

Why exercise may never be effective medicine: an evolutionary perspective on the efficacy versus effectiveness of exercise in treating type 2 diabetes

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ABSTRACT

Most cases of type 2 diabetes (T2D) can be prevented by adopting a healthy lifestyle, highlighting that lifestyle modifications should be the primary defence against developing T2D. Although accumulating evidence suggests that exercise can be an efficacious therapy for T2D, especially in conjunction with pharmacological interventions, its long-term effectiveness remains controversial owing to significant adherence challenges. In this narrative review, we combine an evolutionary perspective with epidemiological and prospective interventional studies to examine the efficacy versus effectiveness of varying volumes of exercise prescriptions for treating T2D. Commonly prescribed and recommended volumes of moderate-intensity physical activity (150 min/week) have demonstrated low-to-moderate efficacy in improving glycaemic control, reflected by improvements in glycated haemoglobin levels. Higher exercise volumes have been shown to enhance efficacy. While exercise can be moderately efficacious under the optimal circumstances of short-term exercise interventions (≤ 1 year), there is little evidence of its long-term effectiveness, primarily due to poor adherence. To date, no study has demonstrated long-term adherence to exercise programmes in individuals with T2D (> 1 year). From an evolutionary perspective, the finding that exercise interventions are often ineffective over time is unsurprising. Although often overlooked, humans never evolved to exercise. Exercise is a counter-instinctive behaviour that can be difficult to maintain, even in healthy populations and can be especially challenging for individuals who are unfit or have T2D morbidities. We conclude by presenting several considerations informed by evolutionary logic that may be useful for practitioners, policymakers and advocates of exercise as medicine to improve exercise adherence.

INTRODUCTION

The prevalence of type 2 diabetes (T2D) has nearly quadrupled worldwide over the last three decades¹ making it one of the fastest-growing diseases with no evidence of slowing. The worldwide prevalence of T2D is estimated to double from over 500 million in 2021 to over 1.2 billion by 2050.² The increasing prevalence of T2D is accompanied by increased costs. Between 2015 and 2030, the total costs in the USA are projected to increase 53% from US\$408 billion to US\$622 billion.³ The current worldwide economic burden of diabetes is estimated to be approximately US\$1.3 trillion.² Despite improvements in treatment, approximately

WHAT IS ALREADY KNOWN?

- ⇒ A healthy diet and physical activity (PA) are the cornerstones for the prevention and management of type 2 diabetes (T2D).
- ⇒ Many people struggle to adhere to effective levels of PA.

WHAT ARE THE FINDINGS?

- ⇒ Prescribed exercise for T2D does not lack efficacy when exercise doses are high enough; rather it suffers from low effectiveness largely because of poor adherence.
- ⇒ To date, no study has demonstrated long-term adherence to exercise programmes in individuals with T2D.
- ⇒ An evolutionary perspective on exercise predicts that humans will not engage in non-discretionary PA unless it is necessary or highly rewarding. As most exercise prescriptions are considered neither necessary nor rewarding, they are prone to failure even when exercise is profoundly beneficial.

HOW MIGHT IT IMPACT ON CLINICAL PRACTICE IN THE FUTURE?

- ⇒ We offer several considerations informed by an evolutionary perspective for practitioners, proponents of exercise as medicine and policymakers to consider moving forward.

half of individuals with T2D have poor glycaemic control⁴ and diabetes remains one of the leading causes of death worldwide.⁵ Further, as T2D prevalence rapidly increases in low-income countries where treatment is less available and affordable, global T2D morbidity and mortality rates will inevitably increase. This worsening epidemic raises a conundrum. On the one hand, no one disputes that a healthy diet and physical activity (PA) are the cornerstones for preventing and helping manage T2D.⁶ On the other hand, lifestyle changes, especially exercise, are difficult for patients to achieve and sustain.

