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A SELECTION OF TEN READINGS ON TOPICS RELATED TO "BASIC OBESITY MANAGEMENT ACCREDITATION (BOMA) COURSE 2"

Some are available as free full text, and in some payment is required

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – CONTINUOUS WEIGHT LOSS TREATMENT MODEL ACROSS LIFESPAN

Bray GA,[1] Ryan DH.[1] Evidence-based weight loss interventions: Individualized treatment options to maximize patient outcomes. Diabetes Obes Metab. 2021 Feb;23 Suppl 1:50-62. PMID: 32969147.

URL: doi: 10.1111/dom.14200PMID: 32969147 (Payment required)

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ABSTRACT
Against the backdrop of obesity as a major public health problem, we examined three questions: How much weight loss is needed to benefit patients with obesity? How well do current therapies do in producing weight loss? What strategies can be used to improve patient outcomes using evidence-based studies? This paper reviews literature on the outcomes of lifestyle, diet, medications, and surgical treatments for obesity using literature searches for obesity treatments. Current treatments, including lifestyle, diet, and exercise, produce a weight loss of 5 to 7 percent on average. Despite continued attempts to identify superior dietary approaches, most careful comparisons find that low carbohydrate diets are not significantly better than low-fat diets for weight loss. The four medications currently approved by the US Food and Drug Administration for long-term management of obesity are not as effective as surgery, adding about 5 percent on average to lifestyle approaches to weight loss. Two new medications that are under investigation, semaglutide and tirzepatide, significantly improve on this. For all treatments for weight loss, including lifestyle, medications, and surgery, there is enormous variation in the amount of weight lost. Examination of this literature has yielded evidence supporting baseline and process predictors, but the effect sizes associated with these predictors are small and there are no prospective studies showing that a personalised approach based on genotype or phenotype will yield uniform success. Because obesity is a chronic disease, it requires a "continuous treatment model" across the lifespan.

READING 2 – LONG-TERM WEIGHT LOSS STRATEGIES

Kheniser K,[1] Saxon DR,[2] Kashyap SR.[3] Long-Term Weight Loss Strategies for Obesity. J Clin Endocrinol Metab. 2021 Jun 16;106(7):1854-1866. PMID: 33595666.

URL: doi: 10.1210/clinem/dgab091. PMID: 33595666 (Free full text)

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ABSTRACT
CONTEXT: Obesity is a chronic disease that is difficult to manage without holistic therapy. The therapeutic armamentarium for obesity primarily consists of four forms of therapy: lifestyle modification (i.e., diet and exercise), cognitive behavioural therapy, pharmacotherapy, and bariatric surgery.

EVIDENCE ACQUISITION: Evidence was consolidated from randomised controlled trials, observational studies, and meta-analyses.

EVIDENCE SYNTHESIS: After two years, lifestyle interventions can facilitate weight loss that equates to ~5 percent. Even though lifestyle interventions are plagued by weight regain, they can have substantial effects on type 2 diabetes and cardiovascular disease risk. Although 10-year percentage excess weight loss can surpass 50 percent after bariatric surgery, weight regain is likely. To mitigate weight regain, instituting a multifactorial maintenance programme is imperative. Such a programme can integrate diet, exercise, and pharmacotherapy. Moreover, behavioural therapy can complement a maintenance programme well.

CONCLUSIONS: Obesity is best managed by a multidisciplinary clinical team that integrates diet, exercise, and pharmacotherapy. Bariatric surgery is needed to manage type 2 diabetes and obesity in select patients.

READING 3 – LOW CARBOHYDRATE DIET HAS LONG-TERM LIMITATIONS

Barber TM,[1,2,3] Hanson P,[1,2,3] Kabisch S,[4] Pfeiffer AFH,[4,5] Weickert MO.[1,2,6] The Low-Carbohydrate Diet: Short-Term Metabolic Efficacy Versus Longer-Term Limitations. Nutrients. 2021 Apr 3;13(4):1187. PMID: 33916669.

URL: doi: 10.3390/nu13041187. PMID: 33916669 (Free full text)

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ABSTRACT

BACKGROUND: Diets have been a central component of lifestyle modification for decades. The Low-Carbohydrate Diet (LCD), originally conceived as a treatment strategy for intractable epilepsy (due to its association with ketogenesis), became popular in the 1970s and has since risen to prominence as a weight loss strategy.

