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ABSTRACT & COMMENTARY

Combined GIP/GLP-1 Agonist: Safe for Type 2 Diabetes Patients?

By Tim Drake, PharmD, MBA, BCPS

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SYNOPSIS: In the SURPASS-2 trial, tirzepatide showed noninferiority and superiority vs. semaglutide in decreasing A1c levels in patients with type 2 diabetes.

SOURCE: Frías JP, Davies MJ, Rosenstock J, et al. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. *N Engl J Med* 2021;385:503-515.

Metformin continues to be the drug of choice to treat patients with type 2 diabetes.[1] Glucagon-like peptide 1 (GLP-1) agonists quickly gained favor and now are recommended second line after metformin because of their ability to cause weight loss, lower cardiovascular risk, and their low risk of causing hypoglycemia.[2] Other agents to treat type 2 diabetes include sodium-glucose cotransporter-2 inhibitors, sulfonylureas, thiazolidinediones, and insulin.[1] Important characteristics to consider when choosing a drug to treat diabetes include effectiveness at lowering blood sugar, cardiovascular and renal effects, weight loss or weight gain, and risk of hypoglycemia.[3]

Tirzepatide is a dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 that is injected once weekly. GLP-1 agents work by stimulating insulin secretion in hyperglycemic states and reducing appetite by delaying gastric emptying. GIP works by stimulating insulin in hyperglycemic states and stimulating glucagon in hypoglycemic conditions.[4] In theory, an agent that enhances both pathways should offer a better glucose-lowering benefit.

The authors of the SURPASS-2 trial compared the glucose-lowering effect of various doses of tirzepatide to semaglutide. This was an unblinded, parallel-group, randomized, active-controlled trial. Adult patients who had not achieved a glycosylated hemoglobin (A1c) level < 7% on metformin alone were randomly assigned to inject tirzepatide 5 mg, 10 mg, 15 mg, or semaglutide 1 mg on a weekly basis for 40 weeks. The primary endpoint was the change in A1c. Secondary endpoints included body weight change and achieving an A1c level < 7% and < 5.7%.

Financial Disclosure: Dr. Brunton, physician editor, reports he is on the speakers bureau for AstraZeneca, Bayer, Lilly, and Novo Nordisk; and is a retained consultant for Abbott, Acadia, AstraZeneca, Bayer, Novo Nordisk, Sanofi, and Xeris. The relevant financial relationships listed have been mitigated. None of the remaining planners or authors for this educational activity have relevant financial relationships to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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The authors included 1,878 patients in the results. Baseline characteristics were similar among the four groups. The starting mean A1c was 8.28% and the average weight was 93.7 kg. At the end of the study, the 5 mg tirzepatide group lowered A1c by 2.01%, the 10 mg group by 2.24%, and the 15 mg group by 2.30%. The A1c was lowered by 1.86% in the semaglutide group. The tirzepatide was superior to semaglutide for A1c-lowering for all three groups ($P = 0.02$ for 5 mg, $P < 0.001$ for 10 mg and 15 mg).

Tirzepatide was superior to semaglutide treatment for weight loss, with mean body weight reductions for 5 mg, 10 mg, and 15 mg tirzepatide groups of 7.6 kg, 9.3 kg, and 11.2 kg, respectively. The semaglutide group lost an average of 5.7 kg ($P < 0.001$ for all groups).

A total of 82% of patients in the 5 mg group met the < 7% target vs. 86% in the 10 mg and 15 mg groups and 79% in the semaglutide group. The 5 mg group was noninferior, and the 10 mg and 15 mg groups were superior to semaglutide treatment ($P < 0.05$). Twenty-seven percent of patients in the 5 mg group met the < 5.7% target vs. 40% in the 10 mg and 46% in the 15 mg group and 19% in the semaglutide group. The 5 mg group was noninferior, and the 10 mg and 15 mg groups were superior to semaglutide ($P < 0.001$).

The most common adverse event in all groups was gastrointestinal (17% to 22%). Most cases were mild to moderate and occurred during the dose escalation phase of the study. Clinically significant hypoglycemia was low, with three, one, and eight patients in the 5 mg, 10 mg, and 15 mg groups, respectively, compared with two patients in the semaglutide group. There was one case of severe hypoglycemia in the 5 mg group and one case in the 15 mg group. There were two cases of pancreatitis in the tirzepatide group and three cases in the semaglutide group. Overall, the discontinuation rate for tirzepatide was 8.5% vs. 4.1% for semaglutide.

