

A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO DIABETES MELLITUS UPDATE

Some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – TRENDS IN MEDICATION USE, GLYCEMIC CONTROL, AND OUTCOMES

Tan YZ(1), Cheen MHH(1), Goh SY(2), Bee YM(2), Lim PS(1), Khee GY(1), Thumboo J(3). Trends in medication utilization, glycemic control and outcomes among type 2 diabetes patients in a tertiary referral centre in Singapore from 2007 to 2017. J Diabetes. 2018 Dec 16. [Epub ahead of print.]

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ABSTRACT

BACKGROUND: Use of glucose-lowering agents is a cornerstone in combating type 2 diabetes (T2DM). Treatment guidelines have changed significantly over the past decade. We report temporal trends in medication utilisation, glycemic control, and rate of severe hypoglycemia in T2DM patients at a tertiary referral centre in Singapore.

METHODS: We analysed data of 36,924 T2DM patients seen at Singapore General Hospital (SGH) from 2007 to 2017. Annual age-, sex- and ethnicity-standardised proportions of patients (a) prescribed with each class of glucose-lowering agent; (b) on various glucose-lowering regimens; and (c) with an HbA1c of <6%, 6 to <7%, 7 to <8%, 8 to <9% or ≥9% were estimated using logistic regression. Poisson regression estimated standardised rate of severe hypoglycemia.

RESULTS: From 2007 to 2017, use of metformin (45.9% to 59.6%) and insulin (24.4% to 57.9%) increased, while utilisation of sulphonylureas (52.0% to 44.9%) decreased (all $p < 0.001$). Utilisation of dipeptidyl peptidase-4 inhibitors (1.2% to 31.2%) and sodium-glucose cotransporter-2 inhibitors (0.5% to 7.4%) increased from 2008 to 2017 and 2012 to 2017 respectively (all $p < 0.001$). More patients were prescribed with a combination of insulin and oral agents (17.3% to 46.0%, $p < 0.001$). Proportion of patients with HbA1c ≥8% increased (33.7% to 36.0%, $p < 0.001$). Rates of severe hypoglycemia (5.0 to 8.4 per 100 patient-years, $p < 0.001$) also rose.

CONCLUSION: Medication utilisation patterns have changed significantly over the past 11 years with a shift towards newer agents. Glycemic control has remained stable, and rate of severe hypoglycemia increased. Further analysis is required before causal relationships can be inferred.

READING 2 – PAST DECADE IN T2DM AND FUTURE CHALLENGES

Haddad JA(1), Haddad AN(2). Hormones (Athens). The past decade in type 2 diabetes and future challenges. 2018;17:451–9.

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ABSTRACT

There is today an exponential increase in prevalence of type 2 diabetes mellitus (T2DM), especially in young people. This downward shift in age of onset of T2DM has been shown by abundant evidence to be due to an increase in obesity among the young, the latter mainly attributable to unhealthy dietary habits and a sedentary lifestyle. It is therefore obvious that the prevention of diabetes rather than its treatment is of paramount importance.

In the past decade, because concerns about the safety of antidiabetic agents took precedence over the issue of efficacy, almost all studies have been diabetes CVOTs and not traditional CVOTs. Until 2015, the evidence showed that antidiabetic agents are effective in terms of reduction of microvascular, as opposed to macrovascular, complications. However, following publication of the results of some new studies, it became clear that the new class of antidiabetic drugs, e.g., SGLT 2 inhibitors and GLP-1 agonists, are also effective in reducing cardiovascular disease (CVD).

In the coming decade, numerous health challenges are expected to arise, the most important being the greater expansion of the therapeutic armamentarium for T2DM and the adoption of strategies for prevention of CVDs. In parallel, the new generation of antidiabetic agents will target the recently investigated pathophysiologic disorders of diabetes, while, ideally, treatments should include smart drugs without side effects.

