## **ORIGINAL ARTICLE**



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## Glycaemic patterns of male professional athletes with type 1 diabetes during exercise, recovery and sleep: Retrospective, observational study over an entire competitive season

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## **Abstract**

Aims: To analyse glycaemic patterns of professional athletes with type 1 diabetes during a competitive season.

Materials and Methods: We analysed continuous glucose monitoring data of 12 professional male cyclists with type 1 diabetes during exercise, recovery and sleep on days with competitive exercise (CE) and non-competitive exercise (NCE). We assessed whether differences exist between CE and NCE days and analysed associations between exercise and dysglycaemia.

**Results:** The mean glycated haemoglobin was  $50 \pm 5$  mmol/mol (6.7  $\pm$  0.5%). The athletes cycled on 280.8 ± 28.1 days (entire season 332.6 ± 18.8 days). Overall, time in range (3.9-10 mmol/L) was 70.0 ± 13.7%, time in hypoglycaemia (<3.9 mmol/L) was  $6.4 \pm 4.7\%$  and time in hyperglycaemia (>10 mmol/L) was  $23.6 \pm 12.5\%$ . During the nights of NCE days, athletes spent 10.1 ± 7.4% of time in hypoglycaemia, particularly after exercise in the endurance zones. The CE days were characterized by a higher time in hyperglycaemia compared with NCE days (25.2  $\pm$  12.5% vs. 22.2  $\pm$  12.1%, p = .012). This was driven by the CE phase, where time in range dropped to 60.4 ± 13.0% and time in hyperglycaemia was elevated (38.5 ± 12.9%). Mean glucose was higher during CE compared with NCE sessions (9.6  $\pm$  0.9 mmol/L vs. 7.8  $\pm$  1.1 mmol/L, p < .001). The probability of hyperglycaemia during exercise was particularly increased with longer duration, higher intensity and higher variability of exercise.

Conclusions: The analysis of glycaemic patterns of professional endurance athletes revealed that overall glycaemia was generally within targets. For further improvement,

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#### **KEYWORDS**

continuous glucose monitoring (CGM), glycaemic control, hypoglycaemia, observational study, type 1 diabetes

#### 1 | INTRODUCTION

Regular physical exercise is a key component in the management of type 1 diabetes, <sup>1,2</sup> associated with increased longevity and improved cardio-metabolic health. <sup>3</sup> Despite significant advances in supportive technology and guidance, <sup>1,4</sup> exercise poses considerable challenges for people with type 1 diabetes, with fear of hypogly-caemia and inadequate knowledge around exercise management being major barriers. <sup>5,6</sup> Nevertheless, there are examples of people living with type 1 diabetes that undertake ultra-endurance exercise on a regular basis, <sup>7-12</sup> some of them even competing at a professional level. <sup>7,8</sup>

Current guidelines to optimize exercise-related glycaemia suggest insulin dose adaptation and ingestion of additional carbohydrates in the context of physical exercise. A,13 These recommendations are largely based on findings from laboratory-based studies and clinical experience of moderately trained individuals undertaking exercise of limited duration. Yet, the applicability to prolonged endurance exercise is less well known. This is partly because reports on endurance exercise of prolonged duration in people with type 1 diabetes have only been provided over a short period of time, such as an individual race or training period, meaning there is little research describing the associated glycaemic patterns in endurance athletes living with type 1 diabetes beyond a single training camp or competitive event.

Developments in technology to monitor glucose [e.g. continuous glucose monitoring (CGM)] and physical exercise (e.g. power meters and heart rate monitors) enable readily available measurements of factors related to glycaemic management and exercise behaviour, regardless of the training or competition setting and environment. Combined monitoring of both glucose and exercise performance for a prolonged study period may allow for novel and expanded insights into the effects of training and competition on glycaemia and the various challenges athletes may face in combining high-performance exercise with type 1 diabetes.

In this retrospective observational study, we assessed glycaemic patterns of professional cyclists with type 1 diabetes over an entire competitive season (October 2018-October 2019). The objective of this study is twofold: (a) to assess and compare glycaemic patterns during phases of competitive exercise (CE) and non-competitive exercise (NCE), recovery and sleep, and (b) to analyse the association of specific exercise-related factors with the occurrence of hypo- and hyperglycaemia during these phases.

