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A SELECTION OF TEN READINGS ON TOPICS RELATED TO 2024 DISTANCE LEARNING COURSE 4 ON BASIC OBESITY MANAGEMENT ACCREDITATION

FPSC124 – SATURDAY, 02 NOV 2024 & SUNDAY 03 NOV 2024: 2.00pm-5.30pm
All are available as PMC free full text

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – EVENING IS THE BEST TIME TO EXERCISE

Sabag A,[1,2] Ahmadi MN,[1-3] Fontana Stamatakis E,[1-3] Postnova S,[1,5] Cistulli PA,[1,6] L,[1,7,8] Francois ME.[4] Timing of Moderate to Vigorous Physical Activity, Mortality, Cardiovascular Disease, and Microvascular Disease in Adults With Obesity. Diabetes Care. 2024 May 1;47(5):890-897. PMID: 38592034.

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ABSTRACT

OBJECTIVE: To assess the association between the timing of aerobic moderate to vigorous physical activity (MVPA) and risk of cardiovascular disease (CVD), microvascular disease (MVD), and all-cause mortality in adults with obesity and a subset with obesity and type 2 diabetes (T2D).

RESEARCH DESIGN AND METHODS: Participants included adults with obesity (BMI ≥30 kg/m^2) and a subset of those with T2D from the UK Biobank accelerometry substudy. Aerobic MVPA was defined as bouts of MVPA lasting ≥3 continuous minutes. Participants were categorised into morning, afternoon, or evening MVPA based on when they undertook the majority of their aerobic MVPA. The reference group included participants with an average of less than one aerobic MVPA bout per day. Analyses were adjusted for established and potential confounders.

RESULTS: The core sample included 29,836 adults with obesity, with a mean age of 62.2 (SD 7.7) years. Over a mean follow-up period of 7.9 (SD 0.8) years, 1,425 deaths, 3,980 CVD events, and 2,162 MVD events occurred. Compared with activity in the reference group, evening MVPA was associated with the lowest risk of mortality (hazard ratio [HR] 0.39; 95% CI 0.27, 0.55), whereas afternoon (HR 0.60; 95% CI 0.51, 0.71) and morning MVPA (HR 0.67; 95% CI 0.56, 0.79) demonstrated significant but weaker associations. Similar patterns were observed for CVD and MVD incidence, with evening MVPA associated with the lowest risk of CVD (HR 0.64; 95% CI 0.54, 0.75) and MVD (HR 0.76; 95% CI 0.63, 0.92). Findings were similar in the T2D subset (n=2,995).

CONCLUSIONS: Aerobic MVPA bouts undertaken in the evening were associated with the lowest risk of mortality, CVD, and MVD. Timing of physical activity may play a role in the future of obesity and T2D management.

READING 2 – IDENTIFYING THOSE REPRODUCTIVE-AGED WOMEN WHO COULD MOST BENEFIT FROM PRECONCEPTION CARE (PCC)

Withanage NN,[1] Botfield JR,[2] Mazza D,[2] Black K.[2,3] Preconception health risk factors documented in general practice electronic medical records. BMJ Sex Reprod Health. 2024 Jul 12;50(3):165-171. PMID: 38336467.

doi: 10.1136/bmjsrh-2023-202038. PMID: 38336467.

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ABSTRACT

BACKGROUND: Documenting medical and lifestyle preconception health risk factors in electronic medical records (EMRs) could assist general practitioners (GPs) in identifying those women of reproductive age who could most benefit from preconception care (PCC). However, it is unclear to what extent PCC risk factors are identifiable in general practice records. This study aimed to determine the extent to which medical and lifestyle preconception health risk factors are documented in general practice EMRs.

METHODS: We conducted an audit of the documentation of medical and lifestyle preconception risk factors in 10 general practice EMRs in Melbourne, Australia. We retrospectively analysed the EMRs of 100 consecutive women aged 18-44 years who visited each practice between January and September 2022. Using a template informed by PCC guidelines, we extracted data from structured fields in the EMR and conducted a descriptive analysis.

RESULTS: Among the data extracted, the more commonly documented medical and lifestyle preconception health risk factors in the EMRs included smoking (79 percent), blood pressure (74 percent), alcohol consumption (63 percent), and body mass index (57 percent). Among the women audited, 14 percent were smokers, 24 percent were obese, 7 percent had high blood pressure, 5 percent had diabetes, 28 percent had a mental health condition, 13 percent had asthma, 6 percent had thyroid disease, and 17 percent had been prescribed and could be using a potentially teratogenic medication.

