Categoría: Health Sciences and Medicine

REVISIÓN



Effect of probiotics on the obese patient. A review study

Efecto de los probióticos en el paciente obeso. Un estudio de revisión

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Cite as: Montachana Crespata MA, Viteri Robayo CP. Effect of probiotics on the obese patient. A review study. Salud, Ciencia y Tecnología - Serie de Conferencias. 2023; 2:549. https://doi.org/10.56294/sctconf2023549

Submitted: 02-07-2023

Revised: 12-10-2023

Accepted: 19-12-2023

Published: 20-12-2023

Editor: Dr. William Castillo-González 回

ABSTRACT

Introduction: the gut microbiota is a potential determining factor in the development of obesity, resulting in dysbiosis, which is related to a lower number of members of the Bacteroidetes division and an increase in Firmicutes leading to a decrease in energy expenditure, it is also associated with the inflammatory process, insulin resistance and type 2 diabetes mellitus.

Objective: to conduct a literature review related to the effects of probiotics on the improvement of the intestinal microbiota in an obese patient and its associated disorders.

Methods: a search of articles in PubMed, Google Scholar and Elsevier from the last five years was conducted using the terms "obesity and probiotics", "effect of probiotics", "gut microbiota and probiotics". A total of 23 articles were included in the selection criteria.

Results: supplementation with probiotics specifically certain strains such as Lactobacillus plantarum and Bifidobacterium could lead to significant weight reductions, in combination with energy restriction and physical activity. However, it is important to develop clinical trials that are properly designed, including all aspects of lifestyle, gut microbiota, metabolites, and genetic background.

Conclusions: despite the beneficial effects, they are not yet considered an alternative strategy in the treatment of obesity due to the lack of research in this field, since the currently available data come from studies conducted in animals that may not present potential in humans. It is important to conduct more large-scale longitudinal studies with longer follow-up.

Keywords: Probiotics; Obesity; Gut Microbiota; Dysbiosis.

RESUMEN

Introducción: la microbiota intestinal es un potencial factor determinante en el desarrollo de la obesidad, ocurriendo una disbiosis, la cual se relaciona con un menor número de miembros de la división Bacteroidetes e incremento de Firmicutes conduciendo a una disminución del gasto energético, además está asociada con el proceso inflamatorio, la resistencia a la insulina y la diabetes mellitus de tipo 2.

Objetivo: realizar una revisión bibliográfica relacionada a los efectos que producen los probióticos en la mejoría de la microbiota intestinal en un paciente obeso y sus trastornos asociados.

Métodos: se realizó una búsqueda de artículos en PubMed, Google Académico y Elsevier, de los últimos cinco años utilizando términos "obesity and probiotics" "Efecto de probióticos", "Microbiota intestinal y probióticos". Se incluyeron 23 artículos con los criterios de selección.

Resultados: la suplementación con probióticos específicamente ciertas cepas como Lactobacillus plantarum y Bifidobacterium podrían conducir a reducciones significativas de peso, en combinación con restricción

© 2023; Los autores. Este es un artículo en acceso abierto, distribuido bajo los términos de una licencia Creative Commons (https:// creativecommons.org/licenses/by/4.0) que permite el uso, distribución y reproducción en cualquier medio siempre que la obra original sea correctamente citada energética y actividad física. Sin embargo, es importante desarrollar ensayos clínicos que estén correctamente diseñados, donde incluyan todos los aspectos del estilo de vida, la microbiota intestinal, los metabolitos y los antecedentes genéticos.

Conclusiones: a pesar de los efectos beneficiosos aún no se consideran una estrategia alternativa en el tratamiento de la obesidad debido a la falta de investigación en este campo, puesto que los datos actualmente disponibles provienen de estudios realizados en animales que no pueden presentar potencial en humanos. Es importante realizar más estudios longitudinales a gran escala con un seguimiento más prolongado.

Palabras claves: Probióticos; Obesidad; Microbiota Intestinal; Disbiosis.