To evaluate an intervention such as exercise, it is necessary to distinguish between its efficacy, defined as its desired effect under ideal conditions such as a randomised controlled trial (RCT), and its effectiveness, defined as how well it works in real-world settings.⁷ Because successful treatments require both qualities, this narrative review compares the efficacy and effectiveness of exercise in the treatment



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of T2D. We begin by considering an evolutionary perspective that predicts PA has high efficacy in preventing T2D and other diseases. However, as a counter-instinctive behaviour, exercise, even if modestly efficacious in the management of T2D, is likely to have low long-term effectiveness due to adherence difficulties for most people. We then compare the evidence for the efficacy of exercise as a treatment for T2D under the conditions of experimental interventions versus the evidence for its effectiveness in real-world settings. Finally, we present several considerations informed by evolutionary logic that may be useful for practitioners, policymakers and advocates of exercise as medicine to improve exercise adherence.

Equity, diversity and inclusion statement

Our research team included two women and three men. Two of the authors were American and the remaining were Scandinavian. The author group was comprised of individuals in various career stages and clinical disciplines.

METHODS

We conducted a narrative review to present a comprehensive overview of the efficacy and effectiveness of exercise in T2D treatment. Our goal was not to address a specific research question or to undertake an exhaustive literature review as this would be suitable for a systematic or scoping review. The literature search for this narrative review focused on peer-reviewed studies published until October 2023. Two databases were searched, PubMed and Google Scholar. This review included all adult age groups and only studies focusing on individuals with T2D were considered. The search criteria were restricted to studies published in the English language.

The paradox of exercise

To compare the effectiveness and efficacy of exercise prescriptions for treating T2D, it is useful to distinguish between PA, defined as bodily movements produced by skeletal muscles that expend energy and exercise, defined as discretionary, voluntary, planned PA undertaken for the sake of health and fitness.⁸ This distinction is critical because humans evolved to engage in life-long habitual PA but never evolved to exercise which is a modern behaviour primarily practised by individuals in industrialised economies. Until a few thousand years ago, all humans were hunter-gatherers who walked an average of 10–15 km per day and often carried heavy burdens. Hunter-gatherers also regularly dig, climb, occasionally run and perform other physical tasks, averaging 135 min of moderate-to-vigorous PA daily;^{9 10} subsistence farmers tend to be even more physically active.^{10 11}

Humans evolved to engage in lifelong PA which allocates energy towards processes that slow senescence and decrease vulnerability to disease.¹² Among its benefits, PA prevents weight gain, burns fat (preferentially visceral adipose tissue) and moderates the levels of reproductive hormones such as oestrogen and progesterone which increase the risk of breast cancer.¹² PA also generates many physiological stresses that activate numerous repair and maintenance mechanisms that promote health and slow senescence, thereby extending the health span.¹² In fact, PA and exercise have been reported as effective primary prevention measures against 35 chronic conditions¹³ and there is an evidence-based basis for prescribing exercise as a medicine for the treatment of 26 different diseases.¹⁴

Although humans evolved under conditions where high levels of PA were necessary for survival, they also evolved under conditions of limited energy availability. Consequently, the instinct to

avoid PA when it is neither necessary nor rewarding was adaptive. However, this strong instinct has become maladaptive in modern environments, characterised by abundant high-energy food and labour-saving devices¹⁵ and the resultant lack of PA throughout life represents an evolutionary mismatch. This term refers to novel environmental conditions to which our bodies are not well adapted that increase the prevalence and severity of diseases such as T2D.¹⁵ Studies of physically active hunter-gatherers and farmers in small-scale subsistence societies indicate that metabolic diseases, such as T2D, are rare to non-existent⁹ even though the modal age of death among hunter-gatherers who survive childhood is 68–78 years.¹⁶ In addition, obesity is rare in these populations and T2D incidence skyrockets wherever and whenever populations industrialise and become sedentary.¹⁷ For all these reasons, T2D can be considered an evolutionary mismatch disease.

An unfortunate consequence of our evolutionary history as physically active hunter-gatherers and farmers who faced constant shortages of energy is that structured exercise is often counter-instinctive. Natural selection favours adaptations that increase survival and reproductive success even if those adaptations come at the expense of other outcomes such as longevity. Because hunter-gatherers struggle to acquire sufficient energy to feed themselves and their dependent offspring, unnecessary PA tends to be non-adaptive as it diverts scarce calories from reproduction and basic somatic maintenance. Therefore, hunter-gatherers are typically physically active only when it is necessary or when highly rewarding. For example, when not foraging or sleeping, Hadza hunter-gatherers in Tanzania avoid non-essential PA and average 9.9 ± 2.4 hours/day of non-ambulatory behaviours such as sitting, as much sitting as industrialised populations.¹⁸ Now, in an evolutionary blink of an eye, people in industrialised countries struggle to overcome similar instincts to avoid unnecessary, discretionary PA (ie, exercise). Only 45% and 65% of American and European adults, respectively, reported meeting the minimum levels of recommended PA^{19–22} and only 23% of American adults and 17% of European adults reported engaging in the recommended strength training two times a week.^{22 23} These numbers likely reflect an overestimation of the population engaging in recommended levels of PA as self-reported activity typically overestimate PA and underestimate sedentary behaviour.^{24 25}