OBJECTIVE: To explore the efficacy, limitations, and potential safety concerns of the LCD.

DATA SOURCES: We performed a narrative review, based on relevant articles written in English from a PubMed search, using the terms "low carbohydrate diet" and "metabolic health".

RESULTS: Evidence supports the efficacy of the LCD in the short term (up to six months) for reduction in fat mass and remission of Type 2 Diabetes Mellitus (T2D). However, the longer-term efficacy of the LCD is disappointing, with diminishment of weight loss potential and metabolic benefits of the LCD beyond six months of its adoption. Furthermore, practical limitations of the LCD include the associated restriction of food choices that restrict the acceptability of the LCD for the individual, particularly over the longer term. There are also safety concerns of the LCD that stem from nutritional imbalances (with a relative excess of dietary fat and protein intake with associated dyslipidaemia and increased risk of insulin resistance and T2D development) and ketotic effects. Finally, the LCD often results in a reduction in dietary fibre intake, with potentially serious adverse consequences for overall health and the gut microbiota.

CONCLUSIONS: Although widely adopted, the LCD usually has short-lived metabolic benefits, with limited efficacy and practicality over the longer term. Dietary modification must be tailored to the individual, with careful *a priori* assessments of food preferences to ensure acceptability and adherence over the longer term, avoidance of dietary imbalances and optimisation of dietary fibre intake (primarily from plant-based fruit and vegetables), and *a posteriori* assessments of the highly individual responses to the LCD. Finally, we need to change our view of diets from simply an excipient for weight loss to an essential component of a healthy lifestyle.

READING 4 – AGEING, OBESITY, AND SARCOPENIA

Colleluori G,[1] Villareal DT.[2] Aging, obesity, sarcopenia and the effect of diet and exercise intervention. Exp Gerontol. 2021 Nov;155:111561. PMID: 34562568.

URL: doi: 10.1016/j.exger.2021.111561 PMID: 34562568 (Payment required)

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ABSTRACT
The number of adults aged 65 years and older is increasing worldwide and will represent 20 percent of the population by 2030. Half of them will suffer from obesity. The decline in muscle mass and strength, known as sarcopenia, is very common among older adults with obesity (sarcopenic obesity). Sarcopenic obesity is strongly associated with frailty, cardiometabolic dysfunction, physical disability, and mortality. Increasing efforts have been made to identify effective strategies able to promote healthy ageing and curb the obesity pandemic. Among these, lifestyle interventions consisting of diet and exercise protocols have been extensively explored. Importantly, diet-induced weight loss is associated with fat, muscle, and bone mass losses, and may further exacerbate age-related sarcopenia and frailty outcomes in older adults. Successful approaches to induce fat mass loss while preserving lean and bone mass are critical in reducing ageing- and obesity-related physical and metabolic complications while at the same time ameliorating frailty. In this review article, we discuss the most recent evidence on the age-related alterations in adipose tissue and muscle health and on the effect of calorie restriction and exercise approaches for older adults with obesity and sarcopenia, emphasising the existing gaps in the literature that need further investigation.

READING 5 – TIME-RESTRICTED EATING

Queiroz JDN,[1] Reischak-Oliveira A,[1] Macedo RCO,[1,2] Tinsley GM.[3] Time-restricted eating and circadian rhythms: the biological clock is ticking. Crit Rev Food Sci Nutr. 2021;61(17):2863-2875.

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ABSTRACT
Meal timing may be a critical modulator of health outcomes due to complex interactions between circadian biology, nutrition, and human metabolism. As such, approaches that aim to align food consumption with endogenous circadian rhythms are emerging in recent years. Time-restricted eating (TRE) consists of limiting daily nutrient consumption to a period of 4-12 hours in order to extend the time spent in the fasted state. TRE can induce positive effects on the health of individuals with overweight and obesity, including sustained weight loss, improvement in sleep patterns, reduction in blood pressure and oxidative stress markers, and increased insulin sensitivity. However, it is not fully clear whether positive effects of TRE are due to reduced energy intake, body weight or the truncation of the daily eating window. In addition, null effects of TRE in some populations and on some parameters of cardiometabolic health have been documented. Some evidence indicates that greater promotion of health via TRE may be achieved if the nutrient intake period occurs earlier in the day. Despite some promise of this dietary strategy, the effects of performing TRE at different times of the day on human cardiometabolic health, as well as the safety and efficacy of this dietary approach in individuals with cardiometabolic impairments, need to be evaluated in additional controlled and long-term studies.

