

出國報告（出國類別：國際會議）

參加 2023 39th ICPE annual meeting

服務機關：國立成功大學醫學院附設醫院

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摘要

本次出國參加第三十九屆藥物流行病學研討會，並且於會中發表論文結果。會議地點為加拿大哈利法克斯。大會議程共包含2天pre-conference education sessions及3天正式會議，前兩天的課程，主要介紹藥物流行病學的概念及研究方法，例如Adherence to Pharmacotherapy、Causal inference與現在很夯的machine learning(ML)於藥物流行病學之應用、如何用scientific方法去設計及研究藥品安全性、疫苗安全性、unmeasured confounders之測量等議題。第3天為正式會議開始，議程有包含keynote、plenary presentation、oral presentation、symposium、poster presentation等。也安排有多種研究領域的方法介紹包含機器學習、pregnancy、adherence等課程。此次指導學生的論文入選為poster presentation，其中有一篇獲選為poster award。會中除吸收他人研究經驗也與其他學者交流討論，收穫頗豐。建議我國主管機關可以派員參加此類會議，了解全球目前的發展趨勢，對於用藥安全的政策可與國際接軌。

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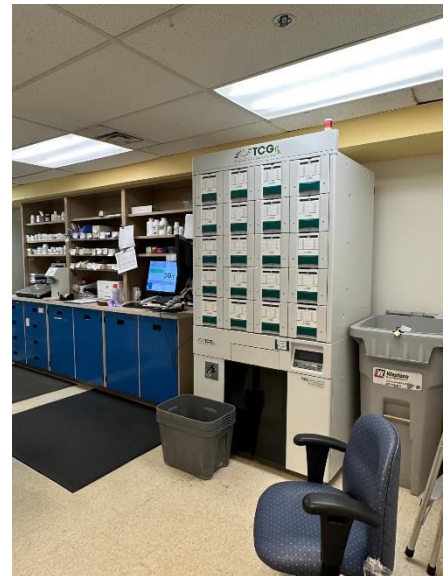
一、目的

本次出國為參加第39屆ICPE annual meeting，指導學生於會中發表論文結果；同時拜訪Baycrest Hospital, Interprofessional Practice and Pharmacy部門的負責人。

二、過程

(一)拜訪Baycrest Hospital Pharmacy部門過程：

Baycrest醫院是位於加拿大多倫多的一家著名醫療機構，專注於老年醫學和神經科學研究。其專業領域包括老年健康、認知功能、阿茲海默氏症、精神健康等。Baycrest醫院藥劑部接受他院藥師訓練和培訓機會，以提高藥師和相關醫療專業人員的專業知識和臨床技能，包含：臨床藥學培訓，以幫助藥師能更理解老年患者的特殊需求和藥物治療，如 polypharmacy或drug-drug interaction等相關主題與跨團隊合作照護的培訓。相信經由4-8周的訓練，可以提高藥師在老年醫學和藥物治療領域的專業知識和臨床技能，以提供給老年患者的最佳藥物治療和臨床照護。



與部內藥師參觀Baycrest醫院住院藥局

(二)參加會議過程：

這次大會共有5天，包括2天的會前教育課程和3天的正式會議。會前教育課程分為兩個部分：一為基礎課程：主要介紹藥物流行病學的基本概念和方法，包括如何用科學方法研究藥品使用趨勢等。還會涵蓋不同領域的研究方法，如藥物基因組學、精準醫療、藥物依從性、因果推斷和機器學習在藥物流行病學中的應用。二為進階課程：包括疫苗安全性、未測量混雜因素的測量、懷孕和兒童族群的藥物監視以及上市後藥物監測。儘管學

校也設有類似的課程，但由於時間限制，通常只能提供基礎概念性的內容。這次的教育課程讓學生們可以更深入地學習和複習藥物流行病學的知識。此外，部分課程還以工作坊的形式進行，這樣學生們可以透過實際操作來內化所學內容。這種實踐性的教學方法有助於學生將理論知識應用到實際研究中，讓他們能夠更好地將所學知識付諸實踐。

8/25-8/27是正式會議，此次會議共有約1500參加實體(另有300人線上參加)、超過1500篇abstract投稿，此次成大臨藥所約有十多人參加，並於會中有壁報論文、口頭報告等發表。



與系上老師、國外學者及指導學生於會場拍照留念

依照慣例，大會會依據當年度較熱門的主題安排幾場重要演講：

1. 8/25 Keynote Plenary: Global Regulatory Forum on Real-World Evidence。這次大會邀請了來自加拿大衛生主管機關和美國FDA的官員，一同討論使用真實世界數據（RWD）和真實世界證據（RWE）等藥物流行病學研究來支持決策制定相關的科學措施，以

及目前方法面臨的關鍵問題。同時，也探討了在特定治療領域，包括腫瘤學、罕見疾病和傳染病等領域中應用RWD的實際案例。透過這些演講，監管機構、學術界、業界以及其他利害關係者得以相互交流觀點，並探討使用RWD支持全球監管科學研究和監管決策所面臨的機會和挑戰。

2. 8/26 Plenary Session: Patient Involvement in the Development and Safe Use of Medicines。近年來，全球各地的地方當局已呼籲加強患者參與藥物的開發和安全使用，例如：歐盟透過IMI-Prefer（偏好研究倡議）收集病患的喜好，以作為醫療產品決策的重要參考依據。美國FDA以「患者關注的藥物開發」（Patient-Focused Drug Development，PDUFA VII Commitment）將患者的意見納入藥物開發和評估的過程中。歐洲藥品管理局（EMA）制定了有關患者參與的額外風險最小化措施，包括工具和有效性指標的選擇，詳見Good Pharmacovigilance Practice（GVP Module XVI, Rev 3）。2022年國際醫學科學組織（CIOMS）的報告也強調了系統性地讓患者參與藥物的整個生命周期的重要性，從早期開發到監管過程，再到醫療護理中的安全使用。這突顯了未來在藥物開發和臨床應用中，納入患者意見的重要性。患者的參與有助於確保藥物的研發和使用更符合實際需求，提高醫療產品的質量和安全性。

3. 8/27 Hot topic: Health Equity and Diversity in Pharmacoepidemiology Research: Making Change Happen 醫療照護公平和差距一直是長期存在的問題，特別是在COVID-19大流行期間，更加凸顯了這些不平等問題，包括種族、民族、經濟和地區方面的不平等。藉由藥物流行病學的應用，我們能夠發現這些問題，並在現實世界人群的健康方面發揮重要作用。然而，藥物流行病學

家如何將健康公平付諸實踐呢？在這個演講中，首先會明確定義在醫療照護公平性研究中的重要概念，並將這些概念納入更廣泛的研究和醫療背景中。也會討論如何應用藥物流行病學研究方法來測量醫療照護差距。台灣是少數有全民健保，且給付包含藥品、處置及檢驗項目最多的國家，因此，對於醫療照護公平性的議題也許並不像其他國家那麼嚴重，但城鄉差距依然存在，導致一些地區的病患在就醫可近性方面存在差異。

會議期間在不同時段參與許多新穎的討論會：

1. Data to Action: Leveraging Drug Utilization Research to Shift Clinical Practice and Health Policy。藥物利用研究（DUR）是藥物流行病學中最古老和基礎的領域之一。這個領域從早期描述用藥情況的研究發展到更高級的使用現實世界數據（RWD）來評估、預測和評估政策以及臨床實踐變化的影響。此 topic 由四位來自澳洲、美國、丹麥與加拿大的專家，分享真實研究和經驗，以說明跨學科的DUR研究所獲得的發現的使用和影響。講者們分享了DUR在老年醫學、疼痛治療、兒童與青少年精神健康及政策制定的相關應用。講者也提及了DUR的研究是 the simple the better，畢竟我們研究究成果是必須能讓做決定的人看得懂才能發揮最大效果。

What kind of questions can we ask?

- Population-based epidemiologic studies using databases at ICES
- Typical types of questions would include:

How often is drug X being prescribed?

How much is drug X costing the Ontario government?

How many people would be impacted if the ODB implemented a new drug reimbursement policy?

Does one drug appear to be safer, or more effective than another similar drug?

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演講者的投影片，說明研究者應該要回答的問題

2. Patient involvement in the development and safe use of medicines。歐美國家近年來更加重視病人參與臨床決策，包含回報用藥的療效及安全性，並且在決策單位公告相關的法規及準則。台灣的醫療雖然已重視病人參與臨床決策”SDM(Shared decision making)” ，但是病人與醫療人員是否具有相同的知識可以完全了解資訊，因此，這是值得我們學習的領域。



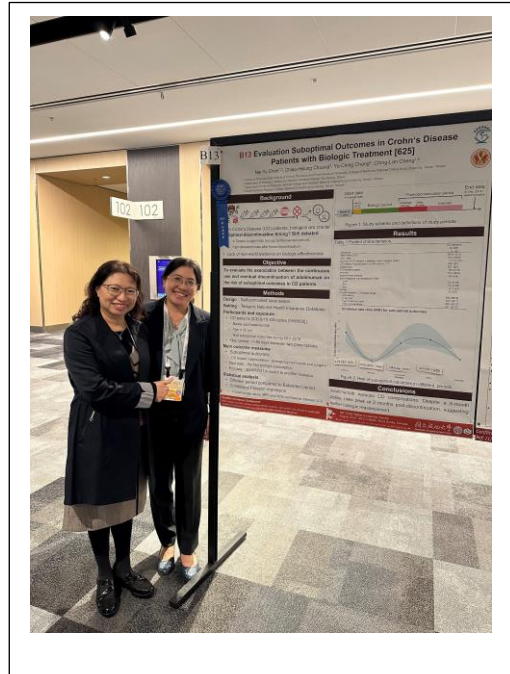
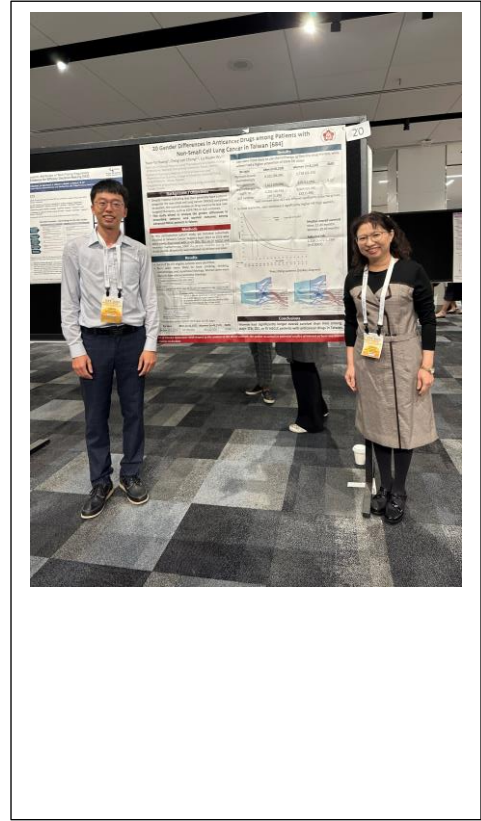
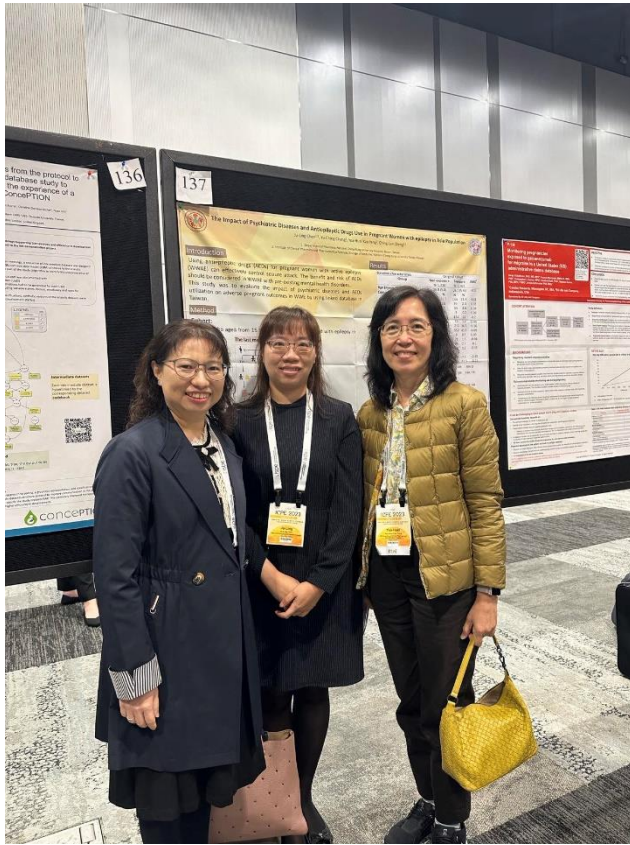
3. Deep Learning for Pharmacoepidemiologists: An Accessible Introduction to Neural Networks。隨著電腦科技及AI演算速度的發展，深度學習方法(DL)於醫學和醫療保健的應用越來越多。在這個領域的研究非常豐富，流行病學家、生物統計學家和其他健康研究人員能夠參與並貢獻於使用深度學習方法的研究非常重要。但在應用此方法提升醫療照護品質的同時，深度學習同時也存在著許多挑戰，我們必須考慮模型的穩健性，應用時的公平性或設計實用性和風險的評估。藥物流病的研究者們可以學習與資訊工程相關專家進行溝通，從而實現改進此技術應用的安全性和效益的合作。
4. Oral presentations: 會議中安排了多個口頭報告，報告者來自世界各地的學生，涵蓋多個研究領域。這樣的安排不僅讓我們能夠了

解各位學者目前的研究主題和進展，還能參考別人如何有效呈現自己的研究成果。透過即時的問答環節，我們可以獲得其他學者對自己研究的建議，這有助於未來的研究方向和改進。這也提供了一個寶貴的學習和交流機會，促進了跨學科和跨國界的知識分享，有助於建立更廣泛的研究網絡。這種互動有助於學術界的持續成長和發展，並推動了新的想法和創新的產生

5. Poster sections: 除了口頭報告，現場還有許多壁報展出。壁報展示提供了一個互動的平台，研究者可以詳細討論他們的研究成果，回答問題，並與對相關領域感興趣的人建立聯繫。這有助於促進學術合作，共同探討新的研究方向，並可能引發新的研究項目。壁報展示也為與會者提供了一個深入了解各種主題和方法的機會，有助於擴大知識領域，促進跨領域的交流和學習。共指導4學生進行壁報發表，發表題目如下表

	題目
1	The Impact of Psychiatric Diseases and Antiepileptic Drugs Use in Pregnant Women with epilepsy in Asia Population
2	The Prescription Pattern of Biologics for Crohn' s Disease Patients in Taiwan.
3	Gender Differences in Anticancer Drugs among Patients with Non-Small Cell Lung Cancer in Taiwan
4	The prescription pattern of biologics for Crohn' s disease patients in Taiwan

相關活動照片如下圖，論文摘要如附錄所示



三、心得

藥物流行病學研究包含藥物使用型態、療效與安全性以及風險管理，隨著電腦科技及運算技術的開發，大數據及真實世界資料分析已是目前全球在此領域發展的趨勢，而國際藥物流行病學會 (ISPE) 成立已有三十多年，其使命在於促進全球藥物流行病學領域的科學信息交流、政策制定、教育推廣以及宣傳，包括議題如藥物警示、藥物使用研究、療效比較評估和治療風險管理等，因此 ISPE 成為這一領域中討論新的研究方法、藥物政策和相關教育的重要平台。

今年 ISPE 在加拿大舉辦第 39 屆國際藥物流行病學大會 (ICPE)，以” The global home for the science of real-world evidence” 為大會的主題，吸引來自世界各國的學者參與，這個會議提供了一個交流和討論的機會。大會包括教育培訓課程，從基礎的方法簡介，到進階的課程，介紹先進的研究方法和模型，讓學生或研究者更新相關資訊。此外，今年度 ICPE 邀請學者討論各國主管機關如何利用 RWE 進行決策，並且在主題演講討論病人參與決策及藥物流行病學家如何促進醫療照護的公平性等議題。此次會議安排的座談會和口頭報告，也包含了先進的 AI 議題，不過也有許多是與 COVID-19 及疫苗相關，參與者可以根據自己的研究領域進行交流和討論，了解世界各地研究學者的最新研究成果和方向。在會議中亦可透過與其他研究者有交流，介紹台灣健保資料庫的內容，不但有助於建立國際合作關係，亦能提升台灣在國際上的知名度。

四、 建議事項

(一)重視藥物安全決策及風險管理：

近年來，許多國家的主管機關，如 FDA 和 EMA，逐漸接受真實世界證據（RWE）作為臨床試驗的替代品，作為決策的參考依據。因此，RWE 的應用前景將逐漸擴大。然而，正確地分析和解釋這些資料庫的資料是一個關鍵議題，需要深入研究和討論。我國的健保資料庫是極為重要的醫療相關研究資料來源，被廣泛應用於藥物安全性、風險評估等重要研究領域。這個資料庫包含了 99%以上全人口的就醫記錄，具有極高的資料完整性和長期追蹤性，因此吸引了眾多學者的關注。許多研究者希望能夠與我國建立合作夥伴關係，以利用這一寶貴的資源進行多國研究合作。這些研究成果有望為衛生主管機關的政策制定提供有力的參考，同時也有助於臨床醫師做出更明智的治療決策，進一步提升醫療照護品質和病患的用藥安全。

(二)學習歐美國家資料管理政策：

除了大型申報或保險資料庫外，歐美國家的研究材料亦包含醫療機構的電子病歷，也被稱為 Electronic Medical Records (EMR)，EMR 可以彌補資料庫中一些缺失的資訊，例如實驗室檢查數據、病人的生活習慣（如抽煙或飲酒），這些資料對於研究非常關鍵。但如何在確保個人資料安全和隱私的前提下進行資料整合，這是一個需要專業知識和政策支持的重要議題。歐美國家雖然在醫療制度與我國不盡相同，但是在病人隱私及資料保護的原則具有許多不同的規範及作法，尤其現在面臨台灣健保資料庫的個資及使用權利的議題，因此，需要更多國內的專家學者以及政府官員參與討論和合作，並透過參與國際會議認識國外學者，互相學習，以制定出適用於國內的最佳實踐和政策。

附錄

壁報摘要-1

The Impact of Psychiatric Diseases and Antiepileptic Drugs Use in Pregnant Women with epilepsy in Asia Population

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Background: Using antiepileptic drugs (AEDs) for active pregnant women with epilepsy (WWE) can effectively control seizure attack. The benefit and risk of AEDs should be considered in WWE with pre-existing mental health disorders.

Objective: This study was to evaluate the impact of psychiatric diseases and AEDs utilization on adverse pregnant outcomes in WWE by using linked database in Taiwan.

Method: We identified a cohort of pregnancy women with active epilepsy in 2009 to 2018 by linking three databases (Maternal and Child Health Database, National Health Insurance Database, and Birth Certificate Database). Active epilepsy was defined as pregnant WWE with at least two epilepsy visits on separate date or at least one hospitalization of epilepsy or had at least one AEDs prescriptions within two years prior to conception. WWE with major depression disorder, bipolar disorder, schizophrenia, sleep disorder and anxiety diagnosis were defined as with psychiatric comorbidities. Prenatal outcomes which included premature rupture of membrane, fetal distress, antepartum hemorrhage and pre-eclampsia/eclampsia and birth outcomes such as maternal complications in delivery, low birth weight, very low birth weight, preterm birth (<37 weeks), low Apgar score (<7), congenital malformations were evaluated as composite adverse pregnant outcomes. The primary analysis was to compare the risk of adverse outcome between AEDs exposure and non-exposure and stratified by psychiatric disease. We conducted a sensitivity analysis to redefined active epilepsy within 6 months period.

Results: There were 1,262 and 1,230 pregnant women met study criteria in exposure and non-exposure group, respectively. Compared to non-exposure group, the adjusted

odds ratio for composite adverse outcome in exposure group was 0.98 [95% CI: 0.84-1.15]. Compared to non-exposure WWE without psychiatry, AEDs exposure WWE with psychiatry was not increase risk of adverse outcome (aOR=1.07 [95% CI: 0.84-1.35]). The stratified analysis showed that the risk was significantly lower in AED exposures than non-exposures among psychiatric subgroup (aOR=0.75, [95% CI:0.60-0.94]. Among non-psychiatric subgroup, AED exposure had marginal higher risk of adverse outcome than non-exposure ones (aOR=1.13, [95% CI:0.79-1.60]) Further sensitivity analysis showed similar results.

Conclusions: Stratified analysis showed that the risk of adverse outcomes of AEDs exposure was different among with/without psychiatric disease. Further study to analyze the interaction between a AEDs exposure and psychiatric disease is needed.

The Prescription Pattern of Biologics for Crohn's Disease Patients in Taiwan

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Background:

Biologics have been reimbursed for Crohn's disease (CD) for more than a decade in Taiwan, including restriction treatment duration and retreatment criteria.

Objectives:

To determine the real-world prescription pattern of biologics in CD patients.

Methods:

This was a retrospective cohort study using Taiwan National Health Insurance Database from 2010 to 2020, enrolled patients newly CD diagnosed, with catastrophic illness certificate, age older than 20 years old, and incident biologics users including adalimumab, infliximab, vedolizumab, and ustekinumab. Utilization patterns were defined as continuing initial biologic, discontinuation (gap was 84 days of two consecutive biologic prescriptions) or switch to another biologic. The treatment course was defined as patients who completed the maintenance phase and meets the criteria of discontinuation. We performed descriptive analysis for prescription pattern and Sankey diagram for switching pattern.

Result:

This study enrolled 590 patients, 407 (69.0%) male, mean age (SD) at the first date of CD diagnosis and the biologic prescription was 37.4 (15.5) and 39.8 (15.4) years old, respectively. Median (IQR) lag time from first diagnosis to first biologic prescription was 1.5 (0.6, 3.7) years. Adalimumab was the most common initial biologic. 343 patients (58.1%) had second treatment course, 188 patients (31.9%) had third course, and 97 patients (16.4%) had fourth course. For treatment transition, after the first course, most patients entered the second course, with 265 (44.9%) using the same biologic and 78 (13.2%) switching. Among those not entering the second course, 129

(21.9%) discontinued biologic, and 118 patients (20.0%) continued their first biologic. The proportion of patients using the same biologic was higher for those treated with adalimumab (80.6%) in the first course compared to vedolizumab (61.5%) and infliximab (57.1%).

Conclusions

This real-world prescription pattern enhances our understanding of biologics in Taiwan's CD patients. It is an important issue for future research to investigate the optimal treatment course of biologics and to identify patients who may benefit from switching.

Gender Differences in Anticancer Drugs among Patients with Non-Small Cell Lung Cancer in Taiwan

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Background: Lung cancer is the most common cause of cancer-related deaths in Taiwan. The first-line drug therapy options for non-small cell lung cancer (NSCLC) include chemotherapy, EGFR tyrosine kinase inhibitor (EGFR TKI), and ALK inhibitor. Although reports have revealed that men have a poorer prognosis for NSCLC compared to women, there have been no studies that have included all the known prognostic factors to evaluate survival in different genders.

Objective: To analyze the gender differences in prescribing patterns and survival outcomes of anticancer drugs among NSCLC patients in Taiwan.

Methods: In this retrospective cohort study, we included individuals enrolled in Taiwan's Cancer Registry from 2012 to 2019 who were newly diagnosed with stage 3a, 3b, or 4 NSCLC and received chemotherapy, EGFR TKI, or ALK inhibitor during the study period. All patients were followed up at least one year. We collected patient characteristics, tumor-related factors, treatment-related factors, and other factors. Continuous variables were presented as mean and standard deviation or median and quartiles, while categorical variables were presented as counts and percentages. For survival outcomes, we calculated the hazard ratio (HR) to estimate survival differences between genders. The difference was estimated using p-value, with <0.05 considered statistically significant.

Results: We identified 16255 eligible patients (8102 men, 8153 women). Men were more likely to have smoking, drinking, radiotherapy, and squamous histology. Women were more likely to have adenocarcinoma histology. The median first prescription time was 34 days for men and 35 days for women. The first prescription types were chemotherapy (58.3 % for men vs 33.1 % for women), EGFR TKI (40.5 % for men vs 65.3 % for women), and ALK inhibitor (1.3 % for men vs 1.6 % for

women). The median overall survival was significantly shorter with men than women (12.43 months vs. 20.43 months; adjusted HR; 1.23; 95% confidence interval [CI], 1.17 to 1.29; $p < 0.0001$).

Conclusion: Women had significantly longer overall survival than men in patients with advanced NSCLC. Further study is required to understand the cause of survival differences between men and women to provide adequate care to patients of either gender.

Keywords: Non-small cell lung cancer, prescribing pattern, overall survival, gender