INTRODUCTION

Obesity has become one of the major global issues. This problem arises from various intrinsic and extrinsic factors such as genetics, diet, and other nutrigenomic factors. In obese individuals, the composition of intestinal microbiota is altered (dysbiosis), leading to reduced energy expenditure. Additionally, obesity is associated with inflammatory processes, insulin resistance, and type 2 diabetes mellitus.⁽¹⁾ However, there are different combinations of therapeutic strategies for controlling this condition, starting with lifestyle changes, the use of drugs or probiotics as treatment, and in critical cases, bariatric surgery, considering that the efficacy of probiotics is considered a potential way to control obesity.⁽²⁾

Currently, obesity is described as one of the main risk factors for many non-communicable diseases such as diabetes, cardiovascular diseases, and others cerebrovascular accidents and various types of cancer Thus, in 2021, obesity caused 2,8 million deaths from noncommunicable diseases in the Americas.

According to the WHO, in 2016, approximately 13 % of the global adult population had obesity, with 11 % being men and 15 % women. There was a rapid growth in middle-income countries, in Southeast Asia and Africa. On the other hand, the prevalence of overweight or obesity in children and adolescents aged 5 to 19 increased worldwide, exceeding 30 %.⁽³⁾ In the case of Ecuador, according to ENSANUT reports, the prevalence estimates show that out of every 100 children, 35 already have overweight or obesity. For adults aged 19 to 59, it was 64,68 %, higher in women (67,62 %) than in men (61,37 %). Obesity rates were higher in women (27,89 %) than in men (18,33 %), while overweight was higher in men (43,05 %) compared to women (39,74 %).⁽⁴⁾

Considering this, it is necessary to incorporate new therapeutic strategies for obesity control, including the use of probiotics as treatment. Several studies have shown considerable expectations regarding their effectiveness, such as modulating the functions of intestinal microbiota, increasing the number of beneficial microorganisms that improve the health of these patients. This study focuses primarily on the metabolic aspect, body fat percentage, body weight, and administration of different microbial strains. Álvarez & Martín pointed out in their study that probiotics have gained significant interest in the treatment of overweight and obesity. Whether used as a single strain or multiple strains, they could have a beneficial effect on weight loss and various anthropometric markers such as body fat percentage, visceral fat area, waist circumference, and Body Mass Index.^(1,5)

Currently, changes in bacterial strains of intestinal microbiota are considered to play a causal role in obesity. Thus, probiotics have emerged as a promising area of research for its treatment. This study aims to provide a review of the current scientific evidence on the use of probiotics in obesity management, demonstrating the underlying mechanisms through which probiotics could influence intestinal dysbiosis, body weight, and improvements in lipid and glucose metabolism.

METHODS

A review of studies regarding the effect of probiotics on obese patients was conducted. For this purpose, databases such as PubMed (86 %), Google Scholar (9 %), and Elsevier (5 %) were utilized for published scientific articles, in English (88 %), Spanish (4 %), French (4 %), and Portuguese (4 %). Bibliographies from the last five years were also used, using keywords: "obesity," "probiotics," "intestinal microbiota." The inclusion criteria were as follows: review articles, original articles, systematic reviews, and randomized controlled trials. With the aforementioned parameters, a total of at least one hundred references were used, of which 23 were predominantly used for this study. During the research, articles with duplicate data, studies that did not meet the inclusion criteria (information from undergraduate studies, studies with only abstract available), and sources from unreliable sources were excluded.

RESULTS

Currently, there are studies mentioning that intestinal probiotics help restore a healthy balance of microbiota, which improves metabolism, especially impacting weight. In a study by Oniszczuk et al., it was

found that probiotics play a crucial role in replenishing intestinal flora, as they promote the development of beneficial bacteria, weight control, and metabolic disorders associated with obesity. ⁽⁶⁾



Figure 1. PRISMA flow diagram showing the article selection process

Over the recent period, preclinical studies have emerged investigating the effects of administering probiotics with multiple strains against obesity development. For instance, supplementation of Lactobacillus curvatus mixed with Lactobacillus plantarum in mice fed a high-fat diet significantly reduced fat accumulation, and the combination showed a synergistic effect on inhibiting genes involved in fatty acid synthesis.⁽⁷⁾

The following studies describe these findings:

Mitev et al. indicate that obese individuals exhibit dysbiosis in their intestinal microbiota, characterized by a lower number of Bacteroidetes members and an increase in Firmicutes such as Clostridium, Eubacterium rectarle, Clostridium coccoides, Lactobacillus reuteri, A mucinophila, Clostridium histolyticum, and S. Aureus. These alterations lead to modifications in gastrointestinal peptides such as gastrin, CCK, somatostatin, and ghrelin, causing decreased satiety and increased appetite.⁽⁸⁾ Soares mentions that the most commonly used strains in obesity treatment were Lactobacillus and Bifidobacterium.