■ COMMENTARY

A different group of researchers recently published the results of the SURPASS-3 trial. This investigation was set up similar to SURPASS-2, except the control group injected the basal insulin degludec instead of semaglutide. The results of SURPASS-3 showed similar results of blood glucose-lowering and weight loss as SURPASS-2.

The authors concluded tirzepatide was superior to insulin degludec for A1c-lowering and weight loss and caused minimal hypoglycemia.[5]

The dual GIP/GLP1 agonist tirzepatide showed impressive results in lowering A1c levels and promoting weight loss in patients with type 2 diabetes who were taking metformin. The dual mechanism could help alleviate the medication burden while delaying the need for insulin. Of note, 46% of patients who took the higher 15 mg dose reached near-normal levels of glycemia with a low risk of hypoglycemia.

It is somewhat expected that a medication with a dual mechanism of action would outperform another with just one mechanism. Additionally, A1c and weight loss do not tell the whole story of an antidiabetic agent. Outcomes showing a reduction in mortality, cardiovascular, renal, and other macro- and microvascular events will help determine if tirzepatide will become an attractive therapy for diabetes. ■

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BRIEF REPORT

Asymptomatic Transmission of COVID-19 in Households

By Carol A. Kemper, MD, FACP

Clinical Associate Professor of Medicine, Stanford University, Division of Infectious Diseases, Santa Clara Valley Medical Center

SOURCE: Ng OT, Marimuthu K, Koh V, et al. SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: A retrospective cohort study. *Lancet* 2021;21:333-343.

Early on during the COVID-19 pandemic, Singapore adopted a comprehensive approach to prevention, diagnosis, and management of COVID-19, with clear guidance for the community and recommendations for mask wearing and social distancing. A network of 800 public health and community clinics was activated to quickly perform contact tracing and quarantine of contacts in the home and in the workplace and to test contacts who developed symptoms, with a medical leave plan for those who became ill. From Jan. 23 to April 3, 2020, 13,026 close contacts were identified, including 1,863 household contacts (with 578 distinct contact groups), 2,319 work contacts (with 225 distinct contact groups), 3,588 social contacts (with 346 distinct contact groups), 2,626 transportation contacts, and 2,630 other contacts.

Of these, 468 household contacts, 332 work contacts, and 458 social contacts were polymerase chain reaction (PCR) tested based on the presence of symptoms. A total of 188 cases were identified as secondary cases based on symptom-driven PCR screening, and another 7,582 completed quarantine without a COVID-19 diagnosis. Based on symptom-based screening, the secondary attack rate was 5.9% for household contacts, 1.3% for work contacts, and 1.3% for social contacts. Cases clearly clustered together within certain households and a few work groups; 86.3% of household contact groups and 91.6% of work contact groups had no apparent secondary cases based on symptom-based PCR screening. Convalescent serologic testing was performed in 30% of household contacts, 9% of work contacts, and 11.8% of social contacts who completed quarantine without a COVID-19 diagnosis. An additional 5.5% of household contacts, 2.5% of work contacts, and 2.1% of social contacts were identified as secondary cases based on positive serology. Among these, two-thirds were asymptomatic and one-third had developed symptoms but had tested SARS-CoV-2 PCR negative.

Activities that increased the risk of transmission included sharing a bedroom, sharing a vehicle, or being spoken to by a COVID-19 PCR-positive person for > 30 minutes. Indirect contact, sharing objects or equipment, sharing a bathroom, and sharing a meal were not associated with SARS-CoV-2 transmission.

Secondary transmission was much more likely for individuals within households (11.4%) than in the workplace (3.8%) or social situations (3.4%), and infections clearly clustered in some households and a few workplaces.