CONCLUSIONS: Better documentation of medical and lifestyle preconception health risk factors in structured fields in EMRs might potentially assist primary care providers including GPs in identifying and providing PCC to women who could most benefit from it.

READING 3 – MANAGING THE EMERGENCE OF OBESITY IN T1DM

Kueh MTW,[1,2] Chew NWS,[3] Al-Ozairi E,[4,5] le Roux CW.[6] The emergence of obesity in type 1 diabetes. Int J Obes (Lond). 2024 Mar;48(3):289-301. PMID: 38092958.

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ABSTRACT
Obesity, a chronic low-grade inflammatory disease represented by multifactorial metabolic dysfunctions, is a significant global health threat for adults and children. The once-held belief that type 1 diabetes is a disease of people who are lean no longer holds. The mounting epidemiological data now establishes the connection between type 1 diabetes and the subsequent development of obesity, or vice versa. Beyond the consequences of the influx of an obesogenic environment, type 1 diabetes-specific biopsychosocial burden further exacerbates obesity.

In the course of obesity management discussions, recurring challenges surfaced. The interplay between weight gain and escalating insulin dependence creates a vicious cycle from which patients struggle to break free. In the absence of weight management guidelines and regulatory approval for this population, healthcare professionals must navigate the delicate balance between benefits and risks. The gravity of this circumstance highlights the importance of bringing these topics to the forefront.

In this Review, we discuss the changing trends and the biopsychosocial aspects of the intersection between type 1 diabetes and obesity. We highlight the evidence supporting the therapeutic means (i.e., exercise therapy, nutritional therapy, adjunct pharmacotherapy, and bariatric surgery) and directions for establishing a more robust and safer evidence-based approach, which influence the work reported in this paper.

READING 4 – YOUTH-ONSET TYPE 2 DIABETES – OVERVIEW OF PATHOPHYSIOLOGY, PROGNOSIS, PREVENTION AND MANAGEMENT

Titmuss A,[1,2] Korula S,[3,4] Wicklow B,[5,6] Nadeau KJ.[7,8] Youth-onset Type 2 Diabetes: An Overview of Pathophysiology, Prognosis, Prevention and Management. Curr Diab Rep. 2024 Aug;24(8):183-195. PMID: 38958831.

doi: 10.1007/s11892-024-01546-2. PMID: 38958831.

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ABSTRACT
PURPOSE OF REVIEW: This review explores the emerging evidence regarding pathogenesis, future trajectories, treatment options, and phenotypes of youth-onset type 2 diabetes (T2D).

RECENT FINDINGS: Youth-onset T2D is increasing in incidence and prevalence worldwide, disproportionately affecting First Nations communities, socioeconomically disadvantaged youth, and people of colour. Youth-onset T2D differs in pathogenesis to later-onset T2D and progresses more rapidly. It is associated with more complications, and these occur earlier. While there are limited licensed treatment options available, the available medications also appear to have a poorer response in youth with T2D. Multiple interacting factors likely contribute to this rising prevalence, as well as the increased severity of the condition, including structural inequities, increasing obesity and sedentary lifestyles, and intergenerational transmission from in-utero exposure to maternal hyperglycaemia and obesity. Youth-onset T2D is also associated with stigma and poorer mental health, and these impact clinical management.

There is an urgent need to develop effective interventions to prevent youth-onset T2D and enhance engagement of affected youth. It is also critical to better understand the differing phenotypes of youth-onset T2D, to effectively target treatments, and to address intergenerational transmission in high-risk populations.

READING 5 – PREDICTING HIGHER CHILD BMI Z-SCORE AND OBESITY INCIDENCE

Salway R,[1,2] Armstrong M,[3] Brady S,[3] Mariapun J,[4] Yasin MS,[4] Reidpath DD,[5] Su TT,[6,#] Johnson L.[7,#] Predicting higher child BMI z-score and obesity incidence in Malaysia: a longitudinal analysis of a dynamic cohort study. BMC Public Health. 2024 May 27;24(1):1408. PMID: 38802803.

doi: 10.1186/s12889-024-18917-9. PMID: 38802803.

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ABSTRACT

BACKGROUND: To target public health obesity prevention, we need to predict who might become obese, i.e., predictors of increasing Body Mass Index (BMI) or obesity incidence. Predictors of incidence might be distinct from more well-studied predictors of prevalence, therefore we explored parent, child, and sociodemographic predictors of child/adolescent BMI z-score and obesity incidence over five years in Malaysia.