READING 6 – CANCER SURVIVORSHIP, EXCESS BODY FATNESS, AND WEIGHT-LOSS INTERVENTION

Anderson AS,[1] Martin RM,[2,3,4] Renehan AG,[5] Cade J,[6] Copson ER,[7] Cross AJ,[8] Riboli E,[8] Grimmett C,[9] Keaver L,[10] King A,[11] Shaw C,[12] Saxton JM[13]; UK NIHR Cancer and Nutrition Collaboration (Population Health Stream). Cancer survivorship, excess body fatness and weight-loss intervention-where are we in 2020? Br J Cancer. 2021 Mar;124(6):1057-1065.

URL: doi: 10.1038/s41416-020-01155-2. PMID:33235316 (Free full text)

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ABSTRACT

Earlier diagnosis and more effective treatments mean that the estimated number of cancer survivors in the United Kingdom is expected to reach 4 million by 2030. However, there is an increasing realisation that excess body fatness (EBF) is likely to influence the quality of cancer survivorship and disease-free survival. For decades, the discussion of weight management in patients with cancer has been dominated by concerns about unintentional weight loss, low body weight, and interventions to increase weight, often re-enforced by the existence of the obesity paradox, which indicates that high body weight is associated with survival benefits for some types of cancer. However, observational evidence provides strong grounds for testing the hypothesis that interventions for promoting intentional loss of body fat and maintaining skeletal muscle in overweight and obese cancer survivors would bring important health benefits in terms of survival outcomes and long-term impact on treatment-related side effects. In this paper, we outline the need for studies to improve our understanding of the health benefits of weight-loss interventions, such as hypocaloric healthy-eating plans combined with physical activity. In particular, complex intervention trials that are pragmatically designed are urgently needed to develop effective, clinically practical evidence-based strategies for reducing EBF and optimising body composition in people living with and beyond common cancers.

READING 7 – PHARMACOTHERAPY FOR ADULTS WITH OVERWEIGHT AND OBESITY

Shi Q,[1] Wang Y,[1] Li J,[1] Xu S,[1] Shen Y,[1] Li L,[1] Yu J,[1] Nong K,[1] Zou X,[1] Zhang X,[1] Qu F,[1] Tian H,[1] Hao Q,[2] Vandvik PO,[3] Guyatt G,[4] Chen Z,[5] Ge L,[6] Sun F,[7] Zhu S,[8] Wang C,[9] Zhang S,[10] Qiao Z,[11] Li Y,[11] Chen K,[11] Jian Z,[12] Wu Y,[13] He Y,[14] Li S.[15] Pharmacotherapy for adults with overweight and obesity: a systematic review and network meta-analysis of randomised controlled trials. Lancet. 2022 Jan 15;399(10321):259-269.

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ABSTRACT

BACKGROUND: Pharmacotherapy provides an option for adults with overweight and obesity to reduce their bodyweight if lifestyle modifications fail. We summarised the latest evidence for the benefits and harms of weight-lowering drugs.

METHODS: This systematic review and network meta-analysis included searches of PubMed, Embase, and Cochrane Library (CENTRAL) from inception to 23 March 2021, for randomised controlled trials of weight-lowering drugs in adults with overweight and obesity. We performed frequentist random-effect network meta-analyses to summarise the evidence and applied the Grading of Recommendations Assessment, Development, and Evaluation frameworks to rate the certainty of evidence, calculate the absolute effects, categorise interventions, and present the findings. The study was registered with PROSPERO, CRD 42021245678.

FINDINGS: 14,605 citations were identified by our search, of which 49,810 participants were enrolled in 143 eligible trials. Except for levocarnitine, all drugs lowered body weight compared with lifestyle modification alone; all subsequent numbers refer to comparisons with lifestyle modification. High to moderate certainty evidence established phentermine-topiramate as the most effective in lowering weight (odds ratio [OR] of ≥5 percent weight reduction 8.02, 95 percent CI 5.24-12.27; mean difference [MD] of percentage body weight change -7.97, 95 percent CI -9-28 to -6.66) followed by GLP-1 receptor agonists (OR 6.33, 95 percent CI 5.00-8.00; MD -5.76, 95 percent CI -6.30 to -5.21). Naltrexone-bupropion (OR 2.69, 95 percent CI 2.11-3.43), phentermine-topiramate (2.40, 1.69-3.42), GLP-1 receptor agonists (2.17, 1.71-2.77), and orlistat (1.72, 1.44-2.05) were associated with increased adverse events leading to drug discontinuation. In a post-hoc analysis, semaglutide, a GLP-1 receptor agonist, showed substantially larger benefits than other drugs with a similar risk of adverse events as other drugs for both likelihood of weight loss of 5 percent or more (OR 9.82, 95 percent CI 7.09-13.61) and percentage body weight change (MD -11.41, 95 percent CI -12.54 to -10.27).

