Incidence and Predictors of Exertional Hyperthermia After a 15-km

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Road Race in Cool Environmental Conditions 2 3 Matthijs TW Veltmeijer, MDa#, Thijs MH Eijsvogels, PhDa,b , Dick HJ Thijssen, PhDa,c , Maria TE 4 5 Hopman, MD, PhDa # Both authors contributed equally to the manuscript 6 7 8 ^aDepartment of Physiology, Radboud University Medical Centre, Nijmegen, the Netherlands; PO 9 Box 9101, 6500 HB Nijmegen, the Netherlands bHenry Low Heart Centre, Department of Cardiology, Hartford Hospital, Hartford, Connecticut, 10 11 USA; ^cResearch Institute for Sport and Exercise Science, Liverpool John Moores University, 12 Liverpool, United Kingdom 13 **Author for correspondence:** 14 Prof. Dr. Maria Hopman, E-mail: Maria. Hopman@Radboudumc.nl 15 16 **Total Word Count: 3000** 17 Word Count Abstract: 249 18 19 **Total Number of Tables: 2 Total Number of Figures: 1** 20 21

ABSTRACT

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- 2 **Objectives:** Current knowledge about the incidence and risk factors for exertional hyperthermia
- 3 (core body temperature ≥40°C) is predominantly based on military populations or small-sized
- 4 studies in athletes. We assessed the incidence of exertional hyperthermia in 227 participants of
- 5 a 15-km running race, and identified predictors for exertional hyperthermia.
- 6 **Design:** Observational study.
- 7 **Methods:** We measured intestinal core body temperature before and immediately after the race.
- 8 To identify predictive factors of maximum core body temperature, we entered sex, age, BMI, post-
- 9 finish dehydration, number of training weeks, fluid intake before and during the race, finish time,
- and core body temperature change during warming-up into a backward linear regression analysis.
- Additionally, two subgroups of hyperthermic and non-hyperthermic participants were compared.
- Results: In a WBGT of 11°C, core body temperature increased from 37.6±0.4°C at baseline to
- 13 37.8±0.4°C after warming-up, and 39.2±0.7°C at the finish. A total of 15% of all participants had
- exertional hyperthermia at the finish. Age, BMI, fluid intake before the race and the core body
- temperature change during warming-up significantly predicted maximal core body temperature
- (p<0.001). Participants with hyperthermia at the finish line had a significantly greater core body
- temperature rise (p<0.01) during the warming-up compared to non-hyperthermic peers, but
- similar race speeds (p=0.34).
- 19 **Conclusion:** 15% of the recreational runners developed exertional hyperthermia, whilst core
- 20 body temperature change during the warming-up was identified as strongest predictor for core
- body temperature at the finish. This study emphasizes that exertional hyperthermia is a common
- 22 phenomenon in recreational athletes, and can be partially predicted.
- 24 Key-words: Heatstroke, Heat Stress Disorders, Body Temperature Regulation, Exercise, Body
- 25 Temperature

1 Introduction

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Current knowledge about the incidence and risk factors for exertional hyperthermia (core body temperature (CBT) ≥40°C) and heat illness is largely based on retrospective studies investigating military populations during military exercises. 1-5 These studies involved well-trained soldiers performing continuous exercise (e.g. long-distance running) superimposed by bouts of highintensity anaerobic exercise (e.g. heavy lifting). This type of exercise is substantially different from a typical athletic event popular in the general public, during which the athletes typically only perform continuous high-intensity exercise. Furthermore, paramount to the general public is that it is characterized by a wide range of individual traits, including a wide diversity in body mass, age and training and health status.⁶ As all these factors may affect thermoregulatory responses differently, each individual may be subject to a different risk for developing heat-related problems, such as exertional hyperthermia or heat illness.4,5,7 Previous studies that did focus on thermoregulation in participants of athletic events or outdoor time trials in cool to moderate conditions are based on relatively small to moderate sample sizes.8-10 These studies reported exertional hyperthermia in 0-23% of their participants, mostly after performing marathon races, and this wide range makes it tenuous to draw any firm conclusions. In addition, no previous authors have confirmed whether this knowledge is applicable to the general public based on measurements in a large and heterogeneous sample size. Based on previous literature, risk factors for heat illness such as metabolic rate (i.e. running speed), 8,11,12 dehydration at the finish line and low fluid intake before and during the race, 13-15 increased body mass index, 3,13,16 poor training,3 advanced age14 and male sex17 could significantly predict CBT at the finish line. However, it has never been confirmed whether these risk factors can be applied to identify athletes at risk of developing hyperthermia during large sports events.