METHODS: The South East Asia Community Observatory in Segamat, Malaysia provided longitudinal data on children and their parents (n=1767). Children were aged 6-14 years at baseline (2013-14) and followed up five years later. Linear multilevel models estimated associations with child BMI z-score at follow-up, adjusting for baseline BMI z-score and potential confounders. Predictors included parent cardiometabolic health (overweight/obesity, central obesity, hypertension, hyperglycaemia), and socio-demographics (ethnicity, employment, education). Logistic multilevel models explored predictors of obesity incidence.

RESULTS: Higher baseline BMI z-score predicted higher follow-up BMI z-score both in childhood to late adolescence (0.60; 95% CI: 0.55, 0.65) and early to late adolescence (0.76; 95% CI: 0.70, 0.82). There was inconsistent evidence of association between child BMI z-score at follow-up with parent cardiometabolic risk factors independent of baseline child BMI z-score. For example, maternal obesity, but not overweight, predicted a higher BMI z-score in childhood to early adolescence (overweight: 0.16; 95% CI: -0.03, 0.36, obesity: 0.41; 95% CI: 0.20, 0.61), and paternal overweight, but not obesity, predicted a higher BMI z-score in early to late adolescence (overweight: 0.22; 95% CI: 0.01, 0.43, obesity: 0.16; 95% CI: -0.10, 0.41). Parental obesity consistently predicted five-year obesity incidence in early to late adolescence, but not childhood to early adolescence. An adolescent without obesity at baseline with parents with obesity, had 3-4 times greater odds of developing obesity during follow-up (incidence OR=3.38 (95% CI: 1.14-9.98, mother) and OR=4.37 (95% CI 1.34-14.27, father) respectively).

CONCLUSIONS: Having a higher BMI z-score at baseline was a stronger predictor of a higher BMI z-score at follow-up than any parental or sociodemographic factor. Targeting prevention efforts based on parent or sociodemographic factors is unwarranted but early childhood remains a key period for universal obesity prevention.

READING 6 – A PROPOSED SIMPLIFIED DEFINITION OF METABOLIC SYNDROME IN CHILDREN AND ADOLESCENTS – A GLOBAL PERSPECTIVE

Zong X,[1,2,#] Kelishadi R,[3,#] Kim HS,[4,#] Schwandt P,[5,#] Matsha TE,[6,#] Mill JG,[7,#] Caserta CA,[8,#] Medeiros CCM,[9,#] Kollias A,[10,#] Whincup PH,[11] Pacifico L,[12] López-Bermejo A,[13-15] Zhao M,[16] Zheng M,[17] Xi B.[18] A proposed simplified definition of metabolic syndrome in children and adolescents: a global perspective. BMC Med. 2024 May 7;22(1):190. PMID: 38715060.

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ABSTRACT

Metabolic syndrome (MetS) is becoming prevalent in the paediatric population. The existing paediatric MetS definitions (e.g., the International Diabetes Federation (IDF) definition and the modified National Cholesterol Education Programme (NCEP) definition) involve complex cutoffs, precluding fast risk assessment in clinical practice.

We proposed a simplified definition for assessing MetS risk in youths aged 6-17 years, and compared its performance with two existing widely used paediatric definitions (the IDF definition, and the NCEP definition) in 10 paediatric populations from nine countries globally (n=19,426) using the receiver operating characteristic (ROC) curve analyses. In general, the total MetS prevalence of 6.2 percent based on the simplified definition was roughly halfway between that of 4.2 percent and 7.7 percent estimated from the IDF and NCEP definitions, respectively. The ROC curve analyses showed a good agreement between the simplified definition and two existing definitions: the total area under the curve (95% confidence interval) of the proposed simplified definition for identifying MetS risk achieved 0.91 (0.89-0.92) and 0.79 (0.78-0.81) when using the IDF or NCEP definition as the gold standard, respectively.

The proposed simplified definition may be useful for paediatricians to quickly identify MetS risk and cardiometabolic risk factors (CMRFs) clustering in clinical practice, and allow direct comparison of paediatric MetS prevalence across different populations, facilitating consistent paediatric MetS risk monitoring and the development of evidence-based paediatric MetS prevention strategies globally.

READING 7 – DIETARY INTAKE, OBESITY, AND METABOLIC RISK FACTORS AMONG CHILDREN AND ADOLESCENTS

Ramadas A,[1] Yasin MS,[2] Rizal H,[2,3] Rajakumar S,[2,3] Su TT,[2,3] Mariapun J,[4] Armstrong MEG.[5] Dietary intake, obesity, and metabolic risk factors among children and adolescents in the SEACO-CH20 cross-sectional study. Sci Rep. 2024 May 17;14(1):11265. PMID: 38760446.

