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*MEDICAL DIARY*

*VOL.26 NO.9 September 2021*

*Nephrology*

*Better Care for Patients with Diabetes and Kidney Disease*





THE **1<sup>ST</sup>**  $\beta_3$ -AGONIST FOR **OAB\* PATIENTS**  
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 PLACEBO-LIKE DRY MOUTH(1.7%) SIDE EFFECT<sup>1</sup>



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\*OAB: Overactive Bladder + LUTS: Lower Urinary Tract Symptoms  
 #  $\alpha_1$ -blockers are often considered the first line drug treatment of male LUTS<sup>3</sup>

Reference: 1. Chapple CR, et al. Neurourol Urodyn 2013 [doi:10.1002/nu.22505] 2. Chapple CR, et al. Eur Urol Supp. 2005; 4:33-44  
 3. Gravas S, et al.EAU Guidelines on the Treatment of Non-neurogenic Male LUTS. European Association of Urology. 2017.

**Abbreviated prescribing information of Harnal OCAS<sup>®</sup> 0.4 mg Tablets**

Version: 002 Pl version: Sep 2013. **Composition:** Tamsulosin HCl **Indication:** Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). **Dosage:** 1 tab daily, can be taken independently of food. **Administration:** Swallow whole, do not chew/crush. **Contraindications:** Hypersensitivity to tamsulosin hydrochloride or to any of the excipients. **Special warnings and special precaution for use:** As with other  $\alpha_1$ -adrenoceptor antagonists, a reduction in blood pressure can occur in individual cases during treatment with Harnal OCAS<sup>®</sup> 0.4 mg Tablets, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared. Before therapy with Harnal OCAS<sup>®</sup> 0.4 mg Tablets is initiated, the patient should be examined in order to exclude the presence of other conditions, which can cause the same symptoms as benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards. Treatment of patients with a history of orthostatic hypotension should be approached with caution. The treatment of patients with severe renal impairment (creatinine clearance of <10 ml/min) should be approached with caution, as these patients have not been studied. The treatment of patients with severe hepatic dysfunction should be approached with caution. The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract and glaucoma surgery in some patients on or previously treated with tamsulosin hydrochloride. IFIS may increase the risk of eye complications during and after the operation. Discontinuing tamsulosin hydrochloride 1-2 weeks prior to cataract or glaucoma surgery is anecdotally considered helpful, but the benefit of treatment discontinuation has not been established. IFIS has also been reported in patients who had discontinued tamsulosin for a longer period prior to the surgery. The initiation of therapy with tamsulosin hydrochloride in patients for whom cataract or glaucoma surgery is scheduled is not recommended. During pre-operative assessment, surgeons and ophthalmic teams should consider whether patients scheduled for cataract or glaucoma surgery are being or have been treated with tamsulosin in order to ensure that appropriate measures will be in place to manage the IFIS during surgery. Tamsulosin hydrochloride should not be given in combination with strong inhibitors of CYP3A4 in patients with poor metaboliser CYP2D6 phenotype. Tamsulosin hydrochloride should be used with caution in combination with strong and moderate inhibitors of CYP3A4. Cases of allergic reaction to tamsulosin in patients with a past history of sulfonamide allergy have been reported. If a patient reports a previously experienced sulfa allergy, caution is warranted when administering tamsulosin hydrochloride. **Undesirable effects:** Common (>1%, <10%): Uncommon (>0.1%, <1%), Rare (>0.01%, <0.1%), Very rare (<0.01%). **Cardiac disorders:** Uncommon: Palpitations. **Gastrointestinal disorders:** Uncommon: Constipation, diarrhoea, nausea, vomiting. **General disorders and administration site conditions:** Uncommon: Asthenia. **Nervous system disorders:** Common: Dizziness (1.3%). Uncommon: Headache. Rare: Syncope. **Reproductive system and breast disorders:** Common: Ejaculation disorders. Very rare: Priapism. **Respiratory, thoracic and mediastinal disorders:** Uncommon: Rhinitis. **Skin and subcutaneous tissue disorders:** Uncommon: Rash, pruritus, urticaria. Rare: Angioedema. **Vascular disorders:** Uncommon: Orthostatic hypotension. **Post-marketing experience:** The following events have also been reported during the post-marketing period. These events are reported voluntarily from a population of uncertain size, therefore it is not possible to reliably estimate their frequency; visual disorders (e.g. blurred vision, visual impairment), dermatitis exfoliative, erythema multiforme and epistaxis. During cataract and glaucoma surgery a small pupil situation, known as Intraoperative Floppy Iris Syndrome (IFIS), has been reported. **Full prescribing information is available upon request.**

**Abbreviated prescribing information of Betmiga<sup>®</sup> prolonged-release tablets**

Version: 003 Pl version: Apr 2016. **Composition:** Mirabegron **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** Adult including elderly 50 mg once daily with or without food. **Administration:** Swallow whole with liquids. Do not chew/divide/crush. **Contraindications:** Mirabegron is contraindicated in patients with - Hypersensitivity to the active substance or to any of the excipients. - Severe uncontrolled hypertension defined as systolic blood pressure  $\geq$  180 mm Hg and/or diastolic blood pressure  $\geq$  110 mm Hg. **Special warnings and precautions for use:** Renal impairment: Betmiga has not been studied in patients with end stage renal disease (GFR < 15 mL/min/1.73 m<sup>2</sup> or patients requiring haemodialysis) and, therefore, it is not recommended for use in this patient population. Data are limited in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m<sup>2</sup>) based on a pharmacokinetic study a dose reduction to 25 mg is recommended in this population. Betmiga is not recommended for use in patients with severe renal impairment (GFR 15 to 29 mL/min/1.73 m<sup>2</sup>) concomitantly receiving strong CYP3A inhibitors. Hepatic impairment: Betmiga has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) and, therefore, it is not recommended for use in this patient population. Betmiga is not recommended for use in patients with moderate hepatic impairment (Child-Pugh B) concomitantly receiving strong CYP3A inhibitors. Hypertension: Mirabegron can increase blood pressure. Blood pressure should be measured at baseline and periodically during treatment with Betmiga, especially in hypertensive patients. Data are limited in patients with stage 2 hypertension (systolic blood pressure  $\geq$  160 mm Hg or diastolic blood pressure  $\geq$  100 mm Hg). Patients with congenital or acquired QT prolongation: Betmiga, at therapeutic doses, has not demonstrated clinically significant QT prolongation in clinical studies. However, since patients with a known history of QT prolongation or patients who are taking medicinal products known to prolong the QT interval were not included in these studies, the effects of mirabegron in these patients is unknown. Caution should be exercised when administering mirabegron in these patients. Patients with bladder outlet obstruction and patients taking antimuscarinics medications for OAB: Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in patients treated with Betmiga; however, Betmiga should be administered with caution to patients with clinically significant BOO. Betmiga should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB. **Undesirable effects:** Summary of the safety profile: The safety profile of Betmiga was evaluated in 8,433 patients with OAB, of which 5,648 received at least one dose of mirabegron in the phase 2/3 clinical program, and 622 patients received Betmiga for at least 1 year (365 days). In the three 12-week phase 3 double blind, placebo controlled studies, 88% of the patients completed treatment with Betmiga, and 4% of the patients discontinued due to adverse events. Most adverse reactions were mild to moderate in severity. The most common adverse reactions reported for patients treated with Betmiga 50 mg during the three 12-week phase 3 double blind, placebo controlled studies are tachycardia and urinary tract infections. The frequency of tachycardia was 1.2% in patients receiving Betmiga 50 mg. Tachycardia led to discontinuation in 0.1% patients receiving Betmiga 50 mg. The frequency of urinary tract infections was 2.9% in patients receiving Betmiga 50 mg. Urinary tract infections led to discontinuation in none of the patients receiving Betmiga 50 mg. Serious adverse reactions included atrial fibrillation (0.2%). Adverse reactions observed during the 1-year (long term) active controlled (muscarinic antagonist) study were similar in type and severity to those observed in the three 12-week phase 3 double blind, placebo controlled studies. List of adverse reactions: The table below reflects the adverse reactions observed with mirabegron in the three 12-week phase 3 double blind, placebo controlled studies. The frequency of adverse reactions is defined as follows: very common ( $\geq$ 1/10); common ( $\geq$ 1/100 to <1/10); uncommon ( $\geq$ 1/1,000 to <1/100); rare ( $\geq$ 1/10,000 to <1/1,000); very rare (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Infections and infestations: Common: Urinary tract infection. Uncommon: Vaginal infection, Cystitis. Psychiatric disorders: Not known (cannot be estimated from the available data): Insomnia\*. Eye disorders: Rare: Eyelid oedema. Cardiac disorders: Common: Tachycardia. Uncommon: Palpitation, Atrial fibrillation. Vascular disorders: Very rare: Hypertensive crisis\*. Gastrointestinal disorders: Common: Nausea\*, Constipation\*, Diarrhoea\*. Uncommon: Dyspepsia, Gastritis. Rare: Lip oedema. Skin and subcutaneous tissue disorders: Uncommon: Urticaria, Rash, Rash macular, Rash papular, Pruritus. Rare: Leukocytoclastic vasculitis, Purpura, Angioedema\*. Musculoskeletal and connective tissue disorders: Uncommon: Joint swelling. Reproductive system and breast disorders: Uncommon: Vulvovaginal pruritus. Investigations: Uncommon: Blood pressure increased, GGT increased, AST increased, AL increased. Renal and urinary disorders: Rare: Urinary retention\*. Nervous system disorders: Common: Headache\*, Dizziness\*, \*observed during post-marketing experience. **Full prescribing information is available upon request.**

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## The Cover Shot



天下第一城 in Beijing is an enormous and prestigious holiday resort with a golf course and surrounded by a large number of lotus ponds. It also has a memorial building containing the exhibit of the life and times of the late Chinese Vice-President of the People's Republic of China 榮毅仁.

The lotus was taken in one of the ponds along the fourways of his golf course.



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# Better Care for Patients with Diabetes and Kidney Disease

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**Co-Editors**

While attention is currently focused on COVID-19, there is another pandemic around the world, diabetes mellitus (DM), which sweeps across the Asia region more than other parts of the world. It is estimated that about 10% of the world population suffer from diabetes<sup>1</sup>. Hong Kong is also facing the same problem.

We all know the implications and consequences of DM, with its morbidity and mortality, cause a major health problem for the patients. In particular, the consequences of DM and diabetic kidney disease (DKD) are very important. In Hong Kong, it was estimated that 37.7% of DM patients had diabetic nephropathy in 2018/19<sup>2</sup>. The true prevalence was likely higher as 14.6% of the study population had undetermined diabetic nephropathy status. Moreover, more than half of the newly diagnosed end-stage renal disease (ESRD) patients on renal replacement therapy are caused by DM. There is a need for us to provide better care for patients with DM.

DM is a major modifiable risk factor for developing DKD. Each healthcare professional plays a slightly different role in patient management. It is important for us to move upstream to slow down the deterioration of kidney failure so that the patients won't go to ESRD. But even more so, if we can do so, is to prevent them from getting kidney disease complications. It can be done, though it is a big challenge, by us the healthcare professionals. There is a call for collective action by everyone.

Recently there has been tremendous progress in diabetes management. New guidelines addressing diabetes management in DKD have also been published<sup>3-4</sup>. It calls for comprehensive and structural care, and teamwork in the patient management of DM and DKD. With this in mind, Hong Kong Society of Nephrology, Hong Kong Kidney Foundation and The Federation of Medical Societies of Hong Kong have jointly organised four live webinars on 'Better Care for Patients with Diabetes and Kidney Disease' from Feb to April 2021. The collaborating partners are Hong Kong College of Family Physicians, Hong Kong Society of Endocrinology, Metabolism and Reproduction (Diabetes Division), Diabetes Hongkong, Hong Kong Dietitians Association, Hong Kong Association of Renal Nurses, Association of Hong Kong Diabetes Nurses and Alliance for Renal Patients Mutual Help Association. In these webinars, the diabetologists, nephrologists, primary care physician, diabetic nurse specialist, renal nurse specialist and dietitian shared the recent guidelines, expert advice and challenges in managing renal disease in diabetes. The last webinar was also open to the public, and diabetic patients were invited to talk about self-management, connecting healthcare professionals and patients together to combat DM and DKD.

This issue of Medical Diary published some of the presentations delivered at the webinars. Dr Li Yim-chu shares the local data on diabetes and DKD and her insight into the challenges and solutions in



managing these problems in the primary care setting. Dr Au Yeung Yick-cheung discusses who would be screened and what parameters would be monitored for diabetic renal complications. Dr Chau Suet-ming gives us an update on the use of anti-diabetic drugs and emphasises the need for an individualised approach for the management of diabetic patients. Dr Sunny SH Wong highlights the current understanding of DKD staging and the clinical action plan, as well as the importance of correcting the cardiovascular risk factors. Ms Cherry PY Law, Ms Veronica SC Hung and Ms Ho Hau-sim also discuss how to improve the diabetic and renal outcomes from the perspectives of the dietitian, diabetic nurse specialist and renal nurse specialist, respectively. Last but not least, Ms Maggie MM Ng shares her story and highlights the patient engagement and self-management that are essential for optimal management.

We would like to thank the contributing authors and everyone involved in the webinars for their effort and great support. We also wish to acknowledge Professor Richard YH Yu for contributing a splendid cover picture for this issue. We sincerely hope the contents addressed will benefit the clinical practice for tackling DM and DKD.

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‡When added to standard of care, which included oral antidiabetic treatment, insulin, antihypertensives, diuretics and lipid-lowering therapies.<sup>3</sup>

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1. Ozempic<sup>®</sup> packing insert.

2. Pratley RE, Aroda VR, Lingway I, et al; SUSTAIN 7 Investigators. Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial. *Lancet Diabetes Endocrinol.* 2018;6(4):275-286.

3. Marso SP, Bain SC, Consoli A, et al; SUSTAIN 6 Investigators. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes.



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OZE-D-20201202

# Challenges in Managing Diabetes Mellitus and Diabetic Kidney Disease in Primary Care Setting

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Dr LI Yim-chu

## DISEASE BURDEN: WORLDWIDE AND HONG KONG

Diabetes mellitus (DM) is one of the most common chronic diseases in both developed and developing countries. The global diabetes prevalence in 2019 was estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045.<sup>1,2</sup> About one in two (50.1%) people living with diabetes do not know that they have diabetes. This implies around half of the people with DM in the world are not aware of having the disease, and are unknowingly at risk of developing cardiovascular and renal complications as well as other health problems. DM is the leading cause of kidney failure, blindness, leg amputations, cardiovascular diseases and stroke.<sup>3</sup>

Diabetic kidney disease (DKD) is the most common cause of the end-stage renal disease (ESRD) in the world, and it is associated with increased morbidity and mortality in diabetic patients.<sup>4</sup> It is defined by elevated urine albumin excretion or reduced glomerular filtration rate (GFR), or both. It takes place in 20% to 40% of all diabetics.<sup>5</sup> The incidence of DKD is increasing each year. It has been estimated that more than 40% of people with diabetes will develop chronic kidney disease (CKD), including a significant number who will develop ESRD requiring renal replacement therapies (dialysis and/or transplantation). Moreover, CKD is the most frequent first comorbidity in type 2 DM. Studies have demonstrated that CKD is the first cardiovascular/renal disease (CVRD) manifestation identified in CVRD-free patients with type 2 DM.<sup>6</sup>

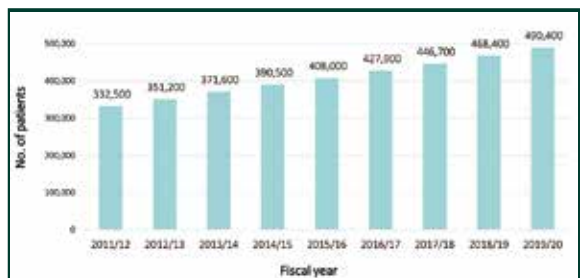
The local situation of DM is comparable to that across the world. According to Population Health Survey 2014/15 carried out by the Department of Health, among persons aged 15-84, 8.4% had DM (either they had previously diagnosed DM or had DM but without a known history of the disease).<sup>7</sup> More people were unaware of their DM (4.5%) than those who had previously diagnosed DM (3.8%). Another 1.0% of persons aged 15-84 had impaired fasting glucose (IFG).

Data of Hong Kong showed comparable findings worldwide that almost half of the new cases of ESRD were due to DM in 2016. (Fig 1)

Cause	Percentage
Diabetes Mellitus	49%
Glomerulonephritis	22%
Hypertension	11%
Unknown reason	9%
Genetic (e.g. polycystic renal disease)	3%
Urinary tract infection	3%
Others	3%

**Fig 1. The cause of new case of end-stage renal failure in Hong Kong (2016) (Excerpted from Hong Kong Hospital Authority Renal Registry)**

In Hong Kong, around 70% of DM patients are being followed up in the public sector. In the year 2019/20, a total of 490,400 DM patients were cared by outpatient settings of Hospital Authority (HA).<sup>8</sup> Among them, 60% are seen at general outpatient clinics (GOPCs) and 40% at specialist outpatient clinics (SOPCs). The number of DM patients was observed to have increased 47%, with additional 158,000 in eight years from 2011/12 to 2019/20 (Fig 2). It is projected to reach 627,000 in 2024.



