ePoster abstracts

A. Pharmaceutical policy and administration

A.1

Accessibility of palliative care medicines

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Aim/Objective: Lack of access to palliative care medicines is observed in some countries. The aim of this work is to assess availability and affordability of essential palliative care medicines in Armenia.

Methods: The List of medicines registered in Armenia and pricelists of main wholesalers were analyzed to assess availability of tracer medicines. Affordability of tracer medicines was calculated using methodology developed by the World Health Organization and the Health Action International. Data on prices were collected from 5 community pharmacies in Yerevan (the capital of Armenia).

Results: 16 of 20 active ingredients listed in the World Health Organization (WHO) Model Essential Medicines List for pain and palliative care were authorized are available in pricelists. However, calculation made with taking into account dosage forms and doses of essential medicines, allowed to reveal that only 52.3% of 44 pharmaceutical forms and 44.4% of 63 strengths recommended by WHO for pain and palliative care medicines were authorized. Only 50.0% of recommended pharmaceutical forms and 33.3% of strengths were found in pricelists of local wholesalers. Cost of treatment with use of 15 essential medicines for palliative care was affordable; cost of treatment with use of two essential medicines for palliative care (lactulose, oral liquid, 3.1–3.7 g/5 ml and midazolam, injection, 5 mg/ml) was not affordable.

Conclusion: Despite the most of active ingredients recommended by the WHO for pain and palliative care are available in Armenia, most of recommended pharmaceutical forms and strengths for tracer medicines are not supplied due to which there is a lack of availability to these essential medicines. Some medicines are not affordable.

Keywords: Palliative care, essential medicines

A.2

Effects of Pharmaceutical Care on Knowledge, Ability of Inhaler Use, and Outcomes in Patients with Chronic Obstructive Pulmonary Disease

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Objective: identify the effects of pharmaceutical care on knowledge, ability of inhaler use, and outcomes in patients with chronic obstructive pulmonary disease (COPD).

Methods: A quasi-experimental study was conducted in COPD patients prescribed with inhaler. COPD patients were recruited from patients visiting COPD clinic at secondary care hospital from 11 February to 10 May 2022. Inclusion criteria included CAT score <10, exacerbation ≥ 2 in the past year and MMRC score 0-1. The clinical pharmacist intervention program included education about COPD knowledge, medication usage, prevention of possible adverse drug effects, lifestyle adjustment, smoking cessation, adherence and inhaler technique e.g. VDO, demonstration and leaflet. Patients were followed up by monthly COPD clinic for 3 months. Data on knowledge, ability to use inhaler, and peak flow rate (PEFR) were collected before and after pharmaceutical care services using a self-administered questionnaire and data collection form. The questionnaire was tested before data collection with Cronbach's alpha 0.756 on knowledge part. Data were analyzed with the use of descriptive statistics that were used to identify the percentage, mean, standard deviation and inferential statistics dependent or paired sample t-test.

Results: Thirty COPD patients were included with mean age 54.4±14.9, patients ≥ 30 years with COPD. Most patients were prescribed with pressurized metered dose inhaler (pMDI.)The average knowledge score pre-service was 9.2±1.5 and post- service was 9.4±1.4 (p=0.032). Knowledge of 90% of the patients increased significantly after receiving pharmaceutical care service (p=0.032). Ability to use inhaler pre- and post-service scores were 27.6±3.1 and 28.4±2.8, respectively (p=0.011). PEFR pre-post service was 76.7±28.6 and 81.0±30.5, respectively (p 0.005). The PEFR increased significantly in 81% of the patients after the service (p=0.005).

Conclusion: Pharmaceutical care services could improve knowledge, ability, and outcome in COPD patients using inhaler.

Keywords: Pharmaceutical care service, chronic obstructive pulmonary disease, knowledge, inhaler

A.3

A survey for investigating the present situation of use of real-world data by pharmaceutical companies and their demand

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Aim/Objective: Real-world data (RWD) are drawing ever-increasing attention in the pharmaceutical industry. We survey to identify the present situation of RWD in pharmaceutical companies and gather their opinions on improving RWD utilization.

Methods: We conducted a survey on RWD utilization related to pharmaceutical companies' conducting and planning RWD studies. A survey was distributed to 181 members of the Korea Pharmaceutical and Bio-Pharma Manufacturers Association and 47 members of the Korean Research-based Pharma Industry Association (KRPIA) on November 10, 2021. All representatives who were interested in the RWD of each company were contacted by email. The questionnaire consisted of closed-ended and open-ended questions and was divided into three main parts: 1) experience of RWD studies, 2) plan of RWD studies, and 3) future of RWD development.

Results: A total of 16 replies were received, of which 13 were pharmaceutical companies with ≥100 billion in annual sales, two were pharmaceutical companies with <100 billion in annual sales, and one was the KRPIA. Five of the respondents (31.3%) reported having experience conducting RWD studies, and eleven (75%) reported having a plan for RWD studies. Most companies (81.3%) responded that no experts or departments were in charge of using RWD, and 93.7% indicated that an education program to foster experts conducting RWD studies was needed. Opinions on RWD utilization included resolving legal issues such as personal information, expanding RWD acceptance by regulatory agencies, revising related regulations, and securing professional personnel.

Conclusion: The response rate may have been low because the questionnaire was not accurately communicated to the survey subjects. However, the survey indicates that most pharmaceutical companies have little experience conducting RWD studies but plan to conduct RWD studies. Therefore, we suggest establishing relevant guidelines for using RWD and nurturing infrastructures that can professionally handle RWD.

Keywords: Real-world data, survey, the pharmaceutical industry

A.4

Application of systematic approaches to assess factors associated with pharmaceutical expenditures: An illustrative study in the type 2 diabetes population

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Background: In Taiwan, pharmaceutical spending has steadily increased over time and reached to around 27% of healthcare expenditures. Such proportion is much higher than that (9-19%) among other developed countries with high-income economies, especially in chronic diseases such as diabetes. However, studies using systematic approaches to assess influential factors with drug expenditures in Taiwan are lacked.

Aim/Objective: We employed a systematic approach consisting of a structured literature review along with expert interviews, regression-based analyses, and expert consensus meetings to identify significant factors associated with total drug expenditures in glucose-lowering agents (GLAs) among type 2 diabetes (T2D) patients.

Methods: Three operational steps were performed: (1) conducting a structured literature review and expert interviews to identify potential factors associated with drug expenditures, (2) applying regression-based statistical methods to select significant factors associated with drug expenditures based on the data of randomly sampled T2D patients (n=16,220) retrieved from Taiwan's National Health Insurance Research Database during 2010-2019 and National Census Reports, and (3) conducting expert meetings to evaluate the applicability of final factors under consideration of clinical relevance and local settings.

Results: According to literature review and expert recommendations, 46 factors were identified and categorized into seven dimensions: patient demographics, socioeconomic status, comorbidities (Charlson Comorbidity Index and Diabetes Complications Severity Index), medical services utilization (e.g., outpatient visits), disease-specific (e.g., diabetes duration), medication-related (e.g., adherence to GLAs), and market-related (e.g., drug price adjustments). 30 and 41 factors were selected using stepwise and LASSO regressions, respectively. A total of 41 factors were finally concluded in the expert meetings as the significant factors.

Conclusion: The systematic approaches applied in this study can be adopted by future studies to assess factors associated with pharmaceutical expenditures. Identifying the influential factors with drug expenditures could facilitate forecasting the healthcare budget and developing effective interventions to mitigate the healthcare economic burden.

A.5

Effectiveness analysis of business intelligence software applied to inhaled medication guidance

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Background: The use of the inhaler device correctly is essential. It is not easy for elders or children to learn to use inhalers properly. However, if the inhaler is not operated correctly, the medicine will not be delivered to the lungs, which will directly affect the therapeutic effect and cause the disease to worsen. In this study, for patients who used the inhaler for the first time, pharmacists conducted health education guidance and performed a medication knowledge test to evaluate the correctness of the operation.

Methods: This study uses a Google form to design a questionnaire to collect pre-and post-tests and satisfaction surveys for pharmacists instructing inhalers from 2020 to 2021. The pre-and post-tests of medication knowledge include the purpose of using inhalers, methods of operation, precautions, and judgment of the remaining amount. All of which were scored on a 5-point Likert scale.

Results: During the study period, 832 cases of inhalers instructions were guided. The pre-test score of the medication knowledge test was increased from 53.20 ± 32.57 to post-test 97.96 ± 6.06; the satisfaction survey score was 4.90 ± 0.29points. Compared with the past, using Microsoft Excel for data collection, it takes 60 minutes to follow up statistical analysis and production of visual reports. Using Power BI only takes 1-2 minutes to wait for the data to be updated. According to the conditions you want to analyze, interactive Click-and-click can quickly display the filtering results, saving a lot of time and cost.

Conclusions: Use business intelligence software to combine data analysis and information technology to provide data mining, statistical analysis, and data visualization, update data in real-time, and quickly grasp the current situation through interactive operations. The time saved allows pharmacists to invest more in the clinical pharmaceutical care business.

A.6

Medicines shortage and falsified medicines as urgent challenges for pharmaceutical policy

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Aim/Objective: Medicines shortages and falsified medicines have become global challenges which compromise population health, put lives of patient at risk and create difficulties for health care systems. Identifying these problems and informing policy-makers is the first step in a process of developing appropriate policy strategies. The objective of this work was to identify pressing problems related to medicines which are able influence population health in Armenia.

Methods: Survey was conducted in different regions of Armenia. 209 pharmacy practitioners participated by completing specially designed questionnaire. Data were analysed with SPSS statistical software.

Results: Most of professionals (84.7%) consider that shortage of medicines for priority diseases is a threat to public health. A half of responders (50.2%) suppose that there is shortage of medicines needed for treatment of priority diseases in Armenia. Some of participants indicate certain medicines for which shortage is observed. 90.0% of professionals believe that strengthening Health care system by introducing policy strategies to manage medicines shortage is essential. The great majority of participants (89.5%) consider that substandard and falsified medicines are also a threat to public health. 77.0% of respondents thinks that substandard and falsified medicines are present on the local pharmaceutical market. The percentage of professionals reporting this problem is higher among those who completed continuing education courses (P=0.007). 81.8% of professionals suppose that unauthorized/unlicensed medicines are also available on the market. 96.2% of participants are sure that strengthening Health care system in Armenia by introducing additional tools for assuring quality of medicines is necessary.

Conclusion: Many pharmacy practitioners consider that there are problems with shortage of medicines needed for treatment of priority diseases in Armenia, as well as with appearance of substandard and falsified medicines. There is an urgent need in developing strategies aimed to solve problems identified.

Key words: Medicines shortages, falsified medicines.

A.7

A Systematics Review of essential antidotes for pesticides toxicity in emergencies care service in Thailand

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Objective: To update evidence of pesticide antidotes lists in Thailand emergency care service and therapeutic effects of add-on magnesium sulfate to standard treatment for organophosphate poisoning on mortality and intubation.

Method: We review guideline antidotes for toxicological emergencies in five countries and systematically searched clinical studies. We use PICO as search strategy tool on literature research by using P (population) is any toxicity or poisoning, I (intervention) is name of pesticide, C (comparation) is placebo and O (outcomes) is mortality, safety, mobility, adverse event. We determined unpublishing and publishing of therapeutic effect of magnesium sulfate for organophosphate poisoning on mortality and intubation during 1990 to 2021. Meta-analysis of each outcome was performed under a random-effects model. I2 was used to quantify statistical heterogeneity.

Results: A total of 2,667 studies were identified in the initial systematic search. After removing duplicated studies and screening title abstract and full text, including reference search. We search for other antidotes and indications especially organophosphate poisoning. We interest in magnesium sulfate which present only in USA guideline. Eight studies related to magnesium sulfate were included in this study. Seven randomized controlled trials and one case series with 483 patients were included. There are 258 patients receiving magnesium sulfate and 225 control patients. The publication bias was tested by Contour-enhanced funnel plot. Sensitivity analysis is dose of magnesium sulfate and study design, we use a random-effects model and forest plots for analysis. The pooled risk ratio (RR) for mortality was 0.36 (95% CI; 0.21 to 0.62, I2 =0.0%), while the RR for intubation was 0.71 (0.58 to 0.87, I2 = 0.0%).

Conclusion: Magnesium sulfate as an add-on treatment to atropine with pralidoxime could significantly reduce mortality and intubation in patients with OP poisoning.

A.8

Effectiveness of pharmaceutical care in patients with chronic kidney disease: an evidence from a tertiary hospital in Taiwan

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Aim/object: Collaboration with pharmacists and multidisciplinary care for pre-end-stage renal disease (preESRD) have been promising. However, evidence of pharmacist`s involvement in chronic kidney disease is limited. The aim of our study was to implement pharmaceutical preESRD care program and evaluate the clinical benefit for people with chronic kidney disease (CKD) stage 3-5.

Methods: We conduct a prospective cohort study in single medical center from December 2021 to May 2022 in Taiwan. Inclusion criteria contained anyone of the following: comorbidities are greater than or equal to two, current medications are greater than or equal to ten, take non-steroidal anti-Inflammatory drug (NSAID) frequently. CKD patients visited pharmacist-led preESRD clinic every three months. The preESRD care consisted of reviewing potential nephrotoxicity prescriptions from different sources, enhancing patients' adherence to medications and drug information education. Effectiveness outcomes, including creatinine, HbA1c and adherence to refills and medications scale (ARMS), were assessed at every visits.

Result: We included 159 patients with second follow-up. The mean age was 68 years, and 56.6% of patients were men. Individuals with multi-comorbidity account for 91.1% with the highest proportion of hypertension (86.16 %). 41.5% and 16.9% with polypharmacy and exposed to NSAID, respectively. Thirty-three prescription suggestions were proposed to clinicians and 93.3% had been accepted. After three-months follow-up, ARMS score was improved from 14.4 (SD: 2.5) to 13.7 (SD: 2.7), however, NSAID exposure revealed no significant difference after education (before: 16.9% vs after: 17.6%, p = 0.88). Level of plasma creatinine was increasing by 0.16 mg/dL (SE: 0.04) and HbA1c declined by 0.02 % (SE: 0.07).

Conclusion: Patients received preESRD pharmaceutical care had improved medication adherence in the early stage of intervention. A long-term follow-up are suggested to investigate further effectiveness in pharmaceutical care.

Keywords: preESRD, pharmaceutical care, pharmacist-led preESRD clinic

A.9

Performance indicators of operation management for refill prescription system in Thailand.