## 2 | MATERIALS AND METHODS

## 2.1 | Participants

This study included data from 12 male professional road cyclists with type 1 diabetes from Team Novo Nordisk over a competitive season (October 2018-October 2019, individual start and end dates of the season varied slightly among athletes). The study was performed in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Canton of Bern ethics committee (Project ID: 2019-01988). All participants provided both verbal and written informed consent. Detailed eligibility criteria are reported in Figure S1 in Data S1.

## 2.2 | Data collection

CGM was performed using Dexcom G6 (Dexcom) throughout the study period and exported using the proprietary manufacturer's software. Glycated haemoglobin (HbA1c) was measured quarterly.

During cycling sessions, participants were equipped with a mobile power meter (SGYPM900H90; Pioneer), a cycling computer (Wahoo Fitness) and a chest strap heart rate monitor (Wahoo Fitness). The following data were monitored at a 1 Hz frequency: power output (W), cadence (rpm), heart rate (HR) (bpm), temperature (°C), latitude (°N), longitude (°E), distance (km) and altitude (m). Data collected from these sensors were exported daily to a central database (TrainingPeaks).

Data collected from cycling sessions were aggregated by day to capture causes of physiological effects of exercise: duration (min), intensity factor and variability index, as well as time in heart rate and power zones (min) based on individualized Coggan heart rate- and power zones<sup>14</sup> (see Table S1 in Data S1 for definitions and further details). If more than one exercise session had taken place during a day, data from the exercise sessions were aggregated cumulatively (i.e. through concatenation). To obtain ventilatory and metabolic thresholds, incremental cardiopulmonary exercise tests were performed on the athlete's personal bike (Colnago C60) attached to a cycle trainer (KICKR; Wahoo Fitness). Together with collected anthropometric data, such as height (cm), body mass (kg) and fat mass (%), these tests yielded the maximum rate of oxygen consumption (VO<sub>2max</sub>) (ml/min/kg), maximum heart rate (HR<sub>max</sub>) (bpm), lactate threshold heart rate (LTHR) (bpm) and functional threshold power (FTP) (W/kg).

In addition, individual travel and competition calendars were collected to differentiate between CE and NCE sessions and adjust for relevant modifying factors including day in the competitive season (counting from the start of the competitive season) and whether travel was undertaken in the current or the previous 2 days. CE was defined as participating in any road cycling event part of the Union Cycliste Internationale (UCI). NCE was defined as any road cycling that did not take place on CE days.

## 2.3 | Analysis of glycaemic patterns

CGM data were analysed in accordance with the international consensus guidelines. 15 For each participant, we calculated the mean glucose (mmol/L), glycaemic variability expressed as coefficient of variation (%), CGM activity (%), time in hypoglycaemia (L1: 3.0 to ≤3.9 mmol/L, L2: <3.0 mmol/L), time in range (3.9-10 mmol/L) and time in hyperglycaemia (L1: >10 to 13.9 mmol/L, L2: >13.9 mmol/L). These statistics were calculated for five phases of the day: (1) the entire day (06:00-06:00 h); (2) wake (06:00-00:00 h); (3) exercise (corresponding to the times of the day that participants recorded cycling exercise; for further analyses, exercise is separated into CE and NCE); (4) recovery (corresponding to the 4 h after exercise, excluding times during subsequent exercise); and (5) sleep (00:00-06:00 h). Phases (1), (2) and (5) correspond to the time frames defined in the international consensus statement, 15 but may not correspond to the actual wake and sleep times of participants. Statistics on glycaemia were calculated for all days that met the inclusion criteria in Figure S1 in Data S1, thus also comprising days without exercise. Summary statistics of glycaemic metrics across individuals are reported as mean ± SD. Glycaemic metrics are compared between CE and NCE days using paired t-tests.

# 2.4 | Association of exercise-related factors with dysglycaemia

To explore the potential association of specific exercise-related factors (i.e. duration, intensity factor, variability index and time in different heart rate/power zones) with the occurrence of hypo- and hyperglycaemia (<3.9 mmol/L and >10 mmol/L, respectively for duration of at least 15 min<sup>15</sup>), we applied multilevel, multiple logistic regression models (see Supplementary Methods) for exercise, recovery and sleep phases, respectively. To account for participant-specific variation in physiology and glycaemia, random intercepts and random slopes were incorporated in the models. The models were fitted for each exercise variable separately, adjusting for the effects of environmental variables. Environmental variables were average temperature (°C) during exercise, average altitude (m) during exercise, day in the competitive season (counting from the start of the competitive season and accounting for a trend over the competitive season) and whether travel was undertaken in the current or the previous 2 days. Further details on the independent variables in this analysis are provided in Table S1 in Data S1.