**Fig 2. Number of DM patients under the care of outpatient settings in HA (Excerpted from Diabetes Mellitus Care Report 2019/20, HA)**

The majority (80%) of DM patients seen at the HA outpatient settings were having CKD Stage 1-2, while the remaining 20% were CKD Stage 3-5 (Fig. 3). This proportion has been static, but the increase in patient number imposes a health burden. Around 14.9% and 31.4% of DM patients in GOPC and SOPC had CKD Stage 3 or beyond.

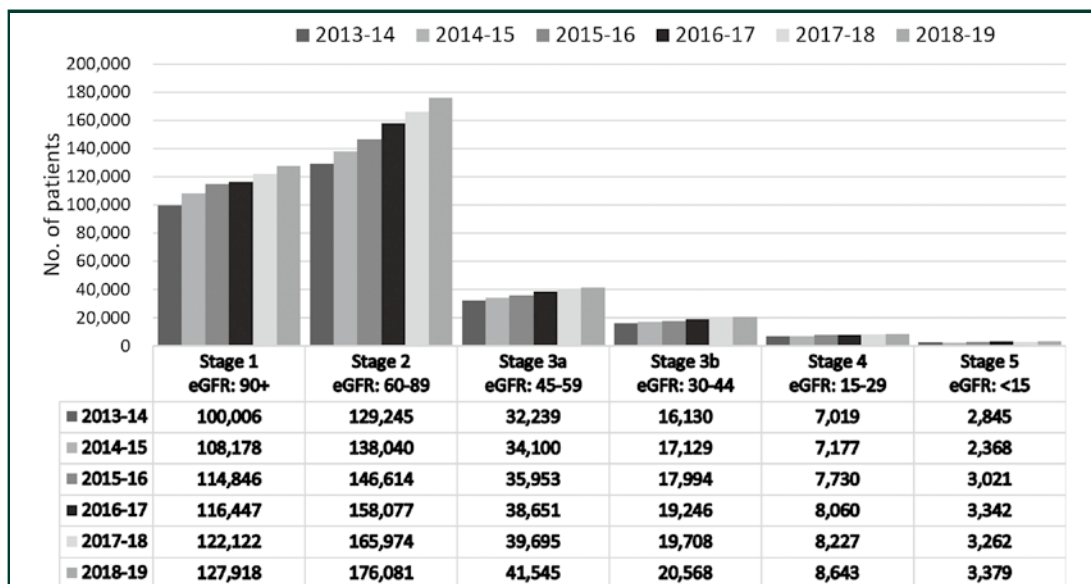


Fig 3. Chronic Kidney Disease Staging of DM Patients (Aged 18 to 85) under the care of outpatient settings in the HA (Excerpted from Diabetes Mellitus Care Report 2019/20, HA)

## THE ROLE OF PRIMARY CARE IN MANAGING DIABETES

Primary care physicians play an important role in managing DM, as more than half of diabetics attend primary care services. Uncomplicated DM patients and those with the absence of recent significant DM complications could be well be managed at the primary care level. As primary care physicians, we provide patient-centred, continuing, coordinated and comprehensive care to patients, in addition to being the first point of contact in the healthcare system.<sup>9</sup> As mentioned earlier, around half of the patients with diabetes are not aware of the problem, which signifies the need for early detection. Monitoring treatment responses and identification of treatment barriers could prevent and delay the development of complications. Coordinated care with other healthcare professionals such as nurses, dietitians, occupational therapists, optometrists, pharmacists and physiotherapists in a multidisciplinary care approach has also been proven to be cost effective in managing diabetes in primary care. In addition, the collaboration between primary and secondary care teams could improve coordinated care for patients. Primary care physicians can also identify high-risk subjects for referral to other experts.<sup>10</sup>

Early detection and management of the renal disease are important to reduce the burden of end-stage renal failure requiring renal replacement therapy (RRT). Primary care physicians can make a timely diagnosis of DKD through regular screening of individuals with DM.<sup>11, 12</sup> Progression of DKD could as well be retarded through optimal glycaemic control, blood pressure control, RAS blockade, and SGLT-2 inhibition. Preventing patients from suffering from acute kidney injury can also avoid progression and deterioration of DKD.

## CHALLENGES FACED IN PRIMARY CARE

Despite the importance of proper management of DM and DKD, and despite various international and local clinical guidelines for primary care physicians to follow, primary care physicians still encounter challenges and difficulties in their practice, no matter whether they are working in the public sector or private market. Three key factors, namely systemic, patient and physician factors, have been identified in contributing to the challenges and difficulties.<sup>13</sup>

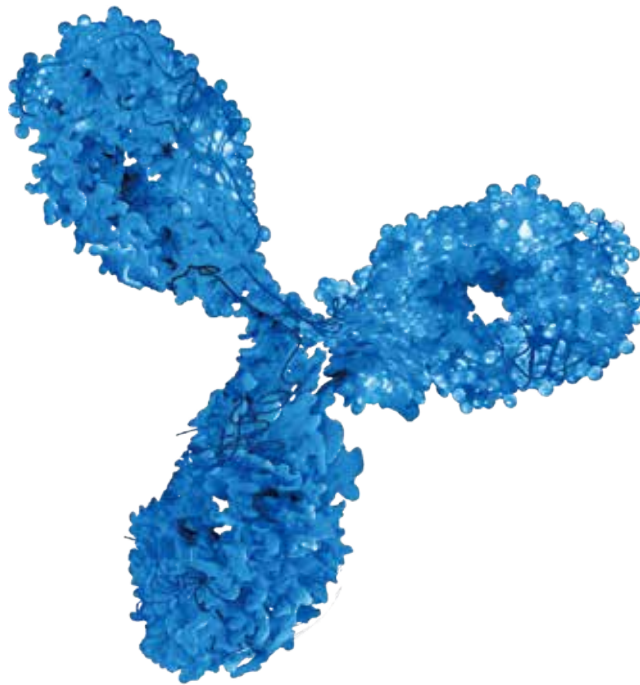
Systemic factors can be further delineated into those found in the public and private sectors. In the public sector, the constraint on resources is a significant factor. Contact time with patients in Hong Kong is relatively short.<sup>14</sup> At general outpatient clinics of the HA, the average consultation time per patient is 6 to 7 minutes, resulting in obstacles to a comprehensive consultation. There are also internal practice guidelines with restrictions on certain drug uses (especially those with cost implications) and on the frequency of complication screening, etc. These obstacles might hinder frontline doctors from fully complying with prevailing international guidelines. Waiting time for specialist referral is also rather long, which delays timely management by the experts. Apart from resource constraints, built-in limitations in the system, such as the difficulty in maintaining continuity of care and the lack of automated reminder system, are faced by frontline doctors.<sup>15</sup> In the private sector, patient care by a multidisciplinary team approach is hard to achieve. Patient autonomy is compromised if the corporate medical scheme confines patients' payments to "listed" doctors, or if the practitioners are employed under group practice. Lack of quality assurance and uncertain compliance with guideline recommendations are also commonly encountered.



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FGF23, fibroblast growth factor 23.

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Secondly, the patient factor frequently contributes to difficult management of DM and DKD. Treatment compliance issue happens regardless where the patient seeks care from. Managing patients with increased complexity in their chronic diseases and in drug management also induces stress to doctors.<sup>16</sup> Some patients carry insufficient awareness of the possible complications of DM and DKD,<sup>17</sup> and hence they are reluctant to have a full set of investigation, e.g. complication screening, especially if co-payment is needed. Financial concern also plays a considerable role. Nowadays, with more introduction of technology like continuous glucose monitoring and telemedicine, patients with low acceptance in technology would be a drawback to better chronic disease management.

With regard to physician factor, studies have pointed out the inadequacy of skill set and knowledge, as well as deficiency in the detection of CKD.<sup>18,19</sup> Clinical inertia is also a contributing factor leading to inadequate management offered to patients.<sup>20</sup> Causes of clinical inertia are multifactorial, but all end up affecting chronic disease control. Too much work stress and frustrations would eventually lead to burnout, which is not uncommon in primary care physicians.

## POSSIBLE FACILITATORS TO OVERCOME CHALLENGES

There is no one-size-fits-all solution to all the factors affecting the management of DM and DKD in primary care, and facilitators to improve the situations could not give rise to instant results. Systemic factors especially those pertaining to drawbacks at the public sector and limitations in the private practices would have to be ironed out by directives from high management level of relevant authorities, and even more ultimately by change in healthcare system such as the health financing system initiated by the government. In recent years, primary healthcare services have been in the limelight at policy address. Public-Private Partnership (PPP) has been established between the HA and her counterparts in the private sector to better manage public services demands and improve patients' access to clinical services.<sup>21</sup> Expansion of PPP with more projects over the years have benefited patients and the system with an overall improvement in service quality.

Another potentially constructive component to primary care, especially in the private sector, would be District Health Centre (DHC), the latter aiming at health promotion at individual and community levels, enhancement of coordination among various medical and social sectors and strengthening primary healthcare at the district level.<sup>22</sup> Via community engagement, and via the multidisciplinary teamwork, networking with private doctors within the local district and/or DHC provides health promotion, health assessment, chronic disease management and community rehabilitation. Hopefully when all districts have their DHCs set up, private doctors could collaborate with nursing and allied health professionals, patients, could be empowered with the knowledge and skills for self-management, and would be more motivated to comply with treatment. The general public would have access to early detection of chronic diseases. Primary care

physicians should also bear in mind to keep their patients healthy in the community through primary prevention with patient education, early detection of diseases and related complications, early intervention to achieve treatment target and referral to specialists as appropriate. Continuing medical education (CME) to keep up-to-date, uphold the professional standard and tackle clinical inertia is essential to primary care physicians in providing quality care to their patients

## CONCLUSION

Diabetes is one of the commonest chronic diseases worldwide and imposes a large economic burden on the healthcare system and the wider economy. A significant proportion of DM patients will develop diabetic kidney diseases. Primary care physicians play an important role in preventing, detecting, managing DM and DKD. Despite all the challenges faced in daily practice, there are positive ways to overcome challenges and to keep patients healthy in the community.

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# Diabetes Mellitus - Who to Screen and What to Monitor for Renal Complications

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*This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 September 2021.*

## KEY MESSAGES

- Diabetic kidney disease (DKD) is a clinical diagnosis based on the presence of albuminuria with or without a decline in estimated glomerular filtration rate (eGFR) in the absence of other primary causes of renal diseases.
- Non-albuminuric DKD may present with a decline in eGFR only (without albuminuria).
- Spot urine albumin-to-creatinine ratio (UACR) is used as a screening test for albuminuria, while estimated glomerular filtration rate (eGFR) is calculated from clinical equations. Various factors may affect the accuracy of the tests, and a repeated test is suggested to confirm the diagnosis.
- Other causes for renal deterioration have to be considered especially when the clinical presentation is not typical for DKD.
- It is recommended for patients with established chronic kidney disease (CKD) stage 3 or above to monitor related complications, e.g. metabolic bone disease, acidosis, and anaemia.

Diabetes is the leading cause of renal failure. It is estimated that around 20 to 30% of patients with type 1 diabetes (T1DM) and 30 to 40% of those with type 2 diabetes (T2DM) have diabetic kidney disease (DKD). DKD typically develops around 5 to 10 years after diagnosing T1DM but may present at diagnosis of T2DM. Patients with DKD typically have a long-standing history of diabetes, retinopathy, albuminuria and progressive decline in eGFR. Most patients with DKD are asymptomatic and the DKD is detected by routine periodic testing. Identifying DKD in diabetic patients enables healthcare workers to monitor and offer treatment for DKD and associated cardiovascular risks.

## PHENOTYPES OF DIABETIC KIDNEY DISEASES

Traditionally, from data among T1DM patients, diabetic nephropathy is described as a progressive disease with microalbuminuria being an early clinical marker (Table 1): the progression of microalbuminuria to macroalbuminuria or overt proteinuria marks the initiation of faster decline in the estimated glomerular filtration rate (eGFR). This albuminuria-centric model

has been challenged by epidemiological studies that show diverging prevalences of albuminuria and reduced eGFR.<sup>1,2</sup>

**Table 1. Classically described 5-stage course of DKD (Excerpted from *Hormones*. 2017 Oct;16(4):351–61<sup>4</sup>)**

	Underlying pathology	Clinical features
Hyperfiltration	- Glomerular hyperfiltration	- Raised glomerular filtration rate (GFR) - Normoalbuminuria
Silent	- Early histological changes e.g. glomerular basement membrane thickening, focal mesangial sclerosis	- Normal GFR - Normoalbuminuria
Incipient	- Mesangial expansion, glomerular basement membrane thickening	- GFR normal or mildly decreased - Microalbuminuria
Overt	- Marked glomerular basement membrane thickening, diffuse mesangial sclerosis	- GFR decreased - Increased albuminuria
End stage renal failure (ESRF)	- Diffuse global glomerulosclerosis	- GFR < 15ml/min - Decreasing albuminuria

**Table 2. Two phenotypes of DKD (Excerpted from *Nutr Metab Cardiovasc Dis*. 2019 Nov;29(11):1127–50<sup>5</sup> & *Front Med*. 2017 Sep;11(3):310–8<sup>6</sup>)**

	Classical albuminuric DKD	Nonalbuminuric DKD
Proposed course of disease	Microalbuminuria progresses to macroalbuminuria while there is unidirectional eGFR decline	The presence of albuminuria & eGFR are independent of each other; eGFR decline may occur without albuminuria
Suggested screening	Albuminuria	eGFR
Implications	Likely points to glomerular lesions. Associated with macrovascular complications & retinopathy	Likely points to vascular +/- tubulo-interstitial lesions. Associated with macrovascular complications but less with retinopathy

Microalbuminuria may regress to normoalbuminuria, whereas eGFR decline, once initiated, will continue to deteriorate progressively. Some diabetic patients with renal impairment have no significant albuminuria.<sup>1,2</sup> These observations suggest that renal function decline is independent of the development of albuminuria. DKD



is hence used to replace "diabetic nephropathy" for describing a complex and heterogeneous disease that encompasses different types of renal injury in diabetic patients.

In contrast to the "classical albuminuric DKD", "nonalbuminuric DKD" is proposed to be an alternative phenotype of DKD (Table 2). It is unclear whether these two models represent true distinctive underlying pathophysiologic changes. It is, however, commonly accepted that the degree of albuminuria (or proteinuria) does not represent the degree of renal impairment, but the presence of confirmed albuminuria remains a strong predictor of eGFR deterioration.

### DIAGNOSIS OF DIABETIC KIDNEY DISEASE<sup>3</sup>

DKD is a clinical diagnosis based on the presence of albuminuria with or without eGFR decline, in the absence of signs or symptoms of other primary causes of renal damage (Fig. 1). Abnormalities are to be confirmed with two or more samples saved at least three months apart. Although the gold standard for diagnosing diabetic nephropathy is the renal biopsy, it is infrequently performed in clinical practice unless an alternative diagnosis is suspected. Conditions that prompt such suspicion include: a rapid decline in eGFR (> 5 ml/min/1.73 m<sup>2</sup>/ year); acute onset of severe albuminuria (5-10 fold in 1-2 years); the presence of red blood cell casts, dysmorphic red blood cells or white blood cells casts in the urine sediment; the presence of other systemic diseases or medications that are known to cause renal damage (e.g. systemic lupus erythematosus, non-steroidal anti-inflammatory drugs); abnormal serum electrophoresis or free light chain ratio; and family history of renal disease (Table 3).

