Effects of Different Dosages of Interval Training on Glycemic Control in People With Prediabetes: A Randomized Controlled Trial

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ABSTRACT

High-intensity interval training (HIIT) has been used as an alternative to moderate-intensity exercise training. Research has shown that HIIT produces better effects on glycemic control and hence the cardiometabolic risk in prediabetes. This randomized controlled trial was conducted to compare the effect of low-volume HIIT (LV-HIIT) with high-volume HIIT (HV-HIIT) on A1C and fasting blood glucose (FBG) in overweight adults with prediabetes. The trial included 60 young adults with prediabetes (32 male, 28 female). Subjects were randomly assigned to one of three equal-sized groups (n = 20): an LV-HIIT group (10 × 1-minute intervals at an interval intensity of ~90% HR_{max} on a treadmill separated by 1 minute of easy recovery, with total exercise of 25 minutes/session), an HV-HIIT group (4 × 4-minute intervals at 90% of HR_{max} with 3 minutes of active recovery at 70% of HR_{max} between intervals, with total exercise of 40 minutes/session), and a control group (no exercise intervention). Exercise programs consisted of 3 sessions/week for 12 successive weeks. All participants followed a low-calorie diet for the 12-week intervention period. A1C and FBG were measured before and at the end of the 12-week trial. There were statistically significant effects on A1C and FBG from both exercise interventions (P <0.05). LV-HIIT and HV-HIIT significantly reduced A1C and FBG; however, HV-HIIT yielded a greater reduction in A1C than LV-HIIT (26.07 vs. 14.50%) and in FBG (17.80 vs. 13.22%) after exercise training, respectively. HIIT was found to be effective for glycemic control in prediabetes, with HV-HIIT being more effective than LV-HIIT in reducing A1C, FBG, and progression to type 2 diabetes in young adults with prediabetes.

During the past decade, the prevalence of type 2 diabetes has increased alarmingly worldwide. Prediabetes is a state of intermediate hyperglycemia that occurs when individuals progress from normal glucose tolerance to type 2 diabetes (1). Prediabetes is characterized by impaired glucose tolerance (blood glucose 140–200 mg/dL), impaired fasting glucose (blood glucose 110–125 mg/dL), or both and elevated A1C levels of 5.7–6.4% (2).

Most people with prediabetes are overweight or obese (3) and are at a great risk to develop type 2 diabetes and cardiovascular disease (CVD) within a 3- to 5-year period (4). Lifestyle changes such as increased regular exercise are important for treatment and prevention of type 2 diabetes (5).

Several professional associations recommend at least 150 minutes/week of moderate- to high-intensity exercise for people with type 2 diabetes (6). High-intensity interval training (HIIT) is a form of exercise that involves short repeated bursts of vigorous exercise interspersed with periods of rest or recovery. A growing body of evidence demon-

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strates that HIIT is an alternative effective exercise modality to moderate-intensity continuous training (MICT) for adults with prediabetes. HIIT had effects that were similar to (7,8) and sometimes better than (9,10) those of MICT for improving a variety of cardiovascular risk factors, including cardiorespiratory fitness, endothelial function, and muscle metabolic capacity in people with type 2 diabetes. An acute bout of HIIT reduces postprandial hyperglycemia in people with type 2 diabetes (11).

HIIT can be individually tailored and does not have to involve all-out exercise. The intensity of the bursts of vigorous exercise that characterize HIIT is not standardized, but rather is based on individuals' cardiorespiratory fitness. For example, the intensity of the "on" or "exercise" phase of HIIT for an overweight individual with type 2 diabetes may involve brisk or uphill walking (12). Some researchers have used low-volume HIIT, which involves 10 × 1-minute vigorous intensity efforts at ~90% of maximal aerobic capacity (HR_{max}) interspersed with 1-minute rest periods in three sessions per week (13,14). Others have used different protocols of longer length, fewer repetitions, and longer rest intervals, which was considered to be high-volume HIIT (HV-HIIT) and involved 4 × 4-minute intervals at 90% of HR_{max} with 3-minute active recovery periods at 70% of HR_{max} between intervals (15,16).