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Long waiting time and unsatisfied the hospital service is severe problem in Thailand. National Health Scheme Organization (NHSO) launched refilled prescription system for NCD patients in community pharmacy since October 2019. Lamphun province is the top area where patients engage the system. Twenty-one drugstores registered to be partner with Lamphun hospital. Pharmacist individually designed operation in their shops. We aimed to investigate the patterns of operation and to design standardized performance measurement for this system. Inventory and logistic of medication of each patient was covered by the hospital. We did a semi-structure in-depth interview and observed the service at each drugstore. Totally, there were 5 patterns of operation. All of them valued the process of dispensing and counseling, it took average 8.39 minutes for each patient. Clinical outcome and adherence monitoring were done only some cases. It took longer service time for dispensing but patients appreciate it. Community pharmacists wasted a long time to complete patient and medication profile in the reimbursement system. They expected for connecting information system with the hospital to reduce working load. Currently, pharmacist fee for refill prescription in this pilot policy is 70 baht/prescription. It was more or less when there was no drug-related problem in each prescription. Conclusion, patients satisfied the refilled prescription service at drugstore. We need more network to serve this demand. For national level, increasing of patients consent in this system was the primary performance indicator. We suggest further collect time consuming to complete the process of each prescription. The good performance of operation is reducing total process time, but increase value counselling time with patient.

A.10

Drug expenditure target ensures drug quality in Taiwan

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Aim/Objective: Much attention is paid to the quality improvement of generic drugs and the control of healthcare expenditure by the government of Taiwan, resulting abundant studies of the relationship between the quality of generic drugs and the reimbursement price of national health insurance. Excluding the drugs for rare diseases and with characteristic exceptional conditions, Drug Expenditure Target (DET) has been conducted yearly to adjust the reimbursement price for those items that are out of patent, enlisted < 15 years and enlisted ≥ 15 years by National Health Insurance Administration (NHIA) since 2014. The items that have been adjusted for reimbursement price were analyzed in the study. The study aimed to assess the impact of DET on hospital drug expenditure.

Methods: The items that are adjusted for reimbursement price according to DET were published in the website of NHIA and accessed to be downloaded. The data were then sorted and processed on the basis of Anatomical Therapeutic Chemical Classification (ATC) and categories of common generic drugs, drugs with BE/(BA + clinical trials), original drugs and BE comparator drugs.

Results: A total of 16,027 items of drugs were collected and analyzed. Among them, 13,336 (83.21%) were items enlisted ≥ 15 years, 12,695 items (79.21%) were local generic drugs, 12,221 (76.25%) were common generic drugs, 8,956 (55.88%) were oral forms, and 8,443 (52.68%) were adjusted owing to lack of quality-related proof.

Conclusion: Local generic drugs enlisted ≥ 15 years and without quality-related proof are major items for reimbursement price adjustment, indicating the primary aim of DET is to ensure drug quality.

A.11

The willingness of healthcare workers to get vaccinated against SARS-CoV-2: A systematic review and meta-analysis

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Objective: To demonstrate the willingness of healthcare workers (HCWs) across different continents to vaccinate against SARS-CoV-2 during the pandemic and to determine factors that influence their intentions.

Methods: A systematic review and meta-analysis were conducted using articles published in PubMed and Scopus from January 1st, 2020 to April 10th, 2021. Meta-analysis was performed using "meta" and "metafor" packages in R version 4.1.2. The rates of vaccine acceptance, refusal, and hesitancy were pooled using random-effect methods. Sub-group and sensitivity analyses were performed. We used meta-regression to detect the change in HCWs' intentions over time. Factors that influenced HCWs' intentions were also systematically analyzed.

Results: A total of 30 studies across 28 countries were included. The rates of vaccine acceptance among HCWs ranged from 23% to 96%. Pooled rates for vaccine acceptance, refusal, and hesitancy were 0.67 (95%CI:0.61-0.72, I2 = 99.5%), 0.23 (95%CI: 0.18 – 0.28, I2 = 99.5%), and 0.23 (95%CI: 0.19 – 0.29, I2=99.2%), respectively. Acceptance rates varied across countries in Asia, while Africa had the lowest rate of vaccine acceptance. HCWs' intentions remained largely unchanged over time. Age, gender, occupation, behavior toward vaccination, trust in governments, and trust in COVID-19 vaccines were associated with HCWs vaccine intention.

Conclusion: The vaccine acceptance rates in HCWs were moderate and varied across continents. Educational campaigns targeting influencing factors should be implemented for HCWs in particular areas to increase vaccine acceptance.

Keywords: SARS-CoV-2, vaccine acceptance, healthcare workers

A.12

Law Enforcement of Regulations on Place, Equipment and Good Pharmacy Practice for Pharmacy in Thailand

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The objectives of this survey research are to explore law enforcement of regulation on place, equipment and good pharmacy practice for pharmacy in Thailand. Population and sample for this study were 782 pharmacists who work in the division of consumer protection and public health pharmacy, the provincial health office in 76 provinces throughout Thailand. Data were collected by questionnaire mail survey where respondents can response by paper questionnaire or online questionnaire via link or QR code provided. A total 192 questionnaires were returned with 155 completed questionnaires. The results shown that the majority of respondents were females 66.4%, average age was 37.84 year-olds, 10 years' experience or more 57.4%, less than 10 years' experience 58.7%, Holding drugstore licensee 18.1%, Pharmacist in the drugstore 32.1, Position as Professional pharmacist 63.9, working in northern and northeastern 35.5% and 32.3% respectively. Most of the respondents were used to inspect drugstore 92.9%. Consumer protection are the most favorable strategy used in consumer protection, followed by law enforcement 31.0%. The opinion of deputy pharmacist toward place, equipment and the good pharmacy practice classified by drugstore license, being drugstore pharmacist and experience in drugstore inspection status are not significant. Multivariable linear regression analysis shown that attitude toward general law enforcement affected opinion on difficulty of regulation and impact to consumer significantly p-value < 0.001.

A.13

Predictors for readmission in patients with surgical site infection in a tertiary care setting

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Aim/Objective: To build a model for predicting readmissions in patients with surgical site infection (SSI).

Methodology: 549 patients diagnosed with SSI from January 1, 2016 to August 25, 2021 admitted to orthopedics (n=334), general surgery (n=135) and neurosurgery (n=41) departments were enrolled in the retrospective study. The study was initiated after the approval of institutional ethics committee. Clinical and socio-demographic data, treatment pattern and microbial isolates were collected using a predesigned case record form. The predictors of readmission were identified using backward stepwise regression. Hosmer-Lemeshow test and omnibus test were used to test for goodness of fit. Ability of the developed model to discriminate between positive and negative cases was evaluated by comparing area under the receiver operating characteristic curve (ROC) curve analysis

Results: Of the 549 patients diagnosed with SSI, 137(24.9%) were readmitted. Presence of implant(OR 1.694 [95% CI 1.09- 2.63]), malodorous discharge(OR 2.435 [95% CI 1.35- 4.4]), surgeries in peripheral areas(OR 2.31 [95% CI 1.35 - 3.97]), post-operative use of glycopeptide class of antibiotics(OR 5.75 [95% CI 1.9- 17.4]) and patients who got SSI for the first time without recurrence or reinfection(OR 0.167 [95% CI 0.084- 0.335]) were considered for the readmission prediction model. The area under the curve was estimated to be 0.709 [95% CI 0.66-0.76]. The model showed an accurate prediction of 77.8%.

Conclusion: A model for predicting readmission in surgery patients with SSI was established based on patient related and treatment related risk factors. The model had an acceptable efficiency in predicting the readmission rates in our healthcare setting which could help the clinician identify the patients susceptible to readmission with SSI.

Keywords: Surgical site infection, risk factors, readmission, prediction modelling

A.14

Investigating the impact of Chinese Zero Mark-up Drug Policy on drug costs for managing Parkinson's disease: a single-center analysis

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Objective: The Zero Mark-up Drug Policy (ZMDP), launched in April 2009 to adjust medical institutions' revenue and expenditure structures in China, may influence drug utilization for chronic diseases. This study evaluated the impact of ZMDP on drug costs for managing Parkinson's disease (PD) and its complications from the perspective of healthcare providers.

Methods: This cross-sectional study used the healthcare administrative data from a tertiary hospital in China from January 2016 to August 2018. An interrupted time-series analysis (ITSA) was used to investigate the impact of ZMDP on monthly drug expenditures for managing PD and its complications per outpatient visit or inpatient admission. The step-change (an immediate level change at the intervention, β1) and the trend change (a change of slope compared post against pre-intervention, β2) were reported. ITSA was further conducted on outpatient-related drug costs dichotomized by whether patients of older age (≥65 years), with health insurance coverage and drugs included in the National Essential Medicine List (EML).

Results: Drug costs were derived from 18,158 outpatient visits, and 366 inpatient admissions. As expected, the implementation of ZMDP significantly decreased drug costs for managing PD in outpatients (β1=-200.9) and inpatients (β1=-307.2) (both $P<0.05$). The post-ZMDP trend change of outpatient-related drug costs for managing PD differed by whether patients were covered with healthcare insurance (covered: β2=-11.3; uncovered: β2=16.8) or drugs included in the EML (listed: β2=-1.4; not listed: β2=6.3). Similarly, post-ZMDP drug costs for managing outpatients' PD complications significantly increased in patients with older age (β2=24.3), uncovered by health insurance (β2=12.6), and drugs included in EML (β2=14.7).

Conclusions: The significantly increased post-ZMDP trend in several subgroups may offset decreased drug costs at the implementation of ZMDP. Further research is needed to investigate the policy-induced medical burden and care outcomes, particularly for patients with older age and uncovered by health insurance.

A.15

Seeing eye-to-eye on real-world evidence: Is guidance from Japan and China consistent with recommendations from REALISE in Asia?

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Aim/Objective: The REAL World Data (RWD) In Asia for Health Technology Assessment (HTA) guidance was developed by a regional working group to facilitate the increasing acceptance of real-world evidence (RWE) in Asia. We compared the consistency of REALISE against guidance from Japan and China.

Methods: Country-specific guidance for RWE/RWD use in pharmaceutical development were identified in May 2022 through governmental websites, with validation searches via Google. Sections from local guidance were mapped onto REALISE and categorised as “agree”, “mixed”, “disagree” or “missing” based on coverage/consistency.

Results: Five Japanese and three Chinese documents were mapped. Most sections in Chinese guidance (77%) and 36% of sections in Japanese guidance were tagged “agree” or “mixed”, with general alignment on definitions and good practice considerations (study design, accountability); however, 63% of Japanese sections were tagged “missing” from REALISE. As local documents took the regulatory perspective, they lacked REALISE’s discussion of translating RWD to RWE for HTA/economic evaluations specifically. Local guidance focussed on practicalities of RWD collection in local contexts, including descriptions of specific actions (e.g. evaluating RWD sources, ensuring data security) rather than overarching principles described in REALISE; specifically, Japanese guidance described how to access and analyse databases/registries, reflecting Japan’s landscape of robust sources of national healthcare data, but lacked discussion of other RWE study types, data sources and specialised analytical methods. While Chinese guidance had a broader view of RWD types (more similar to REALISE), they also contained discussions on pharmacovigilance and omics data, communication with regulatory bodies, and incorporation of RWE into the approval pathway for traditional Chinese medicines.

Conclusion: Despite differing purposes (with no RWE guidance from local HTA bodies), local and regional guidance align on general principles/good practice in generating/using RWE, providing common ground for increasing usage of RWE in HTA in Asia.

Keywords: RWE, regulatory guidance, HTA

B. Pharmacoepidemiology and Pharmacovigilance research methods

B.1

Comparison of SNG algorithm with standard tools for causality assessment of adverse drug reactions in South Indian hospital setting

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Objective: To compare the SNG algorithm with other standard tools for causality assessment of adverse drug reactions in the Indian hospital settings.

Methodology: The cases were identified retrospectively from the Pharmacy Practice Department database for adverse events (AE) reporting using previously documented AEs. Patient data were collected from 2012 until 2021, irrespective of demographics and occupation along with comorbidities. All the ADRs were identified and assessed separately for the Naranjo Scale (NS) and Sharma-Nookala-Gota (SNG) scale, which will be used to compare the validity of the SNG algorithm and its effectiveness against NS for CA.

Results: Out of the 758 AEs, 422 (55.7%) AEs were reported in male patients and 328 (43.3%) in female patients. The highest frequency of AEs was observed in age groups 50-59 years with 153 patients. The most frequently assigned causality category in NS and SNG scale was “possible” with the frequencies being 521 and 528, respectively. A disagreement between the interpretations of the two algorithms was observed in 443 (58.44%) cases. The most frequent disagreement was found in the Possible category (SNG) to Probable (Naranjo) with 222 reports.

Conclusion: The most often ascribed causality category in the NS and SNG scale was "possible" out of 758 ADR reports. Probable was the second most common category in NS, followed by definite and then doubtful. The second most common category in the SNG algorithm was doubtful, followed by probable, with no patients falling into the "definite" and "not related" categories.

Keywords: Adverse Drug Reaction, Naranjo Scale, Causality, India

B.2

Knowledge and perception of vaccine pharmacovigilance and adverse event following immunization reporting among pharmacy students - An online-based cross-sectional study

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Objective: In India, the knowledge and perception of vaccine pharmacovigilance and adverse events following immunization (AEFI) reporting among pharmacy students are unknown. To assess the knowledge and perception of pharmacy students towards vaccine pharmacovigilance and AEFI reporting.

Methods: It is a cross-sectional survey conducted for three months. Validated structured questionnaires were circulated through emails and social media (Facebook and Whatsapp) to the pharmacy students in India. The data was then imported in IBM SPSS (Version 22) for analysis.

Results: Total 205 responses were received, out of which 196 consented to participate, and the remaining nine refused to participate in the study. The average knowledge score was found to be 7.54±1.78. In our survey, 82.7% of participants didn't report AEFI. 50% of participants said that vaccine pharmacovigilance is not yet covered in the syllabus, and 66.3% said they were not trained during their studies for AEFI reporting. 96.9% of participants think that Pharmacists should be involved in reporting AEFI, and 95.4% of participants are willing to undergo training on Vaccine pharmacovigilance.

Conclusion: The AEFI reporting system is essential and, in most cases, done by a pharmacist in the Indian scenario; hence it is recommended to add it to the syllabus and practical exposure of vaccine pharmacovigilance and AEFI reporting to the pharmacy curriculum. It is also recommended that the continuous training programs and education to the health care professionals is essential to raise the knowledge and perception regarding vaccine pharmacovigilance and reporting of AEFI.

Keywords: AEFI, Knowledge, Perception, Pharmacy student

B.3

Validation of clinical variables in the SingHealth COVID-19 Registry

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Objective: The SingHealth COVID-19 registry was established in response to the COVID-19 pandemic for operational, research, clinical and pandemic preparedness purposes. It was developed within Electronic Health Intelligence System (eHIntS), a digital-data repository within SingHealth that integrates information from the Electronic Medical Record (EMR). We aim to internally validate presenting signs and symptoms, comorbidities and COVID-19 complications defined within the registry.