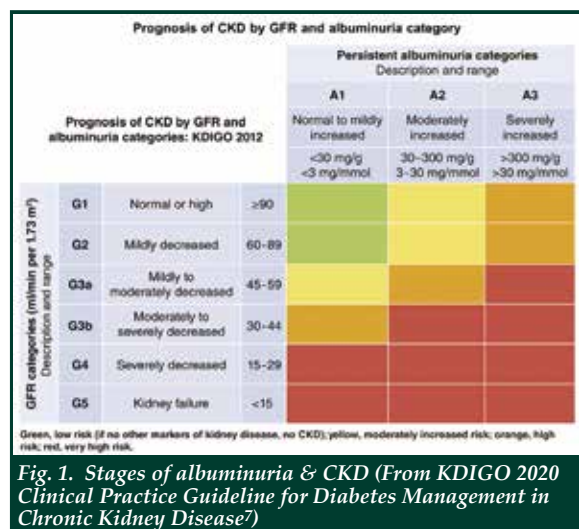


Fig. 1. Stages of albuminuria & CKD (From KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease<sup>7</sup>)

Table 3. Conditions that indicate a need for a workup for causes other than diabetes (Excerpted from ADA Standards of Medical Care in Diabetes -2021<sup>3</sup>)

With albuminuria	Without albuminuria
<ul style="list-style-type: none"> <li>- Rapid decline in eGFR (&gt;5 ml/min/yr)</li> <li>- Acute onset of severe proteinuria or albuminuria with ACR &gt;300 mg/mmol or nephrotic syndrome</li> <li>- Red cell cast or dysmorphic red cells on urine microscopy i.e. active urinary sediment</li> <li>- Other systemic disease that may cause renal diseases</li> <li>- Family history of renal disease</li> </ul>	<ul style="list-style-type: none"> <li>- Vascular risk factors, asymmetrical kidneys, &gt;30% rise in Cr with RAAS inhibitor</li> <li>- Previous AKI</li> <li>- Abnormal serum electrophoresis or free light chain ratio</li> <li>- Medications that coincide with decline in eGFR, eosinophilia, leukocyturia</li> </ul>

### Who to screen and what to monitor for DKD (Table 4)

Checking eGFR is suggested at diagnosis of diabetes or when the acute condition is stabilised (e.g. after an episode of diabetic ketoacidosis) and then every 6 to 12 months or as indicated clinically. For T1DM, the screening for microalbuminuria is arranged at around five years after diagnosis and then annually. For T2DM, the screening is performed at diagnosis or after acute hyperglycemia is controlled and then annually thereafter. The presence of renal impairment in T1DM within five years of diagnosis prompts the workup for causes other than DKD. If a patient is found to have micro- or macroalbuminuria, screening for other comorbidities, especially retinopathy and macrovascular disease, needs to be arranged.

Table 4. Screening for DKD (Excerpted from ADA Standards of Medical Care in Diabetes -2021<sup>3</sup>)

	When	Confirmed diagnosis
Estimated glomerular filtration rate (eGFR) by CKD-EPI equation	every 6 to 12 months or as indicated clinically	2 times < 60 ml/min/1.73m <sup>2</sup> at least 90 days apart
Spot urine Albumin/ Creatinine ratio (UACR)	First time: -T1DM 5 years after diagnosis -T2DM at diagnosis or after severe hyperglycemia controlled Annually thereafter	3 times in 3-6 months (when 2 out of 3 samples are positive)

### Assessment of albuminuria

Urinary albumin-to-creatinine ratio (UACR) in a random spot urine sample (Table 5) is used for checking albuminuria. Timed or 24-hour urine samples are inconvenient and bring no additional clinical benefit. Checking urinary albumin (UA) alone without a simultaneous urinary creatinine (Cr) may be less accurate. A urine albumin excretion ≥ 30 mg/ day or UACR ≥ 3 mg/mmol (some suggest 3.4 mg/mmol as cutoff) is defined as albuminuria.

UACR has a high biological variability in various conditions thus affecting its accuracy, as in conditions that change serum albumin levels (dietary protein

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intake, chronic inflammation), exercise within 24 hours prior to test (transient increase in albumin excretion), muscle build, as well as medical conditions associated with a raised UACR independent of renal damage (heart failure, marked hyperglycemia, menstruation and marked hypertension). Therefore, to confirm the presence of albuminuria, repeated samples in 3 to 6 months are suggested.

### Assessment of estimated glomerular filtration rate (eGFR)

The glomerular filtration rate (GFR) measurement is usually not used in clinical practice as the process is complex, time-consuming, and cumbersome. Estimation of GFR either by measuring creatinine clearance (CrCl) from a 24-hour urine collection or by calculating with equations based on serum creatinine is clinically more practical. The Modification of Diet in Renal Disease (MDRD) study equation and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation are the commonly used equations (Table 6). eGFR of < 60 ml/min/1.73m<sup>2</sup> as obtained via equation(s) is usually defined as decreased GFR.

CrCl by 24-hour urine sample creates inconvenience to patients and usually overestimates GFR (due to increased extrarenal creatinine elimination in advanced renal failure). GFR-estimating equations incorporate variables other than serum creatinine to improve the accuracy; nonetheless, conditions that change creatinine production or secretion (such as drugs interfering with creatinine secretion or dietary changes altering creatinine production) still affect their reliability. Between the MDRD study equation and CKD-EPI equation, the CKD-EPI equation provides better accuracy, especially with normal or mildly reduced GFR.

**Table 5. Definitions of abnormalities in albumin excretion (Data from KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease 7)**

	normal to mildly increased	Moderately increased (Microalbuminuria)	Severely increased (Macroalbuminuria)
Dipstick for protein	negative to trace	trace to 1+	> 1+
24 hour urinary albumin excretion	< 30mg/day	30 - 300 mg/day	> 300 mg/day
Spot urine Albumin/ Creatinine ratio (UACR)	< 3mg/ mmol	3 - 29 mg/mmol	≥ 30 mg/mmol

**Table 6. Equations for estimation of glomerular filtration rate (Data from online nkdep.nih.gov)**

Glomerular filtration rate estimate by CKD-EPI equation in adults	$GFR = 141 \times \min[(Serum\ creatinine/88.4)/kappa, 1]^{alpha} \times \max(Serum\ creatinine/88.4)/kappa, 1]^{-1.209} \times 0.993^{Age} \times Sex \times Race$ For females, Sex = 1.018; alpha = -0.329; kappa = 0.7. For males, Sex = 1; alpha = -0.411; kappa = 0.9. For race: black = 1.159, non black = 1
Glomerular filtration rate estimate by abbreviated MDRD study equation in adults	$Estimated\ GFR = Creatinine\ assay \times (Serum\ creatinine/88.4)^{-1.154} \times Age^{0.203} \times Sex \times Race$ For creatinine assay: IDMS = 175, Non-IDMS = 186 For sex: Female = 0.742, Male = 1 For race: black = 1.21, non black = 1

## COMPLICATIONS OF CHRONIC KIDNEY DISEASE

When a patient's eGFR is less than 60 ml/min/1.73m<sup>2</sup>, healthcare workers need to watch out for potential complications from chronic kidney disease. Monitoring of blood pressure, body weight, fluid status, serum electrolytes, haemoglobin level and markers for metabolic bone disease (serum calcium, phosphate, parathyroid hormones, vitamin D) is needed in follow-up.<sup>3</sup>

## OTHER RISK FACTORS FOR RENAL DETERIORATION

It is common for diabetic patients to have other chronic diseases such as hypertension, hyperlipidemia, hyperuricemia and obesity.<sup>1</sup> Monitoring and proper management of these chronic diseases, together with glucose control, help prevent the deterioration of renal function in diabetic patients.

## CONCLUSION

Screening for DKD is important for diabetic patients as diabetes is one of the leading causes of CKD or ESRD. With the understanding of the phenotype of non-albuminuric DKD, using albuminuria alone for screening of DKD is insufficient. Albuminuria, together with eGFR, are suggested for screening and monitoring of DKD (Fig. 1). It is also important to monitor and offer treatment for other risk factors and complications of chronic renal diseases.

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### Xarelto 2.5 mg film-coated tablet Abbreviated Prescribing Information

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**Composition:** Active ingredient: 2.5 mg rivaroxaban, Excipients: Microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, hypromellose 2910, sodium laurylsulfate, magnesium stearate, macrogol 3350, titanium dioxide (E171), iron oxide red (E172). **Indication and Posology:** Prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events, coadministered with acetylsalicylic acid (ASA). The recommended dose is 2.5 mg twice daily, with a daily dose of 75 - 100 mg ASA. Duration of treatment should be determined for each individual patient based on regular evaluations and should consider the risk for thrombotic events versus the bleeding risks. **Contraindications:** Hypersensitivity to the active substance or any of the excipients; active clinically significant bleeding, lesion or condition considered a significant risk for major bleeding; concomitant treatment with any other anticoagulants except under specific circumstances of switching anticoagulation therapy or when unfractionated heparin is given at doses necessary to maintain an open central venous or arterial catheter; concomitant treatment of CAD/PAD with ASA in patients with previous haemorrhagic or lacunar stroke, or any stroke within a month; hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C; pregnancy and breast feeding. **Warnings and Precautions:** Clinical surveillance in line with anticoagulation practice is recommended throughout treatment. Xarelto should be discontinued if severe haemorrhage occurs. Increasing age may increase haemorrhagic risk. Xarelto should be discontinued at the first appearance of a severe skin rash, or any other sign of hypersensitivity in conjunction with mucosal lesions. Not recommended: in patients with severe renal impairment (creatinine clearance <15 ml/min); in patients receiving concomitant systemic treatment with strong concurrent CYP3A4- and P-gp-inhibitors, i.e. azole-antimycotics or HIV protease inhibitors; in patients with increased bleeding risk; in patients receiving concomitant treatment with strong CYP3A4 inducers unless the patient is closely observed for signs and symptoms of thrombosis; not recommended due to lack of data: treatment in combination with antiplatelet agents other than ASA; in patients below 18 years of age; in patients concomitantly treated with dronedarone; in patients with prosthetic heart valves. Use with caution: in conditions with increased risk of haemorrhage; in patients with severe renal impairment (creatinine clearance 15 - 29 ml/min) or with moderate renal impairment (creatinine clearance 30 - 49 ml/min) concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; in patients treated concomitantly with medicinal products affecting haemostasis; in patients ≥ 75 years of age or with lower body

weight; when neuraxial anaesthesia or spinal/epidural puncture is employed. Patients on treatment with Xarelto and ASA should only receive concomitant treatment with NSAIDs if the benefit outweighs the bleeding risk. In patients at risk of ulcerative gastrointestinal disease prophylactic treatment may be considered. Although treatment with rivaroxaban does not require routine monitoring of exposure, rivaroxaban levels measured with a calibrated quantitative anti-Factor Xa assay may be useful in exceptional situations. Xarelto contains lactose. **Undesirable effects:** Common: anaemia, dizziness, headache, eye haemorrhage, hypotension, haematoma, epistaxis, haemoptysis, gingival bleeding, gastrointestinal tract haemorrhage, gastrointestinal and abdominal pains, dyspepsia, nausea, constipation, diarrhoea, vomiting, increase in transaminases, pruritus, rash, ecchymosis, cutaneous and subcutaneous haemorrhage, pain in extremity, urogenital tract haemorrhage, renal impairment, fever, peripheral oedema, decreased general strength and energy, post-procedural haemorrhage, contusion, wound secretion. Uncommon: thrombocytosis, thrombocytopenia, allergic reaction, dermatitis allergic, angioedema and allergic oedema, cerebral and intracranial haemorrhage, syncope, tachycardia, dry mouth, hepatic impairment, increases in bilirubin, blood alkaline phosphatase and GGT, urticaria, haemarthrosis, feeling unwell, increases in LDH, lipase, amylase. Rare: jaundice, bilirubin conjugated increased, cholestasis, hepatitis (incl hepatocellular injury), muscle haemorrhage, localised oedema, vascular pseudoaneurysm (uncommon in prevention therapy in ACS following percutaneous intervention). Very rare: anaphylactic reactions incl. shock, Stevens-Johnson syndrome/Toxic Epidermal Necrolysis, DRESS syndrome, Frequency not known: compartment syndrome or (acute) renal failure secondary to a bleeding.

**Footnotes:** a) Defined as fatal bleeding, ICH and critical organ bleeding b) The recommended dose is 2.5 mg twice daily, with a daily dose of 75 - 100 mg ASA. <sup>3</sup>vs. aspirin alone

**References:** 1. Anand S.S., Bosch J., Eikelboom J.W. et al. Rivaroxaban with or without aspirin in patients with stable peripheral or carotid artery disease: an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2017; doi: 10.1016/S0140-6736(17)32409-1. 2. Frank U, Nikol S, et al. European Society for Vascular Medicine (ESVM), Guideline on peripheral arterial disease, *Vasa*, 2019;48, Supplement 102; doi: 10.1024/0301-1526/a000834. 3. Xarelto® Hong Kong Prescribing Information 2.5mg (February 2019).



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## MCHK CME Programme Self-assessment Questions

Please read the article entitled "Diabetes Mellitus - Who to Screen and What to Monitor for Renal Complications" by Dr AU YEUNG Yick-cheung and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 September 2021. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. Around 20-40% of diabetic patients have diabetic kidney disease (DKD).
2. Decline in estimated glomerular filtration rate (eGFR) must develop after the development of albuminuria.
3. Checking serum creatinine is adequate for screening for DKD.
4. Diagnosis of DKD is based on the presence of albuminuria with or without a decline in eGFR without other apparent causes.
5. Spot urine albumin-to-creatinine ratio (UACR) is an easy clinical test for screening albuminuria.
6. Calculation of eGFR from clinical equations is NOT reliable.
7. Repeated tests (e.g. UACR and/or eGFR in 2-4 months time) are suggested to confirm the diagnosis of DKD.
8. If the presentation of DKD is not typical (e.g. rapid onset, red cell cast), the workup for other renal pathologies is suggested.
9. Decline in eGFR is expected to be faster in diabetic patients compared to otherwise healthy individuals.
10. Screening for other renal complications (e.g. metabolic bone disease, acidosis and anaemia) is suggested for patients with established chronic kidney disease stage 3 or above.

## ANSWER SHEET FOR SEPTEMBER 2021

Please return the completed answer sheet to the Federation Secretariat on or before 30 September 2021 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

# Diabetes Mellitus - Who to Screen and What to Monitor for Renal Complications

**Dr AU YEUNG Yick-cheung**

MBBS, MRCP (UK), FHKAM (Medicine)  
Specialist in Endocrinology, Diabetes and Metabolism

1  2  3  4  5  6  7  8  9  10

Name (block letters): \_\_\_\_\_ HKMA No.: \_\_\_\_\_ CDSHK No.: \_\_\_\_\_

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Contact Tel No.: \_\_\_\_\_ MCHK No. / DCHK No.: \_\_\_\_\_ (must fill in)

### Answers to August 2021 Issue

Colorectal Cancer Screening for Individuals with Family History

1. F 2. T 3. T 4. T 5. F 6. F 7. T 8. T 9. F 10. T





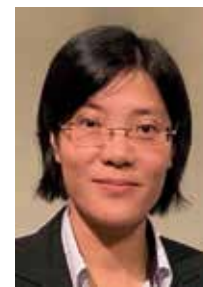


# Optimising the Use of Anti-Diabetic Drugs in Patients with Type 2 Diabetes

## Dr CHAU Suet-ming

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Specialist in Endocrinology, Diabetes and Metabolism



Dr CHAU Suet-ming

### KEY MESSAGES

- An individualised approach is recommended for establishing the glycaemic target for each diabetic patient.
- When treating patients with type 2 diabetes, it is important to identify high-risk patients and patients with established atherosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), and heart failure.
- After metformin, early use of SGLT2 inhibitors and GLP1-RAs are advocated in those who are at risk of progressive renal and cardiovascular disease.
- Patients with type 2 diabetes and CKD should be managed via a comprehensive strategy to reduce the risks of kidney disease progression and cardiovascular disease<sup>1-3</sup>.

Type 2 diabetes is a progressive disease. For most patients, after initiation of monotherapy with metformin, combination therapy is necessary to achieve glycaemic control in the long term. The following paragraphs give an update on optimising the use of anti-diabetic drugs based on the American Diabetes Association (ADA) 2021 guideline<sup>1</sup>, the American Association of Clinical Endocrinologists (AACE) 2020 guideline<sup>2</sup> and the Kidney Disease: Improving Global Outcomes (KDIGO) 2020 guideline<sup>3</sup>.

### GLYCAEMIC TARGET

When we manage patients with type 2 diabetes, their HbA1c and risk factors, particularly the ASCVD risk and the risks of chronic kidney disease or heart failure, are considered first. We set an individualised glycaemic target, aiming to achieve an optimal HbA1c < 6.5%<sup>2</sup>. Young patients with low cardiovascular risk and an absence of comorbidities may encourage their physicians to set a more stringent HbA1c goal. Conversely, the risk of hypoglycaemia in an elderly patient may cause the physician to favour an A1c target that is higher than 8%<sup>1</sup>. All decisions need to be based on medical needs and a balance of risks and benefits of treatment choices. The KDIGO 2020 guidelines take the severity of CKD into account, alongside macrovascular complications, comorbidities, life expectancy, and hypoglycaemia<sup>3</sup> when considering A1c goal setting. In diabetes-induced CKD, a reduction in GFR and concomitant increase in albuminuria are strong predictors of higher cardiovascular risk and hence a poorer prognosis.

### CHOOSING ANTI-DIABETIC AGENTS

If we look at the algorithm from the ADA 2021 guidelines, for patients who are relatively young and low risk, after metformin, the decision depends on the cost, the need for weight loss, the risk of hypoglycaemia, and of course, the patient's own informed choice<sup>2</sup>. We also take into account the feasibility and affordability of the treatment options. After initiation of drug treatment, the glycaemic control is carefully monitored and medication adjusted accordingly.