Therefore, the main purpose of this study was to assess the CBT in a large (n=230) heterogeneous group of participants of a 15-km running race (Seven Hills Run, Nijmegen, the Netherlands). This race is one of the largest running events held in the Netherlands (>30.000 participants), and holds the men's and women's 15-km world records set in 2010 and 2009 respectively. As a secondary purpose, we identified factors that significantly predicted CBT at the finish line using a backward linear regression analysis. The third aim was to assess the differences between athletes finishing with a high CBT versus those with a low CBT, in order to identify key features that may explain the CBT rise during exercise. To that end, we compared body and race characteristics in athletes with a finish CBT ≥40°C (hyperthermic athletes) to an equally sized group of athletes that finished with the lowest CBT of all participants (non-hyperthermic athletes).

Methods

Five-hundred participants of the Seven Hills Run were randomly contacted and, if interested, were sent a study protocol. All volunteers were screened for the presence of any exclusion criteria for using the temperature pill: 1. a history of obstructive or inflammatory bowel disease, or any prior abdominal surgery, 2. the presence of any implanted electric (medical) device, 3. a scheduled MRI scan within 1 week after the event, or 4. pregnancy. Two hundred-thirty participants were included in the study: 111 men and 116 women, were aged 45±11 years and had a BMI of 22.7±2.7 kg/m² (Table 1). Study procedures were approved by the Radboud University Medical Centre Ethics Committee, accorded to the principles of the Declaration of Helsinki, and all participants provided written informed consent before participation.

Prior to the race, participants completed a questionnaire pertaining to their physical training. Participants self-reported their fluid intake from the time of getting out of bed on the day of the race and during the race. Body weight was measured before and after the race in a laboratory set up 50 meters from the finish line. CBT was measured at baseline in the laboratory about 2 hours before the start, 1 minute before the start (i.e. after warming-up), and within 15 seconds after finishing. Due to the large total number of participants in the race, runners started the race phased into in 9 separate 'waves' over a 1 hour period. Ten research assistants measured CBT in 25±1 participants per wave using 5 wireless receivers. Participants with a CBT ≥40°C upon finishing were compared to an equal number of participants that finished with the lowest CBT.

Participants ingested an individually calibrated telemetric temperature pill at least five hours (8 a.m.) before the race (start 1 p.m.) to prevent interaction of the CBT measurements with fluid ingestion during testing.¹¹8 CBT was measured using a portable telemetry system (CorTemp™ system, HQ Inc., Palmetto, USA). This measuring system has been demonstrated to safely and reliably measure CBT.¹¹9.²¹0 The average of three consecutive measurements for each time point

was used for further analyses. The change in CBT during warming-up was calculated by

2 subtracting CBT at baseline from the CBT before the start of the race.

3 Body weight was measured to the nearest 0.1kg using an automatically calibrated balance (Seca

4 888; Hamburg, Germany) before and within 10 minutes after the race. The relative change in

5 body weight was calculated and dehydration was defined as a body weight loss of ≥2%.²¹

Participants were allowed to drink ad libitum before and during the race, whilst they self-reported

the time and amount (standard sized cups, bottles, etc.) of their individual fluid intake before and

during the race. No restrictions were imposed on the type of fluids consumed, though participants

were requested to refrain from drinking between finishing and the second body weight

measurement to avoid overestimating the post-race body weight. Furthermore, body weight

change during the race (delta body weight) was corrected for fluid intake during the race by adding

the fluid intake to the delta body weight.