Before analysis, we standardized independent variables to enable comparisons of the strength of the associations. Variables with more than 30% missing values were excluded. In addition, time in heart rate and power zones were excluded if more than 80% of their values were zero. Missing values in all remaining variables were imputed with their mean. Estimated standardized associations are reported as the odds ratio (95% confidence interval).

## 3 | RESULTS

## 3.1 | Participants

Participant characteristics are summarized in Table 1. Mean  $\pm$  SD age was 25.6  $\pm$  4.4 years, duration of type 1 diabetes was 10.4  $\pm$  4.9 years and HbA1c was 50  $\pm$  5 mmol/mol (6.7  $\pm$  0.5%). All participants were

**TABLE 1** Participant characteristics

Demography and anthropometry			
Sex (male/female)	12/0 (100/0%)		
Age (years)	25.6 ± 4.4		
Weight (kg)	67.4 ± 7.7		
Fat mass (%)	7.6 ± 1.7		
Height (cm)	177.6 ± 5.8		
Diabetes and glycaemia			
Diabetes duration (years)	10.4 ± 4.9		
HbA1c (%)	6.7 ± 0.5		
Days with CGM coverage ≥70%	176.2 ± 88.3		
Insulin therapy (MDI/CSII)	12/0 (100/0%)		
Physical exercise			
Functional threshold power (FTP) (W/kg)	5.0 ± 0.4		
Maximum heart rate (HR <sub>max</sub> ) (bpm)	188.5 ± 7.2		
Lactate threshold heart rate (LTHR) (bpm)	168.9 ± 15.1		
Maximum rate of oxygen consumption $(VO_{2max})$ (mL/min/kg)	70.6 ± 4.0		
Competitive season			
Cycling (days/year)	280.8 ± 28.1		
Competition (days/year)	34.7 ± 15.3		
Distance cycled (km/year)	26 171.6 ± 4841.2		
Average cycling day			
Mean time cycled (h/day)	3.1 ± 0.2		
Mean distance cycled (km/day)	96.6 ± 10.6		
Mean elevation gain (m/day)	1235.0 ± 235.5		

Note: Demographic, anthropometric, diabetes and physical exercise characteristics of (n = 12) professional cyclists. Data are mean  $\pm$  SD or n (%) unless otherwise indicated.

Abbreviations: CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; HbA1c, glycated haemoglobin; MDI, multiple daily injections.

using a basal-bolus insulin regimen administered via multiple daily injections. On average, the athletes cycled on 280.8  $\pm$  28.1 days during a 332.6  $\pm$  18.8-day season, of which 34.7  $\pm$  15.3 days were during a competitive event.

## 3.2 | Analysis of glycaemic patterns

CGM was analysed for a total of 2115 days, where we distinguished between NCE (1536 days) and CE (256 days). Table 2 gives an