The ASCVD risk, presence of heart failure, and CKD are examined and monitored in at-risk patients. Both GLP-1RA and SGLT2i are recommended as the first-line anti-diabetic agents for patients with ASCVD risk, and others are added later if the glycaemic target has not been met. SGLT2i is the treatment of choice for patients suffering from heart failure, and for patients with CKD, GLP-1RA is recommended as an add-on in view of its cardiovascular benefit<sup>1</sup>.

The American Association of Clinical Endocrinology (AACE) 2020 guidelines suggest a similar approach. Assessment of ASCVD risk and CKD risk is recommended before choosing a specific treatment. Metformin is the first-line treatment, and GLP-1RA and SGLT2i are recommended as add-ons for all entry A1c levels, except for A1c > 9%, in which case insulin is recommended for patients with symptomatic hyperglycaemia<sup>2</sup>.

The KDIGO 2020 guidelines recommend the use of metformin and SGLT2i in patients with an eGFR > 30ml/min. GLP-1RA is the preferred add-on for glycaemic control, taking into account the comorbidities and cost of the drug therapies. Furthermore, in susceptible patients with diabetes and CKD, the KDIGO guidelines<sup>3</sup> recommend lifestyle modification, good blood pressure control and lipid management, together with the use of RAS blockade and antiplatelet therapies.

If we look at the profiles of the anti-diabetic drugs that are currently in use, GLP-1RA and SGLT2i are the two choices that offer the greatest renal and cardiac benefits. This paper will focus on these new therapies shortly, but first, there will be a review of the more traditional drug, metformin.



## METFORMIN

Metformin is recommended as the first-line treatment in all patients with type 2 diabetes. However, since there is insufficient safety data in patients with an eGFR < 30 ml/min or dialysis, it is recommended to discontinue its use, or not to initiate the use of metformin in patients with an eGFR < 30 ml/min. The same dose can be continued for those with an eGFR > 60 ml/min (G2). For those with eGFR between 45-59 ml/min (G3a), the same dose can be continued unless patients are prone to hypoperfusion or hypoxemia<sup>3</sup>. In those with an eGFR of 30-44 ml/min (G3b), the metformin dose should be halved, and patients should have their eGFR regularly monitored while on metformin<sup>3</sup>.

## SGLT2 INHIBITORS

This class of therapy has well established anti-glycaemic effect in type 2 diabetes patients. It promotes glycosuria by blocking the paired reuptake of sodium and glucose in the proximal renal tubules. In those with normal or near-normal kidney function, there is an increase in filtered glucose load in parallel with hyperglycaemia, so its glucose-lowering effect is greater in those starting with a higher HbA1c. In general, when comparing to placebo, SGLT2i reduces HbA1c values by 0.79% and 0.61% when used as monotherapy and combination therapy, respectively<sup>4</sup>.

In addition to its anti-glycaemic effect, SGLT2i has a non-glycaemic pleiotropic effect. There is effective weight loss through osmotic diuresis and caloric loss, and a reduction in blood pressure and albuminuria. The postulated mechanism is a reduction in glomeruli hyperfiltration due to afferent arterioles vasoconstriction. Anti-inflammatory and antioxidant effects are also suggested.

EMPA-REG<sup>5</sup>, CANVAS<sup>6</sup> and DECLARE-TIMI 58<sup>7</sup> were the three major cardiovascular outcome trials for empagliflozin, canagliflozin and dapagliflozin, respectively. Most patients in the trials have eGFR > 60 ml/min. They all showed significant risk reduction for their primary endpoint - the 3-point MACE (Major Adverse Cardiac Events) and heart failure benefit. There were significant renal benefits in terms of worsening nephropathy and renal composite endpoints<sup>1</sup>.

CREDESCENCE<sup>8</sup> is a clinical trial using canagliflozin in type 2 diabetes patients with albuminuria CKD. More than half of the patients had an eGFR < 60 ml/min. Significant cardiovascular and renal benefits were demonstrated. The DAPA-HF dapagliflozin trial<sup>9</sup> showed that patients with a history of heart failure (around 18% were normo-glycaemic) had a significant 26% relative risk reduction in worsening heart failure or CV deaths. The result did not differ by diabetes status. There was also a significant relative risk reduction of worsening nephropathy of 29%.

It is observed that the effect of SGLT2i on glycaemic benefit falls as eGFR declines. On the other hand, its effect on reducing CKD progression and CVD risks appear to be independent of eGFR. Currently, the KDIGO 2020 guidelines recommend treating T2DM,

CKD and eGFR ≥ 30 ml/min with an SGLT2i<sup>3</sup>. The FDA did not recommend the use of dapagliflozin or empagliflozin in patients with eGFR < 45 ml/min, although they approved a lower cut-off eGFR for canagliflozin. However, SGLT2i was used up to 30 ml/min in cardiovascular outcome trials (CVOTs), and the dosage was even lower in the more recent trials<sup>3</sup>. The trend of using SGLT2i at lower eGFR is likely to continue as future trial results become available.

## GLP-1 RECEPTOR AGONISTS

The glucometabolic effect GLP1-RAs is due to the incretin effect, which is the stimulation of glucose-dependent release of insulin from pancreatic islet cells with glucose ingestion. Glucagon secretion is reduced, gastric emptying is slowed, and the patient feels full. Its use also facilitates significant weight loss in various major trials. It reduces insulin resistance, and on average, it has an HbA1c lowering efficacy by 1-1.5%<sup>10</sup>. It has also been reported to improve lipid profile, reduce blood pressure, and lower albuminuria.

Most of the major trials for GLP1-RAs recruited patients with established CVD. The REWIND trial<sup>11</sup> of dulaglutide recruited patients with moderate to severe CKD. Significant relative risk reduction in 3-point MACE was noted with LEADER<sup>12</sup>, SUSTAIN-6<sup>13</sup> and REWIND, while CV safety was demonstrated in both ELIXA<sup>14</sup> and ESXCEL<sup>15</sup>. These findings suggest a potential CV class effect of GLP1-RA. Renal benefits were also noted, in which the composite kidney endpoint was mainly driven by a reduction in albuminuria, while no clinically relevant change in eGFR was observed. In AWARD-7<sup>16</sup>, in which dulaglutide was compared with insulin glargine in addition to the use of prandial Humulin, the eGFR did not significantly decline with dulaglutide, but a decrease in eGFR was observed with the use of insulin glargine. The KIDGO 2020 guidelines recommended using GLP1-RAs in addition to metformin and SGLT2i to meet the glycaemic target, or when these two agents could not be used<sup>3</sup>.

When choosing GLP1-RA, since exenatide is renally excreted, it is not recommended to use exenatide in patients with an eGFR < 30 ml/min. There is also limited data on the use of lixisenatide in patients with an eGFR < 30 ml/min<sup>3</sup>. As for other agents, dulaglutide is recommended with eGFR > 15 ml/min, and liraglutide and semaglutide require no renal adjustment<sup>3</sup>.

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# Staging of Diabetic Kidney Disease and the Clinical Action Plan

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### KEY MESSAGES

- Annual screening for the development or progression of Diabetic Kidney Disease (DKD).
- Keep Diabetes Mellitus (DM) under good control with individualised target.
- In the patient with high cardiovascular/renal risk or with overt nephropathy, put the patient on a sodium-glucose cotransporter-2 inhibitors (SGLT2i), followed by a glucagon-like peptide-1 receptor agonist (GLP-1 RA) if necessary.
- In a DM patient with hypertension, or microalbuminuria or above, put the patient on an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB).
- Manage hyperlipidemia. Lifestyle modification, including regular exercise, dietary control and smoking cessation, is an integral part in the management of DKD.
- Work up for alternative causes of renal disease, if the clinical presentation is atypical of DKD.

### INTRODUCTION

DM is a very important healthcare problem worldwide and locally. In Hong Kong, the prevalence of DM is estimated to be 10%<sup>1</sup>. About 30-40% of DM patients will develop DKD, and DKD accounts for 52% of new cases requiring renal replacement therapy in the public hospital in Hong Kong in 2020.

### STAGE AND NATURAL PROGRESSION OF DIABETIC KIDNEY DISEASE

DKD typically evolve through several stages. The first noticeable change is the increase in estimated glomerular filtration rate (eGFR), often called hyperfiltration. This is usually followed by the onset of albuminuria, which typically progresses from normal (< 30 mg/24 hour, or a spot urine albumin-creatinine ration (ACR) of < 3 mg/mmol or 30 mg/g) to moderately increased albuminuria (microalbuminuria) (30-300 mg/24 hour, or a spot urine ACR of 3-30 mg/mmol or 30-300 mg/g), to severely increased albuminuria (macroalbuminuria) (> 300 mg/24 hour, or a spot urine ACR >30 mg/mmol or 300 mg/g). Some patients even progress to nephrotic syndrome. With persistent albuminuria, eGFR usually progressively declines and finally reaches end-stage renal failure. As there is usually a delay in the onset

and diagnosis of type 2 DM, albuminuria may already be present upon diagnosis in some type 2 DM patients.

Although the development of albuminuria is an important landmark of DKD, some type 2 and, to a lesser extent, type 1 patients may develop DKD with progressive decline in renal function without albuminuria. The mechanism is not readily known, but in type 2 DM patients, this may be a result of predominant macrovascular disease.

### PREVENTION AND MANAGEMENT OF DIABETIC KIDNEY DISEASE

As albuminuria usually marked the onset of DKD, screening for its development is important for early diagnosis and aggressive management. The American Diabetic Association (ADA) recommends at least annual screening of urinary albumin for type 1 DM patients with duration  $\geq$  5 years and in all patients with type 2 DM<sup>2</sup>. Renal function by eGFR, blood pressure (BP) and ophthalmologic examination to look for diabetic retinopathy should be done at the same time. More frequent monitoring is warranted with increasing albuminuria and deteriorating renal function<sup>2</sup>.

To prevent the development of DKD, early aggressive glycaemic control has been shown in both type 1 and type 2 DM patients to reduce the risk of moderately increased or severely increased albuminuria<sup>3,4</sup>. So, what should be the target HbA1c to aim at? The Kidney Disease Improving Global Outcomes (KDIGO) 2020 guideline recommends that the HbA1c target be individualised, as the benefits and harms of targeting specific HbA1c levels vary according to key patient characteristics. For the patient with mild chronic kidney disease (CKD), absent or minor macrovascular complications, few comorbidities, long life expectancy, good hypoglycaemia awareness, and not prone to hypoglycaemia, we can aim at < 7% or even < 6.5%. However, for older patients with other clinical characteristics on the other end of the spectrum, an HbA1c target of < 7.5% or < 8% may be selected<sup>5</sup>.

In terms of pharmacological treatment of type 2 DM, metformin remains the first drug of choice as recommended by the KDIGO 2020 guidelines and the ADA 2021 guidelines for its safety, effectiveness in glycaemic control, low cost<sup>5</sup>, and modest long-term benefits in prevention of diabetic complications<sup>6</sup>. SGLT2i with its strong renal and cardiovascular



protective effects, is recommended by the KDIGO guidelines to be used in combination with metformin as first-line treatment in type 2 DM patients and CKD with eGFR  $\geq 30$  ml/min/1.73m<sup>2</sup>. SGLT2i acts by inhibiting renal tubular reabsorption of glucose and sodium chloride, resulting in increased glucose excretion and a modest reduction of blood glucose. The resultant glycosuria produces the diuretic effect. SGLT2i has also been shown to reduce arterial BP and produce weight loss<sup>7,8</sup>. In the cardiovascular outcome trials of EMPA-REG OUTCOME, CANVAS, and DECLARE-TIMI 58 with the use of empagliflozin, canagliflozin and dapagliflozin respectively, cardiovascular benefits including a reduction in hospitalisation for heart failure, myocardial infarction, stroke and cardiovascular death and death from any causes have been demonstrated<sup>8,9,10</sup>. In terms of renal protection, all three cardiovascular trials and the renal outcome trials CREDENCE and DAPA-CKD demonstrated a significant risk reduction in worsening eGFR, new onset end-stage renal failure, renal-related death and albuminuria<sup>8,9,10,11,12</sup>. The strong renal protective effect from the above trials is independent of its glucose lowering effect, which is only modest.

Moreover, for CREDENCE and DAPA-CKD trials, the positive effects were obtained in a background of renin-angiotensin blockade, the only approved class of renal protective medications until recently. The additional renal protective effects offered by SGLT2i further highlights the significance of it as a new class of renal protective medication. One has to be aware that during the early weeks of initiating SGLT2i, an initial dip in eGFR is seen, but thereafter, the decline in eGFR was slower with SGLT2i than placebo<sup>9,11,12</sup>. The initial eGFR dip is due to the reduction in intra-glomerular pressure, which is renal protective in the long term. One is also reminded that SGLT2i may need to be withheld during times of prolonged fasting, surgery or critical medical illness when the risk of ketoacidosis is increased, and also be careful when there is a risk of volume depletion.

In patients with type 2 DM and CKD, who have not achieved glycaemic target despite the use of metformin and SGLT2i, or are unable to use them, a GLP-1 RA is recommended<sup>5</sup>. Glucagon-like peptide-1 (GLP-1) is an incretin hormone secreted in the small intestine upon stimulation by glucose or other food. It results in glucose dependent stimulation of insulin secretion. It also reduces gastric emptying and reduces appetite, which results in weight loss. Liraglutide, injectable semaglutide and dulaglutide have demonstrated a reduction in cardiovascular death, nonfatal myocardial infarction or nonfatal stroke in the LEADER, SUSTAIN-6 and REWIND trials respectively<sup>13,14,15</sup>. In these trials, reduction in new onset or persistent severely increased albuminuria, worsening in eGFR, end-stage kidney disease or death due to kidney disease were also significantly reduced. Overall data of GLP-1 RA is less robust compared with SGLT2i, and the renal benefit is mainly driven by a reduction in urinary albumin excretion<sup>16,14,17,18</sup>.

Hypertension is very common in DM patients and is a very significant risk factor for atherosclerotic cardiovascular disease (ASCVD) and microvascular complications. Numerous studies have shown that

good BP control help to mitigate such risks. ADA recommended that BP target should be individualised. For individuals with diabetes and hypertension at lower risk for cardiovascular disease, the BP target should be  $< 140/90$ . For individuals at higher cardiovascular risk, with existing ASCVD or with CKD and or albuminuria  $> 30$  mg/24 hour, they should go for a BP target of  $< 130/80$ <sup>19</sup>. One may use the following ASCVD risk calculator for risk estimation: <https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#/calculate/estimate/>. In terms of the classes of drugs to use, in patients with diabetes, hypertension and albuminuria, RAS blockade by an ACEi or an ARB should be administered as first-line therapy. RAS blockade has been shown to reduce albuminuria and retard renal progression, independent of their BP lowering effect<sup>20,21</sup>. They should be titrated to the highest approved tolerated dose. Serum creatinine and potassium should be monitored within 2-4 weeks after initiation. An initial rise of serum creatinine is common, reflecting the haemodynamic effect of RAS blocker which is actually renal protective. Therefore, for a rise in serum creatinine of less than 30%, the RAS blocker can be safely continued<sup>5</sup>. Combination therapy with ACEi and ARB can result in further reduction in BP and albuminuria. However, in clinical trials, no difference in the primary endpoint of CKD progression or death or improved cardiovascular outcome has been shown. Moreover, there was a significant increase in hyperkalaemic events and the risk of acute kidney injury doubled<sup>22,23</sup>. Therefore, this combination is not recommended.

Good lipid control and lifestyle modification with smoking cessation, diet control and exercise are important in DKD patients<sup>5</sup>. They are recommended to maintain a protein intake of 0.8 g protein/kg body weight per day. Salt intake should be less than 5 g sodium chloride per day. They are also recommended to undertake moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week, or to a level compatible with their cardiovascular and physical tolerance<sup>5</sup>.

## PATIENT WITH CLINICAL FEATURES ATYPICAL OF DIABETIC KIDNEY DISEASE

One has to be aware of clinical scenarios which are not typical of DKD. It is uncommon for type 1 DM patients with less than five years' duration to develop overt kidney disease. It is also uncommon for type 1 DM patients to develop proteinuria or renal impairment without diabetic retinopathy. Abrupt onset of significant proteinuria and rapid renal deterioration is also atypical of diabetic nephropathy. In these scenarios, another serious renal disease should be suspected. The patient should be referred to a nephrologist for evaluation early. A renal biopsy is commonly required.

## CONCLUSION

DKD is an important complication of DM. Early identification, aggressive management with lifestyle modification and pharmacological therapy is needed to reduce risks of kidney disease progression and cardiovascular disease.