Methods: Validation was completed for patients admitted to 2 acute hospitals (SGH and SKH) from January 2020 to 31st December 2020. We created algorithms by combining various diagnostic codes and other structured clinical data to define comorbidities and COVID-19 complications using eHIntS data. 10% of patients from each institution with at least 1 algorithm detected variable were sampled. We calculated the sensitivity, positive predictive value (PPV), Cohen's Kappa, and prevalence-adjusted and bias-adjusted kappa (PABAK) to measure the performance of the algorithms against the gold standard of manual EMR review for each of the 19 comorbidities and 14 complications.

Results: For 180 (of 1,840) SGH patients and 139 (of 1,377) SKH patients, SGH had and overall PPV of 0.972 (95%CI: 0.935-0.988) and sensitivity of 0.988 (95%CI: 0.959-0.997) while SKH had overall PPV of 0.919 (95%CI: 0.858-0.956) and sensitivity of 0.884 (95%CI: 0.817-0.928). Overall Cohen Kappa and PABAK were 0.345 (95%CI: -0.130-0.821) and 0.922 (95%CI: 0.843-0.968) for SGH and -0.0944 (95%CI: -0.483-0.294) and 0.640 (95%CI: 0.492-0.760) for SKH, respectively.

Conclusion: There was good agreement between our eHints-based algorithms and the gold standard for all variables for both institutions.

B.4

Trends of antibiotic resistance and risk factors of carbapenem resistance in critically ill patients with Klebsiella pneumoniae bacteremia

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Objective: Bacteremia caused by Klebsiella pneumoniae (KP) has high mortality rates. The rapid emergence of antibiotic-resistant KP is a health threat, especially for patients admitted to intensive care units (ICUs). The aim of this study was to investigate the trends of antibiotic resistance of strains responsible for KP bacteremia in ICU patients and the risk factors associated with carbapenem-resistant KP (CRKP) bacteremia.

Methods: We conducted a retrospective study on adult patients with KP bacteremia admitted to the ICUs of a medical center in Southern Taiwan from Jan 1, 2013 to Dec 31, 2020. The antibiotic susceptibility profile and the patients' clinical data were collected from electronic medical records. Cochran-Armitage test for trends was used to assess the trends of antibiotic susceptibility. Univariate and multivariate logistic regression were used to identify risk factors associated with KP bacteremia caused by CRKP.

Results: A total of 266 patients were included in this study. The proportion of KP strains only resistant to ampicillin (wild-type) decreased from 69.0% to 45.2% from 2013 to 2020 (P=0.003). The proportion of CRKP increased from 3.5% to 16.7% (P=0.003) during the study period. The susceptibility of KP to the following antibiotics had dropped to less than 60% in 2020: Ampicillin/sulbactam (50.0%), levofloxacin (52.4%), cefoxitin (56.5%), cefazolin (57.1%), ceftazidime (57.1%), and trimethoprim/sulfamethoxazole (59.5%). The susceptibility of KP to amikacin remained high (95.2%). Length of hospital stay was the only independent risk factor associated with carbapenem-resistant KP bacteremia (odds ratio[OR]: 1.05, 95% confidence interval [CI]: 1.02-1.07, P=0.046).

Conclusion: Our study observed a significant increasing trend in antibiotic resistance in KP bacteremia during the past eight years. The rapid emergence of CRKP is especially alarming. Most KP isolated from bacteremia in critically ill patients remain susceptible to amikacin. Length of hospital stay was a risk factor associated with CRKP bacteremia.

B.5

Claims-Based Algorithms for Lactic Acidosis: What to Do in the Absence of Specific ICD-10 Codes?

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Background: Reliable outcome capture is critical for database studies. However, coding systems do not always capture the precise clinical concept of interest. For example, there is no specific code for lactic acidosis (LA) in either ICD-9 or ICD-10. Previous claims-based studies have relied on codes for acidosis (ICD-9 276.2; ICD-10 E87.2). However, only a small fraction of hospitalizations with acidosis are expected to represent LA.

Purpose: To examine the feasibility of constructing claims-based definitions for LA among patients with type 2 diabetes, assisted by using code position.

Methods: We identified patients with ICD-10 code E87.2 (acidosis) as: (1) admitting and principal diagnosis, (2) admitting and secondary diagnosis, and (3) admitting diagnosis without principal or secondary diagnosis among US Medicare patients age ≥65 from 10/1/2015 to 12/31/2018. Medical charts for 30-50 randomly sampled cases per group were retrieved and reviewed by nephrologists. Confirmed LA was defined as elevated lactate level (≥3mmol/L) and evidence of acidosis (pH <7.35, anion gap >16mmol/L, or serum bicarbonate level ≤21mmol/L). Positive predictive value (PPV) and 95% confidence interval [CI] were calculated by group and overall.

Results: 114 patients were sampled (mean age 75, 60% female). PPVs for confirmed LA were estimated at: 67% [CI 51-83] for group 1 (22/33 charts); 49% [CI 35-63] for group 2 (25/51 charts); 30% [CI 14-46] for group 3 (9/30 charts); and 50% [Cl 36-65] overall.

Conclusion: Our results show that restriction of inpatient acidosis cases to those with both admitting and principal acidosis diagnoses allows identification of LA cases with a PPV of 67%. PPVs were lower for cases with admitting and secondary diagnosis or admitting diagnosis without principal or secondary diagnoses. Code position can be used as a powerful tool to identify precise concepts in the absence of specific codes.

Keywords: Lactic Acidosis Validation; Claims-based definition; Positive Predictive Value;

B.6

Analysis of COVID-19 vaccine-related adverse drug reaction in a medical center in Southern Taiwan

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Aim/Objective: The infection rate of COVID-19 nationwide has exceeded 12.4%, and a total of 4,280 people have died. The infection number in southern Taiwan is still increasing. COVID-19 vaccines greatly reduce the risk of severe illness, hospitalization, and death from COVID-19. However, adverse reactions unlisted in the package insert (unlisted ADR, UADR) appear one after another. Pharmacists can play a crucial role in pharmacovigilance.

Methods: The ADR reports during March 22, 2021, the day when Taiwan's COVID-19 vaccine was first launched, to June 8, 2022 in our ADR database were tested. The UADR of 4 COVID-19 vaccines was counted and UADR signals were detected by proportional reporting ratios (PRRs). We use the Medicines and Healthcare products Regulatory Agency (MHRA) signal selection criteria: PRR≧2, chi-square ≥4, number of case reports ≥3, to detect UADR signals.

Results: During the study period, we received 700 cases of ADR notifications, 725 ADR symptoms including 111 cases of Covishield (38 cases of UADR), 37 cases of Spikevax (17 cases of UADR), 27 cases of BNT vaccine (14 cases of UADR), 8 cases of Medigen (UADR 6 cases). UADRs meeting the MHRA signal selection criteria (PRR; chi-square ≥4; number of case reports) are as follows: suspected Spikevax-induced thrombosis (7.8; 35.6; 7); Covishield-related vision loss (4.6; 13.3; 4), cellulitis (4.6; 13.3; 4), hearing loss (4.3; 8.9; 3), numbness of limbs and trunk (4.3; 8.9; 3), muscle weakness (3.4; 6.1; 3).

Conclusion: We found 6 COVID-19 vaccine UADR signals, which are helpful for medical staffs to prioritize the identification of UADR related to Spikevax and Covishield vaccines. In particular, Spikevax-related thrombus has the strongest signal and needs the most attention. As for vision loss and hearing loss, the signals are also helpful in early detection and treatment. Therefore, pharmacovigilance in COVID-19 vaccines is still important.

Keywords COVID-19, adverse drug reaction, signal, Pharmacovigilance

B.7

Outcomes with concurrent use of proton pump inhibitors and first-line afatinib in patients with advanced non-small cell lung cancer

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Objective: Concomitant proton pump inhibitors (PPIs) use might reduce the plasma concentration of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs), such as gefitinib and erlotinib, and thus might result in worse clinical outcomes in patients with non-small cell lung cancer (NSCLC). This drug interaction clinical results in patients treated with afatinib remain unknown. This study was aimed to evaluate whether the combined use of afatinib with PPIs affected outcomes in patients with advanced EGFR-mutant NSCLC.

Methods: We conducted a multicenter cohort study of patients newly diagnosed with EGFR-mutant NSCLC and treated with first-line afatinib between 2014 and 2019 using an private medical research database based on electronic medical records. Patients who exhibited an overlap between PPIs and afatinib usage days were defined as concurrent use of PPIs. We followed from the index date of afatinib use until treatment failure, death, or the end of 2019. Time to treatment failure (TTF) was defined as the time from the start of the first-line afatinib to the last day of treatment. Association of concurrent use of PPIs and afatinib was evaluated with Cox proportional hazards model.

Results: A total of 918 patients were treated with first-line afatinib, 330 of which took PPIs at the same time and 588 took afatinib only. Patients had similar TTF regardless of concurrent use of PPIs during afatinib treatment (HR 1.08 [95% CI, 0.91 to 1.29]). However, exposure to PPIs during first-line afatinib treatment significantly decreased overall survival compared to that of patients with afatinib only (HR 1.29 [95% CI, 1.05 to 1.59]).

Conclusion: Concurrent use of PPIs was associated with lower overall survival in patients with EGFR-mutant NSCLC under first-line afatinib treatment.

Keywords: proton pump inhibitors (PPIs), epidermal growth factor receptor (EGFR), non-small cell lung cancer (NSCLC), afatinib.

B.8

Treatment with methylphenidate and the risk of fractures among children and young people: a self-controlled case series study

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Introduction: Animal studies suggest that methylphenidate treatment for around 3 months may lead to less mineralized and weaker appendicular bones. Our previous systematic review showed mixed results in the risk of fractures in ADHD treated group compared with the non-treated ADHD, and the results are limited by the study quality. Thus a self-controlled case series (SCCS) study was used to compare the risk before and after treatment initiation.

Methods: We included individuals aged between 5 and 24 years who received methylphenidate treatment and experienced fractures from 2001 to 2020 in Hong Kong using a territory-wide electronic medical record database. Incidence rate ratios (IRRs) and 95% confidence intervals (CIs) of fracture risk were calculated by comparing the incidence rate in the methylphenidate-exposed period compared to the non-exposed period.

Results: Among 43,841 individuals with ADHD medication prescriptions before the year 2020, 2,203 were included in the SCCS analysis. We found a significantly higher risk of fracture in the 6 months before methylphenidate initiation compared to the baseline period (IRR 1.27, 95% CI 1.05-1.53), a similar or marginally similar risk to the baseline period in different periods after treatment initiation with IRRs ranging from 0.75 to 0.87. When compared to the 6-month pre-exposure period, the risk of fractures was decreased by 39% (IRR 0.61, 95% CI 0.45-0.82) in the first 6 months after methylphenidate initiation, 41% (IRR 0.59, 95% CI 0.42-0.84) in 7-12 months after treatment start, and 32% (IRR 0.68, 95% CI 0.55-0.85) during the subsequent exposure period. A similar result was observed in the spline-based SCCS. Negative control outcome analysis did not detect any significant risk of diseases of oesophagus, stomach, and duodenum.

Conclusion: In conclusion, treatment with methylphenidate may lower the risk of all-cause fractures, however, further evidence is needed about the treatment duration and sex effect.

B.9

Association of endocrine-disrupting chemicals exposure and risk of gestational hypertension and preeclampsia: a systematic review and meta-analysis

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Aim and objective: Prenatal exposure to bisphenol A, phthalates, and per or polyfluoroalkyl compounds has been linked to gestational hypertension and preeclampsia. However, the results were conflicting and inconclusive. The present study aims to examine the relationship between EDCs exposure (bisphenol-A, phthalates, and per or polyfluoroalkyl substances) with the risk of gestational hypertension and preeclampsia in pregnant women.

Methods: We searched PubMed and Google Scholar for studies investigating bisphenol-A, phthalates, and per or poly-fluoroalkyl substances and gestational hypertension or preeclampsia. Pooled odds ratio (OR) with 95% confidence interval (CI) were calculated for risk estimate by using the generic inverse variance method, we conducted a meta-analysis.

Results: A total of 20 studies were included. The pooled results demonstrated higher levels of urinary concentrations of mono-isobutyl phthalate (MiBP) (OR:1.52, 95% CI: 1.04,2.21), mono-n-butyl phthalate (MBP) (OR:1.72, 95% CI: 1.26, 2.34) and mono-ethyl phthalate (MEP) (OR:1.37, 95% CI: 1.11, 1.69) were associated with increased risk of gestational hypertension. The higher plasma concentration of PFOS (OR:1.21, 95% CI: 1.09, 1.34) and PFHxS (OR:1.13, 95% CI: 1.02, 1.26) were positively associated with an increased risk of preeclampsia. Whereas, PFUnDA (OR:0.82, 95% CI: 0.72, 0.94) were inversely associated with the risk of preeclampsia. From our analysis, Bisphenol A exposure during pregnancy did not show significant association with the risk of gestational hypertension and preeclampsia.

Conclusion: Our findings indicated that MiBP, MBP, and MEP exposure during pregnancy was associated with increased risk of gestational hypertension. Also, PFOS and PFHxS were associated with an increased risk of preeclampsia. Whereas, PFUnDA was inversely related to the risk of preeclampsia. Since the most of associations have limited evidence, more research is needed to confirm these findings.

B.10

Elevation in serum uric acid levels predicts favorable response to EGFR inhibitors treatment in patients with metastatic NSCLC

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Background: Erlotinib and gefitinib block the activation of EGFR, a transmembrane receptor found in many types of cancer cells. Cancer is halted through EGFR inhibition to inhibit the angiogenesis and impairment of intratumoral microcirculation. Impairment of microcirculation results in intratumoral hypoxia and increases the level of serum uric acid.
The purpose of this study was to determine whether serum uric acid levels related to erlotinib or gefitinib effects on metastatic non-small-cell lung cancer (NSCLC) therapeutic responses.

Methods: These retrospective cohort studies included 125 patients, from Jan 2018 to Dec 2021, with metastatic non-small-cell lung cancer treated for at least 3 months with erlotinib or gefitinib and survivors without disease progression. We recorded and analyzed demographic characteristics, baseline serum uric levels, and 3-month serum uric acid levels.

