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What is the best time of the day to work out?

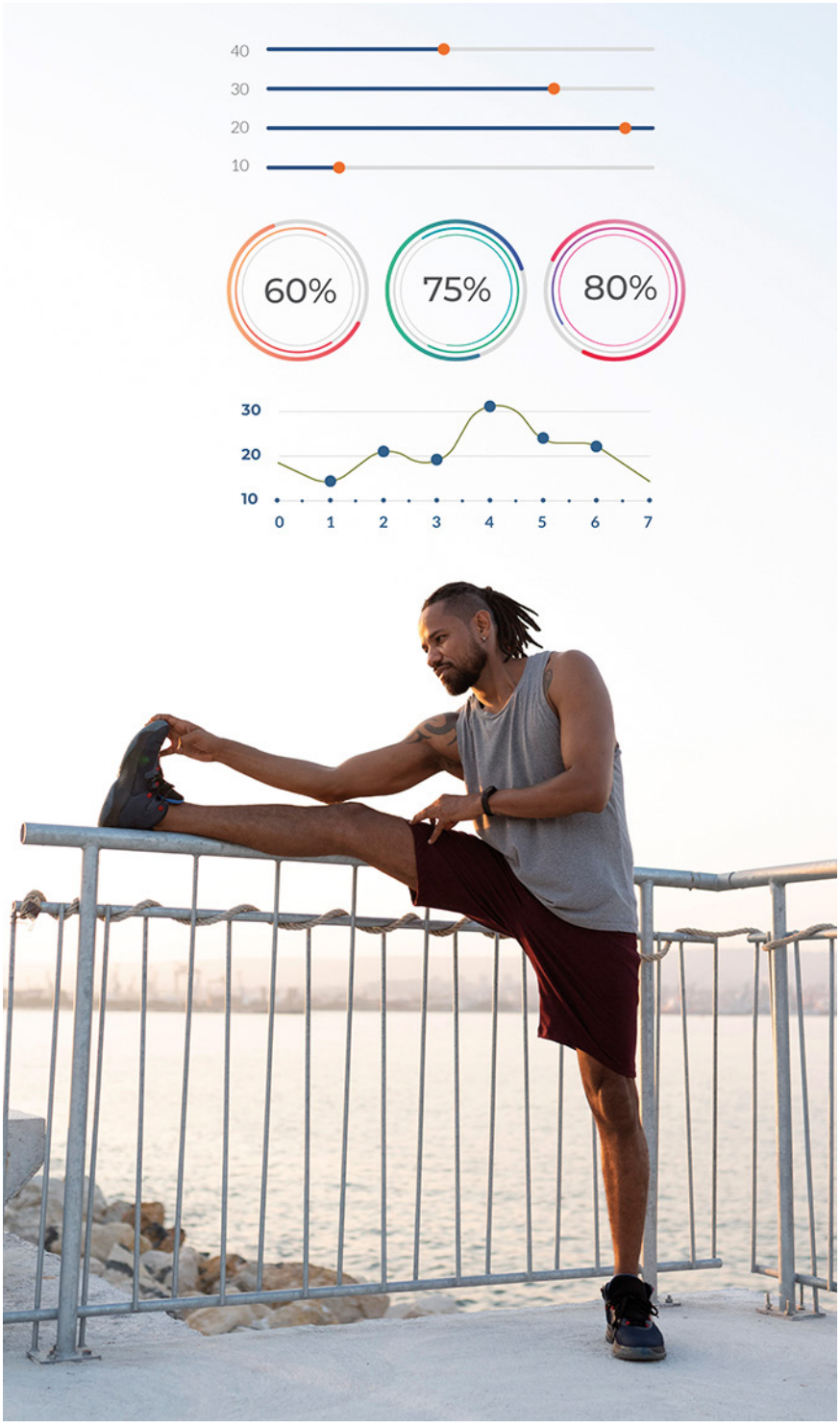
If after fasting for 8-12 hours, your blood glucose level is above 100 milligrams per deciliter, or if 2 hours after an oral glucose load it remains above 140 mg/dL, you likely have diabetes or prediabetes. Glucose accumulates in the blood due to difficulties in transporting it to tissues that use it as an energy source. Glucose transport is mediated by insulin. Therefore, in precise terms, type 2 diabetes is the resistance of tissues to the glucose transport action of insulin. Some diabetes drugs aim to improve this transport by either stimulating the pancreas to produce more insulin (sulfonylureas, meglitinides, GLP-1 analogs), reducing glucose production by the liver (thiazolidinediones, metformin), hindering carbohydrate digestion (alpha-glucosidase inhibitors), or aiding incretins in slowing digestion (DPP-4 inhibitors, metformin). In recent years, drugs that allow glucose to pass from the blood to the urine (SGLT2 inhibitors) have also been used. Finally, when the pancreas begins to deplete its capacity to produce insulin, insulin administration is used.