To our knowledge, no studies have determined the best parameters of HIIT programs that people with diabetes or prediabetes can adopt to improve glycemic control. The purpose of this study was to investigate the effects of different dosages of HIIT on glycemic control in prediabetes.

Methods

Trial Design and Participants

A single-blinded, blocked, randomized controlled trial design was used. The study was conducted at the school of Physical Therapy, Cairo University, Cairo, Egypt, from July 2017 to January 2018. This study conformed to all CONSORT guidelines.

Seventy-seven participants ranging in age from 25 to 45 years were selected from the outpatient clinic of the School of Physical Therapy at Cairo University. Participants were included if they met the following criteria: *1*) overweight with a BMI of 25–30 kg/m^2, *2*) A1C of 5.7–6.4%, *3*) fasting blood glucose (FBG) of 100–125 mg/dL, and *4*) sedentary lifestyle. Participants were excluded if they had a history of diabetes, cancer, prediabetic neuropathy, stroke, pulmonary embolism, or severe musculoskeletal problems restricting physical activity. Of the 77 participants, 9 did not meet the inclusion criteria and 8 declined to take part in the study.

The remaining 60 participants (33 men and 27 women) were randomly assigned to one of three equal groups (each n = 20): a low-volume HIIT (LV-HIIT) group, an HV-HIIT group, or a control group performing no exercise (Figure 1). All participants were instructed to follow a low-calorie diet. Participants' A1C and FBG levels were assessed before and 12 weeks after the exercise program.

All participants provided written informed consent. The Board Council of Higher Education of the School of Physical Therapy, the Institutional Review Board of Higher Education and Research of Cairo University, and the Supreme Council of Universities of Egypt approved the study. The study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12617000631303).

Pre-Experimental Evaluation

Before exercise testing, anthropometric characteristics (i.e., weight, height, and BMI) were measured and participants were familiarized with the laboratory equipment. At their initial laboratory visit, participants performed an incremental cycle test to exhaustion to establish their HR_{max}. The HR_{max} test followed a standard protocol of 2 minutes of baseline cycling at a power output of 20 watts, followed by an incremental test to exhaustion with ramp rates of 30 watts·min^{-1} in men and 20 watts·min^{-1} in women to ensure fatigue within 8–12 minutes. Then the work rates corresponding to 60 and 90% of the HR_{max} were calculated to normalize the training intensity for the HIIT protocols.

Exercise Protocols

LV-HIIT

Individuals randomized to LV-HIIT were prescribed three weekly exercise sessions for 12 weeks involving 10 × 1-minute intervals at an interval intensity of ~90% HR_{max} of uphill running on a treadmill, separated by 1 minute of low-intensity recovery, with a 3-minute warmup and a 2-minute cooldown (for 25 minutes of vigorous exercise). After the supervised training phase, participants were instructed to maintain a regimen of LV-HIIT 3 days/week independently (13).

HV-HIIT

Individuals randomized to HV-HIIT performed uphill running on a treadmill during 3 sessions/week for 12 weeks. They began with warmup for 10 minutes at 70% of HR_{max} before performing 4 × 4-minute intervals at 90% of HR_{max}, with 3 minutes of active recovery (moderate-intensity walking) at 70% of HR_{max} between intervals and a 5-minute cooldown period (for 40 minutes of exercise) (17). Participants were encouraged to adhere to the HV-HIIT regimen for 3 months as a challenge to decrease the chance of progressing to type 2 diabetes.

Low-Calorie Diet

All participants followed a low-calorie diet for the 12-week intervention period. It consisted of a caloric intake of 1,200–1,500 kcal/day for women and 1,500–1,800 kcal/day for men. This was used to achieve a weight loss of 1–2 lb (0.5–0.9 kg) per week (18). Fat intake was limited to 20–35% of total calories, and complex carbohydrates such as whole grains and vegetables