Results: The total number of patients with cancer history was 20; the number of newly diagnosed patients was 105. A total of 54 patients had brain metastases, while 71 patients without metastasis. Of 125 patients, 76 were taking erlotinib and 49 were taking gefitinib. Among the 31 with the uric acid test, 94 were not. When the medication was begun, the average uric acid level was 4.63 mg/dL. After three months, the average uric acid level elevated to 6.08 mg/dL. In the survivors without progression group, we found that serum uric acid levels were significantly different 3 months after starting erlotinib or gefitinib。

Conclusion: There was a significant increase in serum uric acid levels in patients with metastatic NSCLC who responded favorably to erlotinib or gefitinib and did not progress upon erlotinib or gefitinib treatment. However, there are limitations to this study due to the small number of cases detected for uric acid. The serum uric acid biomarker as a novel biomarker for predicting survival in metastatic NSCLC patients requires further study.

B.11

An age-period-cohort analysis of psychiatric medicine related adverse drug reactions from 2010 to 2019 in Jiangsu Province, China

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Background: The adverse drug reactions (ADRs) of psychiatric medicines have been reported a lot in practice. In America, there were 117,414 ADRs caused by psychiatric medicines have been reported between 2004 and 2012. A total of 14,979 psychiatric medicine related ADRs were reported in Australia until 2011. In this study, we aimed to separate the effects of age, year, and birth cohort in association with the incidence of psychiatric medicine related ADRs in Jiangsu Province in China.

Methods: We obtained data for people aged 0-89 years from the regulatory ADR Spontaneous Reporting System in Jiangsu Province during the period between 2010 and 2019. We calculated age-adjusted incidence rates using Poisson regression with the province-wide population as an offset. We further performed the age-period-cohort analysis with an intrinsic estimator algorithm (APC-IE) to estimate the independent effects of age, period, and cohort on the psychiatric medicines related ADRs. We also conducted the stratification analysis by sex.

Result: A total of 16,753 psychiatric medicine related ADRs serious enough for hospital care were identified. The age-adjusted incidence rate of psychiatric medicine related ADRs has increased approximately 4 times from 0.63 to 2.44 per 100,000 population during 2010 to 2019. The risk of psychiatric medicines related ADRs increased with the period. 30-35 age group has highest risk of ADRs than other age groups. The 1930 birth cohort demonstrated 2.56 times higher risk of ADRs in comparison with the 1990 birth cohort, but there has been an upward trend in younger-age birth cohort. Similar age-period-cohort patterns were observed among males and females.

Conclusions: With the increase of diagnosis of mental disorders and the upward trend of psychiatric medicines related ADRs occurrence, we should continue to investing our efforts to promote safer use of psychiatric medicine.

Keywords: psychiatric medicine; adverse drug reactions; age-period-cohort analysis; China

B.12

Identification Tenofovir disoproxil fumarate (TDF) induced nephrotoxicity by using trigger tool

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Objective: To identify Tenofovir disoproxil fumarate (TDF) induced nephrotoxicity by using trigger tool

Method: A retrospective study using chart review was conducted. All patients diagnosed with HIV receiving antiretroviral regimen with TDF at HIV clinic at a secondary care hospital during January 1st 2020 to December 31st 2021. Tenofovir nephrotoxicity was identified using four abnormal laboratory results as triggers for detecting. The trigger tools included estimated glomerular filtration Rate (eGFR) <60 ml/min/1.73m², serum potassium ≤3.5 mmol/L, serum phosphorus ≤2.5 mg/dL, and urine glucose >50 mg/dL

Results: Triggers were observed 149 times in 1,546 medical records were admitted during the study period. Most common triggers were urine glucose >50 mg/dL (42.95%), (eGFR) <60 ml/min/1.73m² (29.53%) , serum Potassium ≤3.5 mmol/L (14.10%) , serum Phosphorus ≤2.5 mg/dL (13.42%). The highest positive predictive value (PPV) was for serum Phosphorus ≤2.5 mg/dL (30.00%) followed by serum potassium ≤3.5 mmol/L (23.80%), urine glucose >50mg/dL (23.44%) and eGFR <60 ml/min/1.73m² (11.36%).

Conclusions: Serum Phosphorus ≤2.5 mg/dL is the most sensitive positive predictive value (PPV) to detecting Tenofovir disoproxil fumarate (TDF) induced nephrotoxicity. Medical profession may benefit from trigger tool method to help them detect TDF induced nephrotoxicity. These triggers might be used as add-on methods to spontaneous method to improve the detection of nephrotoxicity from TDF.

Keywords: trigger tool, pharmacovigilance, Tenofovir disoproxil fumarate (TDF), nephrotoxicity, HIV

B.13

Signal detection of COVID-19 vaccines using spontaneous adverse event reports

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Aim/objective: In order to investigate adverse events (AEs) that might be associated with the COVID-19 vaccines, signals were detected through spontaneous adverse event reports.

Methods: From January 2013 to May 2022, the proportional reporting ratio (PRR), reporting odds ratio (ROR), and information component (IC) was calculated through AE collected by the national medical center from 63 institutions. The proportion of all AEs to COVID-19 vaccines (BNT162 Vaccine, 2019-nCoV Vaccine mRNA-1273, ChAdOx1 nCoV-19, Ad26COVS1) which were for an AE of interest was compared to the same proportion for other viral vaccines in the database, in a 2X2 table. In PRR, ROR, the signal was defined as 3 or more cases, PRR, ROR at least 2, and chi-squared of at least 4; In IC, the signal was defined as the lower limit of the 95% confidence interval was greater than 0.

Results: During the study period, 68,365 cases were reported, among them, viral vaccines-AE pairs were 12,674 patients and 25,758 cases (COVID-19 vaccines 4,179 patients, 12,495 cases; Other viral vaccines 8,495 patients, 13,263 cases). The method identified 36 signals meeting the minimum criteria. The AEs that were not labeled in South Korea regulator of the four COVID-19 vaccines in common were cachexia, dyspepsia, mood swings, and depression, which require further evaluation.

Conclusion: Although not provide causation, these findings might support clinicians and regulators in decision-making for patients who are potentially vulnerable.

Keywords: # COVID-19 Vaccines; Drug-Related Side Effects and Adverse Reactions; Data Mining; Pharmacovigilance

B.14

Assessment of quality of life and depression in Type 2 Diabetes Mellitus female patients in Bihar, India

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Background: Type 2 diabetes mellitus (T2DM) is a chronic, progressive disease characterized by high blood glucose levels. It is frequently accompanied by a variety of comorbidities, including depression, and its impact on quality of life is dramatically expanding.
Objective: To assess the QOL and severity of depression in T2DM female patients using the predefined questionnaires.

Methodology: This is a cross-sectional observational study in which patients over 18 years of age patients were included. Two questionnaires: World Health Organization Quality of Life – BREF (WHOQOL-BREF) and (Patient Health Questionnaire-9) PHQ-9 questionnaires were used to measure QOL and depression, respectively. Data were analyzed through descriptive methods, Chi-square, and Independent t-test using SPSS Ver 25.

Results: Out of 100 T2DM female participants, 47% were in the 51- 65 age group, 84% were postmenopausal, and approximately the same (85%) were of urban residents. Most of the female patients (57 %) had BMI > 30. A significant impact of menopausal status was observed in the physical health domain (p-value = 0.013) and social relationship domain (p-value = 0.009), also patients with diabetic foot had severe “degraded physical health QOL” (23.81 ± 11.44), “psychological QOL” (18.75 ± 5.11), “social relationship QOL” (38.88 ± 6.81), and “environmental QOL” (43.75 ± 6.85). PHQ-9 tool analysis showed, that 77% of the respondents had experienced depression, while 17% were found severely depressed.

Conclusion: This study concluded that depression is prominent among T2DM female patients and that it has a significant impact on diabetes-related complications and quality of life.

Keywords: Quality of Life, Depression and WHO-QOL and PHQ-9

B.15

Pattern of prescription for initial treatment of Systemic Lupus Erythematosus: a descriptive study

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Objectives: To assess nationwide pattern of prescriptions for initial treatment among patients diagnosed as systemic erythematosus lupus (SLE).

Methods: We performed a descriptive study using the nationwide healthcare claims information database of Korea from January 1, 2002 to December 31, 2018. We defined patients with incident SLE during 2006 and 2016 using diagnostic code (International Classification of Diseases, 10th revision code, M32) and rare disease registration code(V136). We analyzed patterns of prescribing antimalarial drug (hydroxychloroquine; HCQ), immunosuppressive drugs (methotrexate; MTX, azathioprine; AZA, mycophenolate mofetil; MMF, cyclophosphamide; CYC), calcineurin inhibitors (tacrolimus; TAC, cyclosporine A; CsA) and biologic agent (rituximab; RTX) within 1 year from initial diagnosis of SLE.

Result: A total of 12,733 patients with incident SLE were identified between 2006 and 2016. The first diagnosis of SLE was the most common in tertiary hospital with 7,963 cases (62.5%). Mean (± Standard Deviation) age at first diagnosis was 37.8 (±15.5), and females occupied 91.6% (n=11,666). The proportion of prescriptions within one year after SLE diagnosis were as follows: HCQ (71.2%, 9,067 patients), AZA (14.3%, 1,826 patients), MTX (9.4%, 1,195 patients), MMF (9.0%, 1,145 patients), CYC (8.3%, 1,055 patients), CsA (5.0%, 642 patients), TAC (2.2%, 274 patients), and RTX (0.1%, 11 patients)

Conclusion: Whereas HCQ is a recommended mainstay treatment in patients with SLE, 71.2% of incident SLE patients were prescribed HCQ within first diagnosis of SLE. Further analysis on longitudinal treatment patterns among SLE patients considering disease activity and comorbidity would be meaningful.

B.16

Risk of Prediabetes Among Population of An Urban Community; Findings of A Community Pharmacy-Based Study

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Aim/Objective: To assess the risk of prediabetes among the urban population

Methods: This prospective cross-sectional study was conducted at four community pharmacies for six months. The general public who was not a known case of diabetes were screened for the risk of prediabetes. The Canadian Diabetes Risk Assessment Questionnaire (CANRISK) was used to assess the risk among the study population. The demographic and anthropometric measurements were collected, documented, and allotted scores. Based on the total score, the study population was categorized as having a low (21 or less), moderate (21-32), and/or high (33 or more) risk of prediabetes.

Results: A total of 431 people were screened. A majority of the participants had a high (63.3%), followed by moderate (29%), and low (7.6%) risk of prediabetes. Gender (male), age (≥45 years), body mass index (≥ 25 kg/m2), waist circumference (≥ 94 cm for men and ≥80 cm for women), systolic blood pressure (>120 mmHg), random blood sugar (>150 mg/dL), history of gestational diabetes, and education (high school or less) were the predictors of moderate or high risk of prediabetes. The Tukey's HSD test revealed a statistically significant difference between participants in all the three risk groups with respect to age (p=0.00092], body mass index (p=0.00505), and waist circumference-women (p=0.03045), and high blood pressure (p=0.00052). There was a statistically significant difference observed between high and moderate (p=0.00001) risk groups with respect to waist circumference-men. Also, there was a statistically significant difference between low and high (p=0.00004), and moderate and high (p=0.00155) risk groups with respect to blood sugar levels.

Conclusion: The prevalence of prediabetes is high among the urban population. The presence of family history, physical inactivity, and non-consumption of fruits and vegetables was not associated with the risk of developing prediabetes among our study population.

Keywords: Community Pharmacy, Prediabetes, Prevalence, Risk-assessment

B.17

Adverse Events and Breakthrough Infections followed by COVID-19 Immunization among Healthcare Professionals in a Tertiary Care Hospital in South India.

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Background: Adverse Events Following Immunization (AEFI) is defined as any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavourable or unintended sign, an abnormal laboratory finding, a symptom, or a disease. Break-through infections are referred to as antigen or SARS-CoV-2 RNA positivity of respiratory specimens more than 14 days after receiving all recommended doses.

Aim: The study was conducted to identify Adverse Events and break-through infections following the precautionary dose of the COVID-19 vaccine among healthcare workers.

Methodology: The study was designed as a cohort event monitoring, all healthcare professionals who received COVID-19 precautionary dose from the study site were included in the study. The study population was actively followed for any Adverse Event Following Immunization (AEFI) through telephonic contact (within 30 days of post-vaccination). Reported adverse events were carefully scrutinized and evaluated by the AEFI investigation team of the study site.

Results: Out of 1229 vaccine beneficiaries, a total of 324(26.36%) individuals were reported with 761 AEFIs. In which 136 (41.98%) individuals were laboratory-confirmed (RTPCR positive) breakthrough cases, while 56 (28.14%) of them had corona like symptoms but didn't tested. Less severity and low morbidity were observed among all the breakthrough cases. According to the WHO causality assessment algorithm, 319 (41.92%) events were vaccine product-related and 442 (58.08%) were co-incidental events.

Conclusion: There was a prevailing outbreak of COVID-19 infection in the study site which resulted in many breakthrough infections soon after immunization. Initially, all breakthrough infections were misleading as vaccine-related events, while this study helped to break the concerns among the study population.

Keywords: Adverse Events Following Immunisation (AEFI), Breakthrough infections, COVID-19 vaccines, precautionary dose.

B.18

Vaccine Safety and Active Surveillance for Adverse Effects Following Immunization in a Tertiary Care Hospital in South India.

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Background: Adverse Event Following Immunization (AEFI) is one of the major branches of pharmacovigilance as like tracking Adverse Drug Reaction (ADR). Unwanted effects after immunization in a healthy individual are always unexpected.

AIM: To conduct an active vaccine safety surveillance and to detect the causality of each reported AEFI. The study also evaluates different predictors of AEFI among the study population.
Methodology
Active vaccine safety surveillance was conducted among all the vaccine beneficiaries from the immunization centre (study site) within a period of 8 months (October 2021 – May 2022). Active surveillance was conducted through two telephonic contacts such as:- 8 days (surveillance I) and 28 days (surveillance II) ± 2 days following immunization. The causality assessment of each reported AEFI was investigated along with the background information and categorized according to WHO's causality assessment algorithm by the expert AEFI investigation panel in the study site.

Results: Out of 4,160 vaccine beneficiaries, a total of 1045 events were identified from 709 individuals. Total AEFI incidence during the study period was identified as 17.04% (n=709). Where incidence rate of adverse events followed by COVID-19 vaccines along contributes 13.27% and the remaining 3.77% was accounted with childhood vaccines. After causality assessment, 70.09% AEFIs were categorized as vaccine product-related reactions and 29.10% events were coincidental events. Three events are classified as indeterminate (category B) which may be new vaccine-linked events. No deaths were reported but 15 AEFIs were considered severe events. The study found out the presence of Comorbidities (Relative Risk: 0.055 and p-value: <0.0001) was a significant predictor other than age and gender.

Conclusion: The study signifies the need for a detailed investigation and assessment of each AEFI along with background information. Therefore many coincidental events following immunization can be ruled out effectively.