TABLE 2 Summary statistics of glycaemia

	Entire day (06:00-06:00 h)	Wake (06:00-00:00 h)	Exercise	Recovery (4 h post-exercise)	Sleep (00:00-06:00 h)
Overall (2115 days)					
Mean glucose (mmol/L)	8.1 ± 1.0	8.2 ± 1.0	8.1 ± 1.1	8.5 ± 1.3	7.7 ± 1.4
CV (%)	38.9 ± 8.5	$38.0 \pm 8.3$	39.7 ± 9.8	36.5 ± 7.1	40.3 ± 9.6
CGM activity (%)	94.3 ± 2.4	94.9 ± 2.1	92.4 ± 3.4	96.4 ± 1.7	92.4 ± 4.6
CGM readings (%)					
Hyperglycaemia (>10 mmol/L)	23.6 ± 12.5	24.5 ± 12.5	24.3 ± 13.8	27.5 ± 14.3	20.8 ± 15.7
L2 (>13.9 mmol/L)	6.7 ± 5.6	$6.8 \pm 5.5$	7.3 ± 5.7	7.7 ± 6.4	6.6 ± 7.7
L1 (>10-13.9 mmol/L)	16.9 ± 7.5	17.7 ± 7.9	17.0 ± 9.1	19.8 ± 9.2	14.2 ± 8.3
Target range (3.9-10 mmol/L)	70.0 ± 13.7	70.1 ± 13.3	70.4 ± 14.8	68.1 ± 13.0	69.5 ± 17.3
Hypoglycaemia (<3.9 mmol/L)	6.4 ± 4.7	$5.4 \pm 4.4$	5.3 ± 5.5	4.4 ± 4.6	9.6 ± 7.2
L1 (3.0-<3.9 mmol/L)	$4.5 \pm 3.0$	$3.8 \pm 2.7$	$3.9 \pm 3.2$	$3.2 \pm 3.1$	6.5 ± 4.8
L2 (<3.0 mmol/L)	$2.0 \pm 2.3$	1.6 ± 2.2	1.4 ± 2.7	1.1 ± 1.5	3.2 ± 3.1
NCE (1536 days)					
Mean glucose (mmol/L)	7.9 ± 1.0	8.0 ± 1.0	7.8 ± 1.1	8.4 ± 1.3	7.6 ± 1.4
CV (%)	38.9 ± 8.6	38.0 ± 8.6	39.7 ± 10.5	36.1 ± 7.1	40.0 ± 9.8
CGM activity (%)	94.5 ± 2.4	95.3 ± 2.2	93.3 ± 3.8	96.6 ± 1.8	92.1 ± 5.0
CGM readings (%)					
Hyperglycaemia (>10 mmol/L)	22.2 ± 12.1	22.8 ± 12.1	21.9 ± 13.9	26.8 ± 14.6	20.2 ± 16.1
L2 (>13.9 mmol/L)	6.1 ± 5.3	6.1 ± 5.1	6.5 ± 5.4	7.3 ± 6.1	6.2 ± 7.3
L1 (>10-13.9 mmol/L)	16.0 ± 7.6	16.7 ± 7.8	15.4 ± 9.2	19.5 ± 9.5	14.0 ± 9.3
Target range (3.9-10 mmol/L)	71.0 ± 13.8	71.3 ± 13.4	72.0 ± 15.3	68.7 ± 13.4	69.8 ± 17.6
Hypoglycaemia (<3.9 mmol/L)	6.9 ± 5.0	5.9 ± 4.9	6.1 ± 6.4	4.5 ± 4.9	10.1 ± 7.4
L1 (3.0-<3.9 mmol/L)	4.8 ± 3.2	4.1 ± 2.9	$4.5 \pm 3.6$	$3.3 \pm 3.4$	6.9 ± 5.2
L2 (<3.0 mmol/L)	2.1 ± 2.4	1.7 ± 2.5	1.6 ± 3.2	1.1 ± 1.6	3.2 ± 2.8
CE (256 days)					
Mean glucose (mmol/L)	$8.4 \pm 0.9^*$	8.5 ± 0.8**	9.6 ± 0.9***	8.9 ± 1.3*	7.8 ± 1.7
CV (%)	$37.2 \pm 9.8$	35.9 ± 8.7	33.3 ± 8.8**	35.8 ± 8.7	36.8 ± 14.5
CGM activity (%)	92.0 ± 4.5	91.5 ± 4.8	87.9 ± 11.1	94.7 ± 5.3	93.6 ± 5.9
CGM readings (%)					
Hyperglycaemia (>10 mmol/L)	25.2 ± 12.5*	27.0 ± 11.3**	38.5 ± 12.9***	29.5 ± 13.7	19.9 ± 19.6
L2 (>13.9 mmol/L)	7.1 ± 6.1	6.9 ± 5.7	11.9 ± 7.7**	9.1 ± 8.4	7.5 ± 10.4
L1 (>10-13.9 mmol/L)	18.1 ± 7.3*	20.1 ± 7.1**	26.5 ± 7.8***	20.4 ± 8.6	12.3 ± 9.7
Target range (3.9-10 mmol/L)	70.1 ± 14.1	69.3 ± 12.0	60.4 ± 13.0**	67.2 ± 12.8	72.2 ± 22.2
Hypoglycaemia (<3.9 mmol/L)	4.7 ± 4.5	$3.6 \pm 3.1$	1.1 ± 1.4*	$3.3 \pm 3.5$	7.9 ± 9.8
L1 (3.0-<3.9 mmol/L)	$3.2 \pm 2.5$	2.6 ± 1.9	0.9 ± 1.0**	2.6 ± 2.5	$5.0 \pm 5.7$
L2 (<3.0 mmol/L)	1.5 ± 2.4	1.1 ± 1.4	$0.2 \pm 0.4$	0.8 ± 1.3	$2.9 \pm 5.2$