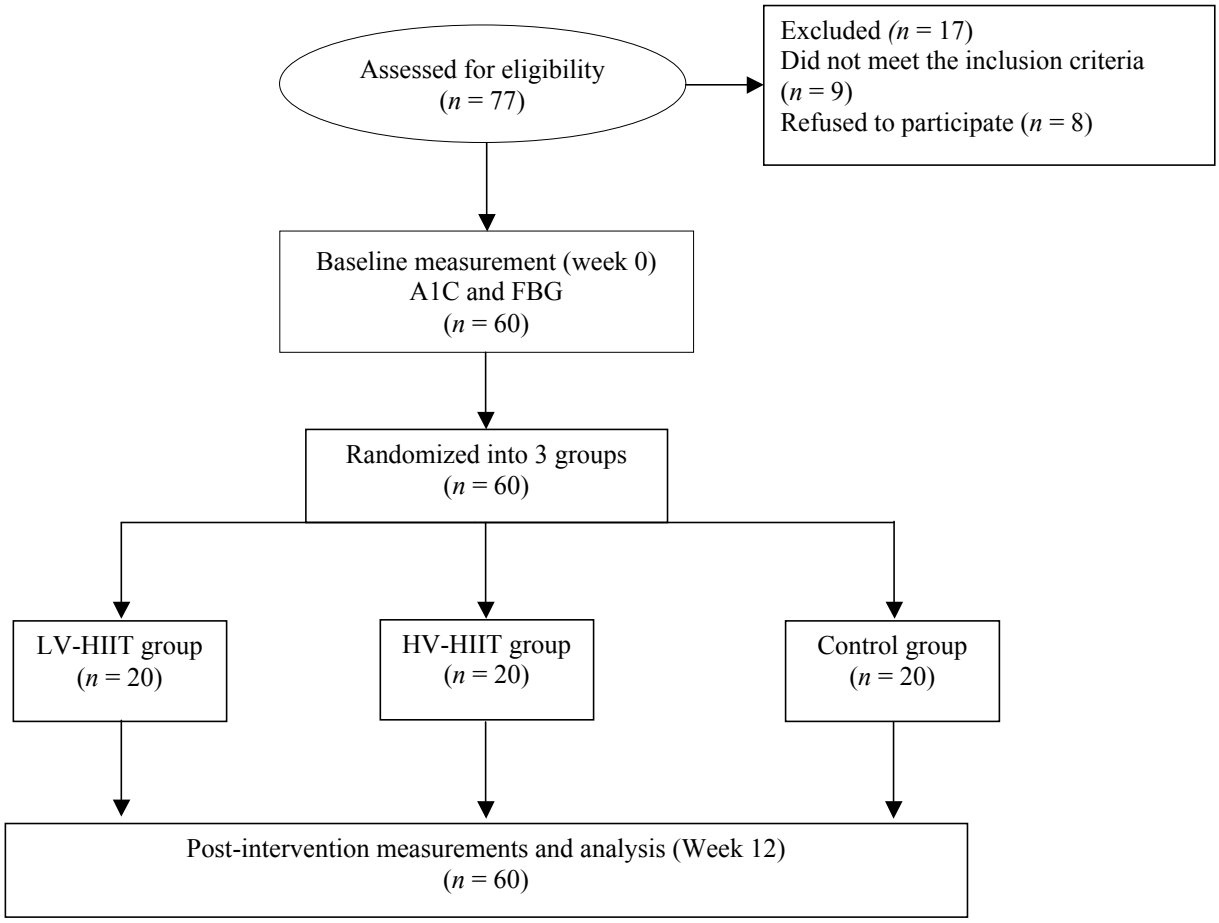

FIGURE 1. Participant flowchart.

made up 45–65% of total calories. Additionally, low-fat protein such as fish, poultry, and legumes made up 15–25% of total calories (19). Adherence to the diet was assessed with a diet logbook in which each participant documented each meal he or she ate every day for 3 months. One day per week was allowed for participants to eat whatever they pleased. However, food eaten on this day was still documented in the logbook. Participants in the control group were instructed to maintain their present lifestyle until the end of the trial.

Measurement Outcomes

Anthropometry Measurements

Height (cm) and weight (kg) were determined at baseline to calculate BMI (kg/m^2). Height was measured using a wall-mounted stadiometer. Weight was taken on a calibrated digital scale.

Biochemical Analyses

Biochemical tests included A1C (Cobas Integra Tina-quant Hemoglobin A1c Gen.2 kit; Roche Diagnostics, Mannheim, Germany) and FBG using glucose oxidase assays (Roche Diagnostics, Indianapolis, Ind.). Blood samples were collected before the intervention for baseline measurements and after 3 months, at the end of the treatment intervention.