READING 3 – METFORMIN EFFICACY AND WEIGHT REDUCTION IN OBESITY

Lentferink YE(1), Knibbe CAJ(2)(3), van der Vorst MMJ(4). Efficacy of metformin treatment with respect to weight reduction in children and adults with obesity: a systematic review. *Drugs*. 2018;78:1887–1901.

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ABSTRACT

BACKGROUND: Obesity and its related complications are increasing health issues. Since generally only minor weight loss is obtained with lifestyle intervention, additional pharmacological therapies such as metformin are often used.

OBJECTIVE: We conducted a systematic review to provide an overview of the efficacy of ≥ 6 months of metformin treatment in children and adults with respect to weight, insulin resistance, and progression toward type 2 diabetes mellitus (T2DM).

METHODS: In September 2018, we searched PubMed, Embase, and the Cochrane Library for studies published in English using the keywords metformin, obesity/overweight, and weight loss. Prospective studies reporting weight/body mass index (BMI) as a primary or secondary outcome in patients with overweight/obesity with ≥ 6 months' metformin treatment were included. Included subjects were children and adults with overweight/obesity who received ≥ 6 months of metformin and/or lifestyle intervention, and/or placebo and/or lifestyle intervention, and/or standard care. Studies were independently screened by two reviewers. Data were extracted by one and verified by the other reviewer, and both reviewers assessed the risk of bias using the Cochrane risk-of-bias tool.

RESULTS: Our review includes 15 pediatric and 14 adult studies. In children, after 6 months, more than half the studies reported a greater reduction in BMI with metformin versus controls. Only six studies had an intervention of >6 months, and these studies found no further improvement in BMI in the metformin users, though their BMI was lower than that of controls. Three studies showed a significant improvement in insulin sensitivity in the metformin versus the control group.

Adults using metformin experienced and maintained small decreases in weight irrespective of duration of intervention. In 11 of 14 studies, a greater reduction in weight/BMI was observed with metformin than with the placebo. Progression toward T2DM was significantly reduced in adults using metformin, ranging from 7 to 31%. The safety and tolerability of metformin, withdrawal of participants, and comparison with other drugs were not taken into account.

CONCLUSIONS: The effects of metformin on weight/BMI vary, with smaller reductions in children than in adults. This could be because of differences in adherence, daily dosage, and insulin status. Metformin significantly reduced the progression toward T2DM in adults. Therefore, metformin should be considered as a treatment for obesity and its related complications.

READING 4 – PLACE OF GLICLAZIDE MR IN T2DM LANDSCAPE

Colagiuri S(1), Matthews D(2), Leiter LA(3), Chan SP(4), Sesti G(5), Marre M(6). The place of gliclazide MR in the evolving type 2 diabetes landscape: A comparison with other sulfonylureas and newer oral antihyperglycemic agents. *Diabetes Res Clin Pract.* 2018;143:1–14.

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ABSTRACT

The sulfonylureas are effective oral glucose-lowering agents with a long history of clinical use. While all have the same general mechanism of action, their pharmacokinetic properties are influenced by factors such as dosage, rate of absorption, duration of action, route of elimination, tissue specificity, and binding affinity for pancreatic β -cell receptor. The result is a class of agents with similar HbA1c-lowering efficacy, but well-documented differences in terms of effects on hypoglycemia, and cardiovascular and renal safety.

This review examines the differences between currently available sulfonylureas with a focus on how gliclazide modified release (MR) differs from other members of this class and from newer oral antihyperglycemic agents in the form of dipeptidyl peptidase-4 (DPP4) and sodium-glucose cotransporter 2 (SGLT2) inhibitors.

The first part focuses on major outcome trials that have been conducted with the sulfonylureas and new oral agents. Consideration is then given to factors important for day-to-day prescribing including efficacy and durability, weight changes, hypoglycemia, renal effects and cost. Based on current evidence, third-generation sulfonylureas such as gliclazide MR possess many of the properties desired of a type 2 diabetes drug including high glucose-lowering efficacy, once-daily oral administration, few side effects other than mild hypoglycemia, and cardiovascular safety.