INTERPRETATION: In adults with overweight and obesity, phentermine-topiramate and GLP-1 receptor agonists proved the best drugs in reducing weight; of the GLP-1 agonists, semaglutide might be the most effective.

READING 8 – ANTI-OBESITY DRUGS: LONG-TERM EFFICACY AND SAFETY

Tak YJ,[1,2] Lee SY.[3,4] Anti-Obesity Drugs: Long-Term Efficacy and Safety: An Updated Review. World J Mens Health. 2021 Apr;39(2):208-221. PMID: 32202085.

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ABSTRACT
As a chronic and relapsing disease, obesity negatively impacts the health of men to a greater extent than that of women, with a higher risk of cardiovascular disease. Since lifestyle modifications alone are often challenging and limited for the maintenance of weight reduction, pharmacotherapy should be considered in a timely manner for obese men or overweight patients with weight-related comorbidities. Recent advances in anti-obesity drugs have enabled the potential of achieving clinically significant weight loss. Increasing evidence has shown that behaviour-based interventions with one of these medications can result in greater weight loss than that elicited by usual care conditions. Data from most recent meta-analyses showed that the overall placebo-subtracted weight reduction (percent) with the use of anti-obesity drugs for at least 12 months ranges from 2.9 percent to 6.8 percent; phentermine/topiramate (-6.8 percent), liraglutide (-5.4 percent), naltrexone/bupropion (-4.0 percent), lorcaserin (-3.1 percent), and orlistat (-2.9 percent). However, they have a high cost and may cause adverse outcomes depending on the individual. Very recently, on 13 February 2020, the US Food and Drug Administration requested withdrawal of lorcaserin from the market as a safety clinical trial showed an increased occurrence of cancer. Therefore, the decision to initiate drug therapy in obese individuals should be made after the benefits and risks are considered. Thereafter, treatment should be tailored to specific patient subpopulations depending on their chronic conditions, comorbidities, and preferences. Herein, we provide an overview of the latest developments in weight loss medications, which may serve as one of the strategies for long-term obesity control.

READING 9 – LONG-TERM EFFECTS OF WEIGHT-REDUCING DRUGS IN PEOPLE WITH HYPERTENSION

Krenn C,[1] Semlitsch T,[1] Winterholer S,[1] Siebenhofer A,[1,2] Jeitler K,[1,3] Horvath K,[1,4] Berghold A.[3] Long-term effects of weight-reducing drugs in people with hypertension.

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ABSTRACT
BACKGROUND: This is the third update of this review, first published in July 2009. All major guidelines on treatment of hypertension recommend weight loss; anti-obesity drugs may be able to help in this respect.

OBJECTIVES: Primary objectives: To assess the long-term effects of pharmacologically-induced reduction in body weight in adults with essential hypertension on all-cause mortality, cardiovascular morbidity, and adverse events (including total serious adverse events, withdrawal due to adverse events, and total non-serious adverse events). Secondary objectives: To assess the long-term effects of pharmacologically-induced reduction in body weight in adults with essential hypertension on change from baseline in systolic and diastolic blood pressure, and on body weight reduction.

SEARCH METHODS: For this updated review, the Cochrane Hypertension Information Specialist searched the following databases for randomised controlled trials up to March 2020: the Cochrane Hypertension Specialised Register, CENTRAL, MEDLINE (from 1946), Embase (from 1974), the World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov. The searches had no language restrictions. We contacted authors of relevant papers about further published and unpublished work.

SELECTION CRITERIA: Randomised controlled trials of at least 24 weeks' duration in adults with hypertension that compared approved long-term weight-loss medications to placebo.