Sample Size

Sample size calculations were performed using G*Power software version 3.0.10 (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). *F* test multivariant analysis of variance (MANCOVA) with global effects was selected. A1C was chosen as the primary outcome measure. The effect size of A1C was estimated to be medium (0.25). Considering a power of 0.95, an α level of 0.05, three groups, and two response variables, a generated sample size of at least 14 participants per group was required. Allowing for a 20% dropout rate, it was necessary to reach a total sample level of at least 70 participants.

Randomization

Randomization was implemented in blocks by means of a computer-generated randomized table using the SPSS program (IBM Corp., Chicago, Ill.), prepared in advance of data collection. A specific identification number was assigned for each participant. These numbers were randomized into three groups. Individual sequentially numbered index cards were secured in opaque envelopes. Participants were given a hand-picked envelope and relocated in the tables accordingly to their treatment groups. Participants

TABLE 1. Demographic Data of Participants

	LV-HIIT Group (*n* = 20)	HV-HIIT Group (*n* = 20)	Control Group (*n* = 20)	*F*	*P*
Age 23–35 years	31.8 ± 5.3	31 ± 5.27	35.9 ± 5.89	2.285	0.121
Sex					
Male	11 (55%)	10 (50%)	12 (60%)	$\chi^2 = 0.242$	0.868
Female	9 (45%)	10 (50%)	8 (40%)		
Weight 65–90 kg	76.8 ± 11.62	78.6 ± 12.38	77.5 ± 11.03	0.06	0.942
Height 158–178 cm	164 ± 10.53	166.8 ± 13.36	164.7 ± 10.31	0.161	0.852
BMI 25–32 kg/m^2	28.37 ± 1.33	28.06 ± 1.47	28.41 ± 1.37	0.189	0.829

Data are expressed as mean ± SD or n *(%).*

were not informed about their assigned group or which treatment they would be receiving.

Blinding

A statistician blinded to the study approach generated the concealed block randomization and allocation sequence and relocated participants to the three groups. A certified physician (blinded to treatment allocations) collected blood samples and took anthropometric outcome measurements before and after treatment. Finally, two certified physical therapists managed each treatment group individually. Both therapists responsible for carrying out the HIIT exercise programs were blinded to the sequence allocation and measurement outcomes.

Data Analysis

Statistical analysis was conducted using SPSS for Windows, version 20 (IBM Corp., Chicago, Ill.). Descriptive statistics were used to describe the means and SDs of participants' characteristics. Descriptive analysis using histograms with a normal distribution curve and testing for homogeneity of covariance and the Shapiro-Wilk test were used to measure normal distribution of the FBG and A1C values among groups.

A 3 × 2 × 2 mixed design MANOVA (group: intervention vs. control; sex: male vs. female; time: baseline vs. post-intervention) was used to compare A1C (%) and FBG (mg/dL) levels between the tested groups, measuring periods, and sexes. Bonferroni corrections were used for comparisons between groups. The level of significance was set at $P \leq 0.05$.

Results

Participant Characteristics

Table 1 lists the general physical characteristics of participants. One-way analysis of variance (ANOVA) revealed that there were no significant differences in mean age, sex, weight, height, or BMI among the three groups with a $P > 0.05$. A Pearson χ^2 test showed no significant difference in sex between groups ($P = 0.868$).

A1C

The 3 × 2 × 2 MANOVA revealed significant differences in change in A1C between groups ($P < 0.0001$). HV-HIIT yielded a greater reduction in A1C by 26.07% compared to LV-HIIT, which yielded 14.5% (Table 2). Pairwise comparisons revealed a significant difference in A1C between the LV-HIIT and HV-HIIT groups ($P = 0.04$), LV-HIIT and control groups ($P < 0.0001$), and HV-HIIT and control groups ($P < 0.0001$). The mean change in A1C between the HV-HIIT and LV-HIIT groups was 0.29 (95% CI 0.017–0.58), between the LV-HIIT and control groups was 1.06 (95% CI 0.77–1.36), and between the HV-HIIT and control groups was 1.36 (95% CI 1.06–1.66) (Table 3).