Efforts to control secondary transmission should be given to households and those contact groups where any case of secondary transmission has been identified. Symptom-based PCR screening of contacts missed nearly half of those who developed secondary infection. At least one-third of secondary transmission cases remained asymptomatic. ■

ABSTRACT & COMMENTARY

Fermented Foods Help the Immune System, Alleviate Inflammation

By Joseph E. Scherger, MD, MPH

Core Faculty, Eisenhower Health Family Medicine, Residency Program, Eisenhower Health Center, La Quinta, CA; Clinical Professor, Keck School of Medicine, University of Southern California, Los Angeles

SYNOPSIS: A diet rich in fermented foods from dairy and other sources reduced 19 inflammatory markers compared with a high-fiber diet.

SOURCE: Wastyk HC, Fragiadakis GK, Perelman D, et al. Gut-microbiota-targeted diets modulate human immune status. *Cell* 2021;184:4137-4153.e14.

Researchers from the Stanford Center for Human Microbiome Studies randomized 36 healthy adults to a high-fiber diet or a diet rich with fermented foods for 10 weeks. Their microbiomes were analyzed before and after the study, along with a variety of inflammatory markers. The high-fiber group ate mainly plant-based, fiber-rich foods. They doubled their fiber intake from 22 grams per day to 45 grams per day, roughly triple the average American intake. The fermented food group went from eating almost no fermented foods to six servings a day of yogurt, kefir, sauerkraut, kombucha, and kimchi. The small study size allowed for a meticulous review of the group compliance.

Those on the fermented food diet showed better diversity of the microbiome, with fewer inflammatory markers and improved immune profiling. These effects were dose-related to the amount of fermented foods. Those on the high-fiber diet showed stable microbiome diversity and no change in these markers. The authors concluded fermented foods may be valuable in improving microbiome diversity and countering the increased inflammation seen in industrialized society.

■ COMMENTARY

When I make food selections, I ask three questions: How healthy is the food? Do I like the food? How good will this food be for my microbiome? After all, we are completely responsible for the health and diversity of our "inner garden" that does so much to keep us healthy. For the second question, I remember a quote I read not long ago: There is no such thing as a food you do not like, there are only foods you do not like yet. Pickles and olives were two foods I avoided because of the taste, but now I eat them heartily when I found out how good they were for my microbiome.

High-fiber foods do produce proven health benefits, and Wastyk et al suggested a follow-up study of the combined effects of a high-fiber diet rich in fermented foods. Meanwhile, we should start recommending fermented foods to our patients as part of a healthy diet. ■

ABSTRACT & COMMENTARY

Vitamin and Mineral Supplements for Cardiovascular Disease

By Rakesh Calton, MD, and Nancy Selfridge, MD

Dr. Calton is Associate Professor, Clinical Foundations, Ross University School of Medicine, Barbados, West Indies.

Dr. Selfridge is Professor, Clinical Foundations Department, Ross University School of Medicine, Barbados, West Indies.

SYNOPSIS: A meta-analysis of systematic reviews and randomized, controlled trials to analyze the role of commonly used dietary supplements for prevention and treatment of cardiovascular disease suggests no significant effect on cardiovascular outcomes or all-cause mortality, although some B vitamins appear to reduce stroke incidence, and B3 appears to increase all-cause mortality.

SOURCE: Jenkins DJA, Spence JD, Giovannucci EL, et al. Supplemental vitamins and minerals for cardiovascular disease prevention and treatment: JACC focus seminar. *J Am Coll Cardiol* 2021;77:423-436.

The use of dietary supplements, such as vitamins B, C, and D and calcium, is on the rise throughout North America, Europe, and other countries.[1-3] However, there is a lack of consensus on the use of these supplements for the prevention and treatment of cardiovascular disease (CVD), although various health authorities and advisories recommend consumption of a well-balanced, plant-based diet to meet daily

requirements for these nutrients.[4,5] To analyze the role of dietary supplements in the prevention and treatment of CVD, Jenkins et al conducted a meta-analysis of recent systematic reviews and randomized, controlled trials (RCTs) in an update to their previous 2018 systematic review and meta-analysis on the same topic.[6]

For this updated meta-analysis, the authors included the systematic reviews and RCTs identified in their 2018 review along with recent studies published up to May 2020. The literature search was conducted according to protocols recommended in the Cochrane Handbook for systematic reviews and meta-analyses. Only meta-analyses and single RCTs were included if they focused on those individual vitamin and mineral supplements previously reported by the authors as commonly used and those supplements that had a significant finding for CVD outcomes or total mortality. Out of 2,999 papers identified in the literature search, 156 total and 35 new RCTs met the inclusion criteria and were added for this updated meta-analysis.