Exercise is not only counter-instinctive but also challenging for individuals with T2D as they often deal with excess body weight and poor fitness levels. The metabolic cost of walking (kcal/kg/m) is 11% more expensive for individuals with a body mass index of 34.0 than 20.0.²⁶ For such individuals, factors such as low aerobic capacity and comorbidities (eg, neuropathies, degenerative joint disease) make exercise difficult and obese individuals often derive less dopamine reward from a given PA.²⁷ Disinclination to exercise can also fuel a vicious cycle in which lack of PA exacerbates cardiometabolic dysfunction which then makes exercise even more demanding and unrewarding.

From an evolutionary perspective, it is predicted that while PA can be highly effective in preventing T2D and other diseases, structured exercise programmes may exhibit low long-term treatment effectiveness owing to adherence challenges. Humans are adapted to be physically active only when the activity is necessary or highly rewarding and for most individuals, non-discretionary exercise rarely fulfils these criteria. While athletes and some non-athletes find exercise rewarding, they are not the majority. This presents a conundrum: Lack of PA is a prime driver of the evolutionary mismatch disease of T2D and a logical solution for engaging in structured exercise is an evolutionary

mismatch itself. Thus, although structured exercise is profoundly beneficial, prescribing it as medicine will likely fail owing to issues with long-term effectiveness.

Efficacy of exercise for preventing and treating T2D

The efficacy of any treatment, including exercise, is a function of its mechanism of action in response to variations in dose (frequency, duration, intensity and type) and factors such as genetics, disease severity, age, sex and fitness level which influence how individuals vary in their response to a given dose. Evidence for the efficacy of PA in preventing T2D is substantial.²⁸ Although diet is also a major risk factor for T2D, extensive research has elucidated diverse mechanisms by which PA, independent of diet, helps prevent metabolic dysfunction, and hence, T2D.^{29–30} In terms of dose, numerous high-quality studies have shown that 150 min of exercise per week reduces the risk of developing T2D by approximately 26%.³⁰ Higher doses of exercise generally have even larger preventive effects; 300 min/week of moderate-intensity exercise is associated with a 36% risk reduction (95% CI, 27% to 46%) and higher doses yield risk reductions of 53% (95% CI, 35% to 66%).³⁰

The efficacy of exercise prescriptions for managing T2D is unclear because of methodological issues and dose variations among studies.³¹ Using changes in glycated haemoglobin (HbA1c) levels following an exercise intervention as a primary outcome measure, the efficacy of exercise in the treatment of T2D ranged from -0.16% to -0.89% depending on the exercise dose prescribed, study length and participant characteristics.^{32–34} For comparison, commonly used oral glucose-lowering medications have been reported to reduce HbA1c levels by 1.12% (95% CI, 0.92% to 1.32%).³⁵ Exercise has been shown to improve glycaemic control and lipid levels in patients with T2D,^{33–36} however, the quality of these studies is generally classified as moderate to low due to an unclear risk of bias.^{33–36} Unfortunately, the efficacy of exercise in preventing microvascular and macrovascular outcomes such as cardiovascular events in patients with T2D is lacking.³¹ Another complication is that participants in studies often have poor baseline glycaemic control and may achieve a large change in HbA1c levels simply by being in a study that monitors and regulates their lifestyle. In other words, participant effects can overestimate the efficacy of the exercise treatment. According to one meta-analysis, 58% of the variance among studies was explained by baseline HbA1c levels and weekly exercise volume.³⁴