DATA COLLECTION AND ANALYSIS: Two review authors independently selected studies, assessed risks of bias, and extracted data. Where appropriate and in the absence of significant heterogeneity between studies (P > 0.1), we pooled studies using a fixed-effect meta-analysis. When heterogeneity was present, we used the random-effects method and investigated the cause of the heterogeneity.

MAIN RESULTS: This third update of the review added one new trial, investigating the combination of naltrexone/bupropion versus placebo. Two medications, which were included in the previous versions of this review (rimonabant and sibutramine), are no longer considered relevant for this update, since their marketing approval was withdrawn in 2010 and 2009, respectively. The number of included studies in this review update is therefore six (12,724 participants in total): four RCTs comparing orlistat to placebo, involving a total of 3,132 participants with high blood pressure and a mean age of 46 to 55 years; one trial comparing phentermine/topiramate to placebo, involving 1,305 participants with high blood pressure and a mean age of 53 years; and one trial comparing naltrexone/bupropion to placebo, involving 8,283 participants with hypertension and a mean age of 62 years. We judged the risks of bias to be unclear for the trials investigating orlistat or naltrexone/bupropion and low for the trial investigating phentermine/topiramate. Only the study of naltrexone/bupropion included cardiovascular mortality and morbidity as predefined outcomes. There were no differences in the rates of all-cause or cardiovascular mortality, major cardiovascular events, or serious adverse events between naltrexone/bupropion and placebo. The incidence of overall adverse events was significantly higher in participants treated with naltrexone/bupropion. For orlistat, the incidence of gastrointestinal side effects was consistently higher compared to placebo. The most frequent side effects with phentermine/topiramate were dry mouth and paraesthesia. After six to 12 months, orlistat reduced systolic blood pressure compared to placebo by mean difference (MD) -2.6 mmHg (95 percent confidence interval (CI) -3.8 to -1.4 mmHg; 4 trials, 2,058 participants) and diastolic blood pressure by MD -2.0 mmHg (95 percent CI -2.7 to -1.2 mmHg; 4 trials, 2,058 participants). After 13 months of follow-up, phentermine/topiramate decreased systolic blood pressure compared to placebo by -2.0 to -4.2 mmHg (1 trial, 1,030 participants) (depending on drug dosage), and diastolic blood pressure by -1.3 to -1.9 mmHg (1 trial, 1,030 participants) (depending on drug dosage). There was no difference in the change in systolic or diastolic blood pressure between naltrexone/bupropion and placebo (1 trial, 8,283 participants). We identified no relevant studies investigating liraglutide or lorcaserin in people with hypertension.

AUTHORS' CONCLUSIONS: In people with elevated blood pressure, orlistat, phentermine/topiramate, and naltrexone/bupropion reduced body weight; the magnitude of the effect was greatest with phentermine/topiramate. In the same trials, orlistat and phentermine/topiramate, but not naltrexone/bupropion, reduced blood pressure. One RCT of naltrexone/bupropion versus placebo showed no differences in all-cause mortality or cardiovascular mortality or morbidity after two years. The European Medicines Agency refused marketing authorisation for phentermine/topiramate due to safety concerns, while for lorcaserin the application for European marketing authorisation was withdrawn due to a negative overall benefit/risk balance. In 2020, lorcaserin was also withdrawn from the US market. Two other medications (rimonabant and sibutramine) had already been withdrawn from the market in 2009 and 2010, respectively.

READING 10 – SEMAGLUTIDE IN ADULTS WITH OVERWEIGHT OR OBESITY, WITH AND WITHOUT T2DM IN EAST ASIA POPULATIONS (SOUTH KOREA & JAPAN)

Kadowaki T,[1] Isendahl J,[2] Khalid U,[2] Lee SY,[3] Nishida T,[4] Ogawa W,[5] Tobe K,[6] Yamauchi T,[7] Lim S[8]; STEP 6 investigators. Semaglutide once a week in adults with overweight or obesity, with or without type 2 diabetes in an east Asian population (STEP 6): a randomised, double-blind, double-dummy, placebo-controlled, phase 3a trial. Lancet Diabetes Endocrinol. 2022 Mar;10(3):193-206. PMID: 35131037.

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ABSTRACT

BACKGROUND: Semaglutide 2.4 mg once weekly has been investigated for weight management in global populations. Differences exist between Asian and non-Asian populations in terms of body composition and definitions of obesity. In the Semaglutide Treatment Effect in People with obesity (STEP) 6 trial, we assessed the effect of semaglutide versus placebo for weight management in adults from east Asia with obesity, with or without type 2 diabetes.