13 Individual split times after 5-, 10- and 15-km were obtained from the organizational measuring

system (ChampionChip®, MYLAPS, Nijmegen, the Netherlands).

Wet bulb globe temperature (WBGT) was measured every 30 minutes throughout the day using

a portable climate monitoring device (Davis Instruments Inc., Hayward, U.S.A.) positioned in the

start/finish area.

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Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 20.0. IBM Corp., Armonk, NY, USA). Data was reported as mean±standard deviation unless otherwise indicated. A backward linear regression analysis was used to identify factors that significantly predicted finish CBT. Age, sex, BMI, finish time, fluid intake before and during the race, the presence of post-finish dehydration, the delta CBT between baseline and the start and the number of training weeks were included as potential factors that could predict finish CBT. Differences between the subgroups of hyperthermic and non-hyperthermic participants were tested using a Student's *t*-test for the continuous data, and a chi-

1	square test for the nominal data (i.e. the presence of post-finish dehydration). The significance
2	level was set at p≤0.05.

Results

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2 The average race time was 79±13 min (range 55-165 min), with a mean running speed of 11.7±1.8 km/h (Table 1). Furthermore, the split times after every 5-km point were comparable 3 (p=0.33) across the race. Under cool environmental conditions (WBGT was stable at 11°C 4 throughout, T_{DRY-BULB} 10.5°C, relative humidity 87%), CBT increased from 37.6±0.4°C at baseline 5 to 37.8±0.4°C after the warming-up at the start, and was 39.2±0.7°C upon finishing (Figure 1). 6 7 CBT could not be measured at the finish line in 18 participants (8%). Thirty-one participants (15%) showed a CBT ≥40°C and were hence classified as being hyperthermic. None of the participants 8 9 reported any apparent heat-related physical complaints. 10 Between baseline and finish, a 1.5±0.6% reduction in total body weight was observed, and 21% 11 of all participants were classified as dehydrated (≥2% decrease in body weight). Self-reported 12 fluid intake before the start of the race was 1.18±0.47L, whilst intake was 0.06±0.12L during the 13 14 race. 15 16 The backward linear regression model (r=0.41, p<0.001) identified age (B = -0.01, p=0.03), BMI 17 (B=0.06, p<0.01), self-reported fluid intake before the race (B=-0.30, p=0.02) and CBT change during warming-up (β=0.56, p<0.001) as parameters that significantly predicted CBT at the finish 18 line (Table 2). Sex, finish time, self-reported fluid intake during the race, the presence of post-19 20 finish dehydration and number of training weeks were also entered into the regression analysis. 21 but did not appear to influence finish CBT. These results remained unchanged when the analysis was repeated after replacing the total finish time for the split time in the last 5-km. 22 23 CBT change during warming-up was identified as the strongest predictor in our model. 24

Accordingly, we were interested in the risk stratification of participants that demonstrated a CBT

change during warming-up that was 2 times higher than the group average (0.2°C). Therefore.

2 we created a new dichotomous variable in which participants were classified to a CBT rise ≤0.4°C

3 or >0.4°C during warming-up. Exertional hyperthermia occurred significantly (p<0.001) more

frequent in the participants with a CBT rise >0.4°C (33.3%) compared to participants with a CBT

rise ≤0.4°C (9%) during warming-up (OR: 5.1, 95% CI: 2.2-11.7).

Two subgroups comprising 31 hyperthermic participants and 31 participants that finished with the lowest CBT of the total group (non-hyperthermic group) were selected for additional analyses with respect to body and race characteristics (Table 1). Within these groups, no differences were found for age, BMI, physical activity, race times, or body weight changes. The CBT change between baseline and the start of the race was significantly greater in the hyperthermic participants compared to the non-hyperthermic group (p<0.01). Furthermore, self-reported fluid intake before the race was significantly higher in the non-hyperthermic participants compared to the hyperthermic participants (p<0.05), whilst self-reported fluid intake during the race was similar in

both groups.