Despite concerns regarding poor experimental design and insufficient dosing, well-designed studies that entailed comprehensive exercise prescriptions have demonstrated modest but meaningful improvements in glycaemic control. For example, the U-Turn Study used a randomised design with 98 adult participants diagnosed with T2D for less than 10 years. Glucose-lowering medications were titrated at least 6 weeks prior to baseline to obtain prespecified treatment targets. During the intervention, all participants were treated using a standardised medical algorithm (with increases or reductions/discontinuation of medication driven by specific predefined HbA1c targets) by a blinded endocrinologist.³⁷ Standard care included medical counselling, education on T2D and lifestyle advice provided by the study nurse at baseline and every 3 months for 12 months. In addition to standard care, the intervention group performed five to six weekly aerobic sessions (lasting 30–60 min), two to three of which included weight training. 74% of participants in the lifestyle intervention group reduced their glucose-lowering medications compared with 26% in the standard care group.

By the end of 12 months, 56% of the participants in the intervention group had completely discontinued all glucose-lowering medications and their HbA1c levels had decreased by 0.31% (95% CI, -0.45% to -0.16%) from a baseline average of 6.65% (SD 0.8).³⁸ Another well-designed study, the Italian Diabetes and Exercise Study (IDES), used objective data and supervised training, demonstrating that a 12-month supervised exercise intervention led to significant improvements in HbA1c levels (-0.30% (-0.49% to -0.10%); $p < 0.001$) compared with the control group receiving standard care.³⁹

Although exercise interventions can have a reasonable degree of initial efficacy in the management of T2D, many studies have reported declining efficacy over time. In the Look AHEAD study, 5145 participants completed a median of 9.6 years of intervention which included a goal of 175 min/week of moderate-intensity exercise combined with a portion-controlled dietary intervention to facilitate weight loss.⁴⁰ However, the study was terminated ahead of schedule because lifestyle interventions did not significantly decrease the primary outcome of cardiovascular events. Average HbA1c levels decreased by -0.64% (SE 0.02) in the intervention group at 1-year follow-up and by -0.36% (95% CI, -0.40% to -0.33%) at the 4-year follow-up.⁴¹ In addition, the percentage of participants in complete remission of T2D defined as fasting plasma glucose < 100 mg/dL and HbA1c $< 5.7\%$ with no glucose-lowering medication was 1.3% (95% CI, 0.9% to 1.8%) after 1 year and 0.7% (95% CI, 0% to 0.4%) after 4 years.⁴² Further, among those not treated with glucose-lowering medication at baseline, 42% of the participants in the intervention group were treated with glucose-lowering medication at the 4-year follow-up compared with 10% at the 1-year follow-up. In the control group, 67% of the participants were treated with glucose-lowering medication after 4 years.⁴¹ In 2014, Balducci *et al* proposed that exercise should be considered a prescribed medication by the US Food and Drug Administration.⁴³ Such approval would require evidence of therapeutic efficacy for a specific condition (T2D), recommended dosing and evidence of effectiveness in the target population. Studies with moderate-to-high bias, along with some well-designed low-bias studies, indicate that the currently recommended volumes of moderate-intensity PA (150 min/week) show low-to-moderate efficacy for T2D.

Higher exercise volumes have been shown to increase efficacy.³⁴ Reductions in HbA1c levels are associated with exercise intensity,⁴⁴ volume⁴⁵ and frequency³⁴ but there is no consensus on the most significant factor. Some studies suggest exercise volume and type of training may be more critical than intensity for T2D therapy.^{46–47} However, a recent systematic review and meta-analysis found that high-intensity training was more effective in reducing HbA1c levels compared with moderate-intensity training.⁴⁸ Thus, when it comes to dosage, there currently is a lack of experimental evidence to determine the optimal exercise dose—if one exists—for the treatment of T2D.³¹

Thus, the efficacy bar appears to be met if the goal is a modest improvement in HbA1c levels; however, work remains to define the appropriate dosage. More importantly, unless the long-term viability (effectiveness) of exercise as a therapy is demonstrated, discussions on trial efficacy and dosage become relatively irrelevant.

Effectiveness of exercise for treating T2D

Although RCT trials have demonstrated the potential efficacy of intensive exercise interventions involving 150 min/week or more of moderate-to-vigorous PA for managing T2D, the modest

outcomes of most RCTs combined with their declining efficacy over time call into question the long-term effectiveness of most exercise interventions. Are these disappointing outcomes due to low efficacy because of disease progression, low effectiveness because of inadequate exercise doses, poor adherence or a combination of these factors?