READING 5 – PHARMACISTS' INVOLVEMENT IN SELF-CARE MANAGEMENT OF PATIENTS WITH DIABETES IS COST-EFFECTIVE

Jamshed SQ(1), Siddiqui MJ(1), Rana B(2), Bhagavathula AS(3). Evaluation of the involvement of pharmacists in diabetes self-care: A review from the economic perspective. *Front Public Health.* 2018;6:244. doi: 10.3389/fpubh.2018.00244. eCollection 2018.

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ABSTRACT

OBJECTIVES: To analyse the studies encompassing the involvement of pharmacists in diabetes self-care. **Method:** We reviewed studies conducted from 2005 to 2017 on the involvement of pharmacists in diabetes self-care. The keywords mainly used in this search were pharmaco-economic analysis, diabetes self-care, pharmacist involvement, cost-effectiveness analysis, cost of utilisation, cost of illness, cost of minimisation and cost-benefit analysis. PubMed, Science Direct, Springer Link and Medline searched for the relevant studies. These databases searched for full-text articles ranging from 2007 to 2017. We tried to limit the search with the inclusion of studies having any sort of pharmaco-economically relevant component.

KEY FINDINGS: Cost of illness varied among the countries in managing diabetes mellitus, and the cost of managing diabetes complications was twice the cost of the management of diabetes. Continuous involvement of the pharmacist in primary healthcare is a cost-effective strategy and was pronounced to be essential for helping diabetes patients in controlling and managing their disease. Implementation of diabetes self-care by pharmacists, such as lifestyle intervention, achieved improved quality of life for the patient without any increase in healthcare cost. Self-care management generated intensive blood glucose control and improved quality of life.

CONCLUSIONS: Implementation of diabetic self-care intervention, including intensive lifestyle intervention, education, self-monitoring of blood glucose and adherence toward medication, resulted in a reduction in the overall healthcare cost of diabetic patients compared to patients relying on only any one of the interventions. Diabetes self-care intervention by pharmacists was reported to significantly reduce the HbA1C levels of diabetic patients along with the reduction of yearly healthcare cost. This review showed that pharmacists' involvement in diabetes self-care interventions proved to be cost-effective and can significantly affect the condition of the diabetic patients for the better and reduce the risk of complications.

READING 6 – QUALITY OF LIFE FACTORS IN PATIENTS WITH T2DM

Jing X(1), Chen J(1), Dong Y(1), Han D(1), Zhao H(1), Wang X(1), Gao F(1), Li C(1), Cui Z(1), Liu Y(1), Ma J(2). Related factors of quality of life of type 2 diabetes patients: A systematic review and meta-analysis. Health Qual Life Outcomes. 2018;16:189. doi: 10.1186/s12955-018-1021-9.

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ABSTRACT

BACKGROUND: Diabetes is a chronic disease and it can affect both health and quality of life (QOL). A lot of studies have reported some predictors of QOL of type 2 diabetes patients. However, their results have not been completely consistent. So the aim of our study was finding out the related factors (including characteristics related to the disease, lifestyles and mental health factors) of QOL of type 2 diabetes patients.

METHODS: We searched the Cochrane library, EmBase, PubMed and CNKI databases for published studies that evaluated the related factors of QOL of type 2 diabetes patients by using a proper statistical method and had effect sizes (OR or β) and 95% confidence intervals from January 1st 2000 to May 31st 2016. All study types were acceptable, but we excluded reviews,

letters, editorials and pooled analyses. The data were analysed using STATA software (Version 12.0; Stata Corporation). Effect sizes and 95% confidence intervals were calculated to evaluate the relationship between these factors and QOL.