Discussion

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This study assessed the incidence of exertional hyperthermia in a large and heterogeneous group of athletes during a 15-km running event. We found that 15% of our participants passed the finish line with a CBT ≥40°C. Taking into consideration that approximately 30.000 participants entered the race, this would mean that as many as 4.200 participants may have developed exertional hyperthermia. We found that age, BMI, CBT change during warming-up and self-reported fluid intake before the race predicted CBT at the finish line, whereas sex, self-reported fluid intake during the race, the presence of post-finish dehydration, and the number of training weeks had no impact on finish CBT. Interestingly, we found no differences in body and race characteristics between the subgroups of hyperthermic athletes and their non-hyperthermic peers, apart from a higher (0.3L) fluid intake before the race by the non-hyperthermic athletes. However, the CBT change after the warming-up was significantly greater, and self-reported fluid intake before the race was significantly lower in the hyperthermic participants compared to the non-hyperthermic participants. Additionally, we found that athletes with a CBT rise after warming-up >0.4°C were significantly more likely (OR 5.1) to develop hyperthermia at the finish line. These results suggest that exertional hyperthermia is a common phenomenon in recreational athletes, does not necessarily result in physical complaints or a reduced exercise performance, and can be partially predicted.

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To our knowledge, this is the first study to measure CBT at the finish line in a large and heterogeneous group of runners. We found that 15% of our participants developed a CBT ≥40°C after 15-km running in cool conditions. Previous smaller-sized studies demonstrated that exertional hyperthermia occurs frequently during military exercises and athletic events,^{9,16,22} and our results are the first that confirm the relatively high incidence in a large sample-size from the general public. Interestingly, the reported incidence of hyperthermia in the present (15%) and

previous studies (50% and 56%)^{9,22} seems to be higher than the reported CBT in several other studies (0%, 3% and 11%).^{10,11,23} The difference may relate to cooler conditions or longer exercise duration that was possibly performed at lower exercise intensity in the studies that found a smaller incidence. Another potential explanation might relate to the use of rectal probes in the three latter studies, which were inevitably inserted several minutes after finishing the race. As passive cooling may result in a CBT drop of 0.2-0.5°C within the first 5 minutes post-exercise,²⁴ the studies measuring rectal temperatures may have in fact underestimated the actual CBT in their participants.

Despite the high incidence of exertional hyperthermia, none of our participants reported any apparent heat-related complaints. Furthermore, we found no differences in race times between the subgroups with and without exertional hyperthermia, nor any differences in split times at the 5-, 10- and 15-km points (i.e. a stable running pace throughout the race). These results suggest that hyperthermia per se does not necessarily result in a reduced exercise performance. Previous authors have questioned the presence of a 'critical' CBT threshold for a reduced exercise performance, 9,25 the latter of which is thought to be caused by a neurologically-mediated sustained decrease in muscle force production.²⁶ Based on a substantially larger sample-size, our results raise the same hesitations. Tolerance for hyperthermia is widely variable amongst athletes, but was demonstrated to be better in ambient conditions that favour low skin temperatures. 9,25,27 The relatively cool environmental conditions in the present study may therefore at least partially explain why both the hyperthermic and non-hyperthermic participants were able to preserve their race times throughout the race. It would be of great interest to further explore this by assessing CBT and skin temperature in a large group of athletes during a similar running event under cool, moderate and hot environmental conditions, and investigate whether hyperthermia only leads to reduced performance levels when skin temperatures are high.

Interestingly, participants who showed a CBT rise >0.4°C between baseline and the start of the race (i.e. after warming-up) had a significantly higher occurrence (OR 5.1) of exertional hyperthermia upon finishing than participants who had a lower CBT rise during warming-up. Furthermore, the hyperthermic participants had a significantly greater CBT rise during the warming-up compared to their non-hyperthermic peers. This finding raises the guestion as to whether a strong CBT rise during warming-up can help in identifying athletes at risk of developing hyperthermia during the race. To our knowledge, no such relationship has been reported previously. However, it has been reported that a previous episode of heat illness predisposes athletes for a repeat event, ¹³ suggesting that an intrinsic predisposition for heat illness may exist. This hypothesis is reinforced by our finding that athletes with the strongest CBT rise after the warming-up were significantly more likely to become hyperthermic at the finish line, which suggests that a similar intrinsic predisposition for developing hyperthermia may exist as well. The clinical implication of this finding is that measuring the CBT rise during warming-up may aid in identifying individuals who should be monitored more carefully, and may help initiate a more direct treatment strategy if problems do occur (i.e. physical complaints or performance detriments). Furthermore, it might also help to identify individuals who are most likely to benefit from any precooling interventions.