Data analysis was conducted using Review Manager 5.3, a software application for meta-analyses created by Cochrane Collaboration. The heterogeneity of the studies was assessed and reported as an I^2 statistic, with an I^2 value > 50% indicating substantial heterogeneity. Publication bias was analyzed on meta-analyses > 10 trials, using STATA software. $P < 0.05$ was considered evidence of a small study effect. The number needed to treat (NNT) and number needed to harm were calculated using the inverse of the respective absolute risk reduction (ARR) values: NNT = 1/ARR, number needed to harm = 1/ARR. Risk bias was addressed for randomization, blinding and allocation concealment, thoroughness of follow-up, and intention-to-treat using the Cochrane Risk of Bias tool. The Grading of Recommendations Assessment, Development, and Evaluation tool was used to assess and categorize the quality and strength of evidence as high, moderate, low, and very low. All RCTs were graded as high-quality evidence, and other studies were downgraded based on identification of limitations using the aforementioned risk of bias tool, high interstudy heterogeneity, imprecision reflected in reported 95% confidence intervals, and publication bias represented by significantly small study effects.

Supplements assessed included vitamin D, vitamin C, calcium, multivitamin formulations, B-complex formulations (at least two of the following: B6, folate, and B12), and antioxidant mixtures (at least two of the following: vitamin A, C, E, and beta-carotene). Vitamin D, vitamin C, calcium, and multivitamins did not significantly affect cardiovascular outcomes or all-cause mortality. Vitamin B-complex and folic acid significantly affected stroke reduction. Niacin increased the all-cause mortality rate. Antioxidant mixtures did not affect CVD outcomes or all-cause mortality.

■ COMMENTARY

This well-designed meta-analysis has some significant strengths, including the use of Cochrane Collaboration Handbook protocols and tools for their systematic review and statistical analyses, and the thoroughness of the literature review. A weakness of this systematic review is that it included no cohort studies, which, because of their longer study duration, may be better for identifying chronic disease risk factors. In this analysis, the authors did not find any beneficial effects of micronutrient supplementation on CVD prevention or mortality. Of supplements most used by patients, multivitamins, vitamin C, vitamin D, calcium, and antioxidants do not show any consistent benefit for the prevention of CVD, including myocardial infarction and stroke, nor a reduction in all-cause mortality. Thus, in general, there is no evidence to support patient use of these supplements for these purposes, and clinicians should refrain from recommending them. The authors cited a potential exception, considering some research evidence suggesting patients on statins may tolerate statins better when they are vitamin D-replete.

Vitamin B-complex and folic acid are shown to be associated with a reduction in stroke incidence, but niacin is associated with increased all-cause mortality. It is reasonable for clinicians to consider recommending daily supplementation with B-complex and folate for patients with increased risk of stroke based on these study results, although caution should be exercised with niacin supplementation. A plant-based diet rich in B vitamins and folic acid currently is supported by United States Preventive Services Task Force recommendations and may be appropriate for patients who do not wish to take supplements. ■

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ABSTRACT & COMMENTARY

Functional Cognitive Disorder: An Important Condition to Recognize

By Lisa Ravdin, PhD

Associate Professor of Neuropsychology in Neurology, Weill Cornell Medicine, New York

SYNOPSIS: Functional cognitive disorder (FCD) can describe cognitive difficulties that are present where there is no biologic cause, but a lack of consensus in diagnostic criteria limits its use in clinical practice and research. The authors proposed an operational definition for FCD as the cognitive phenotype of functional neurological disorder.

SOURCES: Ball HA, McWhirter L, Ballard C, et al. Functional cognitive disorder: Dementia's blind spot. *Brain* 2020;143:2895-2903.

Kapur N, Kemp S, Baker G. Functional cognitive disorder: Dementia's blind spot. *Brain* 2021;144:e37.

Subjective cognitive complaints that present without an identifiable cause or objective evidence of impairment are observed commonly and may present at greater rates in older adults. The term functional cognitive disorder (FCD) has been used to describe unexplainable persistent cognitive complaints and can be seen as a cognitive variant of the broader term, functional neurological disorder (FND).