FBG

The 3 × 2 × 2 MANOVA revealed significant differences in change in FBG between groups ($P < 0.0001$). HV-HIIT yielded greater reduction in FBG by 17.8% than LV-HIIT, which yielded 13.22% (Table 2). Pairwise comparison revealed a nonsignificant difference in FBG between the LV-HIIT and HV-HIIT groups ($P = 0.09$) and significant differences in FBG between the LV-HIIT and control groups ($P < 0.0001$), and the HV-HIIT and control groups ($P < 0.0001$). The mean change in FBG between HV-HIIT and LV-HIIT was 2.7 (95% CI 0.46–5.87), between LV-HIIT and the control group was 10.29 (95% CI 6.94–13.64), and between HV-HIIT and the control group was 13 (95% CI 9.64–16.36) (Table 3).

Discussion

Although it is known that HIIT improves glycemic control in type 2 diabetes and prediabetes, the specific HIIT protocol that results in the greatest improvement in A1C and FBG is unknown. We sought to compare the effects of LV-HIIT and HV-HIIT on glycemic control in overweight adults with prediabetes.

A paucity of research has found that HIIT improves glycemic control, body composition, cardiorespiratory fitness, cardiovascular risk, physical functioning, and well-being in type 2 diabetes (20). In the literature, both acute bouts and long-term HIIT have been shown to rapidly improve glucose control in individuals with type 2 diabetes or prediabetes (11,13).

In our study, two different protocols of HIIT were found to significantly reduce A1C over 12 weeks. Because A1C is a long-term marker of glycemic control, these findings

suggest that individuals accumulating more vigorous-intensity physical activity have reduced odds of developing metabolic syndrome (closely related to prediabetes), independent of their total physical activity levels (21). These results agree with findings from Winding et al. (22), who found that 11 weeks of HIIT significantly decreased A1C, body composition, and android fat mass in type 2 diabetes. According to these authors, the reduction in A1C after HIIT was the result of a lowering of hepatic endogenous glucose production.

Støa et al. (23) investigated the effect of high-volume, high-intensity aerobic interval training (HAIT) on A1C in patients with type 2 diabetes. The HAIT protocol consisted of 4×4 minutes of walking or running uphill at 85–95% of HR_{max} for 12 weeks. They found that HAIT yielded an 8% reduction in A1C compared to the 26.07% reduction found in the present study. These findings imply an important reduction in risk of CVD, since earlier studies have shown a 15–20% reduction in CVD events when A1C was reduced by 1 percentage point (23). For HV-HIIT, this would mean a risk reduction of up to 60% after only 12 weeks of exercise. Although few studies have investigated the effects of HAIT on A1C in type 2 diabetes, Hollekim-Strand et al. (24) found a similar reduction in A1C after 12 weeks of HAIT (from 7.0 ± 1.2 to $6.6 \pm 0.9\%$).

Additionally, in the present study, the training intervention demonstrated a trend toward improved FBG in young, overweight participants with prediabetes. Previous studies showed that short-term HIIT, and even acute HIIT, can rapidly improve glucose control in people with prediabetes (25,26) or type 2 diabetes (27). Conversely, some studies reported that, compared to baseline, short-term sprint interval training improved insulin sensitivity but had no substantial advantage for improving FBG in healthy, sedentary (28), and overweight or obese (29) men.

TABLE 2. Metabolic and Glycemic Responses at Baseline and 12 Weeks After HIIT

	Baseline Mean (SD)			12-Week Mean (SD), % Change			Within-Group Differences (Week 12 Minus Baseline)				Between-Group Differences (Week 12 Minus Baseline)		
							LV-HIIT Group		HV-HIIT Group		Control Group	Overall Effect[a]	
	LV-HIIT Group ($n = 20$)	HV-HIIT Group ($n = 20$)	Control Group ($n = 20$)	LV-HIIT Group ($n = 20$)	HV-HIIT Group ($n = 20$)	Control Group ($n = 20$)	MD	*P*	MD	*P*	*P*	F^b	P^c	Size Effect[d]
A1C (%)	6 (0.25)	6.14 (0.26)	6 (0.25)	5.13 (0.57), 14.5%↓	4.87 (0.34), 26.07%↓	6.25 (0.48), 3.38%↑	0.83	0.0001*	1.26	0.0001*	0.2	0.081	45.51	0.0001*	0.62
FBG (mg/dL)	106.15 (6.11)	106.38 (6.23)	101.17 (3.76)	93.75 (4.16), 13.22%↓	90.8 (4.13), 17.8%↓	103.79 (7.21), 2.9%↑	12.89	0.001*	15.56	0.0001*	3.14	0.075	36.623	0.0001*	0.57