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ABSTRACT
We investigated the association between dietary intake and metabolic risk factors in children and adolescents within a semi-rural Malaysian community.

Using an interviewer-led questionnaire, we surveyed 623 participants aged 7-18 from the South East Asia Community Observatory (SEACO). Anthropometric and blood pressure data were collected from all participants, while a subset (n=162) provided blood samples for biomarker analysis, including fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Metabolic syndrome was determined using the International Diabetes Federation's Definition of Metabolic Syndrome in Children and Adolescents.

Most participants were Malay (66.8 percent), with a median household income of MYR1,500 and a balanced sex distribution. Cereals, processed foods, beverages, fruits, and vegetables were commonly consumed. Obesity and abdominal obesity were prevalent, affecting more than a third of participants. Adherence to dietary recommendations was generally poor (ranging from 19.9 to 58.1 percent) and varied across age, sex, and ethnicity. Notably, some food groups displayed unexpected associations with health markers; for instance, fruit consumption was linked to abdominal obesity in children (abdominal obesity vs normal: 2.4 servings/day vs 1.6 servings/day).

These findings emphasise the necessity of longitudinal studies in exploring the complex relationship between diet and long-term health outcomes, including cardiometabolic diseases, while acknowledging the unique challenges posed by the COVID-19 pandemic on data collection and analysis.

READING 8 – GLP-1 RECEPTOR MECHANISMS AND ADVANCES IN THERAPY

Zheng Z,[1,2,#] Ma Y,[1,2] Tian Y,[1,2] Pang Y,[1,2] Zhang C,[1,2] Zong Y,[3,#] Gao J.[4,5] Glucagon-like peptide-1 receptor: mechanisms and advances in therapy. Signal Transduct Target Ther. 2024 Sep 18;9(1):234. PMID: 39289339.

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ABSTRACT

The glucagon-like peptide-1 (GLP-1) receptor, known as GLP-1R, is a vital component of the G protein-coupled receptor (GPCR) family and is found primarily on the surfaces of various cell types within the human body. This receptor specifically interacts with GLP-1, a key hormone that plays an integral role in regulating blood glucose levels, lipid metabolism, and several other crucial biological functions. In recent years, GLP-1 medications have become a focal point in the medical community due to their innovative treatment mechanisms, significant therapeutic efficacy, and broad development prospects.

This article thoroughly traces the developmental milestones of GLP-1 drugs, from their initial discovery to their clinical application, detailing the evolution of diverse GLP-1 medications along with their distinct pharmacological properties. Additionally, this paper explores the potential applications of GLP-1 receptor agonists (GLP-1RAs) in fields such as neuroprotection, anti-infection measures, the reduction of various types of inflammation, and the enhancement of cardiovascular function. It provides an in-depth assessment of the effectiveness of GLP-1RAs across multiple body systems, including the nervous, cardiovascular, musculoskeletal, and digestive systems. This includes integrating the latest clinical trial data and delving into potential signalling pathways and pharmacological mechanisms.

The primary goal of this article is to emphasise the extensive benefits of using GLP-1RAs in treating a broad spectrum of diseases, such as obesity, cardiovascular diseases, non-alcoholic fatty liver disease (NAFLD), neurodegenerative diseases, musculoskeletal inflammation, and various forms of cancer. The ongoing development of new indications for GLP-1 drugs offers promising prospects for further expanding therapeutic interventions, showcasing their significant potential in the medical field.

READING 9 – SEMAGLUTIDE VERSUS PLACEBO IN PEOPLE WITH OBESITY-RELATED HEART FAILURE

Butler J,[1] Shah SJ,[2] Petrie MC,[3] Borlaug BA,[4] Abildstrøm SZ,[5] Hovingh GK,[5] Møller DV,[5] Einfeldt MN,[5] Lindegaard ML,[5] Rasmussen S,[5] Davies MJ,[6] Kitzman DW,[7] Verma S,[8] Abhayaratna W,[9] Ahmed FZ,[10] Ben-Gal T,[11] Chopra V,[12] Ezekowitz JA,[13] Fu M,[14] Ito H,[15] Lelonek M,[16] Melenovský V,[17] Merkely B,[18] Núñez J,[19] Perna E,[20] Schou M,[21] Senni M,[22] Sharma K,[23] van der Meer P,[24] Von Lewinski D,[25] Wolf D,[26] Kosiborod MN[27]; STEP-HFpEF Trial Committees and Investigators. Semaglutide versus placebo in people with obesity-related heart failure with preserved ejection fraction: a pooled analysis of the STEP-HFpEF and STEP-HFpEF DM randomised trials. Lancet. 2024 Apr 27;403(10437):1635-1648. PMID: 38599221.

