in silico analysis predicted that bacterial production of agmatine might be elevated in people taking metformin[6], future studies are needed to directly assess agmatine levels in people taking metformin. In addition, understanding whether clinical concentrations of metformin increase bacterial agmatine production mediated by cAMP and CRP, and the potential mechanisms mediating these effects, will also be important.

A second key consideration is the systemic concentrations of agmatine that might be achieved with clinical dosing of metformin. Agmatine is produced by both host and bacterial cells during arginine metabolism; however, the majority of agmatine in humans is believed to be derived from bacterial sources[8]. Interestingly, many parallels exist between agmatine and metformin treatment. For example, high dose agmatine supplementation lowers blood levels of glucose in rodent models[8]. Although the mechanisms mediating these effects are unknown, agmatine enhances vasodilation, due to potential activation of α2-adrenergic and imidazoline receptors and the induction of endothelial nitric oxide synthase (eNOS)[8]. Interestingly, metformin also enhances insulin-stimulated vasodilation and blood flow in rodents and humans[9], despite low levels of the drug entering the muscle[2], thereby raising the possibility that agmatine might be important for this effect. In addition, high concentrations of agmatine (1 mM) stimulate insulin release[8] analogous to the incretin effect of metformin, which increases glucagon-like peptide 1 (GLP1) receptor expression in islets via a PPARα-dependent pathway[10]. Given that the effect of agmatine on longevity in *C. elegans* required the PPARα orthologue NHR-49, agmatine might be the potential link between these pathways. Future studies are needed to examine whether increases in agmatine and PPARα are important for mediating the effects of metformin on glucose homeostasis and longevity in rodents.

In conclusion, the present study highlights the need to consider how the microbiota might respond to pharmacological interventions to affect the host. It also raises the possibility of discovering new microbial metabolites that can improve host metabolism. Future studies examining the importance of these pathways in regulating glucose control and lifespan extension in preclinical rodent models and populations of patients are warranted.

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Competing interests
The authors declare no competing interests.

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OBESITY

Gamification and social incentives increase physical activity

John M. Jakicic and Renee J. Rogers

A nationwide study conducted in the USA demonstrated that an intervention combining gamification with social incentives, conducted within the context of a behavioural economics platform, can result in a moderate yet significant increase in physical activity in adults with obesity over a period of 24 weeks with an additional 12 week follow-up.

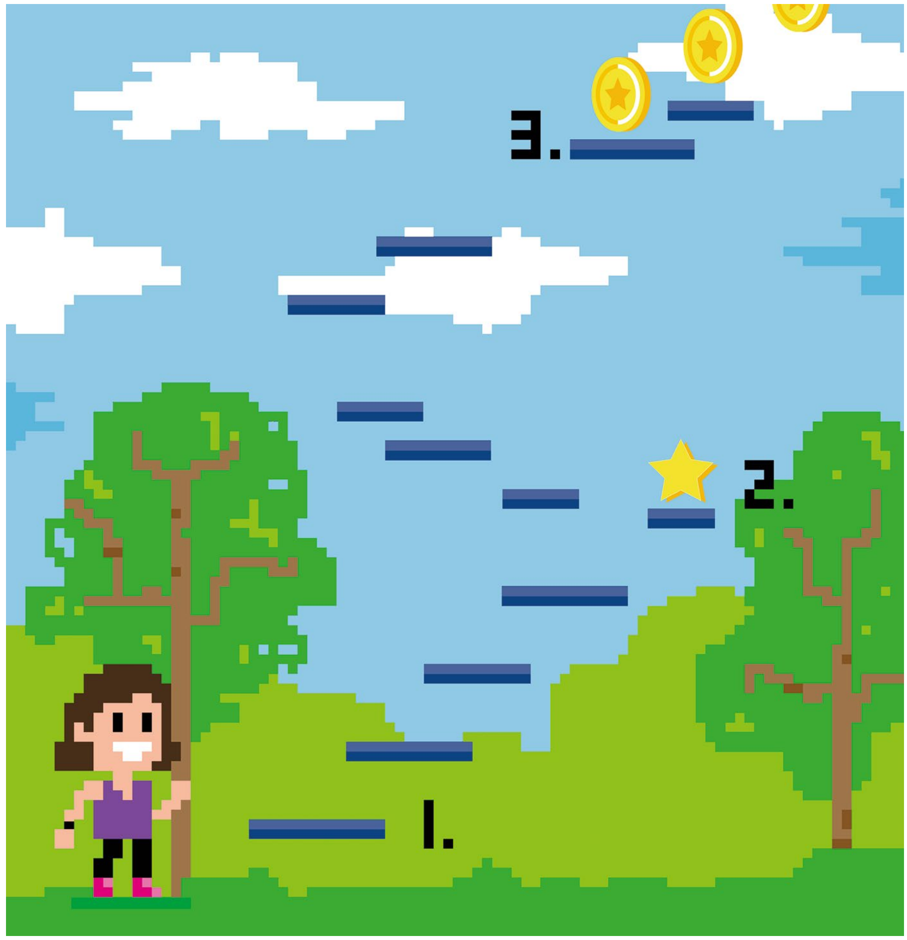
Refers to Patel, M. S. et al. Effectiveness of behaviorally designed gamification interventions with social incentives for increasing physical activity among overweight and obese adults across the United States: the STEP UP randomized clinical trial. *JAMA Intern. Med.* https://doi.org/10.1001/jamainternmed.2019.3505 (2019).