This arsenal of drugs improves the quality of life for people with diabetes and allows them to live longer. But besides taking prescribed drugs, there are other actions that can help maintain controlled glucose levels. One of these aids is exercise. Recent studies from our group show that a single session of exercise, whether aerobic or strength training, does not interfere with the effects of metformin, one of the most widely prescribed drugs for diabetes. Beyond a single session, **a comprehensive training program of 8 to 20 weeks improves the health of people with diabetes**[1]. Exercise strengthens the cardiovascular system and delays the erosion in blood vessels caused by high glucose and insulin levels[2]. It also helps reduce fat in tissues, including liver fat, allowing carbohydrates to appear more slowly in the blood when consumed. It also helps deplete the carbohydrate stored in muscles, called glycogen, buffering glucose spikes after meals[3].

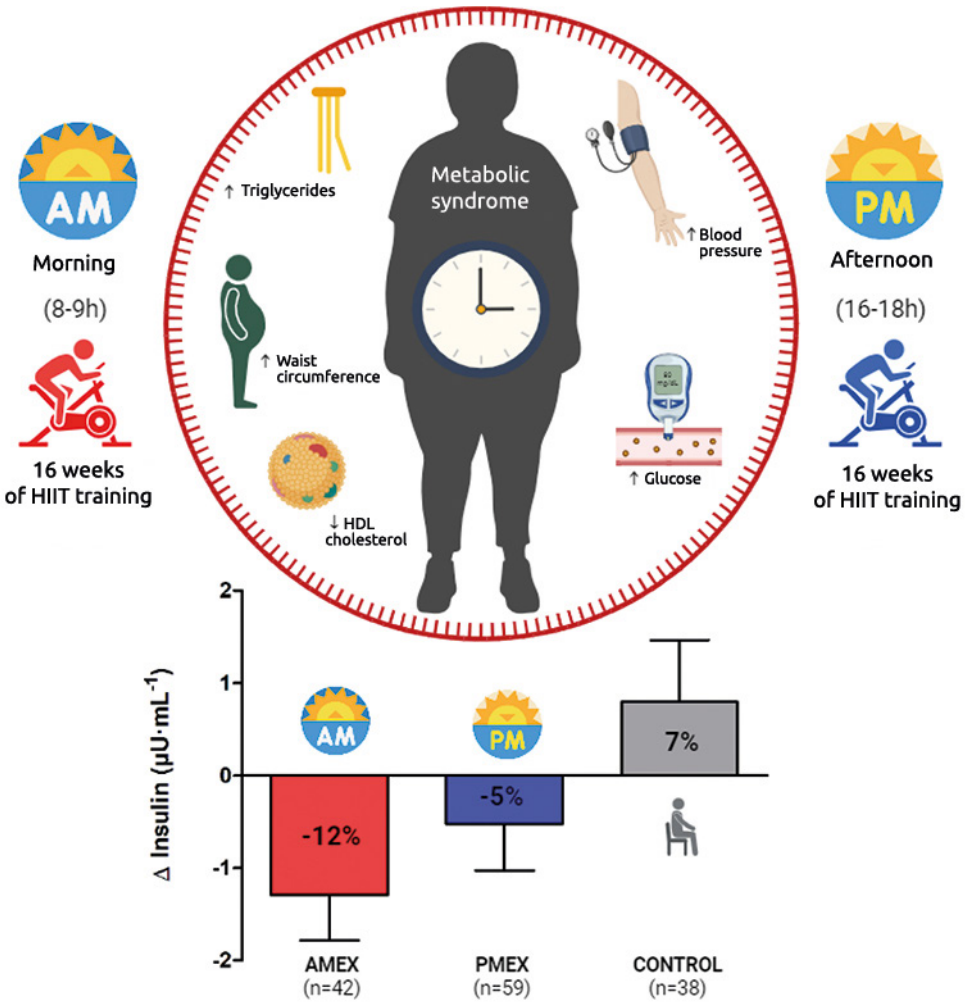
However, these are "side effects" of exercise, and most of these could be achieved with a calorie- and carbohydrate-restricted diet that results in fat loss and depletion of carbohydrate stores. What very few people know **is that exercise not only has beneficial "side effects," but also direct effects on glucose transport**. In 1984, Danish researcher Erik Richter, in Neil Ruderman's lab, made two key observations from his experiments with rats: 1) after exercise, glucose transport in muscle remains elevated even in the absence of insulin, and 2) exercise and insulin stimulate glucose transport through independent pathways, and their effects are additive. In summary, what this scientist demonstrated **is that exercise mimics some actions displayed by insulin**. This explains why people with type 1 diabetes, who do not produce insulin, can run marathons and why there are even cycling teams where all members have type 1 diabetes.