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ABSTRACT

BACKGROUND: In the STEP-HFpEF (NCT04788511) and STEP-HFpEF DM (NCT04916470) trials, the GLP-1 receptor agonist semaglutide improved symptoms, physical limitations, bodyweight, and exercise function in people with obesity-related heart failure with preserved ejection fraction. In this prespecified pooled analysis of the STEP-HFpEF and STEP-HFpEF DM trials, we aimed to provide a more definitive assessment of the effects of semaglutide across a range of outcomes and to test whether these effects were consistent across key patient subgroups.

METHODS: We conducted a prespecified pooled analysis of individual patient data from STEP-HFpEF and STEP-HFpEF DM, randomised, double-blind, placebo-controlled trials at 129 clinical research sites in 18 countries. In both trials, eligible participants were aged 18 years or older, had heart failure with a left ventricular ejection fraction of at least 45 percent, a BMI of at least 30 kg/m^2, New York Heart Association class II-IV symptoms, and a Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS; a measure of heart failure-related symptoms and physical limitations) of less than 90 points. In STEP-HFpEF, people with diabetes or glycated haemoglobin A1c concentrations of at least 6.5 percent were excluded, whereas for inclusion in STEP-HFpEF DM participants had to have been diagnosed with type 2 diabetes at least 90 days before screening and to have a HbA1c of 10 percent or lower. In both trials, participants were randomly assigned to either 2.4 mg semaglutide once weekly or matched placebo for 52 weeks. The dual primary endpoints were change from baseline to week 52 in KCCQ-CSS and bodyweight in all randomly assigned participants. Confirmatory secondary endpoints included change from baseline to week 52 in 6-min walk distance, a hierarchical composite endpoint (all-cause death, heart failure events, and differences in changes in KCCQ-CSS and 6-min walk distance); and C-reactive protein (CRP) concentrations. Heterogeneity in treatment effects was assessed across subgroups of interest. We assessed safety in all participants who received at least one dose of study drug.

FINDINGS: Between 19 March 2021 and 9 March 2022, 529 people were randomly assigned in STEP-HFpEF, and between 27 June 2021 and 2 September 2022, 616 were randomly assigned in STEP-HFpEF DM. Overall, 1,145 were included in our pooled analysis, 573 in the semaglutide group, and 572 in the placebo group. Improvements in KCCQ-CSS and reductions in bodyweight between baseline and week 52 were significantly greater in the semaglutide group than in the placebo group (mean between-group difference for the change from baseline to week 52 in KCCQ-CSS 7.5 points [95% CI 5.3 to 9.8]; p<0.0001; mean between-group difference in bodyweight at week 52 -8.4% [-9.2 to -7.5]; p<0.0001). For the confirmatory secondary endpoints, 6-min walk distance (mean between-group difference at week 52 17.1 metres [9.2 to 25.0]) and the hierarchical composite endpoint (win ratio 1.65 [1.42 to 1.91]) were significantly improved, and CRP concentrations (treatment ratio 0.64 [0.56 to 0.72]) were significantly reduced, in the semaglutide group compared with the placebo group (p<0·0001 for all comparisons). For the dual primary endpoints, the efficacy of semaglutide was largely consistent across multiple subgroups, including those defined by age, race, sex, BMI, systolic blood pressure, baseline CRP, and left ventricular ejection fraction. One hundred and sixty-one serious adverse events were reported in the semaglutide group compared with 301 in the placebo group.

INTERPRETATION: In this prespecified pooled analysis of the STEP-HFpEF and STEP-HFpEF DM trials, semaglutide was superior to placebo in improving heart failure-related symptoms and physical limitations, and reducing bodyweight in participants with obesity-related heart failure with preserved ejection fraction. These effects were largely consistent across patient demographic and clinical characteristics. Semaglutide was well tolerated.

READING 10 – OBESITY HAS A COMMUNICABLE DISEASE ANGLE TO IT

Kalra S,[1] Verma M,[2] Kapoor N.[3] Obesity is a communicable disease. J Pak Med Assoc. 2024 Apr;74(4):820-821. PMID: 38751290.

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ABSTRACT
Obesity has multiple causes and correlates. Usually studied as a metabolic and endocrine disease, with mechanical and musculoskeletal comorbidities, obesity also has a communicable angle to it.

Obesity can be considered a communicable disease from the conventional point of view, as it is associated with viral aetiology in animal and human models. It is also associated with increased prevalence and worse prognosis of infectious diseases. Not only that, obesity is a "socially communicable" disease, as it "spreads" amongst people living in similar environments.