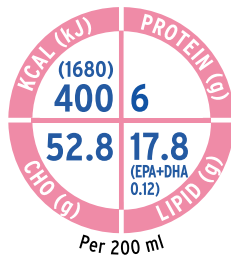
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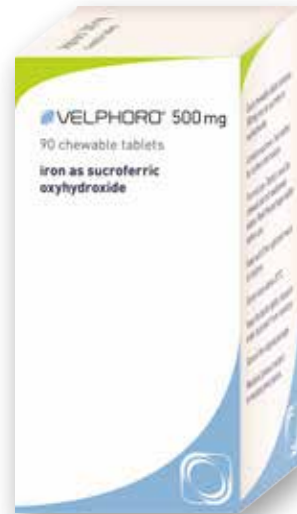
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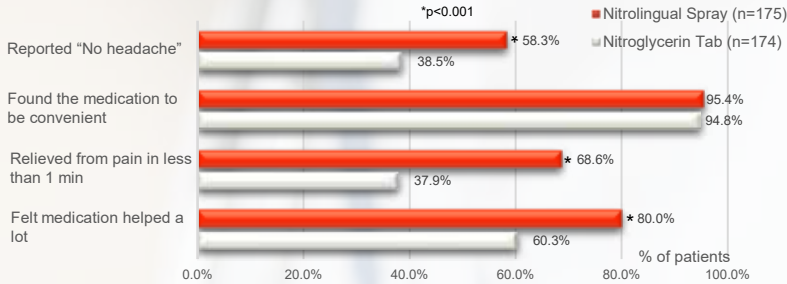
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Reference:  
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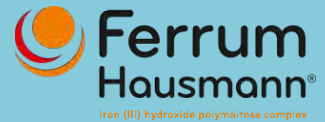
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# Improving Diabetic Control and Kidney Protection: What You Need to Know from Dietitians' Perspective

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Ms Cherry PY LAW

## INTRODUCTION

Diabetes mellitus is the most common cause of end-stage renal failure in Hong Kong. Nutritional intervention is an essential aspect in the management of diabetic kidney disease with the potential for slowing down the disease progression through optimisation of glycaemic, proteinuria, blood lipid and blood pressure control. Nutritional intervention also aims to provide a palatable and attractive diet, to prevent protein-energy malnutrition, and to control oedema and serum electrolytes and phosphorus.

## INDIVIDUALISED HEALTHY BALANCED DIET

Kidney Disease Improving Global Outcomes (KDIGO) 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease (CKD) suggests that "patients with diabetes and CKD should consume an individualised diet high in vegetables, fruits, whole grains, fibre, legumes, plant-based proteins, unsaturated fats, and nuts, and low in processed meats, refined carbohydrates and sweetened beverages".<sup>1</sup> Adherence to a diet high in fibre and low in refined and processed food has been proven to provide numerous health benefits for general populations, and is applicable to patients with diabetic kidney disease.

## PROTEIN

KDIGO 2020 guideline recommends restricting protein intake to 0.8 g/kg body weight/day for non-dialysis-dependent diabetic kidney disease patients.<sup>1</sup> Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline for Nutrition in CKD: 2020 Update recommends restricting protein intake to 0.6-0.8 g/kg body weight/day under close clinical supervision for adults with stage 3 to 5 chronic kidney disease and diabetes.<sup>2</sup> Long-term effects of a high protein diet on kidney function are unknown. A high protein diet may cause harm by increased kidney amino acid excretion. A high protein diet could increase the acid load, which precipitates or worsens metabolic acidosis. It could also increase glomerular hyperfiltration, which causes glomerulosclerosis and tubulointerstitial injury. Excessive dietary protein intake increases the accumulation of metabolic waste products in patients with chronic kidney disease, which in turn may suppress appetite and stimulate muscle protein wasting. Low protein intake could potentially slow down the progression of chronic kidney disease, reduce clinical

symptoms and postpone the need to start dialysis treatment. However, diabetic kidney disease patients may already restrict their dietary carbohydrate and fat intake to manage diabetes and its complications. Following a very low protein diet further reduces their dietary calorie intake, which may cause malnutrition and may make hypoglycemia more common. Both KIDGO and KDOQI guidelines do not have any specific recommendation for the type of protein (plant vs animal) with regard to their respective effects on nutritional status, progression of kidney disease, phosphorus levels and blood lipid profile.<sup>1,2</sup>

## ENERGY

Adequate energy intake is required to spare/preserve dietary protein for tissue protein synthesis. However, excessive intake of dietary calories leads to overweight, which in turn worsens glycaemic and blood pressure control. KDOQI 2020 guideline recommends 25-35 kcal/kg body weight/day (actual body weight for those with underweight or normal body weight, adjusted body weight for those with overweight) for patients with diabetic kidney disease.<sup>2</sup> Dietary energy recommendation is based on individual nutritional needs, such as age, sex, level of physical activity, body composition, weight status goal, stage of chronic kidney disease, concurrent illness and presence of inflammation.

## CARBOHYDRATES

Good glycaemic control delays the progression of diabetic kidney disease. Choosing food high in fibre (such as whole-grain cereals, beans, nuts, fruits and vegetables) and low in glycaemic index helps to improve glycaemic control. People with diabetes should have an individualised meal plan with tailor-made carbohydrate distribution matching their glycaemic control and nutritional needs.

## FAT

Fat is a good source of energy and enhances the flavour of food. American College of Cardiology/ American Heart Association 2013 guideline on lifestyle management to reduce cardiovascular risk recommends dietary saturated fat intake should be limited to no more than 5-6% of total energy, and dietary trans fat intake should be minimal.<sup>3</sup> Food high in saturated fat include fatty meat, animal skin, tallow, lard, butter, high-fat dairy products and food made with palm oil. Trans fat is



commonly found in fried foods, baked goods, fast foods and processed foods.

## SODIUM

Excessive intake of dietary sodium affects the anti-proteinuric effect of angiotensin-converting enzyme inhibitors, as well as, control of proteinuria, hypertension and oedema. KDIGO 2020 guideline recommends restricting sodium intake to no more than 2 g (5 g sodium chloride) per day, except for people with sodium-wasting nephropathy, excessive sodium sweat losses during high temperatures, and high physical activity levels.<sup>1</sup> Hong Kong Population Health Survey 2014/15 showed that Chinese people aged 15-84 years had 8.8 g sodium a day, 4.4 times more than the recommendation.<sup>4</sup> To control dietary sodium intake, sodium-containing seasonings and preserved foods intake should be limited. Diabetic kidney disease patients should be advised the exchanges of sodium-containing seasonings. They are also encouraged to follow low sodium recipes and measure the quantity of sodium-containing seasonings when preparing food at home to improve the compliance with a low sodium diet. Natural seasonings (such as ginger, garlic, pepper, onion, etc.) may enhance the flavour of food. Eating out is a common habit among Hong Kong people. Tips for choosing low sodium menu items should be given to empower patients to make better eating out choices.

## POTASSIUM AND PHOSPHORUS

As renal function declines, people with diabetic kidney disease may have hyperkalemia and hyperphosphatemia. KDOQI 2020 guidelines recommend adjusting dietary potassium and phosphorus intake to maintain serum potassium and phosphorus within the normal range.<sup>2</sup> High potassium food include tea, coffee, soup, beans, nuts, dairy products, fruits, vegetables, mushrooms and low sodium salt. Low potassium fruits and vegetables should be chosen to maintain a low potassium balanced diet. Vegetables should be soaked and boiled to reduce their potassium content. High phosphorus foods include internal organ meat, meat and bone soup, dairy products, beans, nuts, chocolate, whole grain cereals and processed food with phosphorus food additives. Phosphorus additives are widely used in pre-packed foods. Ingredients lists in food labels of pre-packed foods should be checked to determine whether they contain phosphorus additives. Due to poorer phosphorus absorption in plant-based food than animal-based ones, soybeans and their products as protein sources and whole-grain cereals are allowed for people with hyperphosphatemia.

## CONCLUSION

Nutritional intervention is important in the management of diabetic kidney disease. It helps to optimise patients' nutritional status, align conflicting comorbid nutritional requirements, as well as, minimise risks imposed by comorbid conditions and alterations in metabolism on the progression of kidney disease.<sup>2</sup> Dietitians are responsible for carrying out the detailed dietary assessment of patients in order to understand

their needs. They also help patients design their individualised meal plans and empower patients to modify their dietary habits and lifestyles.

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# Better Care for Patients with Diabetes and Kidney Disease

## A Road Map for Diabetes Care: From Risk Assessment to Empowerment

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### INTRODUCTION

According to Diabetes Atlas (2019)<sup>1</sup>, about 463 million global adults have diabetes and the estimates rise to 578 million by the year 2030, and 700 million by 2045.

For the local situation in Hong Kong, the prevalence of diabetes in adults is estimated to be 10%, which means 1 in 10 people is diabetic, half of whom are undiagnosed; for age over 65 years, the estimate is 1 in 5 with diabetes. The Hospital Authority (HA) of Hong Kong, a government-subsidised non-profit organisation, provides over 65% of primary healthcare services and more than 90% of secondary and tertiary healthcare services<sup>2</sup>.

### THE ROLE OF DIABETES CENTRE

The centre is a hut to provide various services to support diabetes care for diabetic patients, their carers and even our healthcare professionals; these services include metabolic risk assessment, patient empowerment, diabetes intensification, help desk and coordination work.

### TARGETED ACTIVE INTERVENTION (TAI)

In the general medical specialist outpatient clinics (SOPC), doctors usually engage with patients with multiple medical problems within a very short consultation time. The referral rate of diabetes patients to structured management is far from satisfactory. The targeted Active Recruitment for Intervention (TAI) programme has been established within the Hospital Authority structure since 2017 to fill this service gap. A key target is for the patient group who have not undergone metabolic assessment within the previous two years. The initial intervention is to perform the metabolic risk assessment.

### CARE PATHWAY OF THE PATIENT JOURNEY

In line with the KDIGO 2020<sup>3</sup> recommendation (Fig. 1), the care pathway of the patient journey is

- ▶ To perform diabetes metabolic risk assessment followed by providing empowerment related to diabetes complication and target of metabolic control and its implications
- ▶ To stratify the risks

- ▶ To identify silent complications for early intervention
- ▶ To make a timely referral
- ▶ To coordinate the care planning

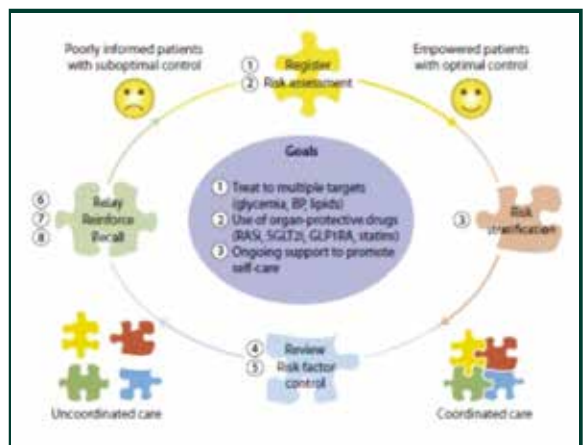


Fig. 1: Care pathway of the patient journey from risk assessment, empowerment, risk stratification, coordination care and review to risk factor control (Excerpted from KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease<sup>3</sup>)

### METABOLIC RISK ASSESSMENT (MRA)

#### Components of MRA

There are pull-down manuals to guide nurses to input data and information onto Clinical Management Service (CMS), including past medical history and family history; lifestyle assessment; medications; technology use; behavioural and diabetes self-management skills; physical assessment (including fundus and foot examination), and laboratory examination. The components of structured MRA is comprehensive comparably to the international guideline Standard of Medical Care in Diabetes 2021<sup>4</sup>.

Among the MRA components, nine parameters are used to evaluate the risk level through the risk engines: laboratory tests including HbA1c, LDL-cholesterol, serum creatinine, urine albumin, as well as clinical assessment including blood pressure, retinal screening, foot surveillance, and smoking status.



## Why is Conduction of MRA Important?

Diabetes is a chronic silent metabolic disease, and if not well controlled, micro and macrovascular disease will develop silently, progressively and can lead to organ damage such as late-stage retinopathy, nephropathy, ischaemic heart and stroke. Landmark studies<sup>6</sup> showed tight metabolic control brings markedly decrease complications.

Two reports are automatically generated: one report is the Metabolic Risk Assessment Report for healthcare professionals, and the other report is the Metabolic Risk Assessment Patient Summary in Chinese version for patients.

MRA can provide healthcare professionals essential biochemical data and metabolic-related risk status so as to take timely interventions to prevent, retard or delay the development of complications and to provide specific individualised treatment care planning. It is crucial that the diabetes patients and their carers have in their hands complete, detailed information on their diabetes condition and take an active role in self-care and self-management.

## EMPOWERMENT

Empowerment is a cornerstone for chronic disease management. Structured education can empower and motivate patients on diabetes self-care management. As patients have to spend most of their time 8,765 hours per year to take care of their metabolic disease, skills and knowledge in coping with changes in circumstances or emergent problems are very important.

There are three formats of education provided: structured educational class, interactive small group education and individualised education.

Structured educational class is usually arranged for those with newly diagnosed diabetes. The structured educational class contents include dietary instructions, exercise, medications, monitoring, the importance of adherence, and engaging diabetes on lifestyle modifications, sick day management, hypoglycaemia and hyperglycemia symptoms and treatment, pregnancy and travel issues. Peer support groups will be invited to share their experience.

Interactive small group education is usually arranged for those newly started on insulin therapy, or those requiring revision of their insulin therapy. During such small group teaching, patients and carers are given a chance to interact with each other and to share their daily encountered problems as well as ways to solve the problems.

Individualised education is usually arranged for those who do not meet metabolic targets or those with an emotional problem. Diabetes nurse carries out thorough assessment, empowerment and protocol-driven treatment intensification, explores the patient's emotions and barriers, personalises goal setting, provides resources and continues support.

## DIABETES TECHNOLOGY

Diabetes monitoring<sup>7</sup> is a key component in diabetes care management, especially as a way to engage patients and carers in daily living self-care. Real-time continuous glucose monitoring (CGM) system provides every 5 minutes interstitial glucose level (which is correlated with blood glucose). A tiny sensor is inserted into the subcutaneous layer; interstitial glucose data are transmitted to the reader or smartphone.

CGM provides information on immediate glucose level, earlier glucose trend, current direction, and the rate of change by an arrow sign (↗ ↘ ↙ ↚ →), thus alerting the patient to take action. There are two types of CGM systems which provide immediate glucose data.

### Real-time (rtCGM) System: 即時連續葡萄糖監測系統

This system automatically transmits a continuous stream of glucose data to the user, provides alerts and active alarm, and transmits glucose data (trend and numerical) in real-time to the smartphone.

### Intermittently Scanned (isCGM) System: 掃描式葡萄糖監測系統

The system provides the same type of glucose data but requires the user to purposely scan the sensor in order to obtain information; this system does not provide alerts and alarms.

Through instant data and the summary report, patients can understand how daily living (such as diet, exercise, medication and adherence) affects their glucose control. They are hence empowered to take on an active role in self-care diabetes.

Provision of comprehensive care focusing on risk evaluation and patient empowerment needs a team-based integrated care approach, involving not only the physician but also the nurse, dietitian, podiatrist, pharmacist, and physiotherapist. Peer group support<sup>3</sup> is also a must. The patient's care plan is reviewed on an ongoing basis, and the goalsetting is individualised according to the patient's personal needs.