Adherence is the dominant problem. In the Diabetes Aerobic and Resistance Exercise trial, participants were randomised into four groups: (1) aerobic exercise three times per week progressing from 15 to 20 to min per session at 60% of HRmax to 45 min per session at 75% of HRmax; (2) resistance training with seven different exercises three times per week; (3) combining both programmes; or (4) sedentary controls. Post hoc analysis showed that adherence affected HbA1c outcomes. In the group that performed only aerobic exercise, adherence to 70% or less of the prescribed exercise dosage was not associated with a significant change in HbA1c levels from baseline to 6 months (0.13% (1 mmol·mol⁻¹); 95% CI, -0.48% to 0.83%) whereas adherence to 90% or more of the prescribed dosage was associated with a significant reduction of 0.69% (95% CI, -1.11% to -0.26%; 8 mmol·mol⁻¹). The same trend was observed in the group that combined aerobic and resistance exercise.⁴⁹ In the U-Turn Study, despite intensive support to promote adherence, only around 30% of participants performed the prescribed dose of exercise after 4 months of intervention and the volume of exercise dose continued to decrease throughout the rest of the study. Adherence to weekly supervised training sessions was just 50% by the end of the study.³⁸ Participants who performed 380 min of exercise per week (upper tertile) experienced a greater reduction in HbA1c -0.7% (95% CI, -1.2% to -0.2%) (p=0.008) and other important clinical outcomes compared with those who performed approximately half of the prescribed dose.⁴⁵ HbA1c (-0.3%; 95% CI, -0.9% to 0.3%; p=0.29) was not significantly different from baseline to 12 months follow-up compared with standard care in the lower tertile who performed 178 min (IQR, 121–213). In addition, although healthier participants in the U-Turn Study might be more likely to have higher adherence, a follow-up study found no difference in baseline glycaemic control between high and low adherers.⁵⁰

Studies aimed at educating and empowering individuals with T2D to engage in exercise have highlighted a common decline in adherence over time. The Look AHEAD study which measured individual PA levels periodically during the study found that only 29% of participants met the goal of 175 min of exercise per week after 1 year, dropping to only 18% after 4 years. Additionally, PA levels relative to baseline increased by less than 10 min/week in the intervention group after 4 years.⁵¹ Similarly, the 3-year IDES-2 behavioural modification study showed that 60% of participants achieved at least 150 min of moderate to vigorous PA per week after 1 year but this fell to 35% by the third year. Additionally, the intervention only increased moderate-to-vigorous PA by 3.1 min per day after 3 years (95% CI, 1.5 to 4.7; p<0.001).⁵² Despite integrating behavioural change science and providing individualised sessions with an exercise specialist,⁵³ the IDES-2 intervention had limited success in enhancing exercise levels over a 3-year period.⁵² While the intervention reduced sedentary time, it minimally impacted exercise adherence. These findings and others highlight the challenges in maintaining long-term adherence to exercise regimes even within the intervention frameworks. Moreover, the exercise doses achieved are generally insufficient for clinically significant glycaemic control effects.^{54 55}

The effectiveness of exercise prescriptions is even more questionable in real-world settings once the interventions are

stopped. A 1-year follow-up study of the U-Turn trial conducted 12 months after its conclusion found reductions in fitness levels as measured by maximal oxygen uptake, indicating that exercise adherence was not maintained. HbA1c levels increased by 2.7 mmol/mol (95% CI, 0.8 to 4.7) and were thus worse compared with baseline and the 12-month results. In the control group, HbA1c increased by 3.2 mmol/mol (95% CI, 0.3 to 6.1) from baseline to the 24-month follow-up. HbA1c levels increased in both groups with no between-group differences.⁵⁶ Similarly, 2 years after the termination of the Look AHEAD RCT study, self-reported PA levels were not different between the intervention and control groups and 200 fewer kcal per week than prior to baseline.⁵⁷ In other words, the intervention failed to increase or even maintain original PA levels.