The authors conveyed that internal inconsistency is at the core of the diagnosis of FCD, which is present when the patient's subjective sense of cognitive dysfunction is discrepant with intact objective test scores, presentation, and independence in activities of daily living, as well as a collateral's report reflecting reduced concern compared to that reported by the affected person. In FCD, there is variability in performance within a particular cognitive domain where an individual shows "the ability to perform a task well at certain times, but with significantly impaired ability at other times, particularly when the task is the focus of attention."

This is not simply normal variability where performance fluctuates over time as in cognitive disorders that have waxing and waning symptoms. Internal inconsistency needs to be seen within a particular cognitive domain. This also is discrepant from individuals who intentionally perform poorly and fail effort testing (i.e., malingerers).

FCD is common in clinical practice but is rarely diagnosed as such. Patients with subjective cognitive complaints with no identifiable neurologic disorder often are diagnosed with mild cognitive impairment (MCI) or subjective cognitive decline. The authors contended FCD terminology also could be useful to de-emphasize the expectation that these subjective cognitive complaints necessarily progress to dementia. Importantly, definitions of FCD lack consensus, and the unclear trajectory of these symptoms, as well as the likelihood of comorbidity with underlying neurodegenerative processes, precludes its common use and understanding in clinical and research settings. The authors proposed an operational definition for FCD as the cognitive phenotype of FND.

In a letter to the editor, Kapur et al indicated some of the main points raised in the formulation of the FCD definition proposed by Ball et al are potential sources of confusion. Specifically, differentiating between internal and external inconsistency and its applicability to the diagnosis is questioned.

These authors noted using this definition does not account for naturally occurring neurologic presentations that have features of inconsistency. It is suggested that this definition of FCD has an overreliance on internal inconsistency. Further, these authors recognized the neuropsychological evaluation examines patterns on cognitive testing, and these exams do, in fact, include consideration of non-organic factors in the interpretation of neurocognitive data, including fluctuating attention, alertness, effort, and environmental factors, both within and between cognitive domains.

■ COMMENTARY

It is not uncommon for individuals to present with cognitive complaints, even when there is no biologic evidence that meets the threshold of a diagnosable disorder. This often is labeled as MCI. When used in this manner, MCI is a term that does not convey diagnostic specificity, essentially creating a blind spot in discriminating subjective vs. objective cognitive compromise. The neuropsychological evaluation can help identify patient-specific factors that contribute to cognitive complaints as well as interpret patterns of performance that can be useful in examining subjective vs. objective cognitive concerns. Patients with cognitive complaints may benefit from evidence-based interventions that target factors that create or amplify the experience of cognitive dysfunction, such as depression, anxiety, sleep problems, substance use, stress, and chronic pain. ■

PHARMACOLOGY UPDATE

COVID-19 Vaccine mRNA Injection (Comirnaty)

By William Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Assistant Clinical Professor of Medicine, University of California, San Francisco.
Dr. Chan is Associate Clinical Professor, School of Pharmacy, University of California, San Francisco.

The FDA has granted full approval for the Pfizer-BioNTech COVID-19 vaccine, a messenger RNA (mRNA) platform, for use in individuals ≥ age 16 years. It has been available under an emergency use authorization (EUA) since Dec. 11, 2020. The EUA will remain for individuals ages 12 to 15 years and as a third dose in certain immunocompromised patients.[1] The agency granted a priority review and fast-track breakthrough designation. The vaccine will be marketed as Comirnaty.

INDICATIONS

Comirnaty can be administered to individuals ≥ age 16 years to prevent COVID-19.[2]

DOSAGE

The recommended dose is two intramuscular doses (0.3 mL each) administered three weeks apart.[2] This solution is available as 0.3 mL single-dose vials.

POTENTIAL ADVANTAGES

Comirnaty is the first COVID-19 vaccine to receive full FDA approval.