Physical activity is an important lifestyle behaviour that is associated with improved health[1]. Of note, health benefits can occur even with moderate increases in physical activity. For example, a systematic review carried out in 2019 suggested that all activity can contribute to health benefits and that interventions that focus on increasing the number of steps per day could be an effective strategy for increasing participation in physical activity[2]. However, the majority of adults in the USA are not sufficiently active; therefore, effective interventions and novel strategies are needed to improve participation in physical activity.

The present study by Mitesh Patel and colleagues[3] reports on a behavioural strategy using gamification, which includes the use of game design elements, in an effort to increase physical activity in adults with overweight or obesity (BMI >25 kg/m^2). The study examined whether the proposed gamification intervention increased physical activity measured in steps per day from a wearable device, across a 24-week intervention period and a 12-week follow-up period. All participants were provided with a wearable device to monitor steps per day of physical activity, which was also integrated with a smartphone application to provide feedback to participants with common behavioural elements. The control arm was provided with the wearable device and the smartphone application but, aside from the feedback provided by this, received no additional intervention components. In the intervention arm, participants were further randomized to one of three social incentive groups, which were designed to further increase their physical activity; these groups included support, collaboration or competition elements. The support arm involved the participant identifying a family member or friend who would be encouraged to support their engagement in physical activity. The collaboration arm involved participants being grouped with three other participants in the study, with the group aiming to work collectively to meet the physical activity goals. The competition arm again involved participants being grouped with three other participants in the study; this group of participants competed with each other on a weekly basis based on their step-based activity.

The results of this study showed that the support (adjusted difference from control 689; 95% CI 267–977; $P<0.001$), collaboration (adjusted difference from control 637; 95% CI 258–1,017; $P=0.001$) and competition arms (adjusted difference from control 920; 95% CI 513–1,328; $P<0.001$) all had significantly higher levels of daily steps than the control arm across the 6-month intervention; however, only the competition arm was significantly greater than the control arm after the 12-week follow-up period (adjusted difference from control 569; 95% CI 142–996; $P=0.009$)[3].

The results of the intervention phase of this study are consistent with the conclusion of the 2018 Physical Activity Guidelines Advisory Committee Report that stated there is strong evidence that wearable activity monitors can help increase physical activity when used in conjunction with goal-setting and other behavioural strategies; however, the strength of this evidence was only at a moderate level when applied to adults with overweight or obesity[1]. In the current study, the magnitude of the higher levels of daily steps in the support, collaboration and competition arms compared with the control group during the 24-week intervention was approximately 600 to 1,000 steps per day[3]. This increase is the equivalent to ~0.5 mile of walking or ~50 additional kcal per day of energy expenditure, assuming that 1 mile of walking is equivalent to ~100 kcal per day. The clinical importance of this magnitude of increase in physical activity needs to be considered, particularly given the participant population was classified as overweight or obesity. The 2018 Physical Activity Guidelines Advisory Committee Report concluded that there is strong evidence that increased amounts of physical activity are associated with attenuated weight gain in adults, with this relationship being most pronounced when physical activity is occurring for at least 150 minutes per week[1,4]. Moreover, other entities have recommended that even higher levels of physical activity might be necessary to achieve successful long-term weight loss[5].



Credit: Jennie Vallis/Springer Nature

The magnitude of the activity increase observed in this current study might not necessarily be large enough to result in a meaningful change in health status, particularly in adults with overweight or obesity. However, a contrasting perspective exists, which suggests that the magnitude of increase in physical activity observed in this study might be clinically meaningful. For example, James Hill and colleagues[6] have suggested that reducing the energy gap by as little as 50 kcal per day would be sufficient to curtail weight gain across the population; therefore, the modest increase in physical activity observed in this study might be sufficient to achieve this goal. Moreover, regarding outcomes such as all-cause mortality and cardiovascular disease, even modest increases in physical activity could be associated with reduced risk of these health outcomes[1,7].

The importance of social support has been demonstrated in other studies of behaviour change in adults with overweight or obesity. For example, Robert Jeffery and Rena Wing[8] demonstrated that an effective behavioural strategy for weight loss involved grouping participants in a manner to provide social support. Moreover, others have demonstrated the importance of social support for increasing physical activity[9].