The discovery that exercise works similarly but independently of insulin has implications not only for rodents but also for people with type 2 diabetes. Thanks to studies conducted by Alessio Bellini et al. at the University of Rome[4], we know that blood sugar can be reduced after a high-carbohydrate breakfast (1 gram per kilogram of body weight) with 30 minutes of brisk walking. This walk must start 15-20 minutes after eating »

EXERCISE MIMICS SOME ACTIONS OF INSULIN IN MUSCLE



FOR PEOPLE WITH TYPE 2 DIABETES, IT IS ADVISABLE TO TAKE A LIGHT WALK AFTER A HIGH-CARBOHYDRATE MEAL, AND IF POSSIBLE, IT IS BETTER TO PERFORM TRAINING IN THE MORNING WITH A MINIMAL BREAKFAST



FIGURE

» and cannot be replaced by walking before the meal.

Our research group, like Bellini's, is also interested in improving blood glucose control in overweight adults. For the past 13 years, we have been training people with pre-diabetes or diabetes who are not yet on insulin for four months. In addition, these individuals are overweight, with high blood fat levels (cholesterol or triglycerides) and hypertension. Our recent study, published in December 2023 in the *Journal of Physiology* revealed that performing these **four months of high-intensity aerobic exercise (HIIT) in the morning was more effective in reducing fasting insulin levels than training in the afternoon[5].** This occurred despite both groups (morning and afternoon) losing the same amount of fat and losing approximately 1 kilogram of weight. Moreover, we monitored their diet and physical activity outside the training program and observed no differences in what they ate or the number of daily steps. We only observed that the caloric intake at lunch (meal) was almost double that of breakfast (828 kcal vs. 424 kcal). We do not know for sure why people who trained in the morning achieved better fasting glycemic control. However, there are several reasons that could explain this superiority of morning exercise, which we present below ***(Figure)***. »

» **Morning exercise and fat oxidation.** If the breakfast of morning participants was light and close in time to exercise, it might not have been enough to offset the liver glycogen depletion that occurs during the 8 hours of fasting while we sleep. This carbohydrate deficit allows for greater fat oxidation during exercise. If this leads to reducing fat that interferes with glucose transport, this could be the reason for the improvement. Studies are analyzing this. In a study conducted at the University of Bath, United Kingom, 22 people with obesity were trained for six weeks. Nine of them trained in a fasted state, while another 12 participants trained the same way but after ingesting 1.3 grams of carbohydrate per kilogram of body weight[6]. At the end of the six weeks of training, those who trained in a fasted state had lower glucose and insulin levels when given an oral glucose load compared to those who trained after carbohydrate ingestion. In the muscle of those who trained in a fasted state, higher levels of the glucose transport protein (GLUT 4) and another protein that is an energy deficit sensor (AMPK) that stimulates fat oxidation were measured. This was achieved in just 6 weeks of aerobic training in people with obesity but without diabetes or pre-diabetes[7]. Something similar might be happening in our study.

Afternoon exercise and heavier dinner. The group that finished training at 6 p.m. might have been hungrier at dinner. A high-intensity exercise program affects the balance of hunger and satiety hormones (ghrelin and leptin), slowing weight loss after the first few months of training[8]. It is possible that the evening group tended to have a larger dinner, while the morning group might have had a more substantial lunch. Spanish nutritionist Marta Garaulet has observed that eating a late and heavy dinner increases melatonin levels. Melatonin is a hormone that, in high concentrations, hinders glucose transport to tissues, alters glucose tolerance, and reduces insulin sensitivity[9]. It is possible that a later and more abundant dinner in the afternoon group opposed the more beneficial effects of training seen in the morning group.

Exercise intensity in the morning. In our HIIT program, we use heart rate to control each participant's exercise intensity. Many of our body's values, such as temperature, breathing rate, body water amount, and blood pressure, vary with the time of day, and this is called the circadian rhythm of physiological variables. Heart rate is not immune to the circadian rhythm and fluctuates with the time of day. Additionally, in the morning, our legs have less strength[10]. Perhaps the morning participants had to put more resistance on the bike to elevate their heart rate to the level requested by supervisors during training. Thus, morning participants might have accumulated more "exercise load," leading to better glycemic control. However, we did not see differences in pedal loads between groups when measured in the study.

In summary, **exercising after an overnight fast and with a light breakfast achieves a greater reduction in insulin levels compared to exercising in the afternoon[5]**. Although this may seem contradictory to Bellini's advice to walk lightly 15-20 minutes after eating, in reality, it is not. **The final advice would be "walk lightly after a high-carbohydrate meal, but schedule your training for the morning with a minimal breakfast**. "Still, the general recommendation for people with type 2 diabetes is to engage in the exercise program they enjoy, as this increases adherence to exercise. A secondary recommendation is, if possible, to perform exercise in the morning. D

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