RESULTS: Eighteen studies were included into our systematic review and meta-analysis, totaling 57,109 type 2 diabetes patients. Doing more physical exercises (the pooled ORs ranged from 0.635 to 0.825 for different scales, less than 1.00) and having more frequent glucose checks [pooled OR (95% CI): 0.175 (0.041, 0.756)] were associated with a better QOL. Presence of complications (the pooled ORs ranged from 1.462 to 3.038 for different scales, more than 1.00), presence of hypertension [pooled OR (95% CI): 1.389 (1.173, 1.644)], longer duration of diabetes [pooled OR (95% CI): 1.865 (1.088, 3.197)], diet with more red meat [pooled OR (95% CI): 2.085 (1.063, 4.089)] and depression (the pooled ORs ranged from 3.003 to 11.473 for different scales, higher than 1.00) were associated with a worse QOL.

CONCLUSION: The results of this study show that physical exercise, frequent glucose checks, complications, hypertension, duration of diabetes, diet with more red meat, and depression affected the QOL of type 2 diabetes patients.

READING 7 – DIABETES AND ANTIPLATELET THERAPY

Rivas Rios JR(1), Franchi F(1), Rollini F(1), Angiolillo DJ(1). Diabetes and antiplatelet therapy: from bench to bedside. *Cardiovasc Diagn Ther.* 2018;8:594–609.

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ABSTRACT

Diabetes mellitus (DM) is a metabolic disorder associated with accelerated atherogenesis and an increased risk of atherothrombotic complications. Multiple mechanisms contribute to the pro-thrombotic status which characterises DM patients, underscoring the importance of antiplatelet therapies used for secondary prevention in these patients. For many years, dual antiplatelet therapy (DAPT) with aspirin and the P2Y12 inhibitor clopidogrel has represented the mainstay of treatment following an acute coronary syndrome (ACS) or in patients undergoing percutaneous coronary interventions (PCI). Although DAPT reduces the incidence of atherothrombotic recurrences, these rates remain high in DM patients, underscoring the need for more efficacious therapies. Oral platelet P2Y12 receptor inhibitors with enhanced potency, such as prasugrel and ticagrelor, as well as antiplatelet therapies such as vorapaxar inhibiting the thrombin-mediated platelet signaling pathway, constitute treatment opportunities for patients with DM and have been shown to be associated with a greater reduction in ischaemic recurrences, albeit at the cost of more bleeding. This article reviews currently available antiplatelet agents and delivers an update on the advances and drawbacks of these agents used for secondary prevention in DM patients experiencing an ACS or undergoing PCI.

READING 8 – BURDEN OF DIABETES, ORAL COMPLICATIONS, PREVENTION AND MANAGEMENT

Nazir MA(1), AlGhamdi L(2), AlKadi M(2), AlBejani N(2), AlRashoudi L(2), AlHussan M(2). The burden of diabetes, its oral complications and their prevention and management. *Open Access Maced J Med Sci.* 2018;6:1545–53.

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ABSTRACT

BACKGROUND: Diabetes mellitus (DM), a chronic disease, is a public health problem that affects 8.5% of the adult population worldwide. The number of adults with DM has risen sharply from 108 million in 1980 to 422 million in 2014. In 2012, 1.5 million individuals died because of DM and an additional 2.2 million deaths occurred because of high blood glucose levels resulting in cardiovascular and other systemic diseases. DM brings huge economic losses to patients, their families, and healthcare systems. Globally, the cost of DM was US\$1.31 trillion in 2015.

AIM: This review article utilised the prevalence data of DM from the World Health Organization and International Diabetes Federation to provide a comprehensive picture of the disease in different parts of the world.

METHODS: Electronic databases such as Google Scholar, Medline via PubMed, Scopus, and Web of Science were used to search the literature. The library resources of Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia were used to retrieve studies on the topics of the present review.

RESULTS: Systemic complications of DM include heart attack, kidney disease, limb loss, blindness, and peripheral nerve damage. More than 90% of diabetic patients were found to have oral manifestations. It is known that DM severely damages oral tissues, causing periodontal disease, tooth loss, xerostomia, caries, burning mouth disorder, taste and salivary gland dysfunction, delayed wound healing, lichen planus, geographic tongue, and candidiasis. The evidence is mounting about a strong bidirectional relationship between DM and periodontal disease. Unfortunately, many diabetic patients are unaware of the association between DM and oral health, and only a small percentage of them visit the dentist for routine dental check-ups. Changes in lifestyle (control of blood glucose levels and self-care practices), regular dental check-ups with emphasis on periodontal assessment, and reinforcement of oral health instructions can effectively prevent oral complications of DM. Scaling and root planning are effective in improving glycemic control among diabetic patients.