METHODS: This randomised, double-blind, double-dummy, placebo-controlled, phase 3a superiority trial was done at 28 outpatient clinics in Japan and South Korea. Eligible participants were adults (aged ≥18 years in South Korea; ≥20 years in Japan) with a BMI of at least 27.0 kg/m^2 with two or more weight-related comorbidities or a BMI of 35.0 kg/m^2 or more with one or more weight-related comorbidity (one comorbidity had to be either hypertension, dyslipidaemia, or, in Japan only, type 2 diabetes) who had at least one self-reported unsuccessful dietary attempt to lose body weight. Participants were randomly assigned (4:1:2:1) to once-weekly subcutaneous semaglutide 2.4 mg or matching placebo, or semaglutide 1.7 mg or matching placebo, plus lifestyle recommendations for 68 weeks. Data for the placebo groups were pooled in statistical analyses. The primary endpoints were percentage change in body weight from baseline at week 68 and the proportion of participants who had achieved a reduction of at least 5 percent of baseline body weight at week 68. Change in abdominal visceral fat area was assessed as a supportive secondary endpoint using computed tomography scanning in a subset of participants. Efficacy outcomes were assessed in the full analysis set, which included all randomly assigned participants according to the intention-to-treat principle. Safety was assessed in all participants who received at least one dose of the study drug. This trial was registered with ClinicalTrials.gov, NCT03811574.

FINDINGS: Between 21 Jan 2019 and 4 June 2019, 437 participants were screened, of whom 401 were randomly assigned to semaglutide 2.4 mg (n=199), semaglutide 1.7 mg (n=101), or placebo (n=101), and included in the intention-to-treat analysis. Estimated mean change in bodyweight from baseline to week 68 was -13.2 percent (SEM 0.5) in the semaglutide 2.4 mg group and -9.6 percent (0.8) in the semaglutide 1.7 mg group versus -2.1 percent (0.8) in the placebo group (estimated treatment difference [ETD] -11.1 percentage points [95 percent CI -12.9 to -9.2] for semaglutide 2.4 mg vs placebo; -7.5 percentage points [95 percent CI -9.6 to -5.4] for semaglutide 1.7 mg vs placebo; both p<0.0001). At week 68, a larger proportion of participants had achieved a 5 percent or higher reduction in baseline body weight in the semaglutide 2.4 mg group (160 [83 percent] of 193 participants) and semaglutide 1.7 mg group (71 [72 percent] of 98 participants) than in the placebo group (21 [21 percent] of 100 participants); odds ratio [OR] 21.7 [95 percent CI 11.3 to 41.9] for semaglutide 2.4 mg vs placebo; OR 11.1 [95 percent CI 5.5 to 22.2] for semaglutide 1.7 mg vs placebo; both p<0.0001). Abdominal visceral fat area was reduced by 40.0 percent (SEM 2.6) among participants in the semaglutide 2.4 mg group and 22.2 percent (3.7) among participants in the semaglutide 1·7 mg group vs 6.9 percent (3.8) in the placebo group (ETD -33.2 percent [95 percent CI -42.1 to -24.2] for semaglutide 2.4 mg vs placebo; -15.3 percent [95 percent CI -25.6 to -4.9] for semaglutide 1.7 mg vs placebo). 171 (86 percent) of 199 participants in the semaglutide 2.4 mg group, 82 (82 percent) of 100 participants in the semaglutide 1.7 mg group, and 80 (79 percent) of 101 participants in the placebo group reported adverse events. Gastrointestinal disorders, which were mostly mild to moderate, were reported

in 118 (59 percent) of 199 participants in the semaglutide 2.4 mg group, 64 (64 percent) of 100 participants in the semaglutide 1.7 mg group, and 30 (30 percent) of 101 participants in the placebo group. Adverse events leading to trial product discontinuation occurred in five (3 percent) of 199 participants in the semaglutide 2.4 mg group, three (3 percent) of 100 participants in the semaglutide 1.7 mg group, and one (1 percent) of 101 participants in the placebo group.

INTERPRETATION: Adults from east Asia with obesity, with or without type 2 diabetes, given semaglutide 2.4 mg once a week had superior and clinically meaningful reductions in body weight, and greater reductions in abdominal visceral fat area compared with placebo, representing a promising treatment option for weight management in this population.