The results of probiotic supplementation included a reduction in body mass index (BMI), waist and hip circumference, body weight, and visceral fat.⁽⁹⁾ Additionally, there was an improvement in insulin resistance, such as a decrease in hyperglycemia, reduction in proinflammatory cytokines, positive changes in lipoproteins such as increased HDL and decreased LDL, as well as reductions in triglyceride and total cholesterol levels. Similarly, a study notes that probiotic administration and clinical trials related to weight control and metabolic health have focused on two groups, Lactobacillus and Bifidobacterium. The latter strain has shown weight maintenance in placebo-controlled studies and improved metabolic health in animal studies by reducing glucose

levels and enhancing insulin sensitivity.⁽¹⁰⁾

Unlike the study by Rahayu et al., where 60 overweight and obese adult volunteers in Indonesia were administered a probiotic in the form of L. plantarum Dad-13 powder (2×10° CFU/gram/packet) for 90 days, various measurement parameters and result analyses were used once a month. These included weight, lipid profile, analysis of short-chain fatty acids via gas chromatography, and fecal pH measurement. However, no significant reduction in body weight, lipid profile, or any other mentioned parameter was observed. Nonetheless, it only resulted in a decrease in the Firmicutes population and an increase in the Bacteroides population, specifically Prevotella.⁽¹¹⁾

Similarly, Sivamaruth et al.'s research demonstrated that the supplementation of probiotic yogurt (YP) and low-fat regular yogurt (YBG) influenced weight loss programs in overweight and obese women. The consumption of YP supplemented with Bifidobacterium lactis and Lactobacillus acidophilus; 10^7 CFU per day for 12 weeks significantly reduced total cholesterol, LDL, and insulin resistance. However, no notable changes were observed in body mass, HDL, fasting plasma glucose, and triglyceride levels. The results suggested that consuming YP with the regular diet did not influence weight reduction but improved lipid profile and insulin sensitivity in obese and overweight women.⁽¹²⁾

Lauw et al. noted that patients with metabolic syndrome experienced decreases in BMI, total cholesterol, LDL cholesterol, tumor necrosis factor- α , and interleukin-6 after receiving fermented milk supplemented with Bifidobacterium lactis for 45 days compared to baseline and a control group. Additionally, it was discovered that using Lactobacillus acidophilus for four weeks in individuals with type 2 diabetes mellitus increased insulin sensitivity.⁽¹³⁾

On the contrary, a review evaluating 25 studies demonstrated that probiotic supplementation, especially of the Lactobacillus population, in overweight and obese patients showed reductions in BMI, weight, and LDL compared to controls. However, they had no effect on systolic blood pressure (SBP), diastolic blood pressure (DBP), HDL, glucose, and triglycerides.⁽¹⁾

In a study conducted by Depommier et al., involving 40 individuals, of which 32 overweight/obese participants completed the study, they were administered 1010 bacteria daily for 3 months in either live or pasteurized form. It was demonstrated that the pasteurized form of A. muciniphila improved insulin sensitivity, insulinemia by approximately 30 %, and total cholesterol levels. Moreover, it reduced body weight and fat mass. The conclusion drawn was that supplementation with A. muciniphila reduced the levels of the most relevant blood markers of liver dysfunction and inflammation, improving various metabolic parameters, while the overall structure of the intestinal microbiome remained unaffected.⁽¹⁴⁾

Quiroz-Erazo et al. used biocompounds such as polyphenols and probiotics with the aim of investigating the resistance to polyphenol-rich extracts of Theobroma cacao L. by Lactobacillales isolated from human fecal microbiota of volunteers (with high consumption of saturated fats). This aimed to advance the understanding of the potential combination of these bioactive compounds, which have shown multiple health benefits. It has been observed that polyphenols enhance the adherence to intestinal mucus of Lactobacillus strains, and both prevent or restore dysbiosis of the intestinal microbiota. However, more studies are required to explore whether these two biocompounds can act synergistically under different conditions. Nevertheless, the potential use of the combination of bacteria and polyphenols as a promising strategy for intestinal elimination of free fatty acids is confirmed.⁽¹⁵⁾