CONCLUSION: Dental professionals should be part of the multidisciplinary team that helps individuals with diabetes.

READING 9 – THE METABOLIC MODEL OF HEART FAILURE AND ROLE OF SGLT2 INHIBITION

Saad M(1), Gomceli U(2), Ravi P(1), Lacoste AG(1), Shah N(1), Vittorio TJ(2). The metabolic model of heart failure: the role of sodium glucose co-transporter-2 (SGLT-2) inhibition. *Drugs Context*. 2018;7:212549.

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ABSTRACT

Heart failure (HF) is one of the leading causes of hospital readmissions and healthcare expenditures. With a vast degree of advancements in the clinical approach and diagnosis, its management protocol is limited in terms of enhancing quality of life and prognosis.

Type 2 diabetes mellitus (T2DM) is considered one of the commonly associated comorbid conditions in the HF population. The understanding of the molecular and metabolic models of HF has led to the utilisation of therapeutic goals of T2DM in improving HF-related complications. In the recent era, SGLT-2 inhibitors have shown success in decreasing cardiovascular mortality in the T2DM population.

This article will help the reader to comprehend the pathophysiology of HF and the potential role of SGLT-2 inhibitors in the management algorithm of HF and its associated risk factors in T2DM.

READING 10 – PROTEINURIA IN T2DM FROM H PYLORI INFECTION

Shi Y(1), Duan JY(2), Liu DW(2), Qiao YJ(2), Han QX(1), Pan SK(2), Tang L(3), Cai GY(3), Chen XM(3), Liu ZS(2), Zhu HY(3). Helicobacter pylori infection is associated with occurrence of proteinuria in type 2 diabetes patients: a systemic review and meta-analysis. Chin Med J (Engl). 2018;131:2734–40.

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ABSTRACT

BACKGROUND: Type 2 diabetes (T2DM) patients are susceptible to *Helicobacter pylori* (HP), and it has been reported that the occurrence of proteinuria is associated with HP infection in T2DM patients; however, this view remains controversial. This meta-analysis aimed to explore the association between HP infection and the occurrence of proteinuria in T2DM patients. In addition, we hope to provide some recommendations to readers in clinical or related fields.

METHODS: Our meta-analysis was conducted with the methodology of the Cochrane Collaboration. Search strategies were formulated by relevant professionals. Case-control studies that compared the occurrence of proteinuria in T2DM patients with and without HP infection were involved in our meta-analysis. Relevant English or Chinese studies were searched on online databases before 2018, including PubMed, the Cochrane library, Medline, Google Scholar, the China National Infrastructure, and Wanfang database. The search strategies were “diabetic proteinuria, diabetic microalbuminuria, diabetic albuminuria, diabetic kidney disease, diabetic renal dysfunction, diabetic renal disease, diabetic nephropathy, diabetic complications, and diabetic mellitus, combined with HP.” The quality of these selected articles was separately assessed by two investigators using the Newcastle-Ottawa Scale (NOS). Odds ratios (ORs) and associated 95% confidence intervals (CIs) were extracted and pooled using fixed-effects models.

RESULTS: Seven studies involving 1029 participants were included. The quality of these seven articles was all above five stars as assessed by NOS, and there was no significant publication bias in our meta-analysis. We found that T2DM patients with HP infection had a 2.00 times higher risk of the occurrence of proteinuria than patients without HP infection (OR: 2.00, 95% CI: 1.48-2.69).

CONCLUSIONS: Our analysis showed that HP infection was associated with the occurrence of proteinuria in T2DM patients. HP radical surgery might be a therapeutic option for protecting kidney function in patients with T2DM.