HONG KONG PHARMACEUTICAL JOURNAL

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The Pharmaceutical Society of Hong Kong
The Practising Pharmacists Association of Hong Kong
The Society of Hospital Pharmacists of Hong Kong

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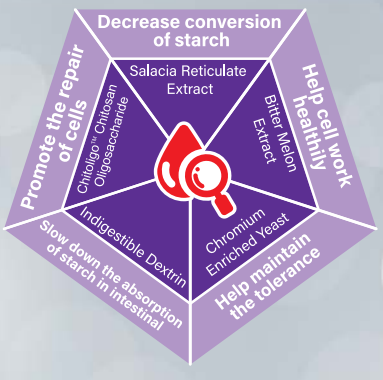
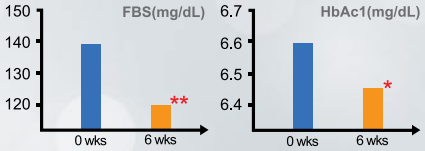


Studies revealed a significant reduction in the fasting plasma glucose levels (FBS) in the subjects after 6 weeks of Salacia containing diet, as well as their HbAc1. [1]



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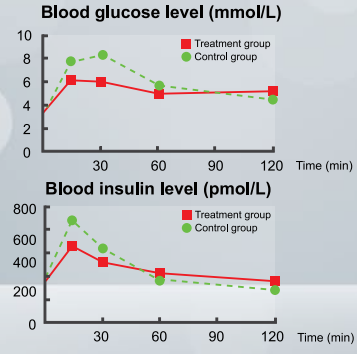

[1] Osami Kajimoto, et, al. J Jpn Soc Nutr Food Sci 2000, Vol.53(5)199-205
[2] Uebanso T, et, al. J Nutr Sci Vitaminol (Tokyo). 2007 Dec;53(6):482-8.

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INSTRUCTIONS FOR AUTHORS

The Hong Kong Pharmaceutical Journal is a journal of the pharmacists, for the pharmacists and by the pharmacists. Submissions are welcome for the following sections:

- Pharmacy Education & Practice
- Drugs & Therapeutics
- Primary Care
- OTC & Health
- Pharmaceutical Techniques & Technology
- Medication Safety
- Herbal Medicines & Nutraceuticals
- Society Activities
- New Products

Comments on any aspects of the profession are also welcome as Letter to the Editor.

There is no restriction on the length of the articles to be submitted. They can be written in English or Chinese. The Editorial Committee may make editorial changes to the articles but major amendments will be communicated with the authors prior to publishing.

It is preferable to have original articles submitted as an electronic file, in Microsoft Word, typed in Arial 9pt. Files can be sent to the following address:

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For detail instructions for authors, please refer to the first issue of each volume of HKPJ.

Challenges and opportunities

As of 30 August 2020, the Covid-19 pandemic has infected over 25.1 M people and causing over 844,000 deaths worldwide. It has changed the way we lived. People are working more at home, conducting meetings and learning via Zoom, social distancing, wearing masks, taking hygienic measures and washing hands to break the chain of transmission. This will continue until sufficient safe and effective vaccines are produced for the low-, middle- and high-income countries. While there are many setbacks during this period, there are opportunities for growth to meet the needs of the public.

During this Covid-19 pandemic, patients do not like to go to the public hospitals and clinics to check up with the doctors to get the medications. HA allow patients with chronic diseases to authorize someone to pick up the medications for them. Since mid-April 2020, Mannings offer the service to pick up the patient's medications from the HA hospitals and clinics and deliver them to a designated Mannings Pharmacy for the patients to pick up the medications with counseling from the pharmacist. The fee is only HK$50 (See page 37). This is good timing to build up the public private partnership and open up the opportunity for community pharmacists to counsel patients on their medications. Other NGOs offer free consultation by medical doctor, free medication and free counselling by a pharmacist. It further develops telemedicine, smart delivery of medications and telepharmacy (See page 39). It is encouraging to see different modes of community pharmacy services developing to meet the needs of patients.

According to the General Household Survey and Thematic Household Survey, the percentage of daily cigarette smokers among persons aged 15 and over in Hong Kong decreased steadily from 23.3% in 1982 to 10.5% in 2015 (except for years from 2000 to 2002). The percentage of male daily cigarette smokers was persistently higher than that of females: in 2015, the percentages of male and female daily cigarette smokers were 18.6% and 3.2% respectively. Smoking increases the risk of coronary heart disease, certain types of cancer, stroke and chronic lung diseases. It is the most preventable cause of morbidity and mortality in Hong Kong.

In the article on page 52, CHAN, Yuk-Pui & CHONG, Donald Wing-Kit wrote about the pharmacological and non-pharmacological options for smoking cessation. Currently, the smoking cessation services are provided by the Hospital Authority, Department of Health, or other institutions with no pharmacist led clinics. Smoking cessation is a potentially appropriate role for community pharmacists because they are encouraged to advise on the correct use of nicotine replacement therapy products and to provide behavioral support to aid smoking cessation. With the development of the Primary Health Care Centre in the 18 districts, smoking cessation could be referred by the health care team in the Primary Health Care Centres to community pharmacists for a service fee. Other than smoking cessation, there are other services such as immunization, medication review, medication reconciliation, filling up of weekly medication pill boxes for the elderlies that the community pharmacists can provide for a service fee. Leaders of the pharmacy profession should grasp the opportunity and voice their opinions to the HKSAR government.

The speech of Professor John W Kao delivered at the Hong Kong Pharmacy Conference 2019 on page 48 is on the challenges and opportunities regarding the development of research products for healthcare use. His main area of research is on wound healing. His team designed the material called Interpenetrating Network (IPN) containing two major polymer components: a polyethylene derivative and a functionalized collagen. The formulation is in liquid and one can apply in situ and form a three-dimensional scaffold. Within the scaffolding, different compounds such as drugs, bioactive cells can be incorporated to correct the underlying pathology. He also explained that translational research is to take technologies whether they are drugs, therapies, devices or diagnostics, from the research side to the patients' bedside, and eventually into a larger community. It is also a bilateral process where we identify community or patient needs to help us designing research. His talk is enlightening and inspirational.

Globalization facilitates the flow of information and distribution of pharmaceutical products, fostering the growth of drug e-commerce. Online pharmacies offer 24-hour limitless medical information access while it also provides a cheaper and faster way for the consumers to procure medicines. In the article on page 41, HAU, Melody, CHONG, Donald & WONG, Vincent wrote about online pharmacies, the current situation of drug e-commerce in different countries and discusses the feasibility of conducting online sales of drugs in Hong Kong.

I hope you enjoy reading this issue and we look forward to suggestions and comments from readers. Stay safe, happy and healthy!

Mary Catherine Cheng
Managing Editor
31 August 2020

Prepared by Howard Chan, Chiu TS Ching

香港萬寧爲市民提供公立醫院標準藥物取藥服務

Date: April 15, 2020

由4月15日開始，香港萬寧為香港市民提供標準藥物取藥服務。醫管局轄下指定7間公立醫院（東區尤德夫人那打素醫院、瑪麗醫院、基督教聯合醫院、瑪嘉烈醫院、伊利沙伯醫院、威爾斯親王醫院及屯門醫院）的專科門診病人經核實資格*後，可在指定的香港萬寧分店取藥，病人可減低因進出醫院的感染風險之餘，更可便捷獲取藥物。只適用於領取標準藥物的專科門診病人。病人需於預約覆診日期前14天內向所屬醫院的專科門診確認可以「免覆診取藥」。此服務不適用於需冷藏藥物或其他需特別處理之藥物。服務流程：

1. 客人到設有專業註冊藥劑師的指定萬寧查詢。合資格客人須向藥劑師提供醫院覆診紙或覆配處方。
2. 經客人同意及授權，萬寧專業註冊藥劑師可於「醫健通」查核客人服藥和藥物過敏記錄。
3. 萬寧派專人到指定公立醫院，將藥物運送到指定萬寧分店。
4. 客人返回指定萬寧分店取回藥物，並獲專業註冊藥劑師教導正確用藥。

萬寧只收取港幣$50作為取藥及藥劑服務之費用。

Source : https://www.mannings.com.hk/zh-hk/promo/mcp

US FDA Approves Dapagliflozin for Heart Failure with Reduced Ejection Fraction

Date: May 5, 2020

The US FDA approved Farxiga (dapagliflozin) oral tablets for adults with heart failure with New York Heart Association (NYHA) functional class II-IV heart failure with reduced ejection fraction (HFrEF) to reduce the risk of cardiovascular death and hospitalization for heart failure. Farxiga is the first in class, sodium-glucose co-transporter 2 (SGLT2) inhibitors, to be approved to treat adults with HFrEF. Farxiga is also FDA-approved to improve glycemic control in adults with type 2 diabetes in addition to diet and exercise, and to reduce the risk of hospitalization for heart failure among adults with type 2 diabetes and known cardiovascular disease or other risk factors.

Farxiga's safety and effectiveness were evaluated in a randomized, double-blind, placebo-controlled study (DAPA-HF). 4744 patients with NYHA functional class II-IV HFrEF were randomly assigned to receive Farxiga (at a dose of 10 mg daily) or placebo, in addition to recommended therapy. The average age of participants was 66 years and more participants were male (77%) than female. The primary outcome was a composite of worsening heart failure (hospitalization or an urgent resulting in intravenous therapy for heart failure) or cardiovascular death. Over a median of 18.2 months, the primary outcome occurred in 386 of 2373 patients (16.3%) in the Farxiga group and in 502 of 2371 patients (21.2%) in the placebo group (hazard ratio [HR], 0.74; 95% confidence interval [CI], 0.65 to 0.85; p<0.001).

Farxiga can cause dehydration, serious urinary tract infections and genital mycotic infections. Elderly patients, patients with kidney problems, those with low blood pressure, and patients on diuretics should be assessed for their volume status and kidney function. Patients with signs and symptoms of metabolic acidosis or ketoacidosis should also be assessed. Serious cases of Fournier's Gangrene have been reported in people with diabetes taking Farxiga.

Source: www.fda.gov

Effects of Allopurinol on the Progression of Chronic Kidney Disease

Date: June 25, 2020

Elevated serum urate levels are associated with progression of chronic kidney disease (CKD). Whether urate-lowering treatment with allopurinol can attenuate the decline of the estimated glomerular filtration rate (eGFR) in patients with CKD are at risk for progression is not known. A randomized, double-blind, placebo-controlled trial at 31 centers in Australia and New Zealand was conducted to test such hypothesis.

Adults with stage 3 or 4 CKD with no history of gout who had a urinary albumin:creatinine ratio of ≥265 (with albumin measured in milligrams and creatinine in grams) or an eGFR decrease of at least 3.0 mL/min/1.73 m^2 of body surface area in the preceding year were randomly assigned to receive allopurinol (100 to 300 mg daily) or placebo. The primary outcome was the change in eGFR from randomization to week 104, calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.

Enrollment was stopped because of slow recruitment after 369 of 620 intended patients were randomly assigned to receive allopurinol (185 patients) or placebo (184 patients). Three patients per group withdrew immediately after

randomization. The remaining 363 patients (mean eGFR, 31.7 mL/min/1.73 m^2; median urine albumin:creatinine ratio, 716.9; mean serum urate level, 8.2 mg/dL) were included in the assessment of the primary outcome. The change in eGFR did not differ significantly between the allopurinol group and the placebo (−3.33 mL/min/1.73 m^2/year and −3.23 mL/min/1.73 m^2/year respectively; mean difference, −0.10 mL/min/1.73 m^2/year [95% CI, −1.18 to 0.97]; p=0.85). Serious adverse events were reported in 84 of 182 patients (46%) in the allopurinol group and in 79 of 181 patients (44%) in the placebo group.

In patients with CKD and a high risk of progression, urate-lowering treatment with allopurinol did not slow the decline in eGFR as compared with placebo.

Source: www.nejm.org

Trial of Roflumilast Cream for Chronic Plaque Psoriasis

Date: July 16, 2020

An oral phosphodiesterase type 4 (PDE-4) inhibitor, apremilast, has been approved for the treatment of moderate-to-severe plaque psoriasis; however, topical PDE-4 inhibitors are currently not approved for such purposes. The efficacy and safety of two dose levels of a topical once-daily cream consisting of roflumilast was investigated in a phase 2b trial for the topical treatment of plaque psoriasis.

Adults with plaque psoriasis were randomly assigned in a 1:1:1 ratio to use roflumilast 0.3% cream, roflumilast 0.15% cream, or vehicle (placebo) cream once daily for 12 weeks. The primary efficacy outcome was the investigator's global assessment (IGA) of a status of clear or almost clear (assessed on a 5-point scale of plaque thickening, scaling, and erythema) at week 6. Secondary outcomes included an IGA score indicating clear or almost clear plus a 2-grade improvement in the IGA score for the intertriginous area and the change in the Psoriasis Area and Severity Index (PASI) score. Safety was also assessed.

Among 331 patients who underwent randomization, 109 were assigned to roflumilast 0.3% cream, 113 to roflumilast 0.15% cream, and 109 to vehicle cream. An IGA score indicating clear or almost clear at week 6 was observed in 28% of the patients in the roflumilast 0.3% group, in 23% in the roflumilast 0.15% group, and 8% in the vehicle group (p<0.001 and p=0.004 vs. vehicle for roflumilast 0.3% and 0.15%, respectively). Among the approximately 15% of patients overall who had baseline intertriginous psoriasis of at least mild severity, an IGA score at week 6 indicating clear or almost clear plus a 2-grade improvement in the intertriginous area IGA score occurred in 73% of the patients in the roflumilast 0.3% group, 44% of those in the roflumilast 0.15% group, and 29% of those in the vehicle group. The mean change from baseline PASI score at week 6 was −50.0% in the roflumilast 0.3% group, −49.0% in the roflumilast 0.15% group, and −17.8% in the vehicle group. Application-site reactions occurred with similar frequency in the roflumilast groups and the vehicle group.

Roflumilast cream administered once daily to affected areas of psoriasis was superior to vehicle cream in leading to a state of clear or almost clear at 6 weeks. Longer and larger trials are needed to determine the durability and safety of roflumilast in psoriasis.

Source: www.nejm.org

Continuing Glucocorticoids Shown to Provide Safer and Better Outcomes Than Tapering Regimen After Achieving Controlled Rheumatoid Arthritis

Date: July 25, 2020

Glucocorticoids, while commonly indicated for anti-inflammation in patients with rheumatoid arthritis, often raise concerns on undesirable adverse effects upon long-term use. The Steroid Elimination In Rheumatoid Arthritis (SEMIRA) study, with the objective of comparing efficacy and safety of continuing and tapering glucocorticoids, suggested that the former regimen may be a better option for disease control.

SEMIRA is a two-year, double-blind, two parallel-arm randomized controlled trial done at institutions across six European countries. 259 patients with rheumatoid arthritis of stable low disease activity (on tocilizumab and had received prednisone 5mg daily for four weeks or more), confirmed by a Disease Activity Score for 28 joints-erythrocyte sedimentation rate (DAS28-ESR) of <3.2 four to six weeks before and on the day of randomization, were recruited. They were randomly assigned 1:1 to either continue prednisone 5mg daily for 24 weeks or to taper prednisone to 0mg at week 16. The primary outcome was differences in mean DAS28-ESR change from baseline to week 24, with a difference over 0.6 defined as clinically significant.

The difference between estimated mean DAS28-ESR changes of the continuing and tapering regimen from baseline to week 24 was 0.61 (continuing regimen, -0.08 vs tapering regimen, 0.54; 95% CI, 0.35 to 0.88; p<0.0001). Treatment success, the key secondary efficacy outcome defined as low disease activity at week 24, plus absence of rheumatoid arthritis flare for 24 weeks as well as adrenal insufficiency, was reported in 99 (77%) and 85 (65%) of groups receiving continuing and tapering prednisone therapy respectively (relative risk, 0.83; 95% CI, 0.71 to 0.97). Occurrence rate of serious adverse events were similar across two treatment groups (tapering regimen, 5% vs continuing regimen, 3%).

Study results implied that for patients with rheumatoid arthritis being stabilized by tocilizumab and at least 24 weeks of glucocorticoid treatment, continuing regimen at 5mg daily may be a safer and more effective disease control measure.

Source: www.thelancet.com

Community Interim Medication Refill Service (CIMRS)

LAM, Wan
Hong Kong Pharmaceutical Care Foundation

BACKGROUND

Since the outbreak of Covid - 19 in late January 2020, the non-emergency service in public health care system has been stepped down. Hence, many out-patients with chronic diseases were unable to attend their follow up appointments at the Hospital Authority (HA) hospitals. However, they needed the supply of medications without which their disease conditions would deteriorate.

In view of this, the Community Interim Medication Refill Service (CIMRS) was initiated in Feb 2020 to provide an alternative means of medication supply to help patients who were unable to attend HA follow-up appointments to get free and immediate medication replenishment as an interim measure. This project is a joint collaboration between Hong Kong Pharmaceutical Care Foundation (HKPCF) and Hong Kong College of Health Service Executives(HKCHSE) with support from other organizations, including Society for Innovative Healthcare Hong Kong, Health In Action, Easy Healthcare and HKSKH Lady MacLehose Centre Community Pharmacy.

OBJECTIVES

Besides aiming to meet the immediate needs of patients, CIMRS also served as a pilot model of medication supply to HA patients with chronic illnesses through a community-based approach and offered us insight for Public Private Partnership proposal.

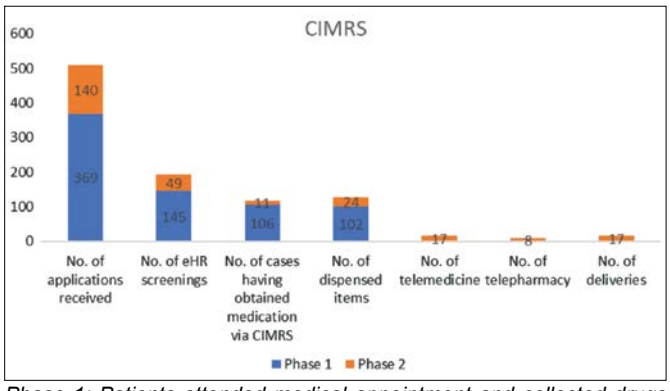
FEATURES

HA patients whose HA follow-up appointment were within 1 month were eligible to obtain 1-4 weeks of medication supply and the entire service (including consultation, medication supply, dispensing and drug counselling) was free of charge which was made possible through generous donations by different sponsors.

SERVICE FLOW

First, patients registered via hotline or online application. Pharmacists in HKPCF determined the suitability of patients according to their electronic health record (eHR) and referred eligible patients to participating doctors in the private sector for consultation who saw patients, prescribed the same medications for a period of 1-4 weeks and explained the objectives and nature of CIMRS and reminded patients to return to HA for future follow-up appointments. Within 3 days, Pharmacists in HKPCF would arrange to dispense medications and gave prescription copies to patients who would present the copies to HA doctors and pharmacists for their records.

RESULTS



Phase 1: Patients attended medical appointment and collected drugs in person.
Phase 2: Patients could opt to see doctors via video conferencing and have their drugs delivered to their homes.

patient inquiries and around 200 of their electronic health records were successfully screened and more than 100 drug items have been prescribed and dispensed, benefiting around 120 patients.

DISCUSSION

The implementation of CIMRS was expeditious and it took around 10 days to proceed from planning to implementation. Besides implementation, the project also boasted short turnaround time. On average, it took a patient 3 days to have their drugs replenished after registration. Complementary to the operation of HA, CIMRS brought healthcare professionals in the private sector to work together to provide an alternative means of medication supply that responded promptly to patients' medication needs and relieved the burden of public healthcare system.

However, there were some barriers. From patient's perspective, the eHR registration procedure seemed complicated and they needed to provide detailed personal information. There was also feedback that the duration of medication supply was too short that the replenished medications could not last until patients' delayed appointments. From the operational viewpoint, an array of drug items were required for refill purpose, but the required quantity of each drug item was not large, which made procurement process expensive and inefficient.

FINDINGS

It is clear that the public healthcare system is overburdened and it alone cannot accommodate all the patients in need, especially those chronically ill patients whose conditions are stable and who can be followed up easily in the primary care setting. GPs and pharmacists in the private sector can be incentivized to share the workload and alleviate the burden of the public healthcare system. Besides, we also provided our experiences in using the eHRSS and made some suggestions to the eHRSS office, such as establishing an interface for patients to know about their registration status, in the hope that better and less complicated eHRSS access service can be enabled in the future. We also found that the drug refill initiative could better support chronic and elderly patient with delivery of drugs to their homes. Hence, we implemented a drug delivery service model which consisted of the following components:

1: Telemedicine - A doctor sees the patient via video conferencing.
2: Smart delivery of medications - The delivery team ensured the integrity of medications en route by utilizing Internet of Things (IoT) Technology where the temperature of drugs was monitored continuously and logged with a smart device which would alert the team once there was a temperature breach. Besides, the location of the delivery team was tracked using an app to reflect the real-time status of deliveries. Different parameters of deliveries were electronically recorded and analyzed to optimize the delivery service and reduce errors.
3: Telepharmacy – A pharmacist provides teleconsultation on medications.

The model was well-received by patients who commended the model for its convenience.

ACKNOWLEDGEMENT

We would like to express our gratitude to all volunteers, including doctors, pharmacists, pharmacy students and the sponsors to this project.

Clarification on HKPJ Vol. 271

In the article "Covid-19: An Overview of its Transmission, Management and Prevention Strategies" published in HKPJ Vol. 271 on page 20-21, the list of references nos. 2, 7, 14, 39, 43, 47, 60 & 75 show a publication date later than the article's submission date. The reason is because a citation tool Zotero has been used and for the references listed above, they were all available as online articles BEFORE the submission date, but the actual publication date in the corresponding physical journals were later than their available online dates, hence the apparent 'improbable' referencing in terms of the dates.

Online pharmacies – An overview and its implications to Hong Kong

HAU, Melody Wing Kei[a]; CHONG, Donald Wing Kit[a]*; WONG, Vincent Wai Shing[a]*
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ABSTRACT

Online pharmacies are pharmacies that operate over the internet to sell medicines to consumers through an online platform. The term 'online pharmacy' has also become increasingly popular in recent decades in which there are more and more countries approving this mode of medication provision. This article provides an overview of online pharmacies, followed by a description of the current situation of drug e-commerce in different countries. In the latter section, it discusses the feasibility of conducting online sales of drugs in Hong Kong and the role of pharmacists upon such implementation.

Keywords: *Online pharmacy, e-pharmacy, e-commerce, telemedicine, counterfeit medicines*

INTRODUCTION

With the rapid development of digital technology, e-commerce such as online shopping/food ordering has become more convenient, and therefore, more prevalent. Online shopping has also been extending to the pharmaceutical field in recent decades, giving rise to a digital revolution in the pharmaceutical field - online pharmacies. Despite several benefits brought by the online pharmacies, there are also increasing ethical, legal and safety concerns regarding the online sales of drugs.

What is an online pharmacy?

Online pharmacies, also referred as e-pharmacy, internet pharmacies or cyber-pharmacies, are vendors that sell medicines through an online platform.[1] The medicines on sale include over-the-counter medications and behind-the-counter medications (also known as pharmacy-only medicines or prescription drugs).

Online pharmacies can be divided into three main types:

(I) independent internet-only pharmacy
(II) online version of the 'brick-and-mortar' pharmacies and
(III) internet sites representing a partnership with neighborhood pharmacies.[2] Taking the rapidly growing trend of online pharmacies into account, the major offline pharmacy chains such as the Boots from the United Kingdom and Walgreens from the United States have also been making strategic moves by pursuing the online development, so as to further extend its offline presence while maximizing the market share.[3]

In general, an online pharmacy might serve the following functions:[4]

- Sales and supply of OTC medicines and prescription drugs
- Sales and supply of other healthcare or herbal products
- Providing medication information
- Providing advice about symptoms and disease control
- Hosting online support groups

In order to ensure a lawful sale and supply of prescription medicines to the consumers, legitimate internet pharmacies will offer online prescription verification whereas patient consultation will be conducted through an online questionnaire or live streaming with a medical professional to assess the appropriateness of medications.[4] Some pharmacies may also extend their services by utilizing modern technology such as creating mobile apps, providing educational videos on different health topics and sending text reminder for refilling repeated prescriptions. The emergence of digital world may provide another convenient and cost-saving alternative to consumers to purchase drugs, but it may also open the door to illicit pharmacies to conduct illegal drug trades or to provide substandard pharmaceutical products. The pros and cons of online pharmacies will be discussed in latter sections.

CURRENT SITUATION OF ONLINE PHARMACIES ACROSS THE GLOBE

Global trend of online pharmacies

Online pharmacies have become more prevalent in recent decades. The term 'online pharmacy' was introduced in January 1999, where Soma.com, the first online pharmacy in the world, went live on the internet.[3] Since then, the online pharmacy landscape has been under a drastic change throughout the decades with the emergence of e-commerce, digital health and globalization of pharmaceutical industries. It is estimated to have approximately 3000 online pharmacies worldwide in 2008,[5] which the number has soared to over 30,000 online pharmacies operating globally by the year 2015.[6]

Apart from the proliferating number of online pharmacies, there is also an increasing trend for different countries to legalize the existence of internet pharmacies. Online pharmacies are officially approved to conduct legal sales of drugs over the internet in several developed countries such as the United Kingdom, the United States and Australia. Among them, the United Kingdom has been a front liner in drug e-commerce history. For developing countries such as India, a spike for such introduction is also observed as the country governmental body had proposed draft rules on online pharmacies operation in 2018.[7] The effort made by the regulatory bodies from different countries is believed to help shape a better environment for the future development of drug e-commerce, which will be further discussed below.

Status of online pharmacies in different countries

The United Kingdom

The United Kingdom has been a pioneer in the development of internet pharmacy with a history of over 20 years. The first pharmacy in the United Kingdom to operate online, Pharmacy2U, was opened in November 1999.[8] In 2005, the national regulation has made it legal for pharmacies to conduct the sales and supply of prescription drugs over the internet. The sales of medicines in the UK are governed by the Medicines and Healthcare products Regulatory Agency (MHRA).[9] The drugs are classified into three main categories: general sales (GSL) medicines (equivalent to over-the-counter medicines), pharmacy-only medications (P) and prescription-only medicines (POM). Online pharmacies are permitted to conduct the sale and supply of GSL, P and POM medications over the internet if the pharmacy is registered with the General Pharmaceutical Council (GPhC), which is an independent regulator responsible for governing the pharmacy premises and pharmacists in the United Kingdom. The internet pharmacy is required to base in Great Britain physically for pharmacy licensure registration.[9] The website supplying the medicines must correctly display the EU Common Logo **(Fig. 1)** in compliance with the MHRA requirement for selling medicines legally online.[10][11] There is also a voluntary internet pharmacy logo scheme run by the GPhC where the accredited pharmacies can display a green cross logo **(Fig. 2)** on their websites as a reassurance that the public is purchasing from a registered internet pharmacy that meets the GPhC requirements.[4]

Figure 1. *EU Online Pharmacy Common Logo*

Figure 2. *Logo of accreditation by the voluntary internet pharmacy logo scheme (GPhC)*

The United States

The sale and supply of drugs in the United States is governed by the US Food, Drug and Administration (FDA), a division of the U.S. Department of Health and Human Service.[12] Online pharmacies in the United States are permitted to conduct sales of over-the-counter medications, prescription drugs and controlled substances (a group of substances with high potential of abuse and dependence subjected to the control under Drug Enforcing Agency, DEA) in compliance with the federal laws and regulations.[12][13] As there is no federal law for pharmacy licensure In the United States, each online pharmacy should be licensed at the state level, in the state which it delivers, distributes or dispenses or offers to deliver, distribute or dispense medicines. The pharmaceutical regulations may slightly differ between states such as drug shipping restrictions but in general, all state laws require the presence of licensed pharmacists to manage the pharmacies with strict standards of good dispensing practices.[14] The internet pharmacies are also requested by law to display a series of information **(Table 1)** on its homepage in a visible and clear manner.

Australia

E-commerce of drugs is permitted in Australia. The sale and supply of drugs are regulated by the Therapeutic Goods Administration (TGA) in which the sales of prescription drugs follow the European Union's standards.[15] For online pharmacy licensure, the pharmacies in Australia are registered at the state or province level as the pharmacies in the United

Table 1. Additional requirements relating to online pharmacies and telemedicine from Legal Information Institute[14]	
(a)	Name and address of the pharmacy same as the one registered with Drug Enforcement Administration
(b)	Contact information i.e. telephone number and email address of the pharmacy
(c)	Name, professional degree, States of licensure and telephone number of the pharmacist-in-charge
(d)	A list of controlled medicines that the pharmacy is licensed to dispense (if applicable)
(e)	A certification that the pharmacy is authorized to deliver, distributes or dispenses controlled medicines by the means of internet. (if applicable)
(f)	Name, address, telephone number, professional degree, and States of licensure of any practitioner who has a contractual relationship to provide medical evaluations or issue prescriptions, through referrals from the website or at the request of the owner or operator of the website, or any employee or agent thereof.
(g)	The following statement, unless upon regulation revision, 'This online pharmacy will only dispense a controlled substance to a person who has a valid prescription issue for a legitimate medical purpose based upon a medical relationship with a prescribing practitioner. This includes at least one prior in-person medical evaluation or medical evaluation via telemedicine in accordance with applicable requirements of section 309.

States. The state boards are incorporated into a federal organization, the Pharmaceutical Society of Australia, which is responsible for providing guidance and policies for safe pharmaceutical practice in the field.[15][16] Pharmacists must be registered in the state or territory where they are practising and exercising their control in an approved premises.[16] Online ordering of medicines from Australian e-pharmacies retain the features of Australian traditional pharmacy landscape in which the pharmacist should only supply the medicines in accordance to the relevant laws and regulations of the state or territory, Commonwealth legislation, the Pharmacy Board of Australia's Guideline and quality assurance standards.[17][18]

India

There are no pharmacy laws governing the online sale of medicines in India currently, yet a draft on the rules of operating an internet pharmacy was proposed by the Union Health Ministry of India in August 2018, with an aim to regulate the online sale of drugs and protect patients from getting substandard or counterfeit drugs from online pharmacies.[7] It is stated that the online pharmacy has to be registered with the Central Drugs Standards Control Organization (CDSCO), a division of the Indian Ministry of Health and Family Welfare, to legally distribute or sell, stock, exhibit or offer the sales of drugs through the internet.[7][19] The conditions of selling different classes of drugs will be following the requirements of the corresponding schedule that they belong to as stated in the Drugs and Cosmetics Rules 1945.[20] Apart from the regulatory actions from the Drugs and Cosmetic Rules, a group of chemical substances listed under the Narcotic and Psychotropic Acts, also referred as 'controlled medicines', are subjected to the control of the Narcotics Control Bureau.[21] The sale and supply of these groups of chemicals, tranquillizers, and drugs with dependence potential have been prohibited for e-commerce.[7] For the attainment of online pharmacy license, it depends on whether it is a new application or not. For existing e-pharmacy, they need to be registered with the Central Licensing Authority through the Central government website while new e-pharmacy must get licensure from CDSCO, India's apex drug regulator and central licensing authority for registration completion.[7] Despite a lack of established regulation governing the drug e-commerce in India currently, some Indian internet pharmacies may also be subjected to inspection by third-party verification organization such as PharmacyChecker.com to safeguard the qualities and standards of internet pharmacies.

Asian countries: Singapore and China

Compared to the above countries such as the United Kingdom, which is with a history of over 20 years to conduct online sales of medicines, the concept of online pharmacies is relatively new to the Asian countries.

E-commerce of drugs is permitted in China to conduct sales of both prescription and non-prescription medicines over the internet. Despite a number of legislations such as《药品经营许可证管理办法》,《药品经营质量管理规范》and《互联网药品交易服务审批暂行规定》governing the authenticity and legality of the drugs supplied by the pharmacies in China, the legislative model has been continuously modified to improve the surveillance over e-pharmacies.[22][23] In April 2018, the General Office of the State Council of China has approved the policy address-《关于促进"互联网+医疗健康"发展的意见》, in which all the prescriptions regarding common diseases and chronic diseases are subjected to the verification by registered pharmacists in China before supplying to further tighten the control of prescription medicines online.[23]

As for Singapore, over-the-counter medications are available online whereas the sale of prescription medications over the internet is not permitted.[24] Taking reference to the successful examples of e-pharmacies in the foreign countries, Singapore is currently looking in the direction of telemedicine. The Licensing Experimentation and Adaptation Programme (LEAP), a regulatory subsidiary under the Ministry of Health of Singapore established in 2018 to incorporate innovative technologies into healthcare delivery, has been looking into different pilot models to sell pharmacy-only and prescription medications through an online platform in April 2019.[24] Asian countries are thus predicted to be moving towards allowing the sale of prescription drugs via the Internet in the coming decades, bringing a revolution to the pharmaceutical industry.

Table 2. Prices for a 3-month supply of top-selling brand name medications				
Drug	**Local U.S. Pharmacy Price (USD)**	**International Online Pharmacy Price (USD)**	**International Online Savings**	**Annual Savings (USD)**
Advair Diskus 250/50mcg	$1,437	$72.93	95%	$5,456.28
Crestor 10mg	$969.30	$24.30	97%	$3,780.00
Nexium 40mg	$863.10	$18.90	98%	$3,376.80
Januvia 100mg	$1,593.90	$72.90	95%	$6,084.00
Synthyroid 50mcg	$151.20	$13.50	91%	$550.80
Ventolin HFA 90mcg	$218.31	$68.86	68%	$597.84
Xarelto 20mg	$1,560.60	$149.40	90%	$5,644.80
Zetia 10mg	$1,260.90	$150.30	88%	$597.84

Sources: Local pharmacy prices at chain drugstores in New York City; International online pharmacy prices based on lowest prices listed on PharmacyChecker.com. All prices obtained on March 2018.[25]

ADVANTAGES

A cost-saving alternative

One of the major benefits offered by the online pharmacies is that they can provide cost-saving deals when compared to the offline stores. Taking the drug prices in the United States as an example, a foreign online pharmacy, which the internet pharmacy is based at a different country where the medicine is purchased, could offer at least 60% savings when comparing to the same drug being purchased in the local U.S. pharmacies.[25] Using an online platform to sell drugs can help drive the prices of the pharmaceutical products down in multiple ways such as reducing the maintenance cost due to an absence of a physical store and decreasing the procurement and transactional costs.[26] A centralized order-processing online system could offer an efficient away for transaction management in which it is reported to release a minimum of 10-hours staff time per week upon the implementation of an internet purchasing system.[27] This, in turn, saves time and money for pharmacy operation and allows more efficient procurement for suppliers to manage contracts with wholesalers and suppliers, thus cutting down the overall operational costs. [27]

Other benefits of online shopping

Drug e-commerce also presents with other inherent advantages of digitalization such as convenience, increased accessibility of information and identity anonymity.[5][28] Purchase of medications through online systems can break the constraint of time and space, allowing people with lower mobility, busy lifestyles or those living in a remote rural area to purchase the required drugs with convenience. Pharmacy websites could also offer 24-hour limitless information delivery, increase the accessibility of the medications and relevant clinical information about medicines and diseases. Some of the websites may also provide links to medical resources such as health associations and government regulatory bodies. FDA will also divert the consumers to the federally-verified online pharmacies to secure legal and safe purchase of genuine medicines.[28] In addition, the identity anonymity offered by the internet could also encourage the patients to seek for the drug information that they may feel embarrassed or would have been avoided when facing the pharmacists at the offline pharmacies.[29] All these factors help increase the ease of consumers to use an online platform to purchase drugs, fostering the growth of drug e-commerce.

DISADVANTAGES

Despite the above benefits brought by the online pharmacies, the internet has also opened the door for the illicit online pharmacies. 'Illicit', 'illegitimate' or 'rogue' pharmacies refer to the pharmacies that fail to comply with national or international regulations or have not been subjected to mandatory regulatory review, relevant licensure and/ or certification.[30] They were also found to be far more common than the legitimate ones in which the illicit pharmacies were estimated to occupy over 95% of all the globally operating online pharmacies.[6] The existence of illegitimate pharmacies could lead to a number of concerns as discussed below.

Provision of substandard or counterfeit medicines

One of the major concerns of online pharmacies is the provision of substandard or counterfeit medicines by the illegitimate pharmacies, which in turn pose health threats to the consumers. The World Health Organization (WHO) estimated that approximately 50% of the drugs on sale online are counterfeit medicines.[31] The defective pharmaceutical products in scope include substandard, spurious, falsely-labelled, falsified and counterfeit drugs, collectively known as SSFFC products.[29][31] Under globalization, illicit pharmacies can utilize the worldwide networking to bypass the regulatory controls and distribute the SSFFC products directly to the consumers, exposing the consumers to numerous health risks such as potential under-treatment, overdose or severe adverse events after ingestion of substandard medicine.[32] Incidents regarding fatality and severe adverse events following the ingestion of counterfeit medicines, formulations with heavy metals contamination and illegal

dispensing of medications without prescriptions online have been increasingly reported in the West and in India, which is suggested to be linked with the growth of online pharmacies globally.[5]

To address this problem, different verification programs were designed for online pharmacies' accreditation to ensure the pharmaceutical products supplied are authentic, genuine and harmless to the consumers. Verified Internet Pharmacy Practice Sites (VIPPS) program **(Fig. 3)**, founded in 1999, is one of the accreditation programs for online pharmacies.[33][34] VIPPS is operated by the National Association of Boards of Pharmacy (NABP), which is responsible in reviewing the compliance of the internet pharmacies in scope towards the U.S. regulations and national practice standards.[34] Another program is LegitScript from Canada **(Fig. 4)**, founded in 2007, which aimed to combat internet crimes associated with drug e-commerce.[35] In 2010, LegitScript has successfully identified over 47000 'rogue' internet pharmacies.[35] According to a research study in 2012, it is found that all the tested prescription drug orders received by the verified online pharmacies were lawfully processed while the medications supplied were authentic and trustworthy.[36] In comparison to the non-credentialed ones, approximately one-tenth of the tested products supplied were counterfeit medicine.[36] Public education is thus essential for the consumers to help identify the online pharmacies verified by certain credentialing entities and purchase drugs from the online pharmacies that are referred by reputable regulatory bodies such as the FDA to secure the product quality and protect personal health.

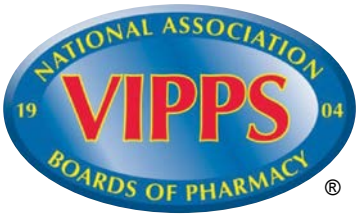

Figure 3. *Logo of Verified Internet Pharmacy Practice Sites (VIPPS) Program*

Figure 4. *Logo of LegitScript verification program*

Loopholes of online service delivery

The nature of pharmacies operating online may also pose inherent safety risks by promoting inappropriate drug use. It is a common practice for illicit pharmacies to label themselves as 'no-prescription' pharmacies as marketing ploys (i.e. selling prescription medicines without the need to provide a valid prescription.[37] No-prescription pharmacies were found to provide virtually all types of medications ranging from over-the-counter medicines to prescription drugs such as cardiovascular disease medications, opioid analgesics or even controlled stimulants.[29] This unhealthy practice can lead to severe consequences if the patient was misdiagnosed of a condition and obtained inappropriate medications as a result. This practice may also promote intentional drug misuse behaviors such as substance abuse.[30][37]

Besides, some e-pharmacies may provide incomprehensive or inadequate prescription verification and patient assessment. A study by *Orizio et al*. found that only 70% of medical questionnaires from the reviewed e-pharmacies had inquired about the pregnancy status of the patients whereas only 17% of them would confirm the validity of the established diagnosis by a medical professional.[38] This study suggested that the use of medical questionnaires by the internet pharmacies to assess the health status of patients may in fact be employed as a business tactic to convey a sense of security and assurance to consumers rather than assessing the appropriateness of medication. Furthermore, these online consultations may neglect the physical evaluation that is considered necessary for certain diseases such as skin and soft tissues infections prior to treatment provision.[5] On the other hand, the patients may also receive inadequate counselling on the special precautions to be taken before taking the prescribed medications, which may lead to potential drug-drug interactions, under-management of serious adverse effects or inappropriate drug use.[5][37]

Cybersecurity threats

Apart from the safety concerns raised by the online pharmacies, cybersecurity and privacy issues shall not be under-addressed. According to a study conducted in 2011, 80% of the studied e-pharmacies were found to have either critical or medium-level vulnerabilities, hinting an inadequate protection of consumers' personal information.[39] Some of the illegitimate pharmacies are also found to be linked to large cross-national criminal networks to carry out fraudulent activities such as financial frauds, identity thefts and data phishing.[40] It may also pose threats to cybersecurity when the illicit online pharmacies use cyber-viruses, malware or spy-ware to commit crimes.

Another major concern regarding the cybersecurity issue will be the anonymity of online pharmacies. In a study by the National Association of Boards of Pharmacy (NABP), there was around one-fifth of the assessed online pharmacies failing to provide a secure and valid address.[37] Different from the traditional 'brick-and-mortar' stores, the internet provides a platform in which the illegal websites could shut down the sites and disappear any time to escape from any potential prosecutions, leaving the least trace and evidence for regulatory actions to be taken. This may thus in turn encourage the growth of substandard pharmacy websites and promote internet crimes.

QUESTIONS TO BE RESOLVED

Drug importation is a common issue encountered during the emergence of e-pharmacies and yet, the answer may be different from country to country. The internet environment may provide a free and open competitive atmosphere for drug e-commerce where the consumers can purchase and import the drugs from the online pharmacies of their own country or those located overseas. This happens to be more common in the United States in which a considerable number of US citizens were found to be importing medications from Canadian online pharmacies, attributing to the long-standing high prices of prescription medicines in the States.[41] There has not been a consensus reached across the globe on drug importation currently, in other words, different countries may have different legislation and restrictions regarding personal drug importation. For instance, the U.S. federal legislation prohibits drug importation from overseas internet pharmacies to protect the consumers whereas the Australian government allows overseas drug importation of no more than 3-month supply per round, given that the medicines are purchased in accordance to the law requirement (i.e. prescription medicines should be obtained upon the presence of a valid prescription by an Australian doctor).[41] Not only does this misalignment cause confusion between consumers, but it also creates loopholes or grey areas for the operation of global illegal drug market. Therefore, collaborations between regulatory bodies from different countries are mandatory for international alignment on purchasing medicines online to effectively combat the illegal drug trade and safeguard consumers' health.

FEASIBILITY OF ONLINE PHARMACIES IN HONG KONG

Reduction of heavy health burden

The introduction of online pharmacies to Hong Kong encourages self-purchasing which might help reduce the health burden of Hong Kong. Online pharmacies offer several benefits that cater to Hong Kong citizens. The healthcare system in Hong Kong is on a dual-track basis and it can be mainly divided into the public sector and private sector.[42] The public sector is delivering medical services for around 90% of the population whereas the private sector is responsible for the remaining 10%.[42] One of the major reasons for such a significant imbalance is attributed to the high rate of subsidies by the public sector, providing approximately 95% subsidies compared to the cost.[43] Online pharmacies enjoy a major benefit of a lower retail price when compared to traditional pharmacies in which it can provide up to 98% savings as mentioned above. Online pharmacies can thus act as an alternative source for citizens to procure medicines other than getting at the local hospital pharmacies and retails stores. Besides, the online platform also brings convenience to the consumers, which specifically caters to the busy lifestyle of Hong Kong people than visiting the pharmacy in person for dispensing. Therefore, introducing online pharmacies in Hong Kong is expected to help divert the patients away from the local healthcare sector, the public sector in particular, thus alleviating the heavy health burden.

Standardization of local pharmacy services

Introducing the online pharmacies to local markets require revision of local legislative framework which in turn may become an opportunity to upgrade and standardize the quality of local pharmacy services. The drug retailers in Hong Kong can be divided into two categories: Listed Seller of Poisons (LSP) and Authorized Seller of Poisons (ASP), depending on the list of drugs that the store is authorized to sell.[44] Among them, community pharmacies occupy a significant portion in supplying over-the-counter medications and prescription drugs. There are two main types of community pharmacies: chain pharmacies and independently-owned pharmacies.[45] As the drug dispensing practice are not strictly regulated in Hong Kong, some of the independently-owned pharmacies were previously reported to fail to comply with the local pharmacy law when dispensing the medicines in which some prescription medications were supplied without the presence of a valid prescription through a non-pharmacist personnel.[45] As community pharmacies are expected to be one of the key sectors to be involved regarding the nature of online pharmacies for drug retailing, introducing such implementation can create an opportunity to re-evaluate the current pharmacy structure and regulations, standardizing and enhancing the overall pharmacy services delivery, especially the community pharmacies.[46] Besides, it can also facilitate a shift of resources from hospital services to community-based health care as the latter one is underdeveloped in Hong Kong currently. This is also expected to help relieve the health burden of hospital sector.[46]

Lack of legislation monitoring

It is relatively tough and difficult to be the pioneer to introduce drug e-commerce in Hong Kong. As there is no relevant legislation or guideline shaping an appropriate environment for such development currently, taking reference to other countries that are with a more established system such as the United Kingdom or the United States can provide groundworks for drafting local guidelines. Revising the legislation regulating the 'brick-and-mortar' stores and relative licensure can help develop new regulations governing the online sale and supply of drugs by e-pharmacies in Hong Kong while aligning the newly proposed rules with the existing one. The development of online pharmacies in Hong Kong should not only rely on the efforts by local regulatory bodies, collaborations between different governmental bodies and organizations such as the Hong Kong

Information Technology Federation and the Office of the Privacy Commissioner for Personal Data, they are also required for ensuring cybersecurity and adequate personal information protection. In general, it remains to be a good direction to consider the future development of online pharmacies in Hong Kong.

ROLE OF PHARMACISTS

Pharmacists are critical in different stages on the development of the online pharmacies. For the operation of online pharmacies, community pharmacists and industrial pharmacists may be involved in maintaining the legality of the online pharmacy store to ensure both over-the-counter and prescription medicines are supplied and sold through the internet in compliance with the local law. On-site pharmacists may also be responsible for providing prescription clinical screening and comprehensive counselling in securing consumers' health. Pharmacists in the regulatory bodies are particularly important in the maintenance of pharmacy licensure and monitoring of the online sale and supply of drugs. Close surveillance and regular inspections are required to ensure the products provided from the online pharmacies are genuine and harmless. The processing of personal information and transaction details should also comply with the relevant regulations to maximize the protection to consumers.

CONCLUSION

Globalization facilitates the flow of information and distribution of pharmaceutical products, fostering the growth of drug e-commerce. Online pharmacies offer 24-hour limitless medical information access while it also provides a cheaper and faster way for the consumers to procure medicines. However, the cybersecurity and safety issues associated with illicit pharmacies shall also be addressed. Public education should be provided to the public to ensure that the medicines are procured from credible sources or those that are accredited by reputable verification programs. Collaborations between regulatory bodies of different countries are also required to create a comprehensive online pharmacy management system and transaction networks to combat internet crimes and global illegal drug trades.

Internet-based technologies are rapidly evolving in the 21st century, from drug e-commerce to e-prescribing, new technologies will continue to change the way of healthcare delivery. Pharmacists should always be well-equipped for the emerging applications and keep up-to-date with the latest trends in the pharmaceutical industries that are likely to impact the current pharmacy practice. With the efforts from the pharmacists of different fields, it is believed to bring the pharmacy profession a better and brighter future.

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Translational Medicine: Stepping up for the Healthcare game – Theme Speech from Professor John W Kao

INTRODUCTION

The Hong Kong Pharmacy Conference 2019 has been successfully conducted on 9-10 March 2019 at the Hong Kong Conventional and Exhibiton Centre, Wanchai. A number of thematic speeches were given by speakers of high caliber from various sectors.

Professor John W Kao was one of the invited speakers of the conference. He is the Chair Professor of Translational Medical Engineering, IMSE and BME of Faculty of Engineering and Li Ka Shing Faculty of Medicine, the University of Hong Kong and Head of the Biomedical Technology Cluster, Hong Kong Science and Technology Park. This issue included the speech of Professor John W Kao on the challenges and opportunities regarding the development of research products for healthcare use.

Figure 1. *Portrait of Professor John W Kao*

THE SPEECH

Thank you so much for the kind introduction and I have to thank the organizing committee for inviting me to give this talk. Thank you very much Phoebe. Prior to coming to Hong Kong, I spent almost twenty years at the School of Pharmacy at the University of Wisconsin Madison. I do not have a pharmacy background, but that was the place where I started my academic career. I came to realize the importance of pharmacy, as you may imagine the School of Pharmacy in the University of Wisconsin Madison is fairly large. It has more than one hundred professoriates and three major divisions, which are pharmaceutical sciences, pharmacy practice, and social administration respectively. I was exposed to a wide range of pharmacy services involving patient care, public policies, and fundamental research of how to discover new therapies including gene therapies, biologics, and small molecules. I also got to know the role of pharmacy, as defined as broadly as possible, beyond just dispensing and service, the role of pharmacy and pharmaceutical sciences in improving the livelihood of patients. It is such a great honor for me to be here, surrounded by very passionate people in this profession. It is really delightful to do that.

I will immediately shift gear, not focusing so much on patient care but what comes before that, which is the fundamental research in devising new drugs, new therapies, and how one translates those discoveries into the clinical setting. I provide that kind of perspective that is a little bit different from the service and the dispensing aspect of pharmacy. I hope you will find some value in this talk. As Secretary Che has already mentioned, pharmacy is very broad. There are a lot

of people involving in fundamental research, and I am focusing on that aspect of our profession.

Instead of taking a very high level look at this very broad field, I will just tell you what I know best and talk about my own story. I think that can bring everything down to a contextual level where we can resonate, and understand the challenges and the opportunities. Take me as a typical case, I do a lot of research in the basic medical area. I am going to walk you through the journey of much of my past 25 years of academic research. I am a very typical professor, trying to make a difference.

My area of research is in wound healing. It does not need an introduction on how important and what a critical clinical need that is. Everything from chronic wounds, acute wounds, surgical wounds are included. We understand the processes of healing fairly well. Wounds are started by injuries induced by many kinds of inducers and is followed by different levels and sequences of inflammation, granulation and remodeling. The cellular and biomolecular aspects of these different stages are known and a lot of people are still doing fantastic work on this.

If you look at what happens within the wound healing domain at a histological and cellular level, you will see it is very hierarchical, multicomponent and dynamic as there are different types of cells, proteins and cells regulating themselves and each other. These biological factors create this orchestra of healing process. Within these very complex processes, if there is any alteration in these natural events, there will be problems in the healing outcomes.

Being a biomedical engineer, we want to understand what kinds of intervention, drugs, and novel therapies we can come up with to influence the outcomes and processes in order to get the ideal outcome. There are several approaches and all these works were done in the School of Pharmacy. These were done with pharmaceutical scientists, clinicians, and people who have a very strong pharmacy background.

Drugs become the central component in our strategy in improving wound healing. The idea is fairly simple. We want to deliver all variety of bioactive small molecules, biologics, and even therapeutic cells to correct the underlying pathology, whether they are diabetic ulcers or acute trauma wounds. We want to deliver this using a biomatrix that will offer a control delivery of these compounds. Going beyond just a systemic injection, where toxicity can be a major issue, we want to localize a drug into a site where these interventions should take place. We developed a hyper material that contains both biological and synthetic components with desirable properties. This becomes more of an engineering strategy, which combines fundamental biology, pharmaceutical approach and engineering undertakings.

We designed this material and I will give you a broad overview. It is called Interpenetrating Network (IPN). Basically, it contains two major polymer components, the red and the orange. The red is a polyethylene derivative and the orange is a functionalized collagen. The formulation is in liquid and you can apply *in situ* and form a three-dimensional scaffold. Within the scaffolding, we can have different loading modality of incorporating different compounds. Some are covalently linked, while some are incorporated physically within this matrix. These are biodegradable matrix so as the drug eludes out into the tissue environment, you can design different delivery mechanisms, which covers dosing, dosage forms, therapeutic windows and things that are really relevant in pharmaceutical sciences.

At the same time, we are developing an advanced therapy that will have a physical presence in the body, and we want to understand some of the physical characteristics of this matrix. There is a wide range of properties that we quantify and measure. By varying the formulation of this matrix, we can have a wide range of physical properties, everything from how much water content incorporated, elasticity, swelling, so on and so forth. All of these have a clinical relevance in terms of how this matrix is being applied, such as the degradation rate and the release rate of the drug.

We also want to make sure that the material is very stable once the material is applied to a tissue. Because the physical contact and stability will have a great impact on the delivery of drugs from the matrix into the tissue bed. We want to measure the force that it would take to peel this material after it is formed onto the tissue. To kind of give you a sense, everybody knows what superglue is, right? Raise your hands if you have ever used superglue before. Keep your hands up if you have ever got superglue in between your fingers. For those who did not put up their hands, I am not saying to let you go home and start doing this. For those who kept their hands up, who had superglue between your fingers, you may try to open your fingers up right? That is a very human reaction. It takes about three to five Newtons of force to open your fingers and it is very painful. Here, it takes about one to three Newtons of force to peel off this matrix from a wet tissue bed. We are very confident that this material is very stable when it is formed onto the tissue. Again, it has a critical application relevancy in terms of drug delivery, tissue compliance, mechanical stability and all kind of that stuff.

What about *in vivo* applications? We want the material to degrade. We looked at a wide range of formulations and we can add materials that degrade within seven days or last more than almost a month in vivo. We published a lot of papers on delivering different kinds of molecules, like KGFs, FGFs, IO1 beta, antibodies, dexamethasone. We now understand the formulation of this biomatrix, how this can be use to deliver therapy in a very localized environment.

This represents two PhD thesis, both from pharmacy students, trying to understand how this material interacts

different cell types in the body including monocytes, keratinocytes and fibroblasts in this orchestration of growth factors and cytokines, and all of these have relevance in wound healing. We took this to small animals and all the way to large animals. In this particular model we used mini pigs and removed the epithelium of the pigs for the study. As part of my appointment was in surgery, I worked along with clinicians to look at how these wounds can be healed. If you ever had a severe injury to your face or get burned, a part of the skin from the leg is shaved off and put on your face. That is the gold standard and that is the model we are re-capitulating. Then there are different treatments to heal the donor site and you can see that with IPN, the healing outcome is very different from the conventional healing. We know when you put the different materials onto a wound it can direct different healing outcomes.

We thought this is fantastic and all the data I show you represent more than ten years of work. As typical researchers, we publish papers, and we understand these materials what is it good for and how can we use it in clinical settings. We looked at cutaneous wound healing and these are some studies done by the Center for Disease Control and Prevention in looking at the cause of trauma-related death. If you look at the disability-adjusted life years, wound healing is a big business. A lot of patients suffer from this. The kicker is that more than 50% wounds remain refractory to current conventional treatments. As pharmacists, you know that there are a lot of diseases that are not very responsive to conventional therapies. As a result, there is the role of creating new types of therapies to serve the patient population. One of the nastiest type of wounds is infective wounds. Clinical definition of infection is 10^4 organisms per tissue. When you have such a high level of infection, these wounds normally do not heal at all. The recourse for this kind of treatment is amputation.

There are lots of clinical needs and we thought that is fantastic because this gives us the chance to explore this material and to deliver different therapies to combat these clinical unmet needs. We incorporated stem cells into the matrix that I showed you. In addition to stem cells we also incorporated small molecule drugs. The idea is that the matrix and the stem cells can promote the healing while the small molecules in the drug can decrease the bio burden, which is a kind of the one-two punch strategy. We are able to see that the cells are viable and were stained in green nicely. Depending on the differentiation medium these mesenchymal stem cells can be differentiated into different lineages so the cells are in trap within the matrix and remain bio-functional.

Then we look at a full thickness wound infected with 10^4 *Staphylococcus epidermidis*. We can see the percentage of wound closure increases nicely when the material incorporated both the cells and the drugs. We thought that this is very exciting. We looked at the quality of the healing, histopathology, as well as epithelial thickness; the treatment containing the stem cells and the drugs have the best healing outcome. In fact, we also saw a decrease in bioburden with the treatment containing the stem cells and the drugs This shows that our original thinking is consistent with the observations.

The question asked by a lot of academics at this stage is: what's next? We are still publishing papers but we still do not have products on the market. Yet, I feel that there is a lot of wonderful results that can make a very compelling argument for translation.

Allow me to shift gear a little bit. Now I am going to focus on the development of technology, not on the research aspect. Translational research, in a nutshell, is to take technologies whether they are drugs, therapies, devices or diagnostics, from the research side to the patients' bedside, and eventually into a larger community. It is also a bilateral process where we identify community or patient needs to help us designing research. It is a two way communication and you can imagine how community pharmacists and hospital pharmacists can play a very important role in this continuum of translational research.

There are a lot of wonderful pipelines and technologies out there, including the researches we did. At universities including the Univertsity of Hong Kong, the University of Wisconsin–Madison , University College London, Stanford University, there are thousands and thousands of patents just sitting there. Because the problem is that after we publish paper, we do not know what is next. There are a lot of downward forces in terms of how to get technology into the market and in the pharmaceutical area. It is called "The Valley of Death".

Raise your hands if you have ever heard of the term "the Valley of Death". (Observes) Very few. I am glad because I am here to explain why it is so difficult to get research into patents. "The Valley of Death" is the time from discovery,the kind of research that I did, through development, the research I want to do, into the market. This takes more than 14 or 15 years at a cost of more than 2 billion USD. Another thing to note is that only one out of ten thousand is approved. That creates a problem when we are talking about antibiotic resistant bacteria. Because without new therapies, we would never be able to get new drugs into the market. That is the value of the research. Why does the process take so long? As you can see, a lot of these processes involve pharmacy. It involves discovery, screening, medicinal chemistry, formulations, and analytical tests to validate. Afterwards, you start looking at the manufacturing processes: how to scale this up from milligrams to grams to kilograms and that is just for small molecules? What about biologics? How big your bio reactor needs to be? What kind of animals are needed for studying the pharmacokinetics and toxicology? All these explain why it takes so long. This is an industry snapshot looking at pre-clinical discovery phase fails. You can see most drugs fail in the discovery phase due to the lack of efficacy and

pharmacokinetics issue. If you look at pre-clinical, phase I, II and III, most drugs fail because either they are too toxic in the early stage or in later stage the blue is efficacy. They just do not work in people. “The Valley of Death” is very serious phase and involves a lot of people from various pharmaceutical science disciplines coming together to resolve the issues.

We thought: “Well, let’s see how far we can take this IPN technology and see what sort of other things we can do at the university to develop this technology.”. One of the things that we start to realize very quickly is that universities cannot do a lot of things in the development phase. We were good in the research phase, but we are horrible in the development phase processes such as scale up, cost, manufacturing, QAQC, quality, validation. We designed the project to work with multiple stakeholders to develop this IPN biomatrix. We wanted to see what kind of system needs to be in place to facilitate the development of a new technology. We looked at things like packaging, sterilization, manufacturing and validation. In addition, we have a quality system set up. These are not basic science, instead they are development type of work. They are really more of a processing design, it takes a lot of planning, specifications checking, risk assessments and design. In fact, these are very iterative processes. At the end, you have a clinical product and you can start doing your clinical phase studies, Gantt charts and everything.

And this is what we got. It is basically clinical grade IPN in two jars in a bag. It is not the product but the processes - how much we learned about taking basic research into really the bedside. It involves a tremendous amount of skill sets from wide range of people, such as pharmacists, engineers, investors, project managers, technology transfer offices, lawyers, clinicians, industry like Merk, and bunch of funding agencies.

The topic of my talk is “Is Hong Kong Ready for this?”. It is now the time for Hong Kong to tackle the problem of the Valley of Death. Hong Kong, in addition to all the wonderful clinical services that we already have, is ready to tackle the next challenge of getting the next exciting drugs into the patients. It really involves academia, government and industry coming together.

Why do I think Hong Kong is ready? This is because there are many unique attributes that Hong Kong has that other regions or regional countries may not have at the moment. Hong Kong has a very robust legal framework that is tremendously important, as intellectual property protection and intellectual protection is very critical. It has a very high quality and internationally recognized research foundation as well as clinical services. Recently, as the Secretary already mentioned, there is a real commitment by the government to do this.In the last budget of Policy Address around innovation and technology, the government has put a significant amount of investment into the innovation and biomedical space. I am talking about 20 billion dollars: 10 billion dollars for the Innovation and Technology Commission, 10 billion dollars for research clusters around artificial intelligence and healthcare technologies. There are a lot of resources that the government is pouring into.

We also have an ecosystem in the making, which is the Hong Kong Science and Technology Park. You all are very familiar with the clinical aspect of the Hong Kong government and I think the Science Park is something that will play a more prominent role in going forward. Because a lot of the funding is funneling through the Science Park to help us create this innovation-healthcare ecosystem. Just to give you a background, the Science Park is roughly divided into five clusters, and biomedical technology is one of the clusters. It covers therapeutics, medical devices, and diagnostics. Therapeutics include small molecules, biologics, and regenerative medicines. The Science Park is a platform they have built where they pour in research from R&D, universities, and different kinds of research agencies. For those who might be interested, for the students in the audience, if you have a good idea and want to take up the value chain, the Science Park has different kinds of programs: everything from internships to incubation programs and even a venture capital to help invest in early phase companies. There are a lot of support already in place for Hong Kong to really step up the game in tackling this healthcare innovation.

Simultaneously, there are a lot of infrastructures in the works. There is an animal pharmacology and drug safety center being considered and discussed. There is also a pilot batch facility, a biobank, tissue banks, and obviously clinical trials in the universities already working much closer with the Science Park and the companies within the Science Park. We have infrastructure, money and talents. That is why I think the time is now for us to think about how to deliver new ways of therapeutics to serve the clinical needs.

In conclusion, I think as a personal story the IPN is an interesting platform that we can deliver different kinds of drugs including cells to meet clinical needs. Through my own personal journey, I come to a deep appreciation of just how important collaboration is. Collaboration across disciplines, pharmacy, engineering, clinical medicines and business, as well as academia, private sectors, and the public sectors. Lastly I share the same excitement with you in terms of where Hong Kong is and where Hong Kong can be in the coming years. We have just started this journey together. Once again, Phoebe thank you so much for having me and I really appreciate your attention. Thank you.

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Pharmacist-led Smoking Cessation: Pharmacological and Non-Pharmacological Options

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ABSTRACT

Smoking cessation is a pressing issue, concerning not only smokers, healthcare practitioners, but also every citizen in Hong Kong, as smoking-led ailments are taking its toll on our healthcare system, and undermining the productivity, not to mention that second-hand smoking can impose deleterious effects on non-smokers. Pharmacists, as the drug expert that are trusted by the public, have the responsibility to educate the public to deter them from smoking, while encouraging smokers to quit. This article summarizes the mechanism, pros and cons of the first line pharmacological options: nicotine replacement therapy, varenicline and bupropion, while suggesting e-cigarettes should not be a suitable aid for smoking cessation. This is followed by introducing about the smoking cessation services provided by the Hospital Authority, Department of Health, or other institutions. Nevertheless, these services currently do not fully incorporate the role of pharmacists. Therefore, it is suggested that more quality local research should be carried out to explore the benefits from pharmacist input in smoking cessation, and in the hope for the future that there will be pharmacists-led smoking cessation clinics in the community.

Keywords: *smoking cessation, pharmacists' roles, nicotine replacement therapy, e-cigarettes*

INTRODUCTION

Tobacco smoking is an abysmal habit that leads to numerous preventable diseases. With taxation, health promotion and pharmacological advancement, the prevalence of smoking has declined slowly, and reached its lowest, i.e. 10.5% of the Hong Kong population in 2017.[1] This figure did not lessen the government's concern, as a study conducted by the Hong Kong University estimated the cost incurred by smoking had amounted to near USD 4.7 billion. Smoking does pose a huge burden on our economy and public health system.[2] There remains room for improvement in smoking cessation rate.

The process of ending tobacco dependence can be arduous, especially without any professional help. According to a global study in developed cities: every year, 70% of smokers are willing to quit; 40% attempt to quit; but only 3 – 7% can do so without any aid.[3] Healthcare professionals have the responsibility and knowledge to promote public health. In particular, pharmacists are equipped with extensive pharmacological knowledge and can take up the role for providing professional advice for other professionals and the public regarding smoking cessation.

This article will first discuss the currently available first-line pharmacological options in Hong Kong, including nicotine replacement therapy (NRT), Varenicline and Bupropion, followed by drugs combination, and the controversy of using electronic cigarettes as a cessation aid. Also, it will elucidate the availability of other smoking cessation aids available in Hong Kong and assess their effectiveness. Lastly, the important roles that pharmacists play in smoking cessation will also be discussed.

PHARMACOLOGICAL OPTIONS

Multiple drugs have been designed to aid smoking cessation, which is a long and difficult journey. It needs persistent effort, and most likely, multiple failures and attempts, combined with long-term follow-up, before tobacco dependence is completely under control. Therefore, it is important to treat tobacco dependence as a chronic disease and prepare for potential relapse. Medications can only increase the success rate of staying abstinence, but may not completely prevent relapse. Relapse rate may be minimized by alternating one medication with another, in addition to psycho-behavioural support.[4]

Nicotine replacement therapy (NRT)

Efficacy

Nicotine is the main substance in tobacco that causes addiction. The mechanism of NRT relies on nicotine's effect to reduce withdrawal symptoms due to smoking

cessation, suppressing the crave to smoke.[5] The substantially lower level and slower onset of action of nicotine from NRT can help reduce the reinforcing effects of cigarettes.[6] NRT has been shown to increase rate of abstinence by 50-60%, compared to placebo or without the use of any aid, with variations between different doses and dosage forms.[7]

Dosage forms

NRT comes in various dosage forms: transdermal patches, buccal absorption products including chewing gum, lozenge and inhaler. However, inhalers are not marketed or registered in Hong Kong. All NRT available in Hong Kong are marketed under the brand names Nicorette® and Nicotinell®.

The various formulations are designed differently, catering to the needs of clients. Their characteristics are summarized in **table 1**. Pharmacists can consider the following factors in order to choose the best dosage form of NRT:

Patient's other medical conditions

Some patients have additional medical conditions that are worth extra attention. For example, dentures and braces may interfere with chewing, therefore, patches and lozenges would be the preferred options.[6] Patients with dermatologic conditions such as psoriasis are more likely to have skin irritation and should consider other NRT formulations.[6]

Patient's dependence level

Patches provide continuous release of nicotine over 16 or 24 hours. Patients with strong morning cravings might benefit from 24-hour patch. On the other hand, NRT gums have a more rapid onset of action and a shorter duration of action, therefore allowing flexible and as needed dosing. The chewing action may be beneficial for patients who desire oral stimulation.[6]

Smokers who have stronger nicotine dependence may experience craving even with patches. Pharmacists may recommend a combination of transdermal patch and an oral dosage form of NRT; the patch can provide a sustained level of nicotine, while gums or lozenges can satiate the immediate urges. Meta-analysis suggested that combining different dosage forms could augment the rate of abstinence compared to monotherapy.[8]

Tolerance to side effects

Differentiating between nicotine withdrawal symptoms and side effects due to NRT is important before the treatment plan can be decided. The common withdrawal symptoms include difficulty concentrating, irritability, anxiety, anger, depressed mood, sleep disturbance, and craving.[9]

The side effect profiles of NRT dosage forms differ. NRT gums and lozenges may cause sore mouth and throat, hiccups and stomach aches. For patients with peptic ulcer, NRT gums and lozenges should be used with caution. NRT gums may also cause jaw pain.

There are counselling tips that can alleviate the side effects from NRT: sore mouth, jaw ache can be prevented by parking the medication in different areas.[10] Nausea, minor degrees of heartburn or indigestion can be alleviated by slow chewing.[11]

Patches can cause skin irritation. Therefore, it is important to rotate the application site daily. Over-the-counter hydrocortisone cream can be applied to relieve

Table 1. Comparison of different NRT dosage forms[4][5][6][61]

Type of NRT	Transdermal Patches	Chewing Gums	Lozenges
Advantages	• Better compliance as it is easy to administer • Either provide 16 hours or 24 hours of nicotine continuously	• Instantly increase the level of nicotine to alleviate the craving for cigarettes • Provide oral stimulation; target patients who identify boredom as a trigger for smoking	• Instantly increase the level of nicotine to alleviate the craving for cigarettes • Simple administration compared to patches and gums • Provide better oral absorption compared to gums
Disadvantages	• May cause skin irritation due to the adhesives (up to 50%) • May detach on wet skin • Does not alleviate the immediate urge of smoking • Long-term use may cause insomnia and sleep disturbance	• If not administered correctly, the absorption can be highly affected • May cause more side effects than patches: sore mouth and throat, hiccups, jaw ache, stomach aches	• If not administered correctly, the absorption can be highly affected • May cause more side effects than patches: mouth and throat irritation, hiccups
Precautions	• To prevent or alleviate skin irritation, can apply to a different site every day; if the irritation persists, try with other brands as they may use different adhesives.	• Nicotine is absorbed in neutral pH environment; thus, users need to avoid acidic food or beverages 15 minutes before taking the gum	• Nicotine is absorbed in neutral pH environment; thus, users need to avoid acidic food or beverages 15 minutes before sucking the lozenges
Current products on the market	• Nicotinell® TTS 10 /20 /30 Pads • Nicorette® Invisipatch® 10/15/25 mg /16Hr	• Nicotinell® Classic/Mint/Fruit Chewing Gum 2mg/ 4mg	• Nicotinell® Mint Lozenges 1 mg (Switzerland)

the irritation. Other than skin reaction, 24-hour patches tend to produce insomnia and vivid dreams; if it is intolerable for patients, 16-hour patches are preferred, so that the patch is removed before sleep. However, the level of nicotine takes 30 minutes to 3 hours to reach adequate level, therefore, 16-hour patches are recommended for smokers who have relatively weaker craving in the morning; otherwise, a short-acting NRT such as gums or lozenges can be used while awaiting for the patch to work.[12]

The number of cigarettes per day

NRT patches and gums come in different strengths, catering to users of variable degrees of dependence on cigarettes. There are guidelines on the choice of dose and duration of these NRT products. Hong Kong Tobacco Control Centre has issued a set of recommended doses and regimen of different forms of NRT.[13] Product-specific information is also listed on the package insert.

Safety

Cardiovascular diseases
According to the EAGLES study, NRT was not found to be associated with a difference in major adverse cardiovascular events in patients with stable cardiovascular diseases.[14] For patients with acute coronary syndrome, the benefits of smoking cessation outweigh the potential risk of NRT in general. However, nicotine carries adrenergic and vasocontrictive effects, which can increase cardiac workload, therefore, patients with unstable cardiovascular conditions such as serious arrhythmia, recent stroke or recent myocardial infarction should seek medical advices before using NRT.

Varenicline

Mechanism

Varenicline possesses therapeutic superiority over other first-line agents, endowed by its dual pharmacological properties; it can activate the α4β2 nicotinic cholinergic receptors in a partial agonist manner, to maintain a certain level of dopamine, relieving the withdrawal syndrome. Also, it competes with nicotine for the α4β2 sites, reducing nicotine's ability to induce dopamine release, thus, undermining the reward from smoking.[15]

Efficacy

Varenicline's efficacy is of the highest among other first-line treatments, i.e. NRT and bupropion. It can increase the quitting rate by at least three times when compared to placebo, which is higher than bupropion and any single form of NRT.[15]

Safety

The most common side effect associated with Varenicline is nausea which is usually mild to moderate and only present in the early phase of the treatment, that is unlikely leading to treatment discontinuation.[16]

Other common side effects are insomnia, headache and abnormal dreams which are also some common nicotine withdrawal symptoms.[17]

In 2008, US Food and Drug Administration (FDA) and European Medicines Agency (EMA) added a black box label to warn about neuropsychiatric adverse events, after the post-marketing surveillance reports had suggested varenicline was associated with increased risk of depression and suicidal behaviour compared to NRT.[5] This was later refuted by two FDA-sponsored epidemiological studies showing there was no increase in risk of neuropsychiatric hospitalizations when compared to NRT. The warning label was removed in 2016 after FDA has determined the risk of serious psychiatric side effects with varenicline is lower than previously suspected based on its review of a large clinical trial.[18] Nevertheless, the risk of these mental health side effects is still present, especially in those with history of or concurrent mental illnesses such as depression, anxiety disorders, or schizophrenia. It is strongly recommended that patients on varenicline should be under close monitoring for neuropsychiatric symptoms.

Another FDA label update was implemented in 2011 to warn users about a small, increased risk of cardiovascular adverse events in patients with underlying cardiovascular diseases after FDA's review of a randomised clinical trial of 700 smokers with cardiovascular disease received either varenicline or placebo. The absolute risk of cardiovascular adverse events with varenicline, in relation to its efficacy in smoking cessation, is small.[19] Patients should notify their healthcare providers of new or worsening CV symptoms and to seek immediate medical attention if they experience signs and symptoms of myocardial infarction or stroke.

Available Product

The only Varenicline marketed in Hong Kong is ChampixTM by Pfizer. It is a prescription drug, indicated for smoking cessation, in the strength of 0.5 or 1mg.

Bupropion

Mechanism

Bupropion inhibits the dopamine reuptake in the nucleus accumbens, thus reducing the dopamine deficiency experienced in nicotine withdrawal and alleviating the withdrawal symptoms.

Bupropion also antagonizes the postsynaptic nicotinic receptors, undermining the pharmacological

effects of nicotine.[20] Concurrently, it blocks the nicotine-induced release of dopamine at the postsynaptic sites, reducing the hedonic effects brought by nicotine. The combined actions help break the reinforcing effects due to chronic nicotine exposure.[21]

Effectiveness

Bupropion was shown by review studies that it could increase the success rate by nearly two times compared to placebo, therefore, it is having a comparable efficacy as to any single form of NRT.[22]

Safety

Having been employed as an antidepressant for decades, bupropion's safety profile is well documented. Bupropion's common side effects include insomnia, headache, dry mouth, nausea which do not lead to a higher discontinuation rate than using NRT.[23] These side effects usually take place during the first two weeks of the treatment, and are rarely extended to three months.[24] For insomnia, pharmacists can counsel patients to take the first bupropion in the morning as early as possible, and the second one to be taken preferably four hours before sleep. If the side effects persist and affect compliance, dose reduction to 150mg/day can alleviate the symptoms.[4]

Concurrent medications:

Seizure-causing medications
Seizure is an adverse effect caused by bupropion that pharmacists have to pay attention to, even though they occur very rarely (0.1%),[25] but it can be very serious. These episodes are more prevalent in patients with brain circulation disorders, head trauma, and simultaneous medication lowering the seizure threshold.[26]

Cytochrome p450 2D6 related drugs
Bupropion has multiple actions, including cytochrome p450 2D6 inhibition. It can reduce the metabolism of other drugs by this enzyme.[27] Therefore, it may be necessary to reduce the dose ofdrugs metabolized by CYP2D6 with narrow therapeutic index, for instance, selective serotonin reuptake inhibitors (SSRIs), antidepressant, beta blockers, propafenone, flecainide, risperidone and thioridazine.[4] On the other hand, drugs that require activation by CYP2D6 to be effective, such as tamoxifen, could have reduced efficacy when administered concomitantly with bupropion.

Available Product

Zyban 150mg prolonged release tablet is the brand product licensed for smoking cessation. But the only available brand products in Hong Kong are Wellbutrin sustained release tab and extended release tab, though their indications do not include smoking cessation aid.[28]

Drugs combination

NRT combination

It is proven that adding oral forms to transdermal patches can increase the efficacy, as the ad libitum use of gums or lozenges can satiate the instant craving. Combined NRT can provide a similar abstinence rate as Varenicline. It is safe and effective with better compliance.

Combination of NRT with Bupropion

Bupropion and NRT work in different mechanisms, so they can work synergistically and improve the smoking abstinence rates. However, this effect is only short-term and the improvement will diminish in the long term, i.e. > 6 months.[29] Currently combination of bupropion SR (Zyban) plus nicotine patch is approved by the FDA for smoking cessation.

Combination of NRT with Varenicline

Monotherapy of varenicline can cause great discomfort from withdrawal during the period for the plasma concentration to reach a stable level; although NRT may reduce the withdrawal effects and craving, the action of nicotine may be blocked by varenicline.[4] Trials showed that this combination was safe and did not lead to more serious side effects than NRT monotherapy.[31] This combination was not recommended by guidelines currently.[4][9]

Combination of Bupropion and Varenicline

Combination therapy with varenicline and bupropion may increase the smoking abstinence rates, compared to that observed with monotherapy of both medications.[30] The use was safe, without any increase in depressive symptoms and suicidal ideation.[29] However, only one study was done so far, and more evidence is needed to support the use.

Pharmacological combinations are possibly more effective than monotherapy but stronger evidence from clinical trials are warranted. Nonetheless, considering their associated cost and the side effects, combined options should only be recommended for heavy smokers (e.g. peak consumption exceeded 24 cigarettes,[26] instead of users with low nicotine dependence.[32]

Determining the Quit smoking date

When NRT has been started, smoking has to be stopped immediately to prevent the overdose of nicotine,[33] while bupropion and varenicline can be started 1-2 weeks before the quit date, as to allow the medication concentration to reach a stable level.[4]

E-CIGARETTES

E-cigarettes are currently being promoted as a smoking cessation aid,[34] and praised as being more effective than NRT.[35] However, more studies have revealed that e-cigarettes should not be considered as a smoking cessation aid, let alone being marketed as a healthy alternative to cigarettes, for the following reasons:

E-cigarettes only help reduce the smoking intensity, but not quit smoking

Adkison et al. reviewed studies in several developed countries, and found that e-cigarettes users have significantly reduced their smoking intensity (number of cigarettes per day) only, without producing a significantly higher smoking cessation rate than non-users.[36]

Other population-based studies have even manifested that there was a correlation between e-cigarettes users and lower cigarette quit rate.[37] This was also confirmed by several clinical trials, that e-cigarettes are not efficacious in smoking cessation.[38][39]

Reduction of smoking intensity could be beneficial for patients, but its medical benefits are very limited. The 2014 report of the US surgeon General asserted that the reduction in the number of cigarettes is much less effective than quitting entirely, in preventing smoke-related mortality.[40]

There is no consistent finding for a decrease in intensity leading to lower mortality rate,[41][42] and it was manifested that even light smoking would drastically elevate the risk of cardiovascular diseases.[43] Risk levels of most of the smoke-related diseases, for instance, lung cancer,[44] pancreatic cancer[45] and oesophageal cancer[46] are highly positively correlated with the cigarette exposure duration instead of intensity.

Table 2. Summary of the characteristics of all pharmacological options

Drug	Dosage form and regimen	Advantages	Disadvantages	Specific counselling advice	Contraindication/ Precautions
NRT	• Available forms in Hong Kong: Gum, lozenges, patches	• Robust safety profile • Satiate the needs of smoking • Combined forms showed higher efficacy than any single type of NRT, and is as effective as varenicline	• Some patients tend to avoid nicotine-containing products • Use cautiously in patients with cardiac problems • Patients' techniques of applying the medications affect the efficacy significantly	• Users have to stop smoking immediately when the treatment starts • Need special counselling on how to apply the medication	Contraindications: • Post-myocardial infarction • Severe arrhythmias • Severe or worsening angina pectoris • Pregnancy (under the advice of physicians or pharmacists) Use with cautions: • Peripheral vascular disease • Endocrine disorder (pheochromocytoma, hyperthyroidism, and diabetes mellitus) • Peptic ulcer disease
Varenicline	• Start the drug 1 week before quit date • Day 1-3: 0.5mg once daily • Day 4-7: 0.5mg twice daily • Day 8 and onwards: 1mg twice daily	• Show superior efficacy over other first line medications	• Nausea and insomnia are common side effects	• Treatment is started one to two weeks before the quit-date • Patients need to report any behaviour and/ or mood change to healthcare provider.	Contraindications: • Aged under 18 • Pregnant or breastfeeding Use with cautions: • End-stage renal diseases
Bupropion	• Wellbutrin (the only bupropion available in Hong Kong) has no dosing recommendation for smoking cessation.	• Show equal efficacy as any single form of NRT	• Cause headache, insomnia and nausea • May cause serious epilepsy; contraindicate in patients with risk of epilepsy	• Treatment is started one to two weeks before the quit-date	Contraindications: • Epilepsy; or on medications that lower seizure threshold • Patients undergoing abrupt discontinuation of alcohol or sedatives Users should be cautious: • Recent myocardial infarction or unstable heart disease • Bipolar disorder
E-cigarettes	Not recommended as a pharmacological option	/	/	/	/

Given that smoking reduction is not effective in reducing mortality rate, the key discussion focus would be on whether smoking reduction can lead to complete smoking cessation. However, there is no data or study to shed light on this issue, and extra research is crucial in this respect.

E-cigarettes deliver harmful substances that are both present and absent in conventional cigarettes.

It is irrefutable that e-cigarettes deliver fewer types of harmful chemicals in much less amount to the smoker,[47] and the people around them than conventional cigarettes.[48] Nevertheless, they still provide a wide range of notoriously health-damaging chemicals, including carcinogens. Propylene glycol when heated and vaporized in e-cigarettes can form propylene oxide, a 2B carcinogen;[49] Acrolein in glycerol form can cause respiratory tract irritation.[50] It was shown that e-cigarettes can significantly increase airway resistance,[51] potentially leading to exacerbation of chronic obstructive pulmonary diseases (COPD) and asthma. The increase in resistance could be due to the cytotoxin to human pulmonary fibroblasts, found in the vapor.[52]

The most notable harmful substances created by e-cigarettes would be particulate matters. These particles are able to penetrate into the human circulation either through the lungs or the blood vessels in the head,[53] and they are proven to cause cardiovascular diseases.[54] These fine particles were identified in the vapor from e-cigarettes, at a level and size distribution resembling the smoke from conventional cigarettes.[55]

In summary, e-cigarettes show no efficacy in smoking cessation. At best, it can reduce smoking intensity, which should not be the goal of smoking cessation. The harmful substances delivered by e-cigarettes are not negligible and can cause considerable damage to human health. Thus, it is, by no means, deemed as a smoking cessation aid.

In order to capture the characteristics of pharmacological options, a summary is provided in **table 2**.

NON-PHARMACOLOGICAL OPTIONS

Non-pharmacological means are proven to be effective, and are additive to the pharmacological effects from medications.[9] As a trusted healthcare professional, pharmacists should be able to provide pharmacological counselling, while refer patients to various non-pharmacological aids, to augment their chance of success.

Quit-lines

There are currently five different agencies providing hotline counselling services: Department of Health, Tung Wah Group of Hospitals, Hospital Authority, Pok Oi Hospital and the University of Hong Kong. The University of Hong Kong focuses on young smokers aged 25 or below, while the others target the general public.[13] Both international and local studies have confirmed that hotlines are conducive to smoking cessation, by providing professional cessation counselling, and pharmacological information.[56] The smoking cessation hotline of the Department of Health even provides immediate nicotine dependence assessment, as a reference for the user.

Access to the quit-line services by calling the Integrated Smoking Cessation Hotline through 1833 183, then press the corresponding number to connect to the service, according to **table 3**.

Table 3. Contacts of quit-lines

Quit-line provider	Hotline Number
Department of Health Smoking Cessation Hotline	Press 1
Tung Wah Group of Hospital Smoking Cessation Hotline	Press 2
Hospital Authority Quit-line	Press 3
Pok Oi Hospital Smoking Cessation Service using Acupuncture	Press 4
Youth Quit-line of University of Hong Kong	Press 5

Internet website

Tobacco Control Office launched an online platform to aid smoking cessation. It provides cessation planning, smoking cessation tips and information. In order to attract the younger smokers, it includes games to explain the concepts of smoking cessation.

Access the Interactive Online Cessation Centre by scanning **Figure 1** with your smart device.

Figure 1. *QR code linked to the Interactive Online Cessation Centre*

Psychological counselling

Tung Wah Group of Hospitals have established eight integrated centres on smoking cessation, providing smoking cessation counselling service to the public. Besides doctors and nurses, clinical psychologists and counsellors would also engage in these services. Clinical

psychologists and counsellors' involvement were proven to be able to increase the success rate.[57]

Apps

There are dozens of mobile phone applications (apps) available in the market that aim to help users quit smoking. However, most of them are from private institutions and their sources of information could be questionable. A study reviewing 47 smoking cessation mobile apps, found that most of them had a low level of adherence to the official key guidelines.[58] In order to convey the correct information to the public, the Tobacco Control Office of Department of Health developed an official "Free Quit Smoking Mobile App" to assist smokers to overcome their dependence.[13]

Download the app by scanning **Figure 2** with your smart device.

Figure 2. *QR code to download Free Quit Smoking Mobile App by Tobacco Control Office of Department of Health*

ROLE of PHARMACISTS

Product Recommendation

Pharmacists are the experts on drugs, and they are familiar with the available pharmacological options. There are no studies on the knowledge level of Hong Kong pharmacists regarding smoking cessation, which may be one direction of future research. This is important as pharmacists, especially community pharmacists, are the most accessible front-line healthcare professional, apart from general practitioners.[59] Community pharmacists and pharmacists of other fields should advocate the importance of smoking cessation and recommend appropriate medications to patients who wish to quit, in addition to suggesting other non-pharmacological means.

Patient counselling (5As, 5Rs)

As mentioned, pharmacists can be found in primary care settings easily. High accessibility provides pharmacists an opportunity to encourage patients to quit smoking with the aid of the 5As and 5Rs techniques (**Table 4 and Table 5**)

When approaching a patient who is in need to stop smoking, the pharmacist first needs to assess whether he or she is willing to quit. If the answer is yes, then the pharmacist can employ the 5As techniques to assist quitting. If the patient is not ready to quit, 5Rs and motivational interview techniques (**Table 6**) are conducive to motivate the client.[13]

Table 4. Summary of 5As techniques to help quit

Ask	• Ask about smoking status for a progress record, including daily consumption and years of smoking • Avoid using a condescending tone to create a friendly and trusting environment
Advise	• Convince the patients to stop smoking with a clear, personalized and adamant manner • Use the Fagerstrom test **(Table 7)** or smokerlyzer to analyse the smoking status and motivate them.
Assess	• Assess the client's readiness to quit • Readiness is defined as the client sees quitting as important and feels confident to quit as well • If the client is not ready, 5Rs and motivational interviewing techniques should be employed.
Assist	• Work out with the client on the smoking cessation plan • Provide appropriate techniques for solving foreseeable problems • Recommend pharmacological options • Assist by making referrals to other professionals • Provide pamphlets or quit-line card
Arrange	• Schedule follow-up sessions; ideally to be one week after the quit date • Recognize the progress and encourage to continue • When relapse occurs, encourage to repeat quit attempt and review the cause

Table 5. Summary of 5Rs techniques to motivate quitting

Relevance	• Make sure clients understand why quitting is important to him/her and the people around them • Analyse the previous failed attempts and identify possible improvement
Risk	• Explain the consequences of continuing the smoking habit • Example of risks include: Acute: shortness of breath; impotence and infertility Long-term: heart attack and stroke Environmental: second-hand smoking can cause cancers and asthma • Emphasise the fact that smoking reduction does not minimize the harm
Rewards	• Remind the client of the relevant benefits brought by smoking cessation, both personal benefits and to his/her family
Roadblocks	• Prepare the clients for the various barriers, e.g. withdrawal symptoms
Repetition	• Remind the clients that most smokers make repeated attempts and encourage them to make great effort

SUGGESTIONS

Research on the potential benefits brought by pharmacists

Currently, there is no study assessing the benefits brought by the pharmacists in smoking cessation service in Hong

Table 6. Motivational interview (MI)	
Principles of MI	• Partnership: it is a collaboration between the counsellor and the client • Acceptance: the power of change rests within the client; counsellors only empower them by showing empathy and affirming their strengths and efforts • Compassion: the counselling is focusing on the benefits for the client but not others • Evocation: draw out the client's own thoughts and reasons to change instead of imposing the counsellor's ideas on the client
Core interviewing skills	• Open questions: allow patient to express freely and think more deeply about the issue • Affirmation: recognize the patient's strength and effort • Reflections: apply reflective listening, repeat what the client says, allowing the client to hear again the thoughts • Summaries: recap what has been discussed after the session

Kong. This could be due to the fact that pharmacists are not a major active player in smoking cessation clinic service in Hong Kong. Reflecting upon other countries, a systemic review of randomised controlled trials suggested that trained community-pharmacists can provide counselling service for their clients, which have a significant positive effect on smoking cessation rates.[60] There is a need for a local research in Hong Kong to address the significance of pharmacists in smoking cessation. This serves as compelling evidence to gain support for launching pharmacists-led clinics.

CONCLUSION

There is an urgency to promote smoking cessation in Hong Kong, as smoking puts a heavy burden on our health system and economy. Pharmacists carry the responsibility to encourage the public to quit tobacco dependence, by first introducing all non-pharmacological options, for example, quit-lines and clinics, to help patients finding the suitable supports and information. Equipped with proficient knowledge on drug use, pharmacists can then recommend nicotine replacement therapy, of the correct dosage form that best fits the clients; or refer to the physicians to prescribe varenicline, enhancing the treatment efficacy and increase the cessation rate. Last but not least, in order to advocate the role of pharmacists in cessation service, future research is warranted to assess the benefits that pharmacists could bring in the service and explore the possibility of a community pharmacist-led clinic.

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Table 7. Fagerstrom Test of Nicotine Dependence	
How soon after you wake up do you smoke your first cigarette?	
After 60 minutes	0
31 – 60 minutes	1
6 – 30 minutes	2
Within 5 minutes	3
Do you find it difficult to refrain from smoking in places where it is forbidden?	
No	0
Yes	1
Which cigarette would you hate most to give up?	
The first on in the morning	1
Any other	0
How many cigarettes per day do you smoke?	
10 or less	0
11 – 20	1
21 – 30	2
31 or more	3
Do you smoke more frequently during the first hours after awakening than during the rest of the day?	
No	0
Yes	1
Do you smoke even if you are so ill that you are in bed most of the day?	
No	0
Yes	1
Total Score:	_____
Results analysis:	
Total Score	Advice
≤ 3	Low nicotine dependence
4 -5	Moderate nicotine dependence
6 -10	High nicotine dependence

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Questions for Pharmacy Central Continuing Education Committee Program

(Please be informed that this article and answer sheet will be available on PCCC website concurrently. Members may go to PCCC website (www.pccchk.com) to fill in their answers there.)

2 CE Units

Pharmacist-led Smoking Cessation: Pharmacological and Non-Pharmacological Options

1. ***Which of the followings is the advantage of nicotine transdermal patches?***
   A. For patients who identify boredom as a trigger for smoking
   B. Can be used to alleviate immediate urge of smoking
   C. Better compliance
   D. The patch is designed to avoid skin irritation

2. ***Which of the following descriptions are TRUE for nicotine chewing gums?***
   A. Compared to lozenges, chewing gums' efficacy would not be affected by techniques
   B. "Chew and Park" technique not only helps improve absorption but also reduce the side effects
   C. Nicotine dissolves better in an acidic environment; thus, it is advised to use the gum right after food
   D. Even though gum is an oral dosage form, nicotine is efficiently absorbed through the skin, thus the gastrointestinal side effects of patch and gum are similar.

3. ***Which of the following medications do not require an immediate cessation of cigarettes smoking at the start of drug treatment?***
   i. Varenicline (Champix®)
   ii. Bupropion (Zyban)
   iii. Nicotine patches/gums/lozenges
   A. i, iii
   B. i, ii
   C. ii, iii
   D. i, ii, iii

4. ***Which of the followings is NOT an absolute contraindication of Nicotine Replacement Therapy (NRT)?***
   A. Recent myocardial infarction
   B. Severe arrythmias
   C. Severe angina pectoris
   D. Diabetes Mellitus

5. ***Which of the following has the highest efficacy as monotherapy in smoking cessation rate?***
   A. Varenicline (Champix®)
   B. Bupropion (Zyban)
   C. Nicotine gums/lozenges
   D. Nicotine patches

6. ***How is bupropion (Zyban) interacting with other medications?***
   A. Its level is increased significantly when metabolism is inhibited by CYP450 2D6 inhibitors.
   B. It inhibits CYP450 2D6 enzymes, thus increasing the levels of other 2D6 substrates significantly.
   C. It induces CYP450 3A4 enzymes, thus decreasing the levels of other 2D6 substrates significantly.
   D. It inhibits P-gp proteins, thus reducing the effects of other medications that are P-gp substrates.

7. ***Which of the following is NOT a warning of varenicline (Champix®)?***
   A. Seizures
   B. Cardiovascular events
   C. Pre-existing psychiatric disorder
   D. Liver dysfunction

8. ***Which of the following is not a nicotine withdrawal symptom?***
   A. Irritable
   B. Insomnia
   C. Loss of appetite
   D. Depression

9. ***Which of the following descriptions regarding e-cigarettes is CORRECT?***
   A. E-cigarettes reduce smoke intensity, thus help reduce mortality rate caused by cigarettes smoking.
   B. E-cigarettes reduce smoke duration, i.e. help smoking cessation
   C. E-cigarettes may contain less harmful chemicals than conventional cigarettes, but still pose harm to users.
   D. E-cigarettes, though heavily recommended against by healthcare professionals, are not regulated in Hong Kong.

10. ***Which of the followings is NOT included in the 5R techniques?***
    A. Reduce
    B. Rewards
    C. Roadblocks
    D. Repetition

Answers will be released in the next issue of HKPJ.

CE Questions Answer for 271(D&T)

Medication Management in Patients Undergoing Surgery

1. D 2. B 3. D 4. D 5. D 6. D 7. A 8. A 9. B 10. C

CE Questions Answer for 271(D&T)

COVID-19: An Overview of its Transmission, Management and Prevention Strategies

1. B 2. A 3. C 4. D 5. D 6. D 7. D 8. B 9. C 10. D

SUCRATE® gel

(Sucralfate 1g/5ml)

Actively treat GERD & Gastritis with lesser early relapse
Heal damaged G.I. lesions & promote complete recovery

Indication
Gastro-esophageal reflux disease (GERD), gastritis and peptic ulcers of various origin

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Per 5ml sachet containing 1 gram of sucralfate gel

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- Patented gel form with double surface area of bio-adhesion to ulcerated G.I. tissues
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One sachet 2-4 times a day, according to physician's judgement.

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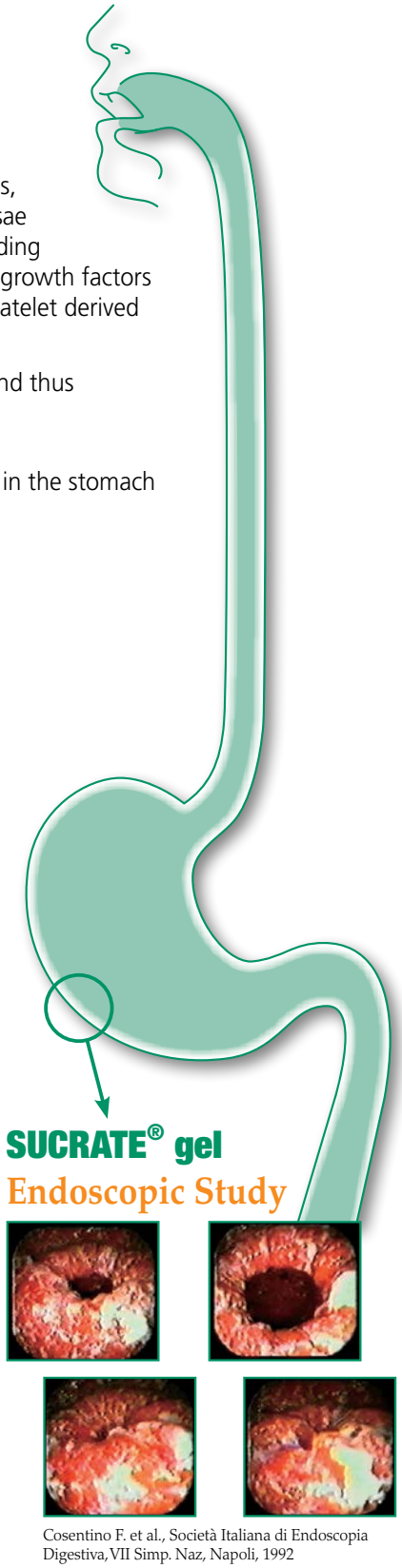

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SHPHK – Keep Calm and Carry On

New Opportunities for Pharmacists in the Midst of COVID-19

In the past few months, there has been continued on and off outbreaks of COVID-19 in the community. Healthcare professionals have been facing huge pressure to meet the public demand for health care. The Society of Hospital Pharmacists of Hong Kong (SHPHK) would like to once again thank its members for upholding their professional responsibilities during these difficult times.

While the challenges are great, so are the opportunities! Despite the severe outbreak of COVID-19, the pandemic offers many new opportunities to pharmacists. Traditionally, the Accident and Emergency Department of public hospitals is the preferred choice of medical service by the general public for minor ailments. However, due to COVID-19, community pharmacies have now become the citizens' first point of contact for health advice, drug information and medical enquiries. In addition, several new pharmacy service models have been developed recently. For example, some of the chain and NGO pharmacies have started to provide drug delivery and counselling services to eligible patients, so that they would be able to continue their treatments without risking themselves to go to the hospital for collecting their repeated prescriptions.

It is encouraging to see the continued evolvement of pharmacists' role in Hong Kong during the pandemic. It is important that hospital pharmacists and community pharmacists are working hand in hand to ensure that patients could have continued access to pharmaceutical care during the pandemic.

SHPHK Telepharmacy Service

The SHPHK Telepharmacy Service was successfully launched in Q2 2020. The first phase of the service would be targeting patients with chronic obstructive pulmonary disease, and have been prescribed with one or more inhalers by the doctor. Pharmacists of the Society would assess patients' inhaler technique and provide counselling on patients' medication use via a teleplatform.

For details, please visit https://www.telepharmacy.hk/.

On 15 July 2020, Mr. William Chui was invited by the Hong Kong Telemedicine Association to give a talk on 'Telepharmacy and Drug Delivery' in an online webinar. In the webinar, the challenges and opportunities for the development of telepharmacy and drug delivery services in Hong Kong were discussed.

CE Activities in Q2 2020

In the second quarter of this year, the Society organised several webcasts to help its members to keep abreast of new drug treatments. For example, webcast on asthma, chronic obstructive pulmonary disease and biotherapy. Pharmacists who have completed the webcast and passed the post-programme assessment would be able to earn CEUs from the Pharmacy Central Continuing Education Committee. In the coming months, the Society will continue to organise webcasts on different clinical topics, including migraine, asthma, biosimilars, immunotherapy, and more! Please stay tuned!

The 33rd SHPHK Annual General Meeting on 15th June 2020

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OFEV®
(Boehringer Ingelheim)

Prepared and edited by Ivy Chan

Active Ingredient:
Nintedanib

Presentation:
Each soft capsule contains 100 mg or 150 mg of nintedanib (as a free base) corresponding to 120.40 mg and 180.60 mg of nintedanib ethanesulfonate (esilate) respectively.

Pharmacological Properties:
Nintedanib is a small molecule that inhibits multiple receptor tyrosine kinases including: platelet-derived growth factor receptor (PDGFR) α and β, fibroblast growth factor receptor (FGFR) 1-3, vascular endothelial growth factor receptor (VEGFR) 1-3 and colony stimulating factor 1 receptor (CSF1R). In addition, nintedanib inhibits the following nRTKs: Lck, Lyn and Src kinases. Nintedanib binds competitively to the ATP binding pocket of these kinases and blocks the intracellular signalling cascades, which have been demonstrated to be involved in the pathogenesis of fibrotic tissue remodelling in interstitial lung disease. In invivo studies, nintedanib was shown to have potent antifibrotic and anti-inflammatory activity.

Indications:
Idiopathic Pulmonary Fibrosis
OFEV (nintedanib) is indicated for the treatment of Idiopathic Pulmonary Fibrosis (IPF).

Systemic Sclerosis-Associated Interstitial Lung Disease
OFEV (nintedanib) is indicated to slow the rate of decline in pulmonary function in patients with systemic sclerosis associated interstitial lung disease (SSc-ILD).

Geriatrics (> 65 years of age):
No dose adjustment is necessary in patients 65 years and older.

Pediatrics (< 18 years of age):
The safety and efficacy of OFEV in pediatric patients have not been studied in clinical trials and therefore, OFEV should not be used in patients under 18 years of age.

Dosage & Administration:

Dosing Considerations
Treatment should be initiated by physicians experienced in the diagnosis and treatment of conditions for which OFEV is indicated.
Hepatic transaminase and bilirubin levels should be investigated just before initiation of treatment with OFEV, then at regular intervals (monthly) during the first three months of treatment and periodically thereafter (e.g. at each patient visit) or as clinically indicated. Conduct liver tests promptly in patients who reports symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice.
Pregnancy testing should be conducted prior to initiating treatment with OFEV and during treatment as appropriate, in females of reproductive potential.

Recommended Dose and Dosage Adjustment
The recommended dose of OFEV is 150 mg twice daily administered approximately 12 hours apart.

Dose adjustments due to adverse reactions
In addition to symptomatic treatment if applicable, the management of adverse reactions of OFEV could include dose reduction (to 100 mg twice daily) and temporary interruption of OFEV treatment until the specific adverse reaction has resolved to levels that allow continuation of therapy. OFEV treatment may be resumed at the full recommended dose (150 mg twice daily) or a reduced dose (100 mg twice daily). If a patient does not tolerate 100 mg twice daily, treatment with OFEV should be discontinued.

Hepatic impairment
Mild hepatic impairment: In patients with mild hepatic impairment, the recommended dose of OFEV is 100 mg twice daily approximately 12 hours apart. Treatment interruption or discontinuation for management of adverse reactions should be considered.
Moderate and severe hepatic impairment: Treatment of patients with moderate or severe hepatic impairment with OFEV is not recommended.

Renal impairment
Adjustment of the recommended dose (150 mg twice daily) in patients with mild to moderate renal impairment is not required. The safety, efficacy, and pharmacokinetics of nintedanib have not been studied in patients with severe renal impairment (<30 ml/min CrCL).

Geriatrics (>65 years of age):
No dose adjustment is required on the basis of a patient's age.

Administration
OFEV capsules should be taken with food, swallowed whole with water, and should not be chewed or crushed.

Missed Dose
If a dose of OFEV is missed, administration should resume at the next scheduled time at the recommended dose. If a dose is missed the patient should not be given an additional dose. The recommended maximum daily dose of 300 mg should not be exceeded.

Forensic Classification:
P1S1S3