POTENTIAL DISADVANTAGES

The commonly reported adverse reactions (reactogenicity) were pain at injection site (88.6%), fatigue (70.1%), headache (64.9%), muscle pain (45.5%), chills (41.5%), joint pain (27.5%), and fever (17.8%).[2] Systemic adverse events (e.g., fever, fatigue, muscle/joint pain) appeared more common with the second dose.[2] There is a higher rate of myocarditis and pericarditis, particularly in men younger than age 40 years, with the highest risk in men age 12-17 years (estimated 65-200 cases/million doses administered).[3] Most recover without sequelae. The vaccine requires specific storage conditions, preferably in an ultra-low temperature freezer between -90°C to -60°C, although limited excursion outside this range may be permitted.[2] The vaccine may be less effective against the B.1.617.2 (delta) variant.

COMMENTS

Comirnaty elicits an immune response to the spike glycoprotein of SARS-CoV-2. Efficacy data were based mainly on participants age 16 years and older who were enrolled from July 27, 2020, follow-up through March 13, 2021, representing up to six months of follow-up after dose 2. Viral variants during the study were mainly B.1.1.7 (alpha) and B1.351 (beta). There were approximately 20,000 subjects in each of the vaccine and placebo groups. Vaccine efficacy (VE) was based on first laboratory-confirmed COVID-19 occurrence from seven days after dose 2 in participants without evidence of prior infection. VE rate (%) was 91.1 (95% CI, 88.8-93.1). This was consistent for ages 16 through 64 years and age ≥ 65 years. VE (%) against first severe disease was 95.3 (95% CI, 70.9-99.9).

The delta variant has become the prevalent strain worldwide, and the effectiveness of the current vaccines against this more transmissible variant is unclear, since VE was established during alpha variant dominance. Several observational studies have been conducted. The authors of a U.K. case-controlled study estimated the effectiveness of Comirnaty against the delta and alpha variants.[4] A two-dose regimen of Comirnaty showed an adjusted vaccine effectiveness of 88% (95% CI, 85-90.1). The CDC conducted an analysis of a cohort study of healthcare personnel, first responders, and other essential and frontline workers in eight U.S. locations to assess vaccine effectiveness during the alpha predominate vs. delta predominate periods.[5] Among 4,217 participants, 65% received Comirnaty and 33% received the Moderna vaccine (mztns-1273). The CDC estimated the adjusted VE to be 66% during the delta predominate period vs. 91% in the alpha predominate period.

The authors of a preprint Mayo Clinic observational study reported the effectiveness of Comirnaty dropped to 42% while mRNA-1273 dropped to 76% during the month where the delta variant became dominant in Minnesota.[6] However, both effectively prevented hospitalization, ICU admission, and death. The most recently reported data to the Advisory Committee on Immunization Practices (ACIP) indicate vaccine effectiveness against hospitalization ranging from 75% to 95%.[7] Effectiveness in those ages > 75 years has dropped slightly, but remains > 80%.

CLINICAL IMPLICATIONS

Comirnaty is the first COVID-19 vaccine to be approved by the FDA. This step is important because

many vaccine-hesitant individuals cited the lack of approval as a reason they were delaying vaccination. Moderna also has applied for full FDA approval for their mRNA vaccine, with approval anticipated before the end of the year. ACIP has issued interim recommendation for use of Comirnaty in individuals age 12-15 years and older than age 16 years.[8] ACIP also has issued an interim recommendation for a third dose for moderately to severely immunocompromised patients. The recommendation for a booster shot for all vaccinated individuals is pending ACIP review.[9] As of Sept. 10, 2021, more than 96 million people in the United States have been fully vaccinated with Comirnaty.[10] ■

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CME QUESTIONS

1. Which statement below describes the results from the SURPASS-2 trial?
a. Tirzepatide was equal to semaglutide in the ability to lower A1c levels.
b. Tirzepatide lowered A1c better than semaglutide, but did not cause weight loss.
c. Tirzepatide caused weight loss, but was inferior to semaglutide at lowering A1c.
d. Tirzepatide lowered A1c better than semaglutide and caused significant weight loss.

2. What is a benefit of eating fermented foods?
a. Lower risk for heart disease
b. Better cholesterol levels
c. Reduced inflammatory markers
d. Fewer episodes of diarrhea

3. According to the meta-analysis by Jenkins et al, which supplement reduced stroke incidence?
a. Vitamin C
b. Multivitamins
c. B-complex
d. Vitamin D

4. The experience of subjective cognitive complaints indicates the presence of an underlying neurologically based disorder.
a. True
b. False

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages, and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.