Note: Summary statistics of CGM of (n = 12) professional cyclists over a competitive season. We distinguish between the entire study period (overall; 2115 days), NCE days (1536 days) and CE days (256 days). Statistics were calculated for five phases of the day: entire day (06:00-06:00 h), wake (06:00-00:00 h), exercise, recovery (4 h post-exercise) and sleep (00:00-06:00 h). Data are mean  $\pm$  SD calculated over all participants. CGM metrics are reported following the international consensus statement. The comparison of glycaemic values between NCE and CE days through paired t-tests are reported with \*\*\*(p < .001), \*\*(p < .01) and \*(p < .05).

Abbreviations: CE, competitive exercise; CGM, continuous glucose monitoring; CV, coefficient of variation; NCE, non-competitive exercise.

overview of glycaemic metrics, including the statistical comparisons between CE and NCE days. Figure 1 shows the glucose concentrations over time during the exercise, recovery and sleep phases for NCE and CE days.

Overall, the percentage of time in range (3.9-10 mmol/L) over an entire day (06:00-06:00 h) was  $70.0\pm13.7\%$ , time in hypoglycaemia (<3.9 mmol/L) was  $6.4\pm4.7\%$ , time in hyperglycaemia (>10 mmol/L) was  $23.6\pm12.5\%$ , and glycaemic variability expressed as coefficient of variation was  $38.9\pm8.5\%$  (Table 2). When looking at individual data, the target for time in range (i.e. >70%) was met by five of 12 participants, the target for time in hypoglycaemia (i.e. <4%) was met by four of 12 participants and the target for time in hyperglycaemia (i.e. <25%) was met by six of 12 participants (Table S2 in Data S1).

During NCE days, time in range was  $71.0 \pm 13.8\%$ , time in hypergly-caemia was  $22.2 \pm 12.1\%$ , and time in hypoglycaemia was  $6.9 \pm 5.0\%$ . Of note, time in hypoglycaemia was high during sleep after NCE  $(10.1 \pm 7.4\%)$ . CE days were characterized by a time in range of  $70.1 \pm 14.1\%$ , a trend towards lower time in hypoglycaemia when compared with NCE days  $(4.7 \pm 4.5\%)$  vs.  $6.9 \pm 5.0\%$ , p = .073) and a higher time in hyperglycaemia  $(25.2 \pm 12.5\%)$  vs.  $22.2 \pm 12.1\%$ , p = .012). This was essentially driven by the CE phase, where time in range dropped to  $60.4 \pm 13.0\%$  and time in hyperglycaemia was considerably elevated  $(38.5 \pm 12.9\%)$ , while there were virtually no hypoglycaemias during CE  $(1.1 \pm 1.4\%)$ . Accordingly, this translated into a significantly higher mean glucose concentration during CE compared with NCE sessions, respectively  $(9.6 \pm 0.9)$  mmol/L vs.  $7.8 \pm 1.1$  mmol/L, p < .001).

Overall, the 4-h post-exercise recovery phase was characterized by comparably high mean glucose (8.5  $\pm$  1.3 mmol/L). On CE days, mean glucose concentrations were significantly higher in recovery compared with NCE days (8.9  $\pm$  1.3 mmol/L vs. 8.4  $\pm$  1.3 mmol/L, p = .041), particularly in the first hours after exercise (Figure 1).

During the sleep phase, time in range was  $69.5 \pm 17.3\%$ , with a time in hypoglycaemia of  $9.6 \pm 7.2\%$ . This pattern was more pronounced on NCE days, where time in nocturnal hypoglycaemia was  $10.1 \pm 7.4\%$ . Nevertheless, targets for time in range overall during sleep were met by seven of 12 participants.