Unfortunately, similarly low adherence to prescribed exercise characterises most general exercise referral programmes. Systematic reviews on the effectiveness of exercise prescriptions have indicated that adherence is typically modest. It has been shown that while approximately two out of three participants were counselled to initiate an exercise programme, only 10% actually increased their level of PA compared with controls and up to 80% dropped out during programmes that lasted 10–12 weeks.^{58–60} Additional systematic reviews have reported that only 12–16% of individuals prescribed exercise reach the goal of 90–150 min of moderate to vigorous exercise per week.^{58 61} Although many factors influence exercise referral schemes, participants with T2D are less likely to adhere to exercise programmes compared with participants referred for primary or secondary prevention of cardiovascular disease or for musculoskeletal or neurological reasons.⁶² In a study that explored 10 years of experience with an exercise programme in the treatment of T2D, participation was above 90% at 6 weeks into the programme but 50% had dropped out at 3 months and only 10% remained in the programme after 1 year.⁶³ Programmes lasting longer than a year almost always have even lower adherence rates⁶⁴ and individuals with T2D⁶⁵ are less physically active than individuals without T2D in terms of step count, energy expenditure and other PA measures.^{66 67} To make matters worse, most exercise programmes prescribe only 150 min/week of exercise which amounts to 21 min/day, most often walking. Although better than no PA, even under ideal circumstances, 21 min/day of walking will only have modest effects on glycaemic control in individuals with T2D.⁶⁸

Adherence to medications is also a significant challenge. At least 45% of patients with T2D fail to achieve adequate glycaemic control (HbA1c<7%) with poor medication adherence being a major contributing factor.⁶⁹ Adherence rates to glucose-lowering medications vary significantly across studies ranging from 36% to 93% for oral hypoglycaemic agents depending on treatment duration, adherence definitions and population.⁷⁰

Nevertheless, the limited effectiveness of exercise interventions in T2D treatment remains a significant challenge as no matter how efficacious a treatment is; if patients do not adhere to it, little is gained.

Where do we go from here?

A 2009 review asked ‘When will we treat physical activity as a legitimate medical therapy...even though it does not come in a pill?’⁷¹ The discouraging answer is that for many healthcare providers and patients prescribing exercise poses a frustrating conundrum: While exercise is medicinal,¹⁴ medicalising exercise rarely works^{58–60} and sometimes backfires. As reviewed above, well-controlled studies have shown that exercise can improve glycaemic control. However, long-term effectiveness is likely