On the other hand, Jacouton et al. used the probiotic strain L. plantarum and its impact on a mouse model of obesity induced by a high-fat diet. They were administered 1 × 109 CFU/day for 12 weeks, showing that treatment with this strain improved insulin sensitivity by reducing fasting serum glucose and fructosamine levels. However, it also affected glucose transport and metabolism, resulting in negative regulation of liver genes Glut-4 and Glucose 6 phosphate. Additionally, L. plantarum reduced LDL-c concentration and regulated hepatic lipid metabolism, similarly restoring the intestinal microbial composition by reducing the Firmicutes to Bacteroidetes ratio. The conclusion drawn was that this probiotic strain represents a potential approach for restoring glucose sensitivity and lipid alteration associated with obesity.⁽¹⁶⁾

Likewise, the mechanism of action of Lactobacillus plantarum L-14 extract was evaluated in vivo, and the effects of its oral intake were assessed in a mouse model with a high-fat diet every 2 days for 7 weeks, resulting in a significant decrease in serum triacylglycerol/high-density lipoprotein cholesterol and steatohepatitis.⁽¹⁷⁾

Similarly, Cai et al. conducted a study using a mouse model fed a high-fat diet for 16 weeks, to which doses of 0,2 ml of 1×10^9 or 1×10^{10} CFU/mL of L. plantarum FRT4 were administered during the last 8 weeks of the diet. This resulted in a reduction of diet-induced body weight, liver weight, body fat, serum cholesterol, triglycerides, and alanine aminotransferase (ALT) levels in the liver. It was also demonstrated that FRT4 positively regulated intestinal barrier function by increasing microbial biodiversity (Bacteroides, Parabacteroides, Anaerotruncus, Alistipes, Itestinimonas, Butyicicoccus, Butyricimonas) and pro-inflammatory biomediators. The conclusion drawn was that this strain could be used as a potential functional food for obesity prevention.⁽¹⁸⁾

Le Barz et al. studied the in vivo potential anti-obesity and anti-inflammatory effects of various previously isolated bacterial strains. In this study, male mice were fed a high-fat and high-sugar diet, and one of the six strains (P35 [Propionibacterium freudenreichii], Lb38 [Lactobacillus plantarum], Lb79 [Lactobacillus paracasei/ casei], Lb102 [Lactobacillus rhamnosus], Bf26, and Bf141 [2 doses of Bifidobacterium animalis spp lactis]) was administered via gavage at 10⁹ CFU/day for 8 weeks. Physiological tests were then conducted, measuring weight, food intake three times per week, and collecting fecal, blood, and tissue samples. Tools such as one-way ANOVA were used to compare the effects of each mentioned strain against the control group, demonstrating that P35, Lb38, Lb102, and Bf141 could prevent weight gain induced by the high-fat and high-sugar diet, improve glucose tolerance, insulin sensitivity, and reduce visceral fat accumulation. However, none of the strains restored dysbiosis of the intestinal microbiota.⁽¹⁹⁾

Similarly, Sun, Chen, & Li conducted experiments in male mice fed a high-fat diet for 12 weeks, showing a significant increase in body weight, white adipose tissue, plasma lipid levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol. Subsequently, Lactobacillus paracasei was administered for 12 weeks, potentially reducing the aforementioned biomarkers. This strain was shown to improve high-fat diet-induced hyperlipidemia, lipid accumulation in the liver, and inflammation associated with intestinal dysbiosis in obese mice.⁽²⁰⁾

On the other hand, the potential anti-obesity of the probiotic Bifidobacterium longum subsp. Infantis was investigated in mice fed a high-fat diet. The results demonstrated that an 8-week intervention reduced the body weight and fat gain of this diet and normalized the levels of total cholesterol and low-density lipoprotein cholesterol.