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By measuring a large number of possible predictive factors for the finish CBT, we were able to predict 16.7% of the total finish CBT. The finding that a higher self-reported fluid intake before the race was predictive for a lower finish CBT in both the total group (regression analysis) and in the non-hyperthermic subgroup *versus* the hyperthermic subgroup could relate to a difference in hydration status prior to the exercise bout. Since we did not measure the participants' hydration status before the start of the race (e.g. through measuring urinary specific gravity at baseline), it is difficult draw any definitive conclusions about this. However, previous literature recommended that the consumption of ~0.4-0.5L of fluids 4 hours before the start of exercise ensures

euhydration at the start of exercise.²⁸ Since the participants of the present study consumed 1.2±0.5L of fluids in the ~6 hour time span prior to the race, it is likely that they started the race in a euhydrated state. Apart from the potential role of fluid intake before the race, we found no other differences between both subgroups of hyperthermic and non-hyperthermic participants. This emphasizes the difficulty to predict CBT during exercise using traditional measures. Previous studies have shown that exercise intensity and physical fitness affect CBT during exercise. 3,12,13 As our study was performed under race conditions, most participants performed in the upper range of their possible exercise intensity levels. This leaves only a small range of exercise intensities to correlate with CBT, and may explain why we did not find a significant relationship between both parameters. The strengths of this study are the inclusion of a large and heterogeneous group of participants, the real-life race setting in which participants reach peak performances that cannot be simulated in a laboratory situation, and the fact that we measured CBT within seconds after finishing instead of several minutes after finishing. However, this study was limited by the fact that no correction was applied for sweat entrapment in the participants' clothing after the race in regard to the body weight measurement after the race. Based on previous literature, it is known that not correcting for sweat entrapment in clothing may lead to a measurement error of 10%.8 As subjects in the present study had an average weight loss of -1.0±0.5 kg, actual sweat losses might have been underestimated by ~0.10 kg on average. However, since the average change in body weight in the present study was already limited and remained below the recommended maximal weight change of 2%,21 we believe that this small underestimation did not substantially influence our

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conclusions.

Conclusion

In cool environmental conditions (WBGT 11°C), 15% of the participants passed the finish line with exertional hyperthermia. The stable and similar race speeds in both the hyperthermic and non-hyperthermic participants suggest that hyperthermia *per se* does not necessarily result in performance detriments. The limited value of the predictors of the increase in CBT and the great similarities between both subgroups of hyperthermic and non-hyperthermic participants, emphasizes the difficulty to predict CBT during exercise. However, we did find that participants with a CBT rise after the warming-up >0.4°C were significantly more likely to develop hyperthermia at the finish line (OR 5.1), which may provide new prospects for predicting CBT and associated heat related problems during exercise.

Practical implications

- Athletes who show sharp rises in their body temperature at an early stage of exercise may
 be at increased risk of developing exertional hyperthermia. This finding could aid in
 identifying any athletes who are at increased risk, so that they can be monitored more
 carefully if desired.
 - Furthermore, identifying athletes with the sharpest rises in body temperature during warming-up may also aid in identifying those athletes that may benefit the most from cooling interventions.
 - We provide evidence that hyperthermia does not necessarily result in a reduced exercise performance or lead to health problems. This implies that no immediate action needs to be taken when an athlete is hyperthermic without presenting with physical complaints or performance detriments.

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- 1 Table 1: Participant demographics, physical activity pattern, race characteristics, CBT, body
- weight, and fluid intake in the total group, a subgroup of hyperthermic participants at the finish
- 3 line and a subgroup of non-hyperthermic participants.