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**A Trusted Intravenous Iron with a Well Established Efficacy and Safety Profile for CKD Patients<sup>1-4</sup>**

**Reliable Iron Delivery<sup>1,5,6,7</sup>**

**30 million patient years<sup>8</sup>**

**Lowest incident rate of hypersensitivity<sup>9,10</sup>**

**Proven safety and efficacy in clinical practice<sup>4</sup>**



#### Venoferr® Abbreviated Product Information

Please refer to the full local Product Insert before prescribing Venoferr®. **Pharmaceutical Form:** Solution for injection or concentrate for solution for infusion. **Indications:** Venoferr® is indicated for the treatment of iron deficiency anaemia where there is a clinical need for a rapid iron supply, in patients who cannot tolerate oral iron therapy or who are non-compliant, or in active inflammatory bowel disease where oral iron preparations are ineffective. Venoferr® should only be administered where the indication is confirmed by appropriate laboratory tests. **Dosage and Administration:** Venoferr® has exclusively to be administered intravenously by drip infusion, by slow injection or directly into the venous limb of the dialyser and is not suitable for intramuscular use and for total dose infusion (TDI), where the full dose of iron required, representing the patient's total iron deficit is administered in one complete infusion. The dose of Venoferr® is determined by the haemoglobin level and body weight, and must be determined individually for each patient according to the total iron deficit. The table in the Product Insert should be used to determine the cumulative iron dose. For intravenous injection, the total single dose per day must not exceed 200 mg of iron given not more than three times per week. For intravenous infusion, the total single dose per day must not exceed 500mg of iron given not more than once per week. **Contraindications, Warnings, Overdose:** The use of Venoferr® is contraindicated in cases of anaemia not caused by iron deficiency, iron overload or disturbances in utilisation of iron, known hypersensitivity to Venoferr® or any of its inactive components, and pregnancy first trimester. Parenterally administered iron preparations can cause allergic or anaphylactoid reactions, which may be potentially lethal. In case of hypersensitivity reactions, healthcare professionals should immediately stop the iron administration. In the case of a mild allergic reaction, antihistamines should be administered; in the case of a serious anaphylactoid reaction adrenaline should be administered immediately. Facilities for cardio-pulmonary resuscitation must be available. Venoferr® should be administered with care in patients with liver dysfunction. Each patient should be observed for adverse effect for at least 30 minutes following each Venoferr® injection. Parenteral iron should only be administered after careful risk/benefit assessment. Venoferr® must be used with care in patients with acute or chronic infection. Hypotensive episodes may occur if the injection is administered too rapidly. Paravenous leakage must be avoided because leakage of Venoferr® at the injection site may lead to pain, inflammation, tissue necrosis and brown discoloration of the skin. **Interactions:** Venoferr® should not be administered concomitantly with oral iron preparations since the absorption of oral iron is reduced. **Pregnancy and lactation:** Data on a limited number of exposed pregnancies indicated no adverse effects of Iron Sucrose on pregnancy or on the health of the foetus/newborn child. No well-controlled studies in pregnant women are available to date. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Nevertheless, risk/benefit evaluation is required. Venoferr® should not be used during pregnancy unless clearly necessary. Treatment should be confined to the second or third trimester, provided the benefits of treatment clearly outweigh the potential serious risks to the foetus. **Undesirable effects:** Common (1% to <10%): transient taste perversions (in particular metallic taste), Uncommon (0.1% to <1%): headache, dizziness, hypotension and collapse, tachycardia and palpitations, bronchospasm, dyspnoea, nausea, vomiting, abdominal pain, diarrhoea, pruritus, urticaria, rash, exanthema, erythema, muscle cramps, myalgia, fever, shivering, flushing, chest pain and tightness, injection site disorders such as superficial phlebitis, burning, swelling. Rare (0.01% to <0.1%): paraesthesia, anaphylactoid reactions, peripheral oedema, fatigue, asthenia, malaise. **Overdose:** Overdosage can cause acute iron overloading which may manifest itself as haemochromatosis. Overdosage should be treated with supportive measures and, if required, with an iron chelating agent. **Legal classification:** Part 1, first and third Schedule poison. **Date of preparation:** 01/2019. Full prescribing information available upon request.

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#### Abbreviations:

CKD = Chronic Kidney Disease, HD = Haemodialysis, IV = Intravenous, ESA = Erythropoiesis Stimulating Agent, TSAT = Transferrin Saturation, Hb = Haemoglobin



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# Nursing Management in Diabetic Patients on Renal Replacement Therapy

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Ms HO Hau-sim

## INTRODUCTION

Diabetes is the leading cause of chronic kidney disease (CKD).<sup>1</sup> Approximately one-third of patients with diabetic nephropathy progress to end-stage renal disease requiring some form of renal replacement therapy (RRT), which in turn carries an impact on glycaemic control and diabetic care.<sup>2</sup> Reducing further macrovascular complications in dialysis patients and preventing hypoglycaemia improve the quality and length of patients' life. The care of diabetic patients on RRT is multifaceted and complex. This paper addresses nursing management in diabetic patients receiving RRT, with the aim of improving their clinical outcomes.

Immediately upon beginning dialysis, the patient's diabetes regimen needs to be reviewed because both peritoneal dialysis (PD) and haemodialysis (HD) each has a different effect on glycaemic control.<sup>3</sup>

## NURSING MANAGEMENT IN PD

Conventional PD solution contains glucose as an osmotic agent to achieve fluid removal. Patients receiving PD treatment are exposed to a high glucose load from the solution.<sup>3</sup> Continuous glucose absorption during dialysis (daily 100 - 300 gm) can result in anorexia, weight gain, elevated blood triglyceride levels and, for diabetic patients, hyperglycaemia.<sup>4</sup> A working alliance with patients and caregivers is required to enhance their capacity for self-care. Nursing care is implemented as detailed below:

1. As cardiovascular disease is the leading cause of death<sup>4</sup>, patient empowerment is essential through home blood pressure monitoring and fluid control. Patients and their caregivers are taught fluid management by being shown how to adjust the strength of glucose PD solution and how to control the patient's diet. Fluid status can be evaluated using a body composition monitor machine. Blood pressure less than 140/90 mmHg is recommended.<sup>5</sup> Regular blood pressure monitoring is important.
2. Patients on PD are more likely to have hyperglycaemia with hyperinsulinemia.<sup>2</sup> They are advised to perform self-monitoring of blood glucose (SMBG), including increasing the frequency of monitoring if needed. They are also educated on the relationship between the effect of PD solution, the action of insulin and its injection schedule. Combining the use of non-glucose based PD solution, such as icodextrin

or amino acid containing solution, to reduce glucose exposure may require. The site for insulin injection should be on the area of non-PD catheter insertion and regularly rotated within the same area to reduce variability in absorption.<sup>6</sup> Injection into the hypertrophic and atrophic areas should be avoided. Targeted glycosylated haemoglobin around 7% in diabetic PD patients, and maybe up to 8.5% in patients at risk for hypoglycaemia, is recommended.<sup>5</sup> Patient and caregivers should be referred back to diabetes nurses for further education if there is consistent high blood glucose.

3. If the patient needs to travel whilst they are on PD, pre-travel preparation should be stressed. Information on PD solution ordering and delivery should be provided, and the patient should be advised to continue blood glucose monitoring during travel. Regular insulin before the meal will be added if appetite improves. Prolonged fasting should be avoided. When planning any period of travel, especially international travel, nephrologist's advice should be sought to discuss the suitability of emptying the abdomen for the long haul. In cases of international travel, it is essential to adjust insulin injections and mealtimes while crossing the time zones.

## NURSING MANAGEMENT IN HD

Haemodialysis normally takes place two to three times a week for four to six hours per session to remove toxins and excess water. Hypoglycaemia may occur due to glucose loss to the dialysis solution and diffusion of glucose into erythrocytes.<sup>7</sup> Some HD patients are discouraged from eating during dialysis as this may cause hypotension and increase the risk of further hypoglycaemia. Nursing assessment on HD schedule, episodes of hypotension or hypoglycaemia, medication compliance and mealtime on HD day needs to be carried out to provide individualised care. The recommended nursing interventions are as follows:

1. Diabetes treatment is adjusted according to the prescribed dialysis regimens.
2. Education on SMBG and insulin adjustment, with particular reference to different insulin doses on HD days versus non HD days and the SMBG profile, is required. Dosage for patients taking twice daily injections of premixed insulin needs to be reviewed to determine whether the dose



needs to be reduced or omitted before dialysis.<sup>7</sup> A smaller dose may be prescribed after dialysis, with the normal dose being given on non-dialysis days.<sup>3</sup>

3. Patients and caregivers need to be taught to differentiate between hypotension and hypoglycaemia. The use of glucose containing dialysis solution to prevent intradialytic hypoglycaemia can be implemented.<sup>7</sup> Rescheduling of mealtimes on HD days may be required, and administration of a prescribed dose of 50% dextrose solution (D50) during HD can be given if hypoglycaemia occurs.
4. Restriction in potassium intake is necessary.<sup>8</sup> Dietary advice, specifically to eat fruits and vegetables that are lower in the potassium content, and to limit the intake of nuts, is an essential element of care. Fruits and vegetables should also be included in line with normal diabetic diet recommendations. The patient's medications are reviewed to avoid using drugs that impair renal excretion of potassium.

## NURSING MANAGEMENT IN KIDNEY TRANSPLANTATION

Kidney transplantation is the preferred form of RRT for end-stage renal disease.<sup>9</sup> The use of long term immunosuppressive drug treatment may impair glycaemic control due to the side effects of high dose steroids and infection.<sup>9</sup>

Providing safe and effective nursing care can minimise avoidable complications and achieve optimal clinical outcomes. The nurse would:

1. Establish a good rapport with the patient and caregivers to enhance mutual goal setting and regain the patient's sense of wellbeing.
2. Educate on the relationship between the effect of immunosuppressive drugs and the action of Insulin.
3. Reinforce the necessity of taking immunosuppressants at a consistent time of the day.
4. Emphasise the importance of patient self-adjustment of anti-diabetes treatment, including medication and diet.
5. Educate on preventive measures, warning signs, daily monitoring strategies, and handling procedures for potential complications.
6. Emphasise and educate on the importance of lifestyle modifications such as weight reduction to prevent diabetes and other metabolic complications.
7. Refer patients for regular metabolic complication screening if necessary.

Furthermore, empowering the patient to actively engage in self-management and lifestyle modification and to make informed choices and decisions is important to achieve optimal diabetes and life goals.

A. The strategies on self-care management are implemented as the following:

1. Quitting smoking is strongly encouraged. Referral to a smoking cessation ambassador may be required.
2. Reducing or stopping alcohol drinking is advised.
3. A high fibre diet and regular exercise are encouraged to prevent constipation.
4. Daily SMBG helps to prevent hypoglycaemia and improves glycaemic control. Recording of pre- and post-meals or pre- and post-PD solution exchange is necessary. Patients are educated to recognise and manage hypoglycaemic symptoms and to adjust the diabetes medications accordingly.

B. In addition, the following strategies on lifestyle modification are needed:

1. Encouraging physical activities  
Patients with diabetes on RRT may have lower levels of physical activity because of functional limitations.<sup>8</sup> Despite these limitations, participation in daily physical activity is recommended. Physical activity can improve insulin sensitivity and endothelial function; and reduce inflammatory markers.<sup>8</sup> Moderate-intensity physical activity for a cumulative duration of at least 150 minutes per week or as much as physically tolerate is encouraged. Aerobic or muscle strengthening exercises such as cycling, use of an exercise bike, Tai Chi, or climbing stairs can be performed, and exercise can be incorporated into the general activities of daily living, such as household chores and shopping. Lifting heavy weights should be avoided.
2. Reduction in carbohydrate intake by rearranging eating patterns  
It is suggested to eat vegetables first, then meat, with carbohydrate foods, such as rice or noodles, to follow. Increasing the intake of non-starchy vegetables, decreasing added sugars and refined grains, and choosing more whole foods over refined and highly processed foods can be implemented.<sup>8</sup>
3. Protein and phosphate diet, and salt modification

### 3.1 Protein intake

Dialysis causes a catabolic response. Amino acid loss on PD and HD and high blood urea leads to depressed appetite, increased catabolism, and decreased muscle mass. A higher protein intake of between 1 and 1.2 g protein/kg/day in diabetic patients undergoing dialysis is recommended to avoid hypoglycaemia.<sup>8</sup> Small but frequent meals can also help a reduced appetite. Patients with low blood albumin or persistent poor appetite are referred to a dietitian for further assessment.

### 3.2 Phosphate intake

Patients are advised to avoid high phosphate foods such as cereal, internal organs, nuts, and milk products.





### 3.3 Salt intake

Patients with CKD are often salt sensitive and cannot regulate blood pressure and extracellular fluid volume when salt intake is high. Patients who are accustomed to consuming high sodium intake may need support in changing to a lower-sodium diet, which may require limiting their favourite foods. Using culturally appropriate foods and incorporating a whole-food diet may help break the cycle of adaptation to a highly processed diet. Patients are advised to buy fresh foods, cook at home, and reduce sauces, both at home and when eating out. This can be achieved in restaurants by asking for any sauces, dressings, and gravies to be served in a separate dish. Pineapple juice or unseasonal rice vinegar offer an alternative to salty sauces like soy sauce. Sweet, sour, bitter, and spicy or hot flavours can be used to season food to enhance taste, instead of salt. Patients are advised on the healthiest diet for their condition, focusing on fresh foods over processed foods, and promoting liaising with a dietitian.

Patients and caregivers are educated to read food labels and choose lower-salt brands when possible. The goal is < 2 g of sodium or 5 g of table salt daily.<sup>8</sup> Salty, processed meats should be avoided.

## CONCLUSION

Optimal management of the diabetic patient with diabetes receiving RRT is a complex, multidisciplinary, cross-functional team effort. Establishing a comprehensive programme including renal and diabetes nursing care is essential to reduce further complications and to improve quality of life, thus optimising the patient's clinical outcomes.

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## HDx Therapy may Improve PROs related to Quality of Life



Expanded Hemodialysis (HDx)

Dialysis patients experience a severe burden of physical and emotional symptoms such as Restless Leg Syndrome (RLS), pruritis, dizziness and headaches.<sup>1</sup>

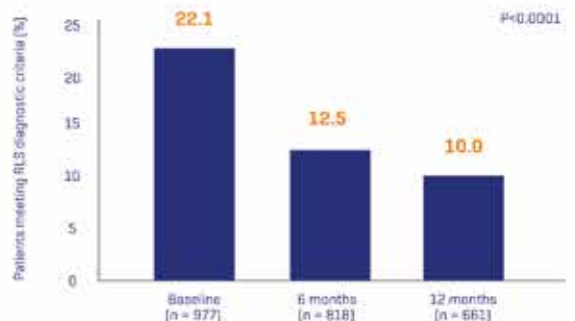
Expanded Hemodialysis (HDx) has emerged as a promising therapy to help patients alleviate these symptoms, thereby allowing them a better quality of life with improved sleep, decreased itching symptoms, dizziness.<sup>3</sup>

## Impact to QoL

Chronic renal patients experience poor quality of life due to the symptoms of end-stage renal disease, accompanied by the physical and emotional burdens of their treatments. RLS, which is commonly observed in these patients, compromises a patient's quality of life - especially when it occurs in its most severe form and is accompanied by depressive symptoms.<sup>2</sup>

A large observational registry study in prevalent HD patients found after 6 months of HDx therapy there was found to be an approximate 50% reduction in the number of patients meeting RLS criteria.<sup>3</sup>

Figure 1. Longitudinal Changes in Patients Meeting Restless Legs Syndrome (RLS) Diagnosis over 12 Months of Follow Up. Abbreviations: RLS, Restless Legs Syndrome. Adapted From Alarcon Et AL.





## Sleep well

Pruritus is a predictor of poor sleep. Together with the physical and emotional burden of end-stage renal disease, it severely impacts a patient's quality of life.<sup>4</sup>

Lim et al. show in a randomized controlled trial (RCT) that even if at baseline, the morning pruritus intensity was worse in the medium cut-off (MCO) group compared with the high-flux group this difference was not observed after 12 weeks of HDx therapy.<sup>5</sup>

After 12 weeks of HDx therapy, patients experienced less symptoms of morning pruritus and less frequent sleep disturbances caused by pruritus-related scratching.

Reduction ratio (%)	BASELINE			12 WEEKS		
	MCO [n = 24]	High-flux [n = 25]	P	MCO [n = 24]	High-flux [n = 25]	P
<b>Severity</b>						
Morning	1.92 ± 1.06	1.40 ± 0.50	<b>0.033</b>	1.54 ± 0.72	1.64 ± 0.86	<b>0.667</b>
Afternoon	2.00 ± 1.14	1.72 ± 0.84	0.332	1.88 ± 0.95	1.84 ± 1.07	0.904
<b>Distribution</b>						
Morning	1.40 ± 0.58	1.48 ± 0.71	0.736	1.29 ± 0.46	1.69 ± 0.64	<b>0.034</b>
Afternoon	1.46 ± 0.59	1.56 ± 0.96	0.659	1.38 ± 0.65	1.56 ± 0.71	0.347
<b>Sleep Disturbance</b>						
Frequency of waking up from sleep	0.83 ± 1.05	0.88 ± 1.28	0.850	0.75 ± 0.89	1.32 ± 1.60	0.126
Frequency of scratching during sleep	0.38 ± 0.92	0.24 ± 0.72	0.571	0.25 ± 0.52	1.00 ± 1.47	<b>0.023</b>
Total score by measuring system	6.58 ± 7.74	7.20 ± 7.58	0.530	5.92 ± 5.98	9.92 ± 8.23	0.152
<b>VAS scoring system</b>						
Morning	2.58 ± 2.24	2.14 ± 2.28	0.496	2.50 ± 1.93	3.34 ± 2.82	0.236
Afternoon	3.04 ± 2.57	2.74 ± 2.53	0.680	3.46 ± 2.32	4.24 ± 3.18	0.335
Average	2.81 ± 2.18	2.44 ± 2.31	0.565	2.98 ± 1.88	3.79 ± 2.91	0.266

Table 1. Assessment of uremic pruritus at baseline and 12 weeks. Abbreviations: MCO, medium cut-off; VAS, visual scale. Adapted from Lim et al.

## Reduce breathlessness and dizziness

Health-related quality of life is a patient-reported outcome that considers a dialysis patient's point of view and supports the evaluation of outcomes and healthcare quality.