The treatment also reduced adipocyte expansion, liver injury, and inflammation; moreover, it was observed to decrease the Firmicutes/Bacteroidetes ratio in obese mice.⁽²¹⁾ Sung-Joon et al. studied how supplementation with Lactobacillus curvatus and Lactobacillus plantarum alleviates obesity by regulating the human intestinal microbiota. A randomized, double-blind, placebo-controlled study was conducted involving 72 overweight individuals over a 12-week period. Participants were administered 1×10^{10} colony-forming units of HY7601 and KY1032, while the placebo group consumed the same product without probiotics. After the treatment, the probiotic group exhibited a reduction in body weight, visceral fat mass, and waist circumference, and an increase in adiponectin compared to the placebo group. Additionally, supplementation modulated the characteristics of bacterial intestinal microbiota and diversity by increasing Bifidobacteriaceae and Akkermansiaceae and decreasing Prevotellaceae and Selenomonadaceae.⁽²²⁾ Below is a summary of probiotics and their effects on obesity and related biomarkers.

| Table 1. Probiotics and their effects related to obesity and its biomarkers | | | | | | |
|---|------|--|-------------------------|---|--|--|
| Referencia | Año | Cepa probiótica | Modelo de estudio | Efectos | | |
| Soares ⁽⁹⁾ | 2019 | Lactobacillus Bifidobacterium. | ln vitro | The results of probiotic supplementation were reduction of body mass index (BMI), waist/hip circumference, body weight and visceral fat, improvement of insulin resistance, reduction of pro-inflammatory cytokines, positive changes in lipoproteins, reduction of triglyceride and total cholesterol levels. | | |
| Rahayu et al | 2021 | Lactobacillus plantarum Dad-13 | ln vitro | The probiotic was administered to overweight and obese patients for 90 days, however no significant reduction in body weight, lipid profile, short chain fatty acids and fecal pH measurement was observed, it simply caused the Firmicutes population to decrease and Bacteroides to increase. | | |
| Sivamaruth et al ⁽¹²⁾ | 2019 | B. lactis BB12 y L. acidophilus | ln vitro | Probiotic Yogurt (containing B. lactis BB12 and L. acidophilus LA5; 10 ⁷ CFU per day) was administered for 12 weeks, the results suggested that its consumption together with the usual diet had not influenced weight reduction, however it improves lipid profile and insulin sensitivity in overweight and obese women. | | |
| Lauw et al. ⁽¹³⁾ | 2023 | Bifidobacterium lactis HN019 Lactobacillus acidophilus NCFM | In vivo | Patients with metabolic syndrome experienced decreases in BMI, total cholesterol, LDL cholesterol, tumor necrosis factor α and interleukin-6. The use of Lactobacillus acidophilus NCFM for four weeks in people with type 2 diabetes mellitus increased insulin sensitivity. | | |