	Total group	Exertional	Non-hyperthermia	P-Value			
	Hyperthermia						
Characteristics							
Sex (male : female)	111:116	15 : 16	16 : 15	0.80			
Age (years)	45 ± 11	43 ± 11	45 ± 11	0.49			
Body mass index (kg/m²)	22.7 ± 2.7	23.0 ± 2.4	22.1 ± 2.6	0.17			
Physical activity pattern							
Number of previous participations in this event	5 ± 4	4 ± 3	5 ± 4	0.30			
Training (weeks)	28 (range 0-52)	30 (range 3-52)	24 (range 0-52)	0.32			
Running exercise (sessions/week)	2.5 ± 0.9	2.4 ± 0.8	2.7 ± 1.0	0.21			
Race characteristics*							
Split time 0-5 km (min)	26.2 ± 3.7	25.8 ± 3.0	25.4 ± 4.0	ANOVA (split times):			
Split time 5-10 km (min)	26.4 ± 3.9	26.0 ± 3.1	25.5 ± 4.0	Time / Group / Time x Group			
Split time 10-15 km (min)	26.6 ± 6.7	26.4 ± 3.5	25.3 ± 4.1	p=0.16 / p=0.46 / p=0.10			
Total race time (min)	79.1 ± 12.8	78.3 ± 9.4	76.2 ± 11.9	0.46			
Total race speed (km/h)	11.7 ± 1.8	11.7 ± 1.5	12.1 ± 1.9	0.34			
Core Body Temperature							
Baseline	37.6 ± 0.4	37.6 ± 0.4	37.4 ± 0.4	0.26			
CBT change during warming-up	0.2 ± 0.5	0.5 ± 0.5	0.1 ± 0.4	<0.01			
Start	37.8 ± 0.4	38.0 ± 0.5	37.5 ± 0.3	<0.001			
Finish	39.2 ± 0.7	40.4 ± 0.4	38.1 ± 0.3	-			
Body weight							
Baseline body weight (kg)	71.7 ± 11.9	72.3 ± 11.4	70.0 ± 12.8	0.46			
Finish body weight (kg)	70.8 ± 11.7	71.3 ± 11.6	69.0 ± 12.6	0.48			
Δ Body weight (%)	-1.5 ± 0.6	-1.7 ± 0.6	-1.5 ± 0.6	0.39			
Classifying as dehydrated** (%)	21	29	24	0.67			
Fluid intake							
Fluid intake before race (L)	1.18 ± 0.47	1.0 ± 0.4	1.3 ± 0.5	<0.05			
Fluid intake during race (L)	0.06 ± 0.12	0.04 ± 0.06	0.07 ± 0.13	0.24			

^{*} Differences in split times were tested using a Two-Way Repeated Measures ANOVA.

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^{**} Participants classified as 'dehydrated' if body weight at the finish line was reduced ≥2%.

1 **Table 2:** Predictors for finish CBT.

Variable		Univariate Analysis			Multivariate Analysis*		
	В	95% CI	β	В	95% CI	β	
Constant				38.7	37.7 – 39.7		
Age	-0.01	-0.02 – -0.001	-0.19 ^C	-0.01	-0.020.001	-0.16 ^c	
ВМІ	0.07	-0.02 – 0.12	0.25 ^B	0.06	0.02 - 0.10	0.21 ^B	
CBT rise after warming-up	0.54	0.30 - 0.78	0.33 ^A	0.56	0.33 - 0.80	0.35 ^A	
Fluid intake before race	-0.28	-0.520.03	-0.17 ^C	-0.30	-0.530.06	-0.18 ^C	

^{*} R^2 for model = 0.167; adjusted R^2 = 0.147

 $^{^{\}text{A}}\,\text{p}$ <0.001; $^{\text{B}}\,\text{p}$ <0.01; $^{\text{C}}\,\text{p}$ <0.05; $^{\text{NS}}$ not significant

CI = confidence interval; β = standardized B

FIGURE LEGEND:

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Figure 1: Frequency distribution of core body temperature (CBT) at baseline (light bars) and finish

line (dark bars). Fifteen percent of the participants had exertional hyperthermia at the finish line

5 after completion of the race.

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