Research from Alarcon JC et al. shows an improved dialysis symptom index (DSI) after 6 months of HDx therapy. All 30 DSI items, each targeting a specific physical or emotional symptom, were reported with marginally significant reductions in shortness of breath, dizziness/light-headedness, and difficulty falling asleep.<sup>6</sup>



DSI Domain	Statistic	BASELINE	6 MONTHS	12 MONTHS	P value
		n = 977	n = 813	n = 842	
Number of symptoms	Mean	10.3	10.3	10.0	0.1 <sup>a</sup>
	SD	6.5	6.7	6.6	
	IQR	10	10	9	
Symptom severity score	Mean	30.7	29.8	28.5	0.00098 <sup>b</sup>
	SD	22.3	22.0	21.7	
	IQR	26	28	31	

Table 2. Changes in Dialysis Symptom Index (DSI) Over 12 Months of Follow Up. <sup>a</sup> by Friedman's test. <sup>b</sup> by ANOVA. Abbreviations: ANOVA, analysis of variance; DSI, dialysis symptom index; IQR, interquartile range; SD, standard deviation. Adapted from Alarcon et al.



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# As a Renal Transplanted Diabetic, How Did I Help Myself?

## Ms Maggie MM NG

*Vice-Chairperson, Hong Kong Kidney Foundation*



Ms Maggie MM NG

I had suffered end-stage renal failure since 1985 and luckily underwent renal transplantation in 1986, following which my life returned to normal. But I would never forget my diet restrictions during the haemodialysis months before the transplantation.

In 1992, I was pregnant; everything went smoothly, although my condition was described as a high-risk pregnancy. However, I started to have high blood pressure at week 19 and gestational diabetes at week 32. I needed to restrict my diet again and even needed to inject insulin. Six weeks passed. The baby was born, and my blood sugar was back to normal. My worries seemed gone.

A few years later, I was diagnosed as a diabetic again. It was a tragic news to me. No matter how well I kept my renal function, I was deemed a sufferer of one more chronic disease “diabetes”. The disease seems to have no symptoms, but I must control my diet thereafter. It is really a punishment for a person who loves food so much. I tried to convince myself: diabetes is better than renal failure; the treatment is only through oral medication and at times insulin injection rather than renal dialysis. I encouraged myself to face one more chronic disease just like how I faced renal failure. I fully understand I will get along with two diseases till my life ends. I reminded myself that I must manage two diseases with the same attitude. I need to make ‘friends’ with them. I should try to learn more about the disease, such as its complications and treatments. Honestly speaking, I need to have the determination to do disease management.

Controlling my blood sugar and keeping it stable is the main task of my diabetes management. I prick my fingertip with a lancet most of the days; dropping my blood on the test kit to check my blood sugar sounds simple but in practice it is hard work. The ten fingertips become painful after years of checking. However, I must check to see if my blood sugar level is too low or too high. It is also a checkbox to see if my eating is right or wrong. As a diabetic, I always keep my blood sugar test kit, medicine and insulin with me. This “tool kit” is especially important when I travel abroad since I am not sure whether I can buy them in foreign countries. If I run into a shortage of the instrument and medicine, it could be life-threatening.

Diabetes management is mainly based on check and balance. Checking blood sugar is correlated with food eating and medicine dosages. The Diabetes nurse, along with the dietician, will teach us how to take a diabetic

diet. They will remind me to inject the insulin dosage based on the blood sugar level and on the “equivalent to the food consumption” level.

The nurse advised me to set up a steady life pattern. Check the blood sugar, take medicine, inject insulin if needed and take three meals routinely. Such a steady life pattern allows stable control of the disease. However, I cannot keep this pattern easily. I need to work, to go out to meet people, and to eat at different restaurants. It is difficult to control the sugar consumption of various cuisines. It will cause fluctuation in my blood sugar level and the insulin level, which will gradually harm my health. I need to have stricter discipline over myself.

Besides the blood test, I use the sensor to check blood sugar as well. For accuracy, I will cross check the sensor with the blood test to find the true figure. The sensor is more convenient for me to check blood sugar when I am on my own, to see if they are too high or too low. The sensor can help me to decide whether to add insulin or take in some sugar in different situations. From my experience, Thai food, Vietnamese food and even Cantonese Yum Chai are at high risk of blood sugar surges. All kinds of starchy food, desserts and fruits are evil to diabetics. I will limit the consumption and will avoid them all.

Diabetes management involves a close relationship with the medical professional. I must have a diary with my blood sugar record. A steady follow up. A full set of blood tests including the HbA1C. I will undertake a full assessment for diabetic complications. Diabetic complications can be life-threatening. I cannot accept myself suffering from heart disease, blindness, limbs amputation ...

Exercise is good for controlling blood sugar level. I have the pleasant experience of seeing my blood sugar level lowered after exercise. I will inject less insulin, and it will benefit my health as well.

Diabetes is troublesome; however, it is, and can be, manageable.



# Dermatology Quiz

**Dr Lai-yin CHONG**

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Specialist in Dermatology & Venereology



Dr Lai-yin CHONG



**Fig.1: Bilateral multiple discrete papules over the cheeks**

This 25-year-old lady developed multiple discrete skin-coloured papules over her cheeks (Fig. 1). These lesions were asymptomatic, but they slowly increased in number over a few years. She was told in a beauty salon that these were infectious warts.

## Questions

1. What are your clinical diagnosis and differential diagnoses?
2. How can you confirm the diagnosis?
3. What is your treatment for these lesions?

(See P.41 for answers)

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 In an observational study on patients with CKD not on dialysis, 1795 (29.7%) subjects initiated dialysis during the study,  
 • After the first 3-month interval following dialysis initiation, the mean Hb concentration started to increase and then stabilized at ~11.5 g/dL  
 • Mean weekly NESP® dose was also relatively stable from Month 6 post-dialysis onwards

**References:** 1. Sinha SO, Bandi VK, Bheemareddy BR, et al. BMC Nephrol 2019;20:50. 2. Galle JC, Addison J, SuranyiMG, et al. Nephrol Dial Transplant. 2016;31:2073-85.

**Abbreviated Package Insert of NESP injection plastic syringe 20 µg/0.5mL, 40 µg/0.5mL, 120 µg/0.5mL or 180 µg/0.5mL.**  
**Composition:** Darbepoetin α. **Indication:** Renal anemia. **Dosage and Administration:** <b>CRD patients</b>: Initial dose: 20 µg single IV inj q1w, (when switching from erythropoietin prep, initial dose: 15-40 µg single IV inj q1w); maintenance dose: 15-60 µg single IV inj q1w. If alleviation of anaemia is maintained by q1w inj, dose can be changed to 2x/dose of the initial dose and administered as IV inj q2w. **<b>ESRD patients</b>:** Initial dose: 30 µg single SC or IV inj q2w, (when switching from erythropoietin prep, initial dose: 30-120 mcg single SC or IV inj q2w); maintenance dose: 30-120 mcg single SC or IV inj q2w. If alleviation of anaemia is maintained by q2w inj, dose can be changed to 2x/dose of the initial dose q1w. **Max: 180 mcg single inj.** **Contraindications:** Hypersensitivity. **Precautions:** Patients w/ MI, pulmonary infarction, cerebral infarction or those w/ history of these conditions who may experience thromboembolism; HTN history of hypersensitivity; allergic predisposition; Start therapy when Hb conc is <10-11 g/dL. Confirm the diagnosis of renal anemia. Assess risk of shock. Monitor Hb conc, Hct, iv, BP, (fluid & electrolyte balance and renal function for patient with CKD not on dialysis) at regular intervals; hypertensive encephalopathy; pure red cell aplasia; hyperkalaemia; Fe deficiency; Shunt occlusion or residual blood in hemodialyzers; Biting & skin exfoliation reactions; Concomitant use w/ erythropoiesis-stimulating agents; Pregnancy & lactation; Children; Elderly. **Clinically significant adverse reactions:** cerebral infarction; cerebral hemorrhage; hepatic function disorder &/or jaundice; hypertensive encephalopathy; shock &/anaphylactoid reactions; pure red cell aplasia; myocardial &/or pulmonary infarction. **PIP:** inj (pre-filled syringe): 20 µg /0.5 mL, 40 µg /0.5 mL, 120 µg /0.5 mL, or 180 µg /0.5 mL. Approved version of package insert Nov 2019.

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 KRHK-NES-D-APP2021



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30		

\* Zoom Lecture Empowering Heart Failure Treatment: the EMPEROR of SGLT2 Inhibition (Sodium-glucose cotransporter-2 Inhibition) – Online

\* Certificate Course on Renal Medicine 2021 (Video Lectures)

\* Zoom Lecture Do Older Adults Require Enhanced Influenza Vaccines? - Online

\* Certificate Course on Respiratory Medicine 2021 (Video Lectures)

\* Certificate Course on Complaint Management 2021 (Video Lectures)

\* Zoom Lecture Spirit of Understanding and Parenting Skills for ADHD Children during the COVID-19 Pandemic - Online

\* Zoom Lecture Long-term Care after Percutaneous Coronary Intervention (PCI) - Online

\* Zoom Lecture Certificate Course for GPs 2021 - Update on Management of Prostate Cancer - Online

\* The Hong Kong Neurosurgical Society Monthly Academic Meeting –To be confirmed

\* Stroke Prevention and Emergency Management: How to Optimize Atrial Fibrillation (AF) Management for your Patients? - Online

\* Certificate Course on Respiratory Medicine 2021 (Video Lectures)

\* Certificate Course on Renal Medicine 2021 (Video Lectures)

\* Recent Update of Treatment of Respiratory Infectious Disease - Online

\* FMSHK Executive Committee Meeting

\* Certificate Course on Renal Medicine 2021 (Video Lectures)

\* Certificate Course on Respiratory Medicine 2021 (Video Lectures)

\* Zoom Lecture HKMA-GHK CME Programme Topic: Update on Minimally invasive spine surgery - Online

\* Certificate Course on Complaint Management 2021 (Video Lectures)

\* Certificate Course on Renal Medicine 2021 (Video Lectures)

\* The Missing Puzzles? Holistic Management of Cardiorenal Disease with Diabetes - the CalMe Approach - Online

\* CME Webinar Liquid Biopsy for Early Cancer Detection in the Nasopharyngeal Cancer Model

\* Certificate Course on Respiratory Medicine 2021 (Video Lectures)

\* Patient Benefit on Inhaled Corticosteroids Usage in Post COVID Era - Online

\* Certificate Course on Renal Medicine 2021 (Video Lectures)





Date / Time	Function	Enquiry / Remarks
<b>1 WED</b> 2:00 PM	<b>Zoom Lecture</b> <b>Do Older Adults Require Enhanced Influenza Vaccines? - Online</b> Organiser: Hong Kong Medical Association Speaker: Dr TSANG Kay-yan	HKMA CME Dept. Tel: 2865 0943 1 CME Point
	7:00 PM <b>Certificate Course on Respiratory Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Maureen WONG	Ms Vienna LAM Tel: 2527 8898
<b>2 THU</b> 7:00 PM	<b>Certificate Course on Renal Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Sze-kit YUEN, Dr Chun-hay TAM	Ms Vienna LAM Tel: 2527 8898
<b>3 FRI</b> 2:00 PM	<b>Zoom Lecture</b> <b>Empowering Heart Failure Treatment: the EMPEROR of SGLT2 Inhibition (Sodium-glucose cotransporter-2 Inhibition) - Online</b> Organiser: HKMA-Shatin Community Network Speaker: Dr Anthony Yiu-tung WONG	Ms. Candice Tong Tel: 2865 0943 1 CME Point
<b>7 TUE</b> 7:00 PM	<b>Certificate Course on Complaint Management 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Suk-chong LEUNG, Ms Asha SHARMA	Ms Vienna LAM Tel: 2527 8898
<b>8 WED</b> 7:30 AM	<b>The Hong Kong Neurosurgical Society Monthly Academic Meeting -To be confirmed</b> Organiser: Hong Kong Neurosurgical Society Speaker(s): Dr Victor Ka-ho HUI Chairman: Dr Danny Tat-ming CHAN Venue: Conference Room, F2, Department of Neurosurgery, Queen Elizabeth Hospital; or via Zoom meeting	CME Accreditation: 1.5 points College of Surgeons of Hong Kong Enquiry: Dr Calvin MAK Tel: 2595 6456 Fax. No.: 2965 406
	7:00 PM <b>Certificate Course on Respiratory Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr CM WONG	Ms Vienna LAM Tel: 2527 8898
<b>9 THU</b> 2:00 PM	<b>Zoom Lecture</b> <b>Certificate Course for GPs 2021 - Update on Management of Prostate Cancer - Online</b> Organiser: HKMA-KLN East Community Network, HA-United Christian Hospital & HK College of Family Physicians Speaker: Dr LAM Ho-ching, Dr CHAN Hoi-chak	Ms Elise Haw Tel: 2660 7720 1 CME Point
	2:00 PM <b>Zoom Lecture</b> <b>Myths of Coughing in Children - GP Perspective - Online</b> Organiser: HKMA-HK East Community Network Speaker: Dr Philip Chak-on SHAM	Ms Candice Tong Tel: 2865 0943 1 CME Point
	7:00 PM <b>Certificate Course on Renal Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Gensy Mei-wa TONG, Dr Elaine Tsz-ling HO	Ms Vienna LAM Tel: 2527 8898
<b>10 FRI</b> 2:00 PM	<b>Zoom Lecture</b> <b>Long-term Care after Percutaneous Coronary Intervention (PCI) - Online</b> Organiser: HKMA-KLN City Community Network Speaker: Dr Henry Ying-lung KOK	Ms Candice Tong Tel: 2865 0943 1 CME Point
<b>14 TUE</b> 2:00 PM	<b>Zoom Lecture</b> <b>Spirit of Understanding and Parenting Skills for ADHD Children during the COVID-19 Pandemic - Online</b> Organiser: HKMA-YTM Community Network Speaker: Dr CHONG King-ye	Ms Candice Tong Tel: 2865 0943 1 CME Point
	7:00 PM <b>Certificate Course on Complaint Management 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Kai-ming CHOW	Ms Vienna LAM Tel: 2527 8898
<b>15 WED</b> 2:00 PM	<b>Zoom Lecture</b> <b>Stroke Prevention and Emergency Management: How to Optimize Atrial Fibrillation (AF) Management for your Patients? - Online</b> Organiser: HKMA-Central, Western & Southern Community Network Speaker: Dr Lee Chi-nam	Ms Antonia Lee Tel: 2865 0943 1 CME Point
	7:00 PM <b>Certificate Course on Respiratory Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr HC FAN, Dr YK LAM	Ms Vienna LAM Tel: 2527 8898
<b>16 THU</b> 2:00 PM	<b>Zoom Lecture</b> <b>Recent Update of Treatment of Respiratory Infectious Disease - Online</b> Organiser: HKMA-KLN East Community Network Speaker: Prof. Ivan Fan-ngai HUNG	Ms Antonia Lee Tel: 2865 0943 1 CME Point
	7:00 PM <b>Certificate Course on Renal Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Cherry Pui-ye LAW, Dr Desmond Yat-hin YAP	Ms Vienna LAM Tel: 2527 8898
	8:00 PM <b>FMSHK Executive Committee Meeting</b> Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Nancy CHAN Tel: 2527 8898
<b>21 TUE</b> 2:00 PM	<b>Zoom Lecture</b> <b>HKMA-GHK CME Programme</b> <b>Topic: Update on Minimally invasive spine surgery - Online</b> Organiser: Hong Kong Medical Association and Gleneagles Hong Kong Hospital Speaker: Dr. Eric Cheung-hing LAM	HKMA CME Department Tel: 2865 0943 1 CME Point
	7:00 PM <b>Certificate Course on Complaint Management 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Kim-lian ONG	Ms Vienna LAM Tel: 2527 8898
<b>23 THU</b> 7:00 PM	<b>Certificate Course on Renal Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Anthony Kai-ching HAU, Dr Joseph Ho-sing WONG	Ms Vienna LAM Tel: 2527 8898
<b>28 TUE</b> 2:00 PM	<b>Zoom Lecture</b> <b>Patient Benefit on Inhaled Corticosteroids Usage in Post COVID Era - Online</b> Organiser: HKMA-KLN West Community Network Speaker: Dr. Veronica Lee CHAN	Ms Antonia Lee Tel: 2865 0943 1 CME Point







Date / Time	Function	Enquiry / Remarks
<b>29 WED</b> 7:00 PM	<b>Certificate Course on Respiratory Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr CF CHOY	Ms Vienna LAM Tel: 2527 8898
<b>30 THU</b> 2:00 PM	<b>Zoom Lecture</b> <b>The Missing Puzzles? Holistic Management of Cardiorenal Disease with Diabetes - the CaReMe Approach - Online</b> Organiser: HKMA-New Territories West Community Network Speaker: Dr Kelvin Ki-wan CHAN	Ms Antonia LEE Tel: 2865 0943 1 CME Point
2:00 PM	<b>CME Webinar</b> <b>Liquid Biopsy for Early Cancer Detection - the Nasopharyngeal Cancer Model</b> Organiser: The Hong Kong Chinese Medical Association Speaker: Dr Jacky LAM	Ms Katrina TONG hkma100@gmail.com
7:00 PM	<b>Certificate Course on Renal Medicine 2021 (Video Lectures)</b> Organiser: The Federation of Medical Societies of Hong Kong Speaker: Dr Wai-yan LAU, Dr Ka-fai YIM	Ms Vienna LAM Tel: 2527 8898



## Society News

## The Hong Kong Orthopaedic Association

## HISTORY

In September 1962, a group of orthopaedic surgeons came together and formed the Hong Kong Orthopaedic Club. With the effort of Prof Hodgson, the Club Chairman, and all the other founding members, an inaugural meeting was held on 4 November 1965. Since then, the Hong Kong Orthopaedic Association (HKOA) was formally established. Prof Hodgson was voted into the office as the first President of the HKOA, and Dr Arthur Yau was being elected as the first Honorary Secretary.



## MISSIONS

The HKOA aims to promote the science, art and practice of orthopaedic surgery and its allied disciplines. We determine to develop, support, and augment the education of individuals who are engaged in the practice of orthopaedic surgery for the public benefit. We also strive to support the research and education on orthopaedic medicine and therapy.

## SUBSPECIALTY CHAPTERS

Orthopaedic surgery has been rapidly growing and developing with more and more diversification. In response to the advancement of orthopaedic knowledge and surgical technology, five subspecialty chapters have been formed under the HKOA. They are the Sports Medicine Chapter, the Foot and Ankle Chapter, the Spine Chapter, the Adult Joint Reconstruction Chapter and the Paediatric Orthopaedics Chapter. Each of these subspecialty chapters are operated by their own chapter council and under the supervision of the HKOA. Academic activities, including seminars and hands-on practical workshops are regularly organised by the chapters for our fellows and members.

## HONG KONG ORTHOPAEDIC ASSOCIATION ANNUAL CONGRESS

Since 1981, the HKOA Annual Congress has always been the annual highlight event as well as the important platform in sharing our clinical research and practice with both the local and international orthopaedic community. Distinguished guests and scholars are invited every year to join the Congress and enlighten us with their clinical experience, research findings and up-to-date knowledge.

With the great effort of our Annual Congress Co-Chairmen, Dr Wong Tak-Man and Dr Edmund Yau, as well as the Organising Committee, our 41<sup>st</sup> HKOA Annual Congress will be held on 6 - 7 November 2021 at the Hong Kong Convention and Exhibition Centre. The theme of this year is "Challenges in Orthopaedics - COVID-19 and Beyond".

## INTERNATIONAL COLLABORATION

Ambassador programme with other national orthopaedic Associations has been established since 1988. We are inviting ambassadors from our overseas sister associations to join our Annual Congress every year, while we send our fellows and members in exchange for their scientific meetings. Through this exchange program, we are building friendship, exchanging ideas as well as establishing a connection with the international orthopaedic communities.

Dr WONG Yau-bun  
President, the Hong Kong Orthopaedic Association



## Answers to Dermatology Quiz

### Answers:

1. Clinically, the most likely diagnoses include syringoma and trichoepithelioma. The other differential diagnoses include colloid milium, eccrine hidrocystoma, trichofolliculoma, plane wart, and other benign adnexal tumours.
2. The only way to confirm the diagnosis is by doing a small punch biopsy for histopathology. Clinically it is difficult to be certain about the definitive diagnosis of these adnexal neoplasms. However, just like this lady, most patients are reluctant to have a biopsy on the face because of the unwanted scar after the biopsy. Plane warts are excessively and wrongly diagnosed in Hong Kong nowadays, especially by beauticians and aesthetic doctors.

Syringoma and trichoepithelioma are two relatively common benign adnexal tumours over the cheeks. Though the final diagnosis relies on histopathology, some useful clinical clues might be useful in differentiating between the two conditions. In general, the lesions of syringoma tend to be smaller, more flat-topped, and with a yellowish pink hue, while those of trichoepithelioma are more waxy, cystic and translucent. Syringoma is more evenly distributed over cheeks and eyelids, and can be generalised in eruptive type, affecting the neck, anterior chest, abdomen and genitalia, while trichoepithelioma is more over cheeks and nasolabial area. Positive family history will favour trichoepithelioma, as it can be inherited in autosomal dominant mode via mutation in the CYLD gene, while syringoma is usually sporadic.

3. Both syringoma and trichoepithelioma are harmless benign, slowing growing adnexal tumours. Treatment, if necessary, is usually for aesthetic reasons. The options include carbon dioxide laser, radiofrequency, electrocautery and trichloroacetic acid. Cryosurgery generally is unsatisfactory and might cause disfiguring pigmentary changes over the face. All these treatment modalities have the potential risk of scarring and subsequent medico-legal disputes. The recurrent rate is also high due to the partial removal of the lesions.

### Dr Lai-yin CHONG

MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)  
Specialist in Dermatology & Venereology

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## Once-daily TRESIBA®: Ultra-long duration of action<sup>1,2</sup>

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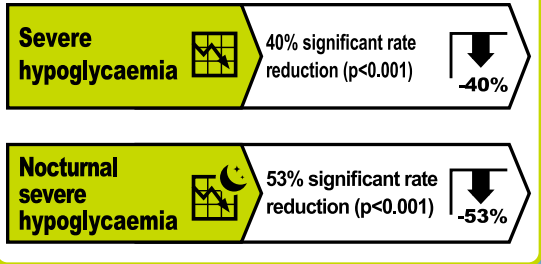


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In 7,637 patients with type 2 diabetes at high risk of cardiovascular events\*

At baseline: mean age was 65 years, diabetes duration was 16.4 years, HbA<sub>1c</sub> was 8.4%, and 83.9% were on insulin therapy\*



\* Once daily (OD) plus additional antidiabetic treatments in accordance with standard of care.  
# Treatment of diabetes mellitus in adults, adolescents and children from the age of 1 year, elderly patients, renal and hepatic impairment patients.

#### Abbreviated prescribing information

Tresiba® (insulin degludec) 100U/100 units/mL insulin solution for injection in a pre-filled pen (FlexTouch). Consult Summary of Product Characteristics before prescribing.

Presentation: Tresiba® FlexTouch®, All presentations contain insulin degludec. Tresiba® 100 units/mL – 1 mL of solution contains 100 units insulin degludec (equivalent to 3.66 mg). One pre-filled device or one cartridge contains 300 units of insulin degludec in 3 mL solution. Indications: Treatment of diabetes mellitus in adults, adolescents and children from the age of 1 year. Posology and administration: Tresiba® is a basal insulin for once-daily subcutaneous administration any time of the day, preferably at the same time of day. On occasions when administration at the same time of the day is not possible, Tresiba® allows for flexibility in the timing of insulin administration. A minimum of 8 hours between injections should be ensured. In patients with type 2 diabetes mellitus, Tresiba® can be administered alone, or in any combination with oral antidiabetic medicinal products, GLP-1 receptor agonists and bolus insulin. In type 1 diabetes mellitus, Tresiba® must be used with short-acting insulin. Administration by subcutaneous injection only. Tresiba® is available in 100 units/mL. For Tresiba® 100 units/mL a dose of 1–60 units per injection, in steps of 1 unit, can be administered. The dose counter shows the number of units regardless of strength. No dose conversion should be done when transferring a patient to a new strength. When initiating patients with type 2 diabetes mellitus the recommended daily starting dose is 10 units followed by individual dosage adjustments. Transferring from other insulins: in type 2 diabetes changing the basal insulin to Tresiba® can be done unit-to-unit, based on the previous basal insulin component, and when transferring from a twice daily regimen or from insulin glargine (300 units/mL) a dose reduction of 20% should be considered; in type 1 diabetes a dose reduction of 20% based on the previous insulin dose or basal component of a continuous subcutaneous insulin infusion should be considered with subsequent individual dosage adjustments. Doses and timing of concomitant treatment may require adjustment. Using Tresiba® in combination with GLP-1 receptor agonists in patients with type 2 diabetes mellitus, when adding Tresiba® to GLP-1 receptor agonists, the recommended daily starting dose is 10 units; when adding GLP-1 receptor agonists to Tresiba®, it is recommended to reduce the dose of Tresiba® by 20% to minimize the risk of hypoglycaemia. In all cases doses should be adjusted based on individual patients' needs, fasting plasma glucose is recommended to be used for optimizing basal insulin doses. In elderly patients and patients with renal/hepatic impairment glucose monitoring should be intensified and the dose adjusted on an individual basis. In paediatric population, when changing basal insulin to Tresiba®, dose reduction of basal and bolus insulin needs to be considered on an individual basis in order to minimise the risk of hypoglycaemia. Tresiba® comes in a pre-filled pen, FlexTouch®, designed to be used with NovoFine® needles. Contraindications: Hypersensitivity to the active substance or any of the excipients. Special warnings and precautions: Too high insulin dose, omission of a meal or unplanned strenuous physical exercise may lead to hypoglycaemia. In children care should be taken to match insulin doses (especially in basal-bolus regimens) with food intake and physical activities in order to minimize the risk of hypoglycaemia. Reduction of warning symptoms of hypoglycaemia may be seen upon tightening control and also in patients with long-standing diabetes. Administration of rapid acting insulin is recommended in situations with severe hypoglycaemia. Inadequate dosing and/or discontinuation of treatment in patients requiring insulin may lead to hyperglycaemia and potentially to diabetic ketoacidosis. Concomitant illness, especially infections, may lead to hypoglycaemia and thereby cause an increased insulin requirement. Transferring to a new type, brand or manufacturer of insulin should be done under medical supervision and may result in a change in dosage. When using insulin in combination with pioglitazone, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between the two strengths of Tresiba® and other insulins. Hypoglycaemia may constitute a risk when driving or operating machinery. Pregnancy and lactation: There is no clinical experience with use of Tresiba® in pregnant women and during breastfeeding. Animal reproduction studies have not revealed any difference between insulin degludec and human insulin regarding embryotoxicity and teratogenicity. Undesirable effects: Refer to SmPC for complete information on side effects. Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/10,000); rare (≥1/10,000 to <1/100,000); not known (cannot be estimated from the available data). Very common: Hypoglycaemia. Common: Injection site reactions. Uncommon: Lipodystrophy and peripheral oedema. Rare: Hypersensitivity and urticaria. With insulin preparations, allergic reaction may occur; immediate-type allergic reactions may potentially be life-threatening. Injection site reactions are usually mild, transitory and normally disappear during continued treatment. FlexTouch®, NovoFine®, Penfill®, and Tresiba® are registered trademarks of Novo Nordisk A/S.

#### References

- Tresiba® FlexTouch Insert, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100.
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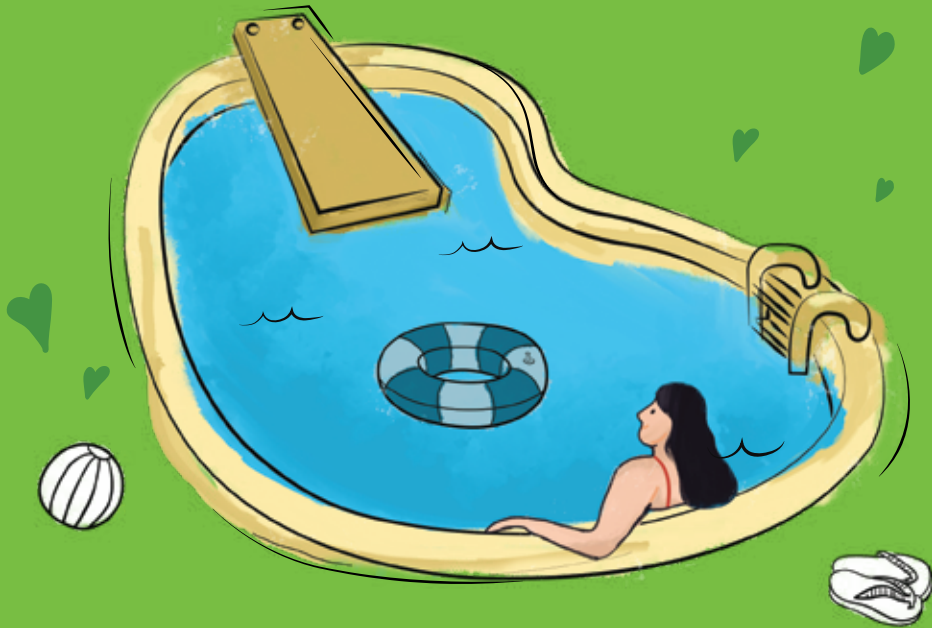
Further information is available from  
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TRE-D-20200302

# THE STATIN

with No Dose Adjustment Required Across All CKD Stages<sup>1,2</sup>



 **LIPITOR**  
atorvastatin calcium  
tablets

# LIPITOR®: Safety Comes First

Most selected lipid-lowering agent by interviewed physicians in Hong Kong for best renal safety profile<sup>3</sup>

- Lipitor 10mg and 80mg showed no adverse effects on eGFR and proteinuria.\*<sup>4</sup>
- “A more recent study (PLANET I) found atorvastatin was found to have more renoprotective effects than high-dose rosuvastatin in patients with diabetes who have progressive renal disease.”<sup>5</sup>



\* From a post hoc analysis of the TNT study. Data showed consistent increase in mean change eGFR from baseline for participants with CKD (9.9% with 80mg of atorvastatin and 6.6% with 10mg of atorvastatin) and participants with normal eGFR (7.6% with 80mg of atorvastatin and 5.2% with 10mg of atorvastatin).

**Abbreviations:** CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; TNT, treating to new targets

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#### LIPITOR SUMMARY OF PRODUCT INFORMATION

**TRADE NAME:** Lipitor. **INDICATIONS:** Prevention of Cardiovascular Disease in Adults: In adult patients without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease, such as age, smoking, hypertension, low HDL-C or a family history of early coronary heart disease, LIPITOR is indicated to reduce the risk of myocardial infarction, stroke, revascularization procedures and angina. In patients with type 2 diabetes, and without clinically evident coronary heart disease, but with multiple risk factors for coronary heart disease, such as retinopathy, albuminuria, smoking, or hypertension, LIPITOR is indicated to reduce the risk of myocardial infarction and stroke. In adult patients with clinically evident coronary heart disease, LIPITOR is indicated to reduce the risk of non-fatal myocardial infarction, fatal and non-fatal stroke, revascularization procedures, hospitalization for Congestive Heart Failure and angina. **Hyperlipidemia** - LIPITOR is indicated as an adjunct to diet to reduce elevated total-C, LDL-C, apo B, and TG levels and to increase HDL-C in patients with primary hypercholesterolemia (heterozygous familial and non-familial) and mixed dyslipidemia (Fredrickson Types Ia and IIb); As an adjunct to diet for the treatment of adult patients with elevated serum TG levels (Fredrickson Type IV). For the treatment of adult patients with primary dysbetalipoproteinemia (Fredrickson Type III) who do not respond adequately to diet; To reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable; As an adjunct to diet to reduce total-C, LDL-C, and apo B levels in pediatric patients, 10 to 17 years of age, with heterozygous familial hypercholesterolemia if after an adequate trial of diet therapy the following findings are present: (a) LDL-C remains  $\geq 190$  mg/dL or (b) LDL-C remains  $\geq 160$  mg/dL and; there is a positive family history of premature cardiovascular disease or two or more other CVD risk factors are present in the pediatric patient. **DOSE & ADMINISTRATION:** The recommended starting dose is 10 or 20mg once daily. Patients who require a large reduction in LDL-C (more than 45%) may be started at 40mg once daily. The dosage range is 10 to 80 mg once daily. LIPITOR can be administered as a single dose at any time of the day, with or without food. **CONTRAINDICATIONS:** Active liver disease, which may include unexplained persistent elevations in hepatic transaminase levels; hypersensitivity to any component of this medication; pregnancy and lactation. **WARNINGS & PRECAUTIONS:** Skeletal muscle - Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria. Myopathy. Liver dysfunction. Endocrine function - Increase in HbA1c and fasting serum glucose levels. CNS toxicity. Used in patients with recent stroke or TIA. **INTERACTIONS:** Strong inhibitors of CYP 3A4, clarithromycin, combination of protease inhibitors, itraconazole, grapefruit juice, cyclosporine, letemovir, glecaprevir and pibrentasvir, elbasvir and grazoprevir, gemfibrozil, other fibrates, niacin, rifampin or other inducers of cytochrome P450 3A4, digoxin, oral contraceptives, warfarin, colchicine, fusidic acid. **PREGNANCY AND LACTATION:** LIPITOR is contraindicated in pregnancy and during breast-feeding. **SIDE EFFECTS:** Nasopharyngitis, arthralgia, diarrhea, pain in extremity, urinary tract infection, dyspepsia, nausea, musculoskeletal pain, muscle spasms, myalgia, insomnia, pharyngolaryngeal pain. Reference: HK PI: DEC2019 Date of preparation: OCT2020 Identifier number: LIP1020

FULL PRESCRIBING INFORMATION IS AVAILABLE UPON REQUEST.

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