Keywords: Active surveillance, Causality Assessment, Predictors, Vaccine safety

B.19

Evaluation of Health Literacy and Medication Regimen Complexity Index among Patients with HIV Infection: A Single-Centre, Prospective, Cohort Study

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Background: A limited number of studies have explored the association between health literacy (HL) and health outcomes. Effectively managing HIV infection expects from the patients the ability to seek medical help, understand the instructions provided by the healthcare professionals, and adhere to the treatment plans. Poor HL may be associated with less optimal disease control, and thereby, a higher burden of medications.

Aim: The aim was to evaluate health literacy and medication regimen complexity index among people living with HIV and determine the associated factors.

Design: This was a prospective, cohort study

Result: Result: The 285 participants, 48.4% were females. The median age of the study participants was 48.00 years (IQR, 39.50–54.00). The median score on the HIV-LT was 3.00 (IQR: 0.00–6.00). Seventy-five (26.3%) scored zero in HIV-LT, and 39 were male and 36 were female; 14 were illiterate, 36 were primary school educated, 24 were secondary school educated, and one had completed college education. A statistically significant increase in the HL scores based on the educational status of the participants was seen ($x2 = 87.324$, $p < 0.001$).

The 285 participants took a total of 639 drug formulations, and the median number of medications taken was 8.0 (IQR, 6-12) per person per day, The median score for MRCI was 8 (6-12). 16 (13-22) in those with diabetes mellitus; 12 (9-16) in hypertensives.The median number of drugs consumed daily was not significantly different between genders (males, 8 [8-14]; females, 8 [4-12]; $p = 0.579$).

Conclusion: Health literacy skills are important for day-to-day self-care in patients living with HIV. Our study showed that health literacy, as assessed using the HIV-LT tool, was less than satisfactory in majority of the studied patients with HIV infection, including those with college education. Poor health literacy was not associated with an increased medication regimen complexity.

B.20

High-Dimensional Propensity Score: improved confounder selection through employing conditional bias factors for candidate variables

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Aim/Objective: In treatment effect studies, the magnitude of confounding impact of a binary covariate is a well-defined function of its prevalence in the treatment groups and its association with the binary outcome of interest. This property is formally embedded in the high-dimensional propensity score (HDPS) algorithm which is a popular method for empirically selecting confounder candidates in pharmacoepidemiological studies. However, a shortcoming of the standard HDPS approach is that the impact of a confounder variable on the outcome is assessed only by its respective univariate and not conditional (on other covariates) risk ratio estimate on the outcome. Therefore, in the presence of non-independent covariates, selection of confounder variables may be suboptimal due to confounding of estimated confounder effects. We demonstrate the shortcoming of univariate bias factors currently implemented in the HDPS and propose an effective solution through employing conditional bias factors.

Methods: We employ established bias formulas and Monte-Carlo simulation studies to illustrate impact of misspecifying the confounding impact of a candidate covariate using univariate bias factors.
We formally derive an extension of the bias factor approach to mirror conditional and not only univariate covariate effects on the outcome. We apply the proposed approach to a high-dimensional dataset on adverse drug reactions previously described in the literature.

Results: Univariate bias factors led to suboptimal selection of confounder candidate variables within the HDPS variable pre-selection step: confounding impact of candidate variables was estimated with considerable bias, leading to inappropriate ranking and/or complete omission by the HDPS.

Conclusion: Covariate pre-selection using univariate bias formulas may lead to sub-optimal confounder sampling within the high-dimensional propensity score algorithm. While we believe that the HDPS has important benefits in large-scale pharmacoepidemiologic studies, we recommend applying conditional bias formulas within the HDPS to improve selection of candidate covariates.

Keywords: high-dimensional propensity score, confounder selection, bias formula

B.21

Community pharmacist-led Diabetes Risk Assessment Services; An Initiative In South Indian Community Pharmacies

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Aim/Objective: To implement and evaluate diabetes risk-assessment services at community pharmacies

Methods: Community pharmacists were trained on diabetes risk assessment using the Canadian Diabetes Risk Assessment (CANRISK) tool. The on-site training program involved an interactive introductory session on CANRISK tool and its scoring system. This session was followed by hands-on training to calculate body mass index and measure waist circumference, blood pressure, and blood sugar, adopting the simulated patient technique. In addition, the community pharmacists were trained on skills related to communicating results to the participants and management strategies depending on the risk categories. A 5-point Likert scale was used to evaluate the effectiveness of the training program by the community pharmacists. At the same time, a six-item questionnaire was used to assess the general public's satisfaction with the community pharmacist-led diabetes screening programs. The results are presented descriptively.

Results: Twenty community pharmacists participated in the diabetes risk-assessment training program. The mean (±SD) age and years of practice of community pharmacists were 42±12 and 16±11 years, respectively. The median score for all the eight components of the self-reported post-training evaluation scale was 4 out of 5, indicating high adequacy and effectiveness of the training program. Four community pharmacists actively engaged in diabetes risk-assessment service at their practice sites screened 431 participants over six months. The participants with a moderate or high risk of developing diabetes were referred to general practitioners for further evaluation and management. The median score for all the six items on the satisfaction questionnaire by the general public was 4 out of 5, indicating a high level of satisfaction with the service.

Conclusion: The diabetes risk-assessment service at community pharmacies will help in detecting and managing people at risk of developing diabetes mellitus.

Keywords: Community pharmacy, Diabetes risk assessment, Canadian Diabetes Risk Assessment tool

B.22

Validation study for risk assessment of febrile neutropenia in patients with malignant lymphoma.

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Aim: In Japan, few validation studies have been conducted to confirm the accuracy of diagnostics codes in claims databases by comparing them with the information in medical records. we conducted a validation study for febrile neutropenia (FN), which occurs frequently in patients with Non-Hodgkin's lymphoma (NHL).

Methods: NHL patients who received a CHOP-like regimen (CHOP, THP-COP, CHOEP, any addition of R) between April 2018 and March 2021 at Nippon Medical School Hospital were included. Diagnosis Procedure Combination (DPC) data were used to identify patients who received chemotherapy. FN was identified from medical records by checking body temperature, neutrophil count, and the presence of empirical antimicrobial therapy. From the DPC data, algorithms were created using the combination of the ICD-10 code for agranulocytosis (D70), infection (part of codes A, B, J, K, L, N, and R), bacterial culture as a test, and intravenous cefepime, meropenem and tazobactam/piperacillin as drugs. The number of FN events per hospitalization period was checked for each algorithm, and sensitivity, specificity, and positive predictive value (PPV) were calculated to determine the optimal FN definition based on DPC data.

Results: During the period, 149 patients received 217 cycles of chemotherapy. As interim analysis, we report the results of 7 of these eligible patients for the 12 hospitalizations during which chart verification was completed (6 FN events in 3 patients). When the algorithm for these patients was examined, the highest sensitivity, specificity, and PPV were 50.0%, 83.3%, and 75.0%, respectively, when only the ICD-10 code for agranulocytosis was used. The PPV was 66.6% for the combination of ICD-10 code for agranulocytosis +bacterial culture identification test ±antimicrobial administration.

Conclusion: We conducted a validation study for FN. It seemed that the use of agranulocytosis as a diagnostics code would be the optimal definition of FN.

Keywords: validation study, Febrile Neutropenia, DPC

B.23

The Manipal deep venous thrombosis registry: epidemiology, clinical characterization, treatment patterns, and 2-year outcomes of dvt patients in India

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Background: Deep vein thrombosis (DVT) is associated with significant morbidity and mortality due to its recurrence and complications. The recent substantial data on DVT and its complications and long-term outcomes are limited in India.

Aims: This Manipal DVT registry is describing the epidemiology, clinical characteristics, treatment patterns, and outcomes of DVT patients.

Methods: This is a retrospective observational registry study carried out on all patients with a diagnosis of DVT confirmed by Doppler ultrasonography between 2014 and 2018 in a tertiary care center in South India. We have followed up with the patients for 2-years for the DVT-related outcomes and correlated with the risk factors.

Results: A total of 612 eligible patients with DVT were included with a mean age of 49.5±15.3 years. Among all, 420(68.6%) were males and 192 (31.4%) were females. One hundred eleven (18%) patients who have had a previous history of DVT and hypertension, malignancy, trauma/surgery, and varicose veins were presented in 154 (25.2%), 44 (7.2%), 96 (15.7%), and 143 (23.4%) patients respectively. Four hundred forty-six (72.9%) and 96 (11.6%) patients received warfarin and newer oral anticoagulants (NOAC) respectively. In composite major adverse outcomes, pulmonary embolism 66 (10.8%) was major followed by DVT recurrence 33 (5.4%) and death 16 (2.6%). A total of 123 (20.1%) patients were readmitted with DVT-related complications. The previous history of DVT and malignancy and smoking were the significant risk factors associated with 2-year composite outcomes with a p-value < 0.05.

Conclusion(s): Manipal DVT registry provides information about risk factors, clinical presentation, and treatment of DVT. A previous history of DVT, smoking, and presence of varicose veins, and the discoloration of the limb is associated with an increased risk of readmission, major adverse cardiovascular events (MACE), or death. Patients with DVT associated with malignancy have reduced survival.

B.24

Post-authorization Experience of COVID-19 vaccinations in Four Provinces in Thailand

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Background: As Coronavirus 2019 (COVID-19) disease has attacked globally. It caused more than 4 million deaths over the world. In year 2021, vaccines against COVID-19 have been approved for emergency use in Thailand. As there is less rigorous data from long-term use on the safety of COVID-19 vaccines, post-marketing surveillance of adverse event data is crucial to make safe use and less serious unexpected events. Among 76 provinces and 4 regions of Thailand, Kalasin, Mahasarakham, Khon-Kaen and Roi-et are four provinces located in the central of southeastern region, covered around 5 million people. Four COVID-19 vaccines were applied: AstraZeneca, Pfizer BioEnTech, Sinopharm and Sinovac Life Science. Adverse events were monitored in all patients. 8 vulnerable patients (patient who was elderly, pregnant women, being cancer, having cardiovascular disease, chronic kidney disease, cerebrovascular disease, DM, and severe respiratory disease) were closely observed. Active pharmacovigilance monitoring after COVID-19 vaccination is needed to prevent and document possible adverse reactions related to COVID-19 vaccines.

Objectives: This study is aimed to examine the adverse events (AEs) among patients who received three COVID-19 vaccines in four provinces of Thailand.

Methods: The retrospective active surveillance of adverse events after immunization of COVID-19 vaccines in four provinces were retrieved to learn the patients 'characteristic and other relevant factors. AE from vulnerable group was also studied. Time period was January- August 2021.

Results: Total 128,892 AEs were reported. The majority were female (63.20%). Patient at age 31-45 years were most reported. Among 8 vulnerable group, mostly were elderly. Myalgia were the most reported (19.46%), followed by headache (16.51%), fever (14.71%) and fatigue (11.56%). No serious events were found.

Conclusions: Post-marketing surveillance of COVID-19 vaccinations in four provinces of Thailand found no serious AEs. Continuous surveillance is recommended to the COVID-19 vaccine immunization to Thai patients.

Keywords: COVID-19, adverse events, vaccines

B.25

Clinical trial eligibility for Paxlovid in a real-world COVID-19 population in Taiwan

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Objective: To estimate the percentage of COVID-19 patients who initiated the Paxlovid in Taiwan meeting the major eligibility criteria for EPIC-HR trial (Evaluation of Protease Inhibition for Covid-19 in High-Risk Patients).

Methods: This was the cross-sectional study from two hospitals in the northern Taiwan between February 1, 2022 and May 12, 2022. We applied the major eligibility criteria of EPIC-HR trial to the real-world COVID-19 patients who initiated the Paxlovid, including (1) at least one underlying condition associated with an increased risk of developing severe illness from COVID-19, such as age over 60 years, BMI over 25 kg/m2, smoking, etc; (2) initial onset of COVID-19 signs/symptoms within 5 days; (3) no pregnancy or breastfeeding; (4) no active liver diseases; (5) not receiving dialysis or known renal impairment (e.g., CKD stage 3 or more advanced stage); (6) no concurrent active systemic infection other than COVID-19; (7) no recent hospitalization and/or surgery. We calculated the percentage of COVID-19 patients initiating the Paxlovid meeting eligibility criteria for EPIC-HR trial.

Results: A total of 117 COVID-19 patients initiating Paxlovid (mean age: 63.4 years old; female: 47.8%) were identified, and all of them had at least one underlying condition associated with an increased risk of developing severe illness from COVID-19. We found only 61.5% (72/117) of real-world COVID-19 patients meet the major eligibility criteria of EPIC-HR trial. Among COVID-19 patients ineligible for EPIC-HR trial, the exclusion reasons included recent hospitalization and/or surgery (25/45, 55.6%), active liver diseases (12/45, 26.7%), advanced renal diseases (5/45, 11.1%), concurrent active systemic infection (4/45, 8.9%), initial onset of COVID-19 signs/symptoms over 5 days (3/45, 6.7%) and pregnancy or breastfeeding (1/45, 2.2%).

Conclusions: About one-third COVID-19 patients in routine care in Taiwan were ineligible for EPIC-HR trial. Further studies should evaluate the treatment effectiveness in these populations.

Keywords: Eligibility; COVID-19; Paxlovid

B.26

The Association of Nonsteroidal Anti-Inflammatory Drugs and New Onset Chronic Kidney Disease Stages3-5 in Elderly Patients with Hypertension in Thailand

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Background: Chronic kidney disease (CKD) presents a major challenge to the 21st century global health policy. The relationship between non-steroidal anti-inflammatory drugs (NSAIDs) and CKD stage 3-5 has been clearly established. We aimed to identify the association of NSAIDs and new onset CKD stage 3–5 in Thai elderly patients with hypertension.

Methods: we conducted a nested case-control study in Thai elderly patients with hypertension visited hospitals during 2014-2018. Data were extracted from the Standard Health Care Data from 4 community hospitals in Chiang Mai, Thailand. Case was patients with CKD stage 3-5 defined by a diagnosis with ICD10 N18.3-18.5 confirmed with 2 lab results of eGFR < 60 ml/minute/1.73 m2 before index date. We matched case and control using 1:1 caliper matching. NSAIDs exposure was defined as NSAIDs use (any NSAIDs prescribed in 1 year after 90 days from index date), NSAID dose (defined daily dose, DDD unit/day, range 0-1, >1), and cumulative NSAIDs use (number of DDDD in 1 year). We analyzed NSAIDs exposure by drug class and individual NSAID, compared with no NSAIDs exposure. Logistic regression analysis was performed in this study.