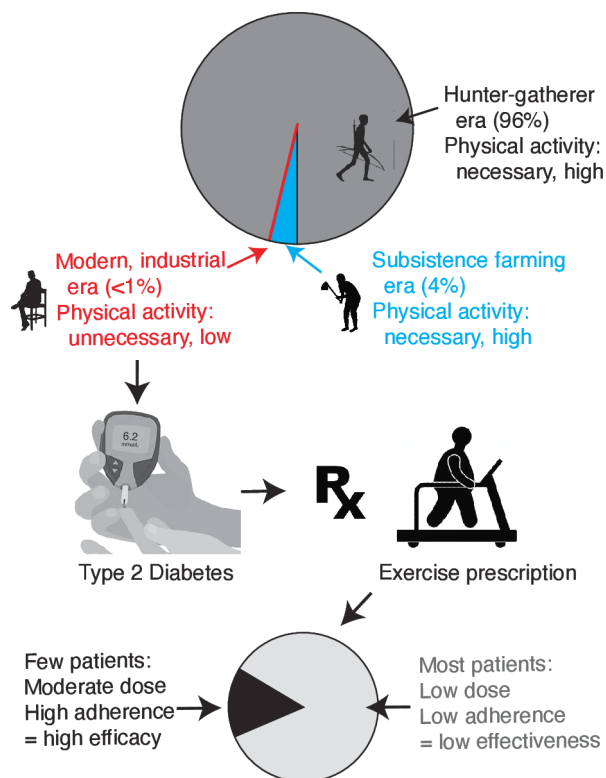


Figure 1 Throughout 99% of human evolutionary history when all humans were hunter-gatherers or farmers (the last 4% of human history), high levels of non-discretionary physical activity were necessary. Although billions of people worldwide still rely on high levels of non-discretionary physical activity for survival in the last 150 years (0.04%), modern technology has made most physical activity optional in some regions, especially high-income countries. In turn, lack of moderate levels of lifelong physical activity is an evolutionary mismatch contributing to increased rates of metabolic disorders like type 2 diabetes (T2D). Although many healthcare professionals prescribe physical activity to alleviate or reverse the symptoms of diabetes, moderately high levels of exercise are needed for high efficacy. However, because it is a basic instinct to avoid unnecessary or unrewarding physical activity, especially when one is unfit or unwell, most efforts to prescribe exercise result in poor adherence leading to a cycle of inactivity and worsening health. As a result, exercise prescriptions tend to have low effectiveness. An evolutionary perspective suggests that instead of medicalising exercise, we need to find ways to make it more necessary and more rewarding.

to be low due to poor adherence. Adherence is commonly an issue for patients with T2D but is especially problematic for those with underlying medical conditions. While the progression and duration of the disease state unquestionably play a role in reducing the efficacy of interventions,^{42–56} the effectiveness of exercise prescriptions is often poor even during relatively short interventions (≤ 1 year). Furthermore, the lion's share of the decline in outcome measures, such as HbA1c levels in long-term interventions (1–4 years), appears to be driven by the inability to adhere to exercise prescriptions of sufficient doses to have any clinically meaningful effect on T2D. To the best of our knowledge, no study to date has demonstrated effective long-term adherence to exercise programmes among individuals with T2D. The medical model of prescribing exercise focuses on physiological benefits and often frames PA as a duty or chore that is necessary to avoid illness. Although this approach is

Box 1 An evolutionary lens provides three key considerations for practitioners, advocates of exercise as medicine and policymakers

1. Acknowledge that the disinclination to exercise is normal.
2. Patients and healthcare providers should recognise that a lack of motivation to exercise is an ancient adaptation that has only recently become maladaptive. It is not a character flaw.
3. Help individuals engage in socially rewarding exercise.
4. As highly social beings, humans are more likely to adopt and adhere to exercise programmes that are socially based and supervised.
5. Implement systemic solutions for systemic problems.
6. Systemic problems require systemic solutions. To make physical activity (PA) necessary and rewarding, environments and cultural norms that encourage PA are essential to counteract the strong evolutionary instinct to avoid discretionary movement.

scientifically sound, it overlooks important behavioural, psychological and social instincts and factors that influence human activity patterns. From an evolutionary perspective, the conclusion that prescribed discretionary exercise does not lack efficacy, but instead suffers from low effectiveness is unsurprising because exercise is a counter-instinctive, modern behaviour that is difficult to maintain and often unrewarding for individuals who are unfit and has morbidities related to T2D (see figure 1).

Understand it is an adherence problem

While exercise can be moderately efficacious in the treatment of T2D, it often fails long-term due to low adherence. Addressing adherence is crucial; however, exercise studies rarely include adherence as the primary or secondary outcome. A recent systematic review of adherence to PA interventions in patients with T2D revealed that only 11 studies reported adherence as a primary or secondary outcome with only one study having a low risk of bias.⁷² Although large-scale cultural and structural changes are likely to be necessary to deeply influence PA and exercise adherence, these changes will be slow and uncertain. Therefore, additional research is needed to identify the factors that enhance adherence to exercise interventions in patients with T2D.

Recognising when something does not work may be discouraging; however, it is an opportunity to change approaches. Given that nothing in biology makes sense except in the light of evolution, we propose that an evolutionary perspective can offer both an understanding of why adherence is a significant problem as well as inspiration for potential solutions. To reiterate, because humans were selected to be physically active in energy-limited conditions, it is an instinct to be disinclined to engage in substantial levels of PA unless it is necessary or rewarding.⁸ As most exercise prescriptions fulfil neither criterion, they fail even when exercise is profoundly beneficial. The fact that no intervention to date has documented effective long-term adherence to exercise in patients with T2D does not mean that efforts to promote exercise should cease. However, it highlights the fact that despite extensive research into behavioural change science and ambitious lifestyle interventions such as the IDES and U-Turn trials, adherence remains a significant challenge. An evolutionary lens (see box 1) provides three important

considerations that practitioners, advocates of exercise as medicine and policymakers should keep in mind:

Acknowledge that the disinclination to exercise is normal

PA should be considered a clinical vital sign;⁷³ however, prescribing exercise to individuals with low PA levels is often ineffective because of instincts to avoid non-essential PA. The inclination to not move unless it is rewarding or necessary is as strong, if not stronger, than the instinct to move as evident from data showing that highly active hunter-gatherers sit as much as industrialised Westerners.⁷⁴ Disinclinations toward exercise are further exacerbated by low fitness, obesity and other comorbidities that can make exercise even harder and less rewarding. As a result, compassionate, non-judgmental efforts to prescribe exercise should include helping individuals appreciate that their disinclinations to exercise are not signs of laziness but rather are normal, universal instincts to avoid unnecessary PA. In other words, patients and healthcare providers alike would benefit from considering that the lack of motivation to exercise is an ancient adaptation that has only recently become maladaptive and is not a character flaw. Understanding that one is not abnormal can be an empowering and critical first step toward increasing motivation.

Help individuals engage in socially rewarding exercise

While instincts to avoid unnecessary physical exertion are strong, so too are instincts to engage in socially rewarding activities that involve movement such as playing, dancing and walking with friends. As humans are ultrasocial, it is unsurprising that socially based and supervised exercise interventions increase both adoption and adherence to exercise.^{33,36} Unfortunately, many people live in environments that neither require nor facilitate, let alone promote, socially based PA. Solutions to these problems include helping individuals make PA rewarding in their environment.

Adherence to exercise in groups, especially those with high social cohesiveness, was higher compared with individual training.⁷⁵ Furthermore, social factors were associated with higher levels of enjoyment and energy during exercise.⁷⁵ Finally, social reasons ranked highest when it came to motivation to attend a run (61%) compared with reasons related to training (37%) or competition (2%).⁷⁶

Implement systemic solutions for systemic problems

The great technological leaps of the last 100 years have systematically engineered considerable PA out of many people's daily lives. This leaves the average person fighting strong internal programming and systemic forces which motivate them to avoid PA. Creating an environment in which PA is necessary helps to solve this problem. The greatest and most consistent evidence for PA interventions incorporating several techniques for behaviour change is seen in school-based and workplace-based programmes.⁷⁷ Considering the substantial portion of life spent in school and work, it makes sense to intervene on these fronts. While these are only two potential systemic solutions, any effort to make PA opportunities both accessible and essential at a societal level could help prevent new T2D cases. Furthermore, systemic changes could expand PA access for underrepresented groups as disparities in participation have been documented among women, people with disabilities, migrants and individuals with lower income or education.^{78–80}

CONCLUSION

Achieving sustained exercise adherence in T2D populations remains elusive. Initiatives such as Exercise is Medicine and

advocacy for the Physical Activity Vital Sign have been pivotal in raising awareness. However, their impact on engagement in and adherence to exercise programmes, particularly for T2D, remains limited.

Prescribed exercise for T2D does not lack efficacy; rather it suffers from low effectiveness largely because of poor adherence. As we seek new ways to overcome ancient disinclinations to engage in sustained discretionary PA, it is useful to keep in mind the profound technological advancements of the last century that have reduced PA levels for billions of people. Consequently, individuals find themselves in a continual struggle with internal programming and systemic forces that discourage PA. This is no excuse to abandon efforts to promote exercise as medicine because there is high-quality evidence that moderate to high levels of exercise have profound benefits on outcomes such as HbA1c levels and the need to take glucose-lowering medications. However, a nuanced approach that acknowledges the limits and pitfalls of medicalising PA is necessary to enhance the promotion of exercise as both a treatment and prevention strategy for T2D. Equally important is committing to systemic changes that reintegrate PA into people's lives. In addition, there is an urgent need to study better methods to improve adherence to exercise because no matter how effective a drug or therapy might be, nothing is gained if patients do not take it. Finally, adherence to exercise regimens is a widespread challenge that is not confined to T2D. Although this review focuses on T2D, the adherence problem extends to other chronic diseases. We found no long-term studies (≥ 12 months) that demonstrated high adherence to exercise interventions for other chronic diseases indicating that this is a systemic issue that demands comprehensive attention if exercise is to be considered as an effective treatment intervention for lifestyle-related conditions.

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