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| Mayta- Tovalino et al. | 2023 | Lactobacillus | In vivo | Consisting of 25 overweight and obese patients, with a follow-up range of two to six months, it was shown that supplementation reduced BMI, weight and LDL but had no effect on systolic blood pressure, diastolic blood pressure, HDL or triglycerides. |
|--|------|--|----------|---|
| Depommier et al. ⁽¹⁴⁾ | 2019 | A. muciniphila | ln vitro | Supplementation in pasteurized form of A. muciniphila improved insulin sensitivity, insulinemia by approximately 30 % and total cholesterol levels, as well as decreased body weight and fat mass. |
| Quiroz-Eraso et al. ⁽¹⁵⁾ | 2023 | Theobroma cacao & Lactobacillales | In vitro | Theobroma cacao enhanced the intestinal mucus adhesion of Lactobacillus strains, highlighting that both biocompounds restore intestinal microbiota dysbiosis, as well as the potential use of the combination of bacteria and polyphenols as a strategy for intestinal elimination of free fatty acids. |
| Jacouton et al. ⁽¹⁶⁾ | 2023 | Lactobacillus plantarum CNCM I-4459 | In vivo | It improved insulin sensitivity by decreasing fasting serum glucose and fructosamine levels, reduced LDL-c concentration and regulated hepatic lipid metabolism, and restored intestinal microbial composition by reducing the ratio of Firmicutes to Bacteroidetes. |
| Lee et al. ⁽¹⁷⁾ | 2021 | Lactobacillus plantarum L-14 (KTCT13497BP) | ln vivo | Significant decrease in serum triacylglycerol/high- density lipoprotein cholesterol and steatohepatitis. |
| Cai et al. ⁽¹⁸⁾ | 2022 | Lactobacillus plantarum FRT4 | ln vivo | L. plantarum FRT4 significantly reduced high-fat diet-induced body weight gain, liver weight, fat, serum cholesterol, triglycerides and liver alanine aminotransferase (ALT) levels. |
| Le Barz et al. | 2019 | Propionibacterium freudenreichii, Lactobacillus plantarum, Lactobacillus rhamnosus, Bifidobacterium animalis spp lactis | In vivo | Four bacterial strains were finally identified for their probiotic effects in preventing the development of obesity, as well as associated metabolic and inflammatory disorders (they prevented weight gain, improved glucose tolerance, insulin sensitivity and reduced visceral fat accumulation). |
| Sun et al. ⁽²⁰⁾ | 2023 | Lactobacillus paracasei (L9) | In vivo | Male mice were acquired and fed a high fat diet for a period of 12 weeks, Lactobacillus paracasei (L9) was administered for another 12 weeks potentially reducing body weight, improving hyperlipidemia, lipid accumulation in the liver and inflammation associated with intestinal dysbiosis in obese mice. |
| Kou et al. ⁽²¹⁾ | 2023 | Bifidobacterium longum subsp. Infantis (FB3-14) | ln vivo | The 8-week intervention (FB3-14) in mice fed a high-fat diet reduced body weight and fat gain, normalized total cholesterol and low-density lipoprotein cholesterol levels. The treatment also decreased adipocyte expansion, liver injury and inflammation. |
| Mo et al. ⁽²²⁾ | 2022 | Lactobacillus curvatus (HY7601) y Lactobacillus plantarum (KY1032) | In vitro | A study was conducted with 72 overweight individuals over a 12-week period, 1×10 10 colony-forming units of HY7601 and KY1032 were administered, showed a reduction in body weight, visceral fat, waist circumference, and an increase in adiponectin. In addition, supplementation modulated the characteristics of the bacterial gut microbiota. |

DISCUSSION

The relationship between gut microbiota and obese individuals has become an area of interest, as probiotics have emerged as a therapeutic intervention for this issue, showing a trend towards improving metabolic profiles. From the studies analyzed, this review demonstrates that the use of probiotics, specifically certain strains such as Lactobacillus plantarum and Bifidobacterium, show several benefits such as improvement in lipid profile, including total cholesterol, LDL cholesterol, and triglycerides, as well as insulin sensitivity. Additionally, these organisms have the capacity to contribute to weight reduction, decrease in BMI, waist-to-hip ratio, and improvement in metabolism through modulation of the composition of intestinal microbiota, thereby improving dysbiosis in various in vitro and in vivo trials. ^(16,22)

However, when comparing the efficacy of probiotics in studies conducted on humans and animals, it is evident that while most animal research shows better outcomes regarding body weight, visceral fat, and other metabolic markers, ^(16,17) it is due to the lack of human cohort trials, the absence of long-term follow-up studies,

and significant differences in probiotic strains, their mechanisms, effective doses, and treatment durations. All of this indicates a significant need for studies and research to tailor interventions and/or treatments according to the individual needs and characteristics of each patient.

Nevertheless, although probiotics offer promising objectives in regulating gut microbiota and improving obesity-associated biomarkers, it is important to address the identified challenges and complexities, focusing future research on bridging gaps in knowledge and establishing guidelines to translate these findings into effective treatment strategies for obese patients.

CONCLUSIONS

Given that overweight and obesity pose a serious public health problem worldwide, there is currently a great need for more agents to prevent this issue and its associated disorders. In this context, diet and exercise are the foundation of preventive and therapeutic interventions. Particularly, numerous types of probiotic strains have been associated with weight loss; however, despite the beneficial effects, they are not yet considered an alternative strategy in the treatment of obesity, due to the lack of research in this field. Currently available data come from studies conducted in animals that may not translate to humans. On the other hand, corresponding human trials are severely limited by sample size, short follow-up duration, lack of adherence, and even adverse events. It is important to conduct more large-scale longitudinal studies with extended follow-up to assess the therapeutic potential of probiotic intake on obesity and associated disorders.

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FUNDING

Self-funded

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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