The current study also concluded that the addition of competition to the gamification intervention was most effective for sustaining higher levels of physical activity at a 12-week follow up. However, close examination of the data indicated that gamification combined with competition increased physical activity by 920 steps per day after the 24-week intervention compared with control, but this difference decreased to 569 steps per day after the 12-week follow-up period. This pattern of behavioural drop-off is similar to findings of other studies of wearable devices that showed the inability for physical activity to be sustained beyond the initial short-term intervention period[10]. Thus, combining a gamification intervention with competition components, which also includes a wearable device, might provide only modest short-term benefits for increasing physical activity. This finding supports the ongoing need for additional effective strategies to increase and sustain long-term improvement in physical activity in adults.

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J.M.J. is on the Scientific Advisory Board for Weight Watchers International, Inc. R.J.R. declares no competing interests.

SURGERY

Incidence and determinants of mental health service use after bariatric surgery

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Bariatric surgery results in sustained weight loss and improvement in many obesity-related comorbidities. However, the effects of bariatric surgery on long-term mental health are less clear. A recent longitudinal cohort study shows that patients undergoing bariatric surgery seek mental health services at higher rates after surgery than before surgery and identifies specific risk factors for increased psychiatric service use.

Refers to Morgan, D. J. R. et al. Incidence and determinants of mental health service use after bariatric surgery. *JAMA Psychiatry* https://doi.org/10.1001/jamapsychiatry.2019.2741 (2019).

Bariatric surgery is a durable and evidence-based treatment for severe obesity and type 2 diabetes mellitus[1]. Over the past two decades, the number of bariatric surgeries performed in the USA has increased, with sleeve gastrectomy and Roux-en-Y gastric bypass being the predominant surgical procedures[1].

Despite longitudinal studies demonstrating sustained weight loss and improvements in overall health-related quality of life after bariatric surgery, the effects of bariatric surgery on mental health outcomes after surgery are less clear. Although suicide or self-harm are rare after bariatric surgery, population cohort studies have shown an increased rate of these events after surgery[2,3]. While a history of mental illness does not seem to influence post-bariatric surgery weight-loss outcomes, the effect of mental illness on mental health service utilization long term or in large samples is less clear.

The present longitudinal cohort study by David Morgan and colleagues[4] provides an important insight into this issue and leverages large population databases from the Western Australian Department of Health Data Linkage Branch to answer questions related to the effect of bariatric surgery on mental health service utilization and psychiatric complications, such as deliberate self-harm and suicide. The study used data from 24,766 patients who received bariatric surgery between 2007 and 2016 and showed that 16.1% ($n = 3{,}976$ patients) received psychiatric services at least once during the study period. Moreover, 6.9% ($n = 1{,}550$ patients) of all patients in the study had their first documented encounter with mental health services after bariatric surgery. Compared with before bariatric surgery, patients were three times more likely to go to the emergency department (incidence rate ratio (IRR) 3.0) or to be hospitalized for mental health issues (IRR 3.0) after surgery. The authors concluded that this study raises questions about the benefit of bariatric surgery on the mental health of patients with obesity.

The study also adds to the previously reported trends in major psychiatric sequelae, namely patient suicide and self-harm, following bariatric surgery. A previous population cohort study from Ontario, Canada, showed an increase in self-harm emergencies after bariatric surgery when comparing rates 3 years before and after surgery[2]. In the present study by Morgan and colleagues, the rate of suicidal ideation and deliberate self-harm increased 4.7-fold after bariatric surgery, and the suicide rate after the first bariatric surgery was increased compared with the general population (19.4 deaths per 100,000 person-years versus 13.5 per 100,000 person-years). These findings align with a previously published systematic review demonstrating an increased risk of self-harm or suicide attempts using the same population (OR 1.9; 95% CI 1.23–2.95) and an increased risk of mortality from suicide with matched control participant (OR 3.8; 95% CI 1.23–2.95) comparisons after surgery[3].

While bariatric surgery results in sustained weight loss and overall improvement in quality of life, this large data set from Morgan and colleagues further highlights the need to consider the mental health needs of patients who have had bariatric surgery. Identified risk factors for increased mental health service utilization after surgery include a pre-surgery mental health service encounter, young age and a history of bariatric surgery complications[4]. Given that nearly 70% of bariatric surgery candidates have a history of a psychiatric illness, the findings suggest that bariatric clinicians should consider psychiatric risks and stability during the pre-surgery assessment. In addition, patients undergoing bariatric surgery might not experience similar improvements in health-related physical quality of life, as demonstrated in studies showing a decline and marginal improvements in mental health-related quality of life long term[5]. In a separate study that examined psychological and quality of life outcomes 1 year after bariatric surgery, patients who experienced surgical complications did not experience a considerable improvement in mental quality of life[6]. Furthermore, patient expectations of bariatric surgery could also influence psychosocial needs after bariatric surgery, as many patients might expect 'transformative' experiences following bariatric surgery in all areas of their life including psychosocial domains. However, failure to achieve these expectations could be a potential factor contributing to increased mental health service use[7].