[a]$3 \times 2 \times 2$ *MANCOVA.* [b]*Mixed-design ANOVA F ratio, representing interaction effect of time by group on dependent variable.* [c]*Statistical significance P <0.05.* [d]*Partial* η^2*: small >0.01, medium >0.06, large >0.14. MD, mean difference.* **Statistically significant (P <0.05).*

TABLE 3. Effects of LV-HIIT and HV-HIIT on Metabolic and Glycemic Parameters

	Mean Difference (95% CI)			*P*		
	LV-HIIT Versus HV-HIIT	LV-HIIT Versus Control	HV-HIIT Versus Control	LV-HIIT Versus HV-HIIT	LV-HIIT Versus Control	HV-HIIT Versus Control
A1C (%)	0.29 (0.017–0.58)	1.06 (0.77–1.36)	1.36 (1.06–1.66)	0.038*	0.0001*	0.0001*
FBG (mg/dL)	2.7 (0.46–5.87)	10.29 (6.94–13.64)	13 (9.64–16.36)	0.09	0.0001*	0.0001*

**Statistically significant (P <0.05).*

This finding is also consistent with Terada et al. (30), who found that HIIT produced large acute reductions in blood glucose as assessed before and after each session of a 12-week training program. The authors explained their findings as being the result of the increase in catecholamine and glucagon release in response to HIIT, which stimulates the release of hepatic glucose stores, and which in turn enhances hepatic insulin sensitivity. Elevated hepatic glucagon production during HIIT results in marked glucose reduction. From this, we can postulate that adopting HV-HIIT with a longer "on" phase decreased the production of endogenous glucose of hepatic origin to a greater extent than LV-HIIT. The discrepancy in FBG resulting from HV-HIIT and LV-HIIT may be attributable to differences in protocols, intervention durations, or numbers of repetitions.

The improvement of A1C and FBG may be the result of the combination of a low-calorie diet and HIIT. This result agrees with findings from the study by Francois et al. (31), who reported that a low-calorie diet with interval exercises improved glucose tolerance more than a low-calorie diet alone in obese adults. This result is also consistent with the findings of Weiss et al. (32) that caloric restriction and exercise have additive beneficial effects on glucoregulation. These data support that the addition of a low-calorie diet to interval training is important for the prevention of type 2 diabetes in people with prediabetes.

Our study did not assess adherence to HIIT; it only encouraged participants to comply with the exercise prescription and adhere to their exercise protocol. Such research is needed to determine whether HIIT is a viable health-enhancing exercise strategy in the real world.

There were several limitations to our study. First, adherence to HIIT protocols were not assessed. Thus, more research is needed to determine whether individuals with prediabetes can adhere to HIIT over the long term (12 weeks). Second, our sample size was small, so larger studies are warranted to confirm and expand our preliminary findings. Factors unrelated to the study also limited the follow-up of participants 1 month after exercise. There are natural safety concerns when implementing vigorous exercise. All participants in our study completed 12 weeks of supervised HIIT with no complications reported, but the study was not designed to examine safety and musculoskeletal injuries in response to HIIT in each protocol. The small sample size of this investigation did not permit an accurate assessment of the safety or injury risk potential of each HIIT protocol. Further studies are also needed with older populations.

Conclusion

Our results show that HIIT may be incorporated to reduce FBG and A1C in people with prediabetes and may prevent progression to type 2 diabetes. Adopting HV-HIIT may be more helpful than LV-HIIT for glycemic control in prediabetes.

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Duality of Interest

No potential conflicts of interest relevant to this article were reported.

Author Contributions

S.S.R. designed the study, collected and analyzed the data, and wrote the manuscript. M.K.T. screened participants, contributed to the discussion, and critically reviewed and revised the manuscript. S.S.R. is the guarantor of the study 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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