## 3.3 | Association of exercise-related factors with dysglycaemia

The associations of exercise-related factors with the occurrence of hypo- and hyperglycaemia during exercise, recovery and sleep phases are shown in Figure 2. Overall, CE, higher variability index and time in the highest power zones were associated with a decreased probability of hypoglycaemia (Figure 2A). Conversely, exercise of longer duration, higher intensity factor and higher variability index was associated with increased probability of hyperglycaemia during exercise (p < .001 for all comparisons, Figure 2A). Time in higher heart rate zones and in higher power zones were positively associated with the probability of hyperglycaemia during exercise was significantly more probable during competitions (p < .001, Figure 2A).

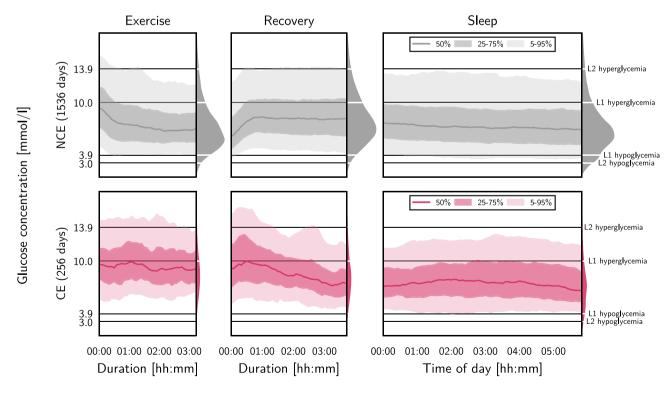
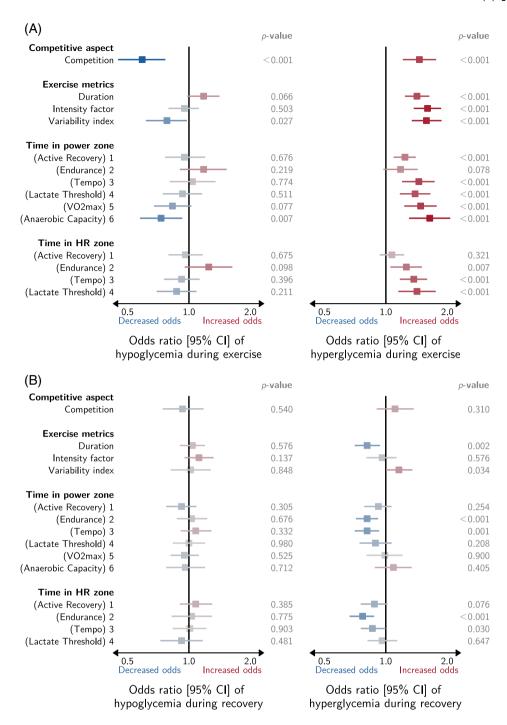


FIGURE 1 Glucose concentrations over time. Glucose concentrations over time during exercise, recovery (4 h post-exercise) and sleep (00:00-06:00 h). We distinguish between non-competitive exercise (NCE) days (1536 days) and competitive exercise (CE) days (256 days). Glucose concentrations are shown with 50th percentile (median), 25th-75th percentile (interquartile range) and 5th-95th percentile. The distribution of glucose concentrations is shown on the right-hand side of each panel.



**FIGURE 2** Association of exercise-related factors with dysglycaemia. Estimated associations of the exercise variables (Table S1) with the odds ratio (95% CI) of hypo- and hyperglycaemia during (A) exercise, (B) recovery and (C) sleep. Listed are p-values. Associations are presented on a logarithmic scale, with red and blue colour indicating an increase and decrease in odds ratio, respectively, and colour intensity indicating the strength of the association. Note that 'Time in HR zone 5 (VO<sub>2max</sub>)' was excluded from the analysis because of the large number of zero values (i.e. 82%). CI, confidence interval; HR, heart rate.

During the recovery phase, the probability of hyperglycaemia was reduced with longer duration of previous exercise (p = .002, Figure 2B), while a variability index of exercise was associated with a higher probability of hyperglycaemia (p = .034, Figure 2B). The association between time in higher power zones and probability of hyperglycaemia was non-linear, revealing decreased probability for power

zones 2 and 3 (endurance and tempo). This pattern was confirmed for heart rate zones, where zones 2 and 3 were also negatively associated with the probability of hyperglycaemia.

The probability of hypoglycaemia during sleep was significantly increased after exercise in the endurance zones (both for power and heart rate, Figure 2c).

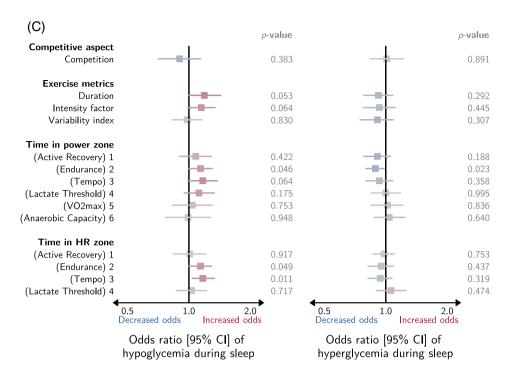


FIGURE 2 (Continued)

## 4 | DISCUSSION

To our knowledge, this is the first study to report on glycaemic patterns of professional athletes with type 1 diabetes over a prolonged study period of an entire competitive season. The most important findings of this analysis are four-fold. First, despite the high physical demands and related challenges of professional high-performance endurance exercise, these athletes revealed an overall time in target range of 70%, matching the general consensus target for individuals with type 1 diabetes. Second, CE was associated with a significantly higher time in hyperglycaemia compared with NCE. Of note, hyperglycaemia during both CE and NCE was significantly associated with a longer exercise duration, higher intensity factor and higher variability index. Third, the post-exercise recovery period was characterized by comparably high glucose concentrations, particularly in the first hour after CE. Fourth, sleep phases revealed a considerable percentage of time spent in hypoglycaemia, particularly after NCE days. Nocturnal hypoglycaemia was more frequent after exercise performed in the endurance zones.

Given the enormous challenges associated with the life of a professional cyclist, the average time in range (70.0  $\pm$  13.7%) and HbA1c (6.7  $\pm$  0.5%) of these athletes is remarkable. This may reflect the fact that the study participants have generally developed strategies to manage glycaemia during different situations (i.e. training, competition, recovery, etc.). On the other hand, the present findings may indicate that there is still room for improvement. Furthermore, our results may give information on specific aspects that athletes, team staff and caregivers may want to focus their attention upon.

During CE, we observed significantly elevated glucose concentrations compared with NCE, along with more time spent in hyperglycaemia.

These findings may be attributed to several factors. First, during competition, strict avoidance of hypoglycaemia is vital to avoid direct withdrawal from the race. Consequently, the athletes may deliberately aim for safety margins by increasing glucose values to higher levels before and during a race. Second, during competition, the athletes are generally advised to follow a diet that is higher in carbohydrate content than during training. 16 because energy demands are high and it is considered metabolically more efficient when competing under high carbohydrate oxidation to optimize performance. 17,18 While data on nutrition and insulin doses were unavailable for this study, previous reports of the Team Novo Nordisk athletes revealed an average consumption of 76 ± 23 g/h carbohydrates during a 7-day World Tour stage race. In training camp conditions, a group of athletes from the same team consumed on average fewer carbohydrates  $(41.9 \pm 6.8 \text{ g/h})$ . Third, previous research suggests that the competitive aspect of a race is related to an increased risk of hyperglycaemia through an elevation of counterregulatory stress hormones.<sup>19</sup>

During the 4-h post-exercise recovery window, there was a distinct pattern of elevated glucose concentrations, particularly during the first hour. Values were significantly higher on CE days compared with NCE days. This may reflect the intake of substantial amounts of carbohydrates post-exercise, and in particular after competitions, to replenish glycogen stores, along with cautious application of insulin because of increased insulin sensitivity. The consistent pattern of post-exercise hyperglycaemia suggests that athletes may benefit from implementing a more structured post-exercise recovery routine to not only help manage glycaemia but optimize training adaptation and recovery.<sup>20</sup>

Our data suggest that hypoglycaemia is a substantial hazard in the overnight periods, in particular on NCE days. Given that many athletes spend the majority of the season in individual training, this merits particular consideration and calls for measures to improve monitoring and to reduce risks. The percentage of time spent in hypoglycaemia during the nocturnal period is even more concerning, considering the dangerous repercussions of hypoglycaemia<sup>21,22</sup> and the increased risk of subsequent hypoglycaemia because of blunted counter-regulatory response the following day,<sup>23</sup> increasing risks for accidents. In addition, sleep is critical for athletic performance, particularly regarding the regenerative processes and adaptations following training and competition.<sup>24–27</sup> As sleep deficiency has been associated with a range of negative health outcomes<sup>28,29</sup> and impaired athletic performance,<sup>27</sup> greater attention should be given to improving overnight glycaemia (particularly focused on reducing hypoglycaemia), to optimize sleep in athletes with type 1 diabetes.

The challenges highlighted by this analysis, particularly in the post-exercise period, raise the question as to whether changing insulin therapy from multiple daily injections to an automated insulin delivery (AID) system or other hybrid insulin regimen may optimize glycaemia in athletes with diabetes. Hybrid closed-loop systems are generally known to increase time in range and quality of life of users. 30-32 While exercise continues to be a challenge for hybrid closed-loop systems because of the rapid increase in insulin sensitivity and changes in contraction-mediated glucose uptake into the skeletal muscles, there is growing evidence on the efficacy of AID systems during and after exercise. 33-35 Studies showed improved time in range overnight. and during exercise with AID systems, 35,36 even under demanding environmental conditions and without pre-planning of exercise. 37,38 An alternative to AID systems has been suggested by an 'untethered' approach with a hybrid regimen of injected insulin and continuous subcutaneous insulin infusion, and with pump removal during exercise.<sup>39</sup> While a recent study by Aronson et al.<sup>39</sup> provides evidence that a hybrid 'untethered' approach may represent a safe and effective insulin delivery regimen, it has yet to be tested formally in athletes with type 1 diabetes in a competitive setting.

The key strength of the present study is that we report on a unique group of professional athletes with type 1 diabetes who engaged in highly competitive endurance exercise over an entire competitive season. Our large dataset provides direct insights into the glycaemic patterns of professional endurance athletes with type 1 diabetes during a significant number of competitive and noncompetitive events. Considering specific factors related to exercise and analysing results according to specific phases (exercise, recovery and sleep) further allowed identifying situations or settings with a negative impact on glycaemia. Nevertheless, we acknowledge certain limitations. First, our findings are based on observational data and are not interventional assessments. For this reason, we emphasize that we only report associations and not causal effects, of individual exercise variables with dysglycaemia. Second, while the amount of data was large, the sample size was limited and exclusively consisted of young male professional endurance athletes with well-controlled type 1 diabetes, thus limiting the generalizability of our findings. Third, we did not have access to insulin, nutritional data and CGM alarm settings in our study. Therefore, we cannot conclude whether the underlying

causes of the observed associations of exercise variables with dysgly-caemia were insulin-, nutrition- or exercise-related changes in metabolism, or other unknown factors. Future research may investigate other characteristics of dysglycaemia, such as length or severity of dysglycaemic episodes.

In conclusion, we provide insights into the glycaemic patterns of a group of professional athletes with type 1 diabetes over an entire competitive season. While overall glycaemia was within range, the substantial challenges associated with the life of a professional athlete with type 1 diabetes may explain that consensus targets were not always reached. Specific emphasis should be put on intensified monitoring and treatment during competitions and overnight periods, not only to improve further the training adaptation, but to reduce shortand long-term risks for athletes with type 1 diabetes.

#### **AUTHOR CONTRIBUTIONS**

Eva van Weenen, Felix Wortmann, Sam N. Scott and Christoph Stettler contributed to the design of the study. Eva van Weenen, Federico Y. Fontana, Kristina Skroce, Charlotte Hayes and Sam N. Scott contributed to data collection. Eva van Weenen, Nicolas Banholzer, Simon Föll, Mathias Kraus, Federico Y. Fontana, Simon Föll and Felix Wortmann contributed to data analysis. Eva van Weenen, Federico Y. Fontana, Thomas Zueger, Stefan Feuerriegel, Vera Lehmann, Sam N. Scott, Felix Wortmann and Christoph Stettler contributed to the interpretation of study results. Eva van Weenen and Sam N. Scott prepared the first draft of the manuscript and all authors reviewed and approved the manuscript. Christoph Stettler is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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## **CONFLICT OF INTERESTS STATEMENT**

The authors have no conflicts of interest to declare.

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## PEER REVIEW

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## DATA AVAILABILITY STATEMENT

The datasets generated during and/or analysed in the current study are not publicly available to protect privacy of the participants, but are available in limited form from the corresponding author upon reasonable request. Code for the analysis of the current study in Python (version 3.7.5) and R (version 3.4.4) is available after publication under https://github.com/im-ethz/TNN-analysis.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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