Results: 1,876 subjects ≥60 years with hypertension were included, 938 cases and 938 controls. Age, gender and index date were not different between case and control groups (p>0.05). Most patients used NSAIDs at low dose (DDD ≤1 unit/day) and only in short-term (median 7 days, interquartile range, 11.25 days, ranged 1-89 days in 1 year). No association between NSAIDs exposure and CKD stage 3-5 was observed in our study (aOR, 0.91; 95%CI, 0.70, 1.18).

Conclusions: This study did not find any associations between NSAIDs exposure and CKD stage 3-5 in Thai elderly patients with hypertension, which might be explained by NSAIDs were prescribed at low dose and short duration for this group of patients.

B.27

Using Administrative Healthcare Data to Identify Drug Repurposing Opportunities: a Case Study of Beta-Blocker Use and Breast Cancer Survival

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Aim/Purpose: Cancer registries are commonly used to evaluate drug repurposing candidates for cancer. Administrative healthcare data is a promising alternative data source given its longitudinal individual-level records and widespread availability. Here, we explored using administrative data to investigate the association between beta-blocker use and breast cancer survival.

Methods: Incident breast cancer cases in women aged ≥50 years were identified from the hospital admission data in Victoria, Australia. The use of beta-blockers and first-line anti-hypertensives were identified during a 120-day baseline period before the admission date using prescription medication claims. Follow-up commenced at initial discharge date. Breast cancer molecular subtypes and metastasis were inferred using an algorithm of commonly prescribed breast cancer antineoplastics and hospitalisation diagnosis codes, respectively. Subdistribution hazards ratios (sHR) and 95% confidence intervals (CI) for breast cancer mortality were estimated using Fine and Gray's competing risk models, adjusted for age, weighted Charlson comorbidity index, congestive heart failure, molecular subtype, metastasis at diagnosis and breast cancer surgery during index hospitalization.

Results: There were 604 beta-blocker users and 1387 users of first-line antihypertensives from a total cohort of 2758 women. There were 185 breast cancer deaths identified over a median follow-up time of 2.6 years. We found no significant association between beta-blocker use and breast-cancer mortality (sHR 0.86, 95% CI 0.57-1.29), or when stratified by beta-blocker type (nonselective, sHR 0.44, 95% CI 0.14-1.37; selective, sHR 0.95, 95% CI 0.63-1.45).

Conclusions: We demonstrated using administrative healthcare data to investigate a drug repurposing candidate for cancer, including methodologies to infer cancer-related clinical information that were lacking in the administrative dataset. However, we did not find an association between beta-blocker use and breast cancer survival, likely due to the small sample size. Further studies using larger sample sizes are required to confirm the feasibility of using administrative data for drug repurposing in cancer.

B.28

The effects of low dose estrogen progestin and obesity on the thrombotic events in the Japanese women

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Aim/Objective: To evaluate the effects of low dose estrogen progestin (LEP) on thrombotic events in obese women.

Methods: The retrospective cohort study using claims database and health checkup information provided from JMDC Inc. was conducted. Women with BMI record were eligible in our study. Among the target population, women with at least one prescription for LEP served as the exposure group, and others as the control group. Women were stratified into obese group with BMI ≧28 kg/m² and non-obese group with BMI< 28kg/m². Time-to-onset of thrombotic event was the outcome. Multivariable COX regression was conducted to examine the interaction effect of obesity and LEP on the thrombotic events.

Results: 53201 women were included in the study. Multivariate COX-regression showed that the adjusted hazard ratios for women with control and non-obese were 1.18 [1.02, 1.35] for women with LEP and non-obese, 1 22 [1.11, 1.50] for control and obese, 1. 35 [1.21, 1.64] for LEP and obese.

Conclusion: Although there are existing reports of the risk of obesity in women with LEP prescription, there have been no previous reports using real-world data from the Asian region. I reported the elevated risk of thrombotic events in obese women with LEP prescription using the claim database in Japan. The prescription of LEP to obese women should be discouraged according to guidelines that do not recommend LEP prescribing in obese women.

B.29

IMPACTS OF THE COVID-19 PANDEMIC ON PATIENTS WITH CHRONIC CONDITIONS IN VIETNAM: A CROSS-SECTIONAL STUDY

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Objective: Individuals with chronic diseases are particularly prone to be affected by the COVID-19 pandemic. We aimed to assess the impact of the COVID-19 pandemic on health, treatment adherence and expectations of patients with chronic diseases in Vietnam.

Methods: We conducted a cross-sectional study using a questionnaire survey to describe the impact of the COVID-19 pandemic on patients with chronic diseases in Vietnam. The study was performed during two months of the most stringent social distancing in Vietnam (between July 21 and September 21, 2021) through an online questionnaire, distributed through social networks and presented on Google Forms.

Results: Among 371 patients, half of them were females, one-third were elderly (60 years old or more) and two-third lived in Ho Chi Minh City. Most of the participants said that the COVID-19 epidemic had affected their daily activities (91.9%), health (53.6%), sleep behavior (52.3%), and mental health (79.8%). During social distancing, three-quarter could not go to hospitals for periodic health examination; nearly half of respondents did not do daily physical activities; a quarter of respondents did not adhere to their recommended diet plan. Factors associated with the effect of the COVID-19 epidemic on patient's health during social distancing period included those living in Ho Chi Minh City ($p = 0.015$), lived alone ($p = 0.027$), uncontrolled chronic conditions ($p < 0.001$), treatment dissatisfaction or experienced anxiety/stress ($p < 0.001$). Factors associated with medication adherence included the elderly ($p = 0.015$), having periodic health examination ($p = 0.012$), direct consultation ($p = 0.003$), and telemedicine ($p = 0.007$).

Conclusions: The COVD-19 pandemic and its preventive strategies has strongly impacted on many aspects of chronic patients (daily activities, health, sleep behavior and mental health). This study highlights the urgent need for better chronic management strategies for the new post-COVID era in Vietnam.

B.30

Incidence of postoperative delirium in Taiwan elderly patients undergoing major elective surgery

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Objective: Delirium is considered a severe neuropsychiatric syndrome among elderly and postoperative patients because it may prolong hospitalization duration and increase all-cause mortality. In the past decades, major elective surgeries for elderly patients have gradually increased due to the aging population in Taiwan. However, the relevant information on postoperative delirium (POD) in Taiwan elderlies remains unknown. Therefore, this study aimed to evaluate the incidence of POD and describe antipsychotics prescription patterns in Taiwan elderlies.

Methods: We performed a retrospective cohort study with the new-user design and retrieved patients aged ≥65-year-old who underwent major elective surgery during 2016-2018 from Taiwan's National Health Insurance Research Database (NHIRD). Because ICD codes were insensitive to most cases of delirium and without timestamp, POD was defined as new antipsychotics prescribed (ATC: N05A, exclude prochlorperazine, droperidol and lithium) postoperatively.

Results: Among 99,418 patients, 1,390 met the definition of POD. The calculated incidence was 1.4%. POD group were older than non-POD group (77.2 ± 6.7 vs. 73.2 ± 6); Proportion of men (50.1% vs. 37.6%) and Charlson Comorbidity Index (1.5 ± 1.5 vs. 1.2 ± 1.3) were higher. Also, inpatient days were longer (9.6 ± 5.2 vs. 6.2 ± 3). Kaplan-Meier analysis demonstrated spine fusion had the highest cumulative incidence of POD, followed by discectomy, lower in hip/ knee replacement and prostatectomy. Approximately 70% of postoperative antipsychotics were initiated in the first 3 days, reaching 95% in the first 7 days. Quetiapine was the most prescribed antipsychotics (55.9%) followed by haloperidol (34.4%). They were mainly short-term used (90.3%, ≤7 days).

Conclusion: Most of POD onset among elderlies were within 3 days after surgery. Spinal surgery seemed to have greater risk, which should be aware of in clinical practice. Identifying specific predisposing and precipitating factors of these populations will further inform clinical care.

Keywords: elderly, postoperative delirium, incidence

B.31

Risk of Major Adverse Cardiovascular Events in Rheumatoid Arthritis Patients Receiving Janus Kinase Inhibitors Versus Receiving Tumor Necrosis Factor Inhibitors

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The major adverse cardiovascular events (MACE) risk of Janus Kinase inhibitors (JAKi) compared with a tumor necrosis factor inhibitors (TNFi) in patients with rheumatoid arthritis has been under scrutiny by regulatory authorities.
To explore two approaches to evaluate safety analysis of the risk of MACE in RA patients receiving JAKi versus those receiving TNFi in a real-world setting.
Using data from the Korean nationwide healthcare claims information database from January 1, 2009, and December 31, 2019, a population-based retrospective cohort study was conducted with patients aged 18 years or older who were diagnosed with rheumatoid arthritis, and prescribed any disease-modifying antirheumatic drugs on the same date. We matched each JAKi user to four TNFi user using a propensity score. The primary composite outcome was defined as the first occurrence of MACE, which was a composite of myocardial infarction, ischemic stroke, and sudden cardiac death. To compare the risk of MACE in patients receiving JAKi compared with those receiving TNFi, hazard ratios (HRs) and their 95% confidence intervals (95% CIs) were calculated using a Cox proportional hazards model and marginal structural model (MSMs) adjusting for both baseline and time-varying confounders.
Out of 7,049 incident patients with RA, 937 (13.7%) were JAKi users. Adjusted HRs of MACE associated with JAKi compared with TNFi users were 0.70 (95% CI; 0.32-1.54) in the Cox proportional hazards model, and 1.05 (95% CI; 0.59-1.84) in the MSM.
In this study, both Cox proportional hazards model and MSMs showed a numerically lower but statistically nonsignificant risk of MACE in RA patients receiving JAKi versus those receiving TNFi. Although similar results were estimated in our study population, MSMs could be used as an effective tool for adjusting time-varying confounders in parallel with standard models.
Arthritis, Rheumatoid; Janus Kinase Inhibitors; Tumor Necrosis Factor Inhibitors; Hazards Models;

B.32

Impact of advertisement on supplement consumption in Indonesia population during COVID-19 pandemic

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Introduction and Aim: The COVID-19 pandemic is a disease outbreak caused by the SARS-CoV-2 virus and contagious. One effort to boost the immune system to avoid COVID-19 is by taking supplements. Supplement advertisements are often to increase public awareness of using supplements during a pandemic. As many as 73% of Indonesians consume more supplements during the COVID-19 pandemic. This study aims to determine the impact of advertising on the supplement's consumption by the public during the pandemic.

Methods: This was an observational study with a cross-sectional method from January to April 2022. The research used an online questionnaire that has been tested for validity and reliability. Statistical analysis was performed using Chi-square and Kruskal-Wallis analysis.

Results: Total respondents included was 404, mostly women with age younger than 25 years old. Almost respondents (87.4%) approached the supplements advertisement on social media, with the top three media like Instagram, YouTube, and Twitter. Respondents (87.1%) agreed and strongly agreed that advertisement helps them to understand the type and benefit of supplements. About 86.4% of respondents consumed supplements to prevent Covid-19 infection. More than 25% of respondents used 2 types of supplements, such as vitamin C, vitamin D, multivitamin, zinc, and herbal supplement. Respondents asked the industry to emphasize the color, graphic design, and halal guarantee in supplement advertisements.

Conclusion: Advertisement affects the public consumption of supplements, especially on color, graphic design, and halal guarantee.

Keywords: advertisement, supplement, public, consumption, Covid-19

B.33

Characteristics and Application of Real-world databases in China

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Objective: This study aims to describe the characteristics and application of current real-world databases in China, including the data structure, access, and detailed information.

Methods: PubMed, Embase, Web of Science and Chinese databases (CNKI, Wanfang, VIP) were searched using the terms “databases”, “electronic medical record”, “registry” and “China” between 2007 and 2019. Studies were included if they were original reviews, guidelines, or consensus in English or Chinese. Studies repeatedly published or not relevant to real-world databases in China were excluded. Information from included studies such as basic characteristics (title, author, publication year, reference type, etc.), real-world database related contents (definition, resource, study aim, design, analysis, etc.) and relevant pharmaceutical characteristics (name, type, treatment, risk, etc.) were parallelly extracted into Excel by two independent reviewers. The consistency of recorded information was tested to maintain accuracy.

Results: A total of 66 English and 82 Chinese publications were included in this study. Ninety publications were primary studies, in which 29 studies were on chemical drugs and 27 were on Chinese medicine. Real-world databases were classified into the primary database (registry data, follow-up platform, health-related longitudinal survey, reporting system) and secondary data (medical insurance data, electronic health records, etc.). Present primary databases in China were collected by observational study, providing rich datasets for pharmacoepidemiology studies to evaluate clinical and health policy-related issues. Secondary databases were built up by various data resources, with a large population and long-term data included, which would better represent real-world clinical practices than clinical trials. However, the access and data quality of secondary databases remain improving.

Conclusion: This study provides a comprehensive description of existing real-world databases in China, giving insights on characteristics, strengths and weaknesses, and real-world application of representative databases.

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C. Drug safety risk monitoring, evaluation and prevention

C.1

Drug therapy-related problems reported by clinical pharmacists in a Critical care unit in a Nepalese hospital

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Aim/Objective: Critically ill patients are more vulnerable to drug therapy-related problems (DTRPs), due to their fragile physiology, polypharmacy, and co-morbidities. DTRPs can interfere with achieving optimal patient outcomes. This study aimed to identify the types and nature of DTRPs occurring among patients admitted to a critical care unit and assess predisposing factors.

Study type: Cross-sectional observational study.

Study site and duration: Department of critical care medicine at Hospital, Kathmandu from August to November 2021.

Inclusion criteria: Patients admitted for more than 48 hours.

Data collection and interpretation: Local and international treatment guidelines, Medscape database, and UpToDate were referred for identifying DTRPs. The Pharmaceutical Care Network Europe (PCNE) classification system version 9.1 was used for DRPs classification.

Results: A total of 120 patients were enrolled. DTRPs were identified in 74.2% (n=89) of patients. The average DTRP per patient was 1.5±0.7. More than one DTRP were identified in 38.5% of patients;these were more common in male. The association between dose selection and gender was significant. Unnecessary drug treatment (40.5%, n=43)was the most common problem identified and improper drug selection was the main cause of DTRPs. Correlations with DTRPs were seen withage (R-0.21; p=0.02), hospital stay (R 0.2; p=0.026), co-morbidities (R-0.21; p=0.019).

Conclusion: A high prevalence of DRPs indicates the need for mechanisms for early identification and mitigation. Routine drug utilization studies with a focus on DTRPs can help identify and prevent DRPs.

Keywords: Critical care, DTRPs, Nepal, Pharmacist.

C.2

The Association between Adverse Pregnant Outcome and Antiepileptic Drugs Discontinuation in Pregnancy in Asia Population

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Background: Considering the seizure attack or safety of AEDs, the consequence of AEDs discontinuation for women with epilepsy (WWE) is still a matter of debate.

Objective: This study was to evaluate the association between prenatal AEDs withdraw and risk of adverse pregnant outcomes in WWE by using linking database in Taiwan.

Methods: We identified pregnancy women with active epilepsy in 2009 to 2018 using linked three database (National Health Insurance Database, Birth Certificate Database, and Maternal and Child Health Database). Active epilepsy was defined as pregnant women 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. The primary analysis was to compare the risk of adverse outcome between exposure and non-exposure groups using fixed time logistical regression. We performed generalized estimating equations (GEE) model to analyze time-dependent AEDs exposure status in three trimesters. The exposure status was classified to non-exposure, single, poly-therapy and switch in three trimesters. Premature rupture of membrane, fetal distress, antepartum hemorrhage, pre-eclampsia/eclampsia and gestational diabetes were evaluated as composite adverse pregnant outcomes.

Results: There were 1,262 and 1,230 pregnant women met study criteria in exposure and unexposed group, respectively. Compared to non-exposure group, the adjusted odds ratio for composite adverse outcome in exposed group was 1.13 [95% CI: 0.88-1.46]. In GEE model analysis, the risk was no significant difference between various AEDs exposure status compared with non-exposure [(1st aOR=1.07, 0.72-1.59), (2nd aOR=1.11, 0.77-1.59), (1st plus 2nd aOR =1.35,0.67-2.72)].

Conclusions: To identify pregnancy women who had high risk of seizure attack and should continue to use AEDs is important and further study is required.

C.3

Maternal Use of Benzodiazepine Receptor Agonists and Risk of Neurodevelopmental Disorders in Offspring: a Population-based Study in Taiwan

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Objective: This study aimed to evaluate the association of maternal benzodiazepine receptor agonist (BZRA) exposure with neurodevelopmental disorders (NDs) in offspring.

Method: This cohort study used data from Birth Certificate Application and National Health Insurance Database in Taiwan. We initially identified pregnant mothers between 2004 and 2012. We then excluded mothers < 20 years old, multiple births, stillbirths, and those with missing data. 197,296 mothers receiving BZRAs from 90 days preconception to the delivery date were defined as the BZRA group and 1,417,439 remaining mothers were identified as the comparison group. We used Cox regressions to calculate the hazard ratios (HRs) of NDs for children with maternal exposure of BZRAs. Those children who had been diagnosed with NDs, including attention-deficit/hyperactivity disorder (ADHD), intellectual disability (ID), reading disorder (RD), speech and language disorder (SLD), motor function disorder (MFD), delayed development, and autism spectrum disorder, during the follow-up period (until 2018) were identified as NDs cases.

Results: The selected mother-child dyads with up to 14.9 years (median 9.5 years) of follow-up. 16.36% of total children had ≥ 1 type of NDs. The NDs incidence rates were 18.89 and 16.96 per 1,000 person-years among BZRA group and comparison group, respectively. The HR of NDs for BZRA group was 1.13 (95% confidence interval [CI]: 1.12-1.14, p<0.001) compared with comparison group. After adjusting for maternal and neonatal characteristics, NDs risk was significantly higher among BZRA group than comparison group (aHR: 1.13). Additionally, after adjustments, BZRAs group still had 1.17, 1.19, 1.14, 1.10, and 1.11-fold significantly higher risk of ADHD, ID, RD, SLD, and MFD, than comparison group, respectively.

Conclusion: This study observed that maternal BZRA exposure increased risk of NDs in offspring in Taiwan. We will perform the subgroups analyses and consider more confounders in the near future.

Keywords: benzodiazepine receptor agonist, pregnancy, neurodevelopmental disorder

C.4

The Association Between Isavuconazole Trough Concentration and QTc Interval Shortening

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Aim/Objective: A newer antifungal agent, isavuconazole, may cause QTc interval shortening, which is different from other triazoles. This study was aimed to evaluate the association between the isavuconazole trough concentration (Ct) and QTc shortening.

Methods: A retrospective cohort study was conducted in a medical center and a regional hospital. Patients ≥ 20 years with at least one isavuconazole Ct between 2019/1/1 and 2022/4/30 were included. Patients who did not complete the loading dose and at least one maintenance dose were excluded. The baseline for QTc interval was defined based on the last EKG report before isavuconazole initiation. QTc shortening was defined as an absolute QTc interval <360 msec or 30 msec decrease compared to baseline. We used the mixed-effects model to analyze the repeated data.

Results: A total of 72 patients were enrolled with 201 blood samples collected. The median age was 57 years. Male (59.7%) and patients with hematological diseases (75.0%) accounted for the majority. Data from 44 patients, with 85 blood samples having EKG reports at the same blood collection time, were included for further analyses. Among them, 24 (54.4%) and 12 (27.3%) patients had prior triazole antifungals and QTc prolongation, respectively. Isavuconazole Ct was associated with the degree of QTc shortening. Patients with Ct greater than 4.65 mg/L had a higher risk of QTc shortening. After adjusting for age, gender, atrial fibrillation and QTc prolongation at baseline, the QTc value decreased by 6.35 msec for every one mg/L increase in Ct ($p = 0.0002$). Only 1 patient experienced QTc interval <360 msec. Subgroup analysis of different baseline QTc intervals and whether they reached steady state yielded similar results.

Conclusion: There was a negative relationship between isavuconazole Ct and QTc with the Ct cut-off point of 4.65 mg/L.

Keywords: Isavuconazole, QTc interval shortening, therapeutic drug monitoring

C.5

Anticholinergic burden and risk of fractures in the middle-aged women – a population-based case-crossover study

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Aim and objective: To compare the risk of fractures among different time periods with various levels of anticholinergic effects (anticholinergic burden) in middle-aged women.

Method: We used a case-crossover design and selected female patients, aged between 45 and 65, who had a record of hospitalization due to fracture during 2012-2018 from the National Health Insurance Database. We defined the first date of fracture as the index date. We defined the hazard period and washout period as 1-60 and 61-120 days before the index date, respectively. We defined a 60-day referent period randomly selecting among 121-180, 181-240, 241-300 days' intervals before the index date. We calculated the anticholinergic burden based on established scales, including the ADS (Anticholinergic Drug Scale), KABS (Korean Anticholinergic Burden Scale), and GABS (German Anticholinergic Burden Scale), and classified the scores into high (10+), moderate (3-9), low (1-2), no (0 points) anticholinergic burden. We performed conditional logistic regression to compare the scores between hazard and referent period within the same individual. We considered no anticholinergic burden as the reference.

Result: We identified a total of 1900 patients with mean age of 57.5 (±5.2) years. We found anticholinergic burden was associated with increased risk of fracture, whatever evaluating by ADS (OR 1.60; 95% CIs, 1.36-1.87), KABS (1.58; 1.35-1.85) or GABS (1.54; 1.31-1.82). Specifically, the risk magnitudes were increased following with the increased levels of anticholinergic burden by ADS (low, 1.35; 1.04-1.74; moderate, 1.64; 1.38-1.94; high, 1.88; 1.43-2.49), KABS (low, 1.45; 1.11-1.90; moderate, 1.59; 1.34-1.88; high, 1.74 ;1.36-2.24) and GABS (low, 1.34;1.07-1.67; moderate, 1.61; 1.34-1.93; high, 1.94; 1.45-2.60).

Conclusion: The results suggested anticholinergic burden was associated with the risk of fractures and potentially had a level-response relationship. The finding warrants clinical attention when using drugs with anticholinergic effects in middle-aged women.

Keywords: anticholinergic burden, fractures, middle-aged women

C.6

Effectiveness and Safety of Fixed-dose Combination of Inhaled Corticosteroid and Long-acting Beta Agonist in Treatment of Bronchiectasis

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Aim: Bronchiectasis is a chronic, inflammatory airway disease that presents with repeated respiratory infection, frequent acute exacerbation and severe symptoms; However, currently little evidence exists to guide treatment decisions. Long-acting bronchodilators, including ICS-LABAs and LAMAs, are widely-used maintenance treatment strategy for bronchiectasis. Nevertheless, ICS-LABAs may cause respiratory infection due to its immunosuppressive effect. Accordingly, we aimed to evaluate the effectiveness and safety of ICS-LABAs in treatment of bronchiectasis.

Methods: We performed a retrospective cohort study using Taiepi Veteran General Hospital electronic medical records. Patients with HRCT-confirmed bronchiectasis during Jan.2008-Mar.2020 were identified. We evaluated the risk of hospitalized respiratory infection, acute exacerbation, all-cause hospitalization of ICS-LABAs, taking LAMAs as active comparison. Furthermore, we compared the difference between three commonly-used ICS-LABA regimens: BEC/FOR, BUD/FOR and FLU/SAL. Propensity score matching and Cox regression model were performed to estimate the hazard ratios between study groups.

Results: The results showed ICS-LABAs have similar risk of outcome occurrence compared to LAMAs, with HR 1.22 (95% CI: 0.81-1.83) for hospitalized respiratory infection, HR 1.06 (95% CI: 0.84–1.33) for acute exacerbation, HR 1.06 (95% CI: 0.82–1.36) for all-cause hospitalization. Among different ICS-LABAs regimens, both BEC/FOR and BUD/FOR were associated with lower risk of outcome occurrence compared to FLU/SAL, with HR 0.48 (95% CI: 0.26–0.86, 0.59 (95% CI: 0.34–1.05) for hospitalized respiratory infection, HR 0.59 (95% CI: 0.43–0.81, 0.68 (95% CI: 0.50–0.93) for acute exacerbation, HR 0.55 (95% CI: 0.37–0.80, 0.75 (95% CI: 0.51–1.10) for all-cause hospitalization, respectively.

Conclusion: For bronchiectasis patients, ICS-LABAs are effective and safe maintenance treatment. Among different ICS-LABA regimens, compared to FLU/SAL, BEC/FOR and BUD/FOR are associated with better effectiveness and safety.

C.7

Age difference in safety profiles on influenza vaccine between adults and older people: a nationwide pharmacovigilance study in South Korea

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Objective: Safety profile of influenza vaccine may differ between adults and older people due to physiological changes associated with aging, but clinical evidence on this is limited. Therefore, we aimed to identify the difference in characteristics and safety signals between adults and older people.

Methods: We conducted a nationwide pharmacovigilance study on influenza vaccine using the Korea Adverse Event Reporting System Database from 2005 to 2019. Between the two age groups (adults: 19-64 years old; older people: ≥65 years old), we compared basic characteristics (including sex and seriousness) and the detected safety signals using three disproportionality-based data mining methods: a) proportional reporting ratio (PRR), b) reporting odds ratio (ROR), and c) information component (IC). A signal detected by any of three methods was defined as an AE.

Results: Among 18,117 AE-pairs following influenza vaccination, 15,986 and 2,131 AE-pairs were reported in adults and older people, respectively. AEs were reported more frequently in women in adults, compared with older people, accounting for 77.64% and 61.07% of the samples, respectively. Serious AEs following the influenza vaccine in older people were markedly higher than in adults, accounting for 11.98% and 2.85%, respectively. We identified higher proportions of central & peripheral nervous system disorders and gastro-intestinal system disorders in older people compared with adults. Neuritis, pharyngitis, asthenia, and arthralgia were only detected in older people. In addition, we detected sweating increased, injection site inflammation, and headache in both age groups, but we observed higher values of PRR, ROR, and IC in older people.

Conclusion: In this study, we identified distinctive basic characteristics and safety profiles following influenza vaccination by different age groups, suggesting that older people vaccinated with influenza vaccine need more careful monitoring although further studies are required to confirm our findings.

Keywords: Influenza vaccine; Vaccine safety; Signal detection; Age difference

C.8

Hypoglycemia Risk with Inappropriate Renal Dosing of Glucose-Lowering Drugs in an Ambulatory Setting: A Retrospective Cohort Study

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Aim/Objectives: To estimate the frequency of inappropriate dosing of glucose-lowering drugs and evaluate the subsequent risk of hypoglycemia in patients with chronic kidney disease (CKD).

Methods: We conducted a retrospective cohort study of outpatients with an estimated glomerular filtration rate (eGFR) of <50 mL/min/1.73 m2 who were treated with glucose-lowering drugs in a medical center from January 1, 2015, to December 31, 2018. We divided the outpatient visits according to whether the prescription of glucose-lowering drugs included dose adjustment according to eGFR or a condition of not recommended or contraindicated use. We performed a Kaplan–Meier analysis for the cumulative incidence and a Cox proportional hazards analysis for the risk of hypoglycemia events.

Results: A total of 89,628 outpatient visits were included, 29.3% of which received inappropriate dosing. The incidence rate of the composite of all hypoglycemia was 76.71 events per 10,000 person-months in the inappropriate dosing group and 48.51 events per 10,000 person-months in appropriate dosing group. After multivariate adjustment, inappropriate dosing of glucose-lowering drugs was found to lead to an increased risk of composite of all hypoglycemia (hazard ratio 1.53, 95% confidence interval 1.35, 1.75) in patients with CKD. In the subgroup analysis, poorer renal function (eGFR < 30 mL/min/1.73 m2) significantly increased the effects of inappropriate dosing of glucose-lowering drugs on the risk of the composite outcome of all hypoglycemia (P for interaction = 0.003).

Conclusion: Inappropriate dosing of glucose-lowering drugs in patients with CKD is common and associated with a higher risk of hypoglycemia.

C.9

A machine learning approach to predict serum levels in valproate-treated patients

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Objective: Valproate is an important drug for bipolar disorder, and blood levels shall be monitored to avoid insufficiency or toxicity. If the frequency of blood drawing can be reduced with a certain blood concentration prediction accuracy, it will be of great help to clinical practice.

Methods: We initially screened 31,439 samples from 11,166 hospitalized patients between 2002 and 2019 and used the following inclusion criteria: 1) Patients should take the same daily dose for at least 5 consecutive days prior to the blood draw (steady-state concentration); 2) No chronic kidney disease; 3) Serum valproate level data were 0–100 μg/ml; 4) Blood samples were drawn 8–16 hours after the last dose. We extacted 125 features, including sex, age, characteristics of valproate prescription, comorbidities, concomitant medications, and laboratory data. The outcome targets had both binary variables (0–50 μg/ml or 50–100 μg/ml) and continuous variables (serum valproate value). All data is divided into training/validation set and test set (9:1 propensity score matching). Five machine learning algorithms were used to predict binary or continuous outcomes, namly logistic/linear regression (LoR/LiR), support vector machine (SVM), random forests (RF), and extreme gradient boosting (XGBoost). We applied a 5-fold cross-validation to develop the above models and then used an independent test set to evaluate their performance, mainly accuracy.

Results: A total of 5786 serum level samples were included. For binary prediction, the accuracies of LoR, SVM, RF and XGBoost were 0.81, 0.80, 0.83, and 0.86, respectively. For continuous prediction, the accuracies (the error value between prediction and reality is within 20μg/ml) of LiR, SVM, RF and XGBoost were 0.78, 0.77, 0.88, and 0.72, respectively.

Conclusion: This study provides a potential tool for predicting valproate concentrations, reducing the frequency of monitoring serum levels, and aiding clinical decision-making.

Keywords: bipolar disorder; machine learning; therapeutic drug monitoring; valproic acid

C.10

Incidence of drug-drug interaction in hepatitis C virus infected patients with direct-acting antiviral agents: A multicenter study in Taiwan

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Aim/Objective: With different metabolic pathways of direct-acting antiviral agents (DAAs), drug-drug interaction (DDI) may occur and lead lack of effectiveness and/or adverse drug reaction (ADR) especially in hepatitis C virus (HCV) infected patients with polypharmacy. However, the incidence and correlation between DDI and ADR among different classes of DAAs were still an unmet need.

Methods: A retrospective cohort study was conducted using a multicenter electronic medical records (EMR) database from May 2017 to Feburary 2022 in Taiwan. HCV patients receiving at least 1 examination for genotyping and completing DAA (sofosbuvir/Velpatasvir, SOF/VEL; glecaprevir/ pibrentasvir, GLE/PIB) course were included. DDA-related DDIs were identified and the severity was established according to the University of Liverpool database. We further analyzed the impact of DDIs on biochemical data change. The logistic regression was applied to estimate the association between presence of DDI and ADR.

Results: A total of 3396 SOF/VEL and 3403 GLE/PIB users with mean age 62.0 years were enrolled. Most of patients were genotype 2 HCV (42.4%), and the incidence rates of contraindicated DDI were significantly higher in SOF/VEL group (4.5% vs. 2.6%, $p < 0.01$). Results demonstrated that hypoglycemia was positively associated with patients who had DDI (0.5% vs. 1.3%, $p < 0.01$), even when restricted to patients with diabetes. In logistic regression analyses, the presence of DDI was associated with higher risk of hypoglycemia (odd ratio: 2.6, 95% confidence interval: 1.4 – 4.7). After DAA treatment, a significant decreasing was found in the fasting BG, especially in patients with DDI (-9.4, vs. -18.2 mg/dL, $p < 0.01$).

Conclusion: Present findings support the results from previous studies and have showed that patients who had DDA-related DDIs were at risk of hypoglycemia. Monitoring of BG or considering other anti-diabetes agent if necessary is recommended.

Keywords: Direct-acting antiviral agents; hepatitis C virus; drug interactions.

C.11

Association of non-steroidal anti-inflammatory drugs (NSAIDs) with risk of acute kidney injury (AKI) in advanced chronic kidney disease (CKD) patients

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Aim/Objective: We aimed to explore the risk of NSAIDs associated with AKI in patients with diagnosed with CKD stages 5 who enrolled pre-ESRD pay for performance (Pre- ESRD P4P) program in Taiwan.

Methods: We conducted a retrospective cohort study, new-user design, using National Health research Insurance Database (NHID) in Taiwan. We identified CKD stage 5 adults (≥ 20 years old) who ever received EPO after enrolled Pre-ESRD P4P program between 2012 and 2017. Index date was defined as first prescription of EPO. NSAIDs users was defined as patients who had at least one prescription of NSAIDs within 3 months since index date, otherwise as non-NSAID users. We performed multivariable Cox proportional hazard models to estimate adjusted hazard ratio (aHR) and 95% CI, after adjusting for age, gender, comorbidities and co-medications.

Results: There were 24,057 patients with CKD stage 5 in this cohort study. We identified NSAID users (n = 5,758) and non-NSAID users (n = 18,299) from 2012 through 2017 in the P4P program. The mean age of these patients were 65 years old and 52% were male. NSAID users had higher rate of HTN, heart failure, gout, osteoarthritis and influenza than non-NSAID users. For medications history, NSAID users also had higher rate of diuretics, antithrombotic agents, anti-platelets, anticoagulants, steroids and opioids than non-NSAID users. After adjusting these covariates, the result showed NSAID users has significantly higher risk of AKI than non-NSAID users (crude HR 1.52, 95% CI 1.35-1.71; adjusted HR 1.35, 95% CI 1.20-1.52).

Conclusion: Use NSAID is associated with increased risk of AKI among advanced CKD patients, further intervention and monitoring is particularly warranted in these patients.

C.12

A Quantitative Bias Analysis on Oral Non-Vitamin K Antagonist Anticoagulants and Risk of Gastrointestinal Bleeding using Real-World data

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Background: Oral non-vitamin K antagonist anticoagulants (NOACs) have been increasingly used in place of warfarin to reduce the risk of stroke in patients with atrial fibrillation. However, administrative database studies have reported an increased risk of gastrointestinal (GI) bleeding, but lack information on potential confounders such as smoking, alcohol consumption, race, and obesity.

Aim/Objective: To perform quantitative bias analyses (QBA) on the impact of potential confounders on the association between NOACs and GI bleeding compared to warfarin. Smoking, alcohol consumption, race, and obesity were selected as potential confounding factors among the known risk factors of GI bleeding, which are typically uncaptured or incompletely captured variables in electronic healthcare data.

Methods: This study used the National Health and Nutrition Examination Survey (NHANES) to estimate population proportions of confounders among users of NOACs and warfarin and results from the literature review, which provided relative risk estimates of associations between the confounders and GI bleeding. The potential confounding effects from smoking, alcohol consumption, race, and obesity were evaluated using three approaches to QBA: array approach, rule-out approach, and E-value approach.

Results: Findings from QBA approaches suggest that the inability to account for smoking, alcohol consumption, race, and obesity in the analysis would have minimal impact on the validity of the previously reported results. QBA results indicated the prevalence of confounders in the NOACs population must be remarkably higher than that in the warfarin population in order to introduce significant confounding.
Conclusion: Results from QBA indicated that the differences between the prevalence of the confounders in NOAC-prescribed populations and warfarin-prescribed populations were minimal, which suggests that these two populations are largely similar in many aspects. This provides greater confidence in the validity of previously-reported results using electronic healthcare databases despite their inability to measure some confounders.

Keywords: Quantitative Bias Analysis, Confounding, NOAC, Gastrointestinal Bleeding

C.13

Prediction models of adverse events associated with antineoplastic drugs: a narrative systematic review

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Objective: Prediction models have been developed to understand antineoplastic drugs-related adverse events (AE), whereas the limited quality of prediction model studies may complicate the clinical utility. Currently, data looking at the quality of the models are still lacking. This narrative systematic review aims to describe the current status of the methodological and reporting quality of prediction models for antineoplastic drugs-related AE.

Methods: Databases including PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched up to January 17, 2022. We included prediction model development studies of antineoplastic drugs-related AE. Methodological and reporting quality of the studies were assessed by the Prediction model Risk Of Bias ASsessment Tool (PROBAST) and the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement, respectively. Results were presented descriptively, which was supported with visual plots of the data. This study was performed according to the PRISMA guideline.

Results: A total of 39 studies were identified, including 29 (74.36%) development (with internal validation) studies and 10 (25.64%) development with external validation studies. Regarding the methodological quality assessed by PROBAST, 26/29 (89.66%) development studies and 9/10 (90.00%) external validation studies were rated as high overall risk of bias, respectively. Regarding the reporting quality, the median adherence to TRIPOD statement was 80.00% [range: 61.29%-97.14%] in development studies and 84.29% [range: 57.14%-88.57%] in external validation studies, respectively.

Conclusion: Although a certain number of prediction models of antineoplastic drug-related AE have been developed in recent years, most of them are identified as evident risk of bias in the analysis domain and lack clear and transparent reporting of methods and results. Rigorous-design and well-reporting prediction models are still warranted for antineoplastic drug-related AE.

C.14

CAR-T therapies and Cardiovascular Adverse Events: An Observational, Retrospective, Pharmacovigilance Study with Machine Learning Approach

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Aim/Objective: Chimeric antigen receptor T-cell (CAR-T) therapy are paradigm-shifting therapeutics in patients with hematological malignancies. However, some concerns remain that CAR-T may cause serious cardiovascular adverse events (AEs), for which data are scarce. This study aimed to identify cardiovascular complications associated with CAR-T.

Methods: We applied a gradient boosting machine algorithm-based model to investigate the possible association between the use of CAR-T (tisa-cel, axi-cel, brexu-cel, liso-cel) and cardiovascular AEs using the WHO-Vigibase through Jan 2022. First, we constructed an input dataset for CAR-T comprising positive controls listed in product information and negative controls that were not listed in product information and observed in works of literature. Given the input dataset, we trained the model and validated its performance by measuring the area under the precision-recall curve (AUPRC). Second, we implemented the model to calculate the probability of cardiovascular AEs defined by preferred terms included in important medical event lists from EMA. We determined that specific cardiovascular AE is significantly associated with CAR-T, if the probability is greater than 0.9.

Results: Vigibase contained 5,321 reports of CAR-T (2,859 [53%] axi-cel, 2,175 [40%] tisa-cel, 219 [4%] brexu-cel, and 68 [1%] liso-cel). Of 5,321 reports in patient who received CAR-T, we identified 678 AEs, comprising of 487 [71%] postive controls, 112 [16%] negative controls. In training and validation process, we developed the prediction model with comparable performance on binary classification of positive and negative controls (AUPRC: 0.9604). Among 22 cardiovascular AEs, our model predicted six cardiovascular AEs significantly associated with CAR-T (atrial fibrillation, 72 reports, probability: 0.98; cardiac arrest, 45, 0.95; bradycardia, 28, 0.99; cardiac failure, 27, 0.97; pericardial effusion, 20, 0.99; ventricular tachycardia, 20, 0.90).

Conclusions: Our findings suggest that clinicians should be alert for serious cardiovascular toxicities when the use of CAR-T is required.

Keywords: CAR-T, Cardiovascular AEs, Machine learning algorithm

C.15

Doxycycline use and adverse pregnancy or neonatal outcomes: a descriptive study using

the Food and Drug Administration adverse event database

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Objective: To describe the adverse event reports of use of doxycycline in pregnant women that resulted in adverse pregnancy/neonatal outcomes using the United States Food and Drug Administration adverse event reporting system (FAERS).

Methods: A database analysis of the adverse event reports of doxycycline, as a suspect or concomitant medication, in pregnant women under the standardized Medical Dictionary for Regulatory Activities Queries (SMQ) category 'pregnancy and neonatal topics' reported to FAERS from first quarter of 2004 to third quarter of 2021 were assessed. OpenVigil version 2.1 was used for data extraction. Duplicate and unrelated cases were identified manually.

Results: During 2004 to 2021, 20 relevant reports were identified in the FAERS database: 5 belonging to the SMQ 'congenital, familial and genetic disorders'; none under 'foetal disorders'; 3 under 'neonatal disorders'; 6 under 'termination of pregnancy and risk of abortion'; 6 belonging to 'pregnancy, labor and delivery complications and risk factors (excl. abortions and stillbirth).' Doxycycline was the suspect medication in 13/20 (65%) reports; it was a concomitant medication in the other reports. The common adverse event terms reported were congenital anomalies with or without foetal death in 6 reports, spontaneous abortion in 6, premature baby in 6, and intrauterine death in 2.

Conclusion: The number of reported events of adverse pregnancy/neonatal outcomes following doxycycline use in the FAERS database is small; also, these are not necessarily causally related. A large number of duplicate cases were identified. Given the presence of comorbidities and concomitant medications which could have contributed to the outcome, there does not seem to be strong signal of harm, although this needs to be confirmed by prospective studies given the limitations of adverse event database analysis.

C.16

Signal Detection for Adverse Events of Chlorthalidone using the Korea Adverse Event Reporting System database, 2016-2020

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Aim/Objective: Chlorthalidone is a thiazide-like diuretic, and its use is expanding as an antihypertensive drug. However, few safety studies have investigated chlorthalidone's adverse events (AEs) using a spontaneous adverse event reporting database. To confirm the safety of chlorthalidone, we analyzed the characteristics and frequency of the AE reports and detected potential signals.

Methods: We used the Korea Adverse Event Reporting System (KAERS) database between 1 January 2016 and 31 December 2020. We conducted a disproportionality analysis to detect the signals. We compared chlorthalidone (ATC code C03BA04) with all other diuretics. We calculated proportional reporting ratios (PRR), reporting odds ratios (ROR), and information components (IC) indices. Criteria for detecting signals were PRR ≥ 2 or ROR ≥ 2, chi-squared ≥ 4, and number of AEs ≥ 3. Also, the criteria for the IC value were that the 95% confidence interval, and that their lower limit was greater than 0. We defined a signal that satisfied all the three indices' criteria. Then, the signals were confirmed with the drug label in Korea.

Results: A total of 12,786 reports, of which 36 out of 60 reports related to chlorthalidone were women and 33 reports were older than 65 years. The most frequent AEs after taking chlorthalidone were dizziness (11.7%), hyponatraemia (7.45%), hypokalaemia (6.38%), and insomnia (5.32%). We found 9 AEs as safety signals of them, insomnia, hypotonia, face oedema, and oedema peripheral were not included in Korean drug labels.

Conclusions: We detected four unexpected signals related to chlorthalidone by signal detection. Insomnia was a frequent AE and a signal but was not included in Korean drug labels. Also, chlorthalidone has increased over the past years in Korea, but the reported AEs could not be enough. Therefore, further analyses are needed using accumulated data.

Keywords: KAERS database, Chlorthalidone, signal detection

C.17

Adverse Event Reporting Rates and its Predictors Among Individuals with Adverse Events After COVID-19 Vaccination: A Nationwide Web-based Survey

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Aim/Objective: Spontaneous adverse event (AE) reporting system plays a key role in identifying AEs following emergency use of COVID-19 vaccines; however, under-reporting remains a big challenge. We evaluated AE reporting rates and its predictors among individuals with AEs after COVID-19 vaccination.

Methods: We conducted a cross-sectional, web-based survey from December 2-20, 2021. Participants were aged 18-49 years who elapsed >14 days since completing a primary series of COVID-19 vaccination and were stratified by age, sex and regions (nationally representative) using a proportional allocation method. Reporting rate was calculated by dividing 'the number of participants who reported AEs to the reporting system' by 'the number of those who responded experiencing AEs in our survey'. We estimated adjusted odds ratios (aORs) with 95% confidence intervals (CIs) using multivariate logistic regression models to determine factors associated with the reporting rate.

Results: Among 2,993 participants (mean age [SD]: 34.6 [8.9] years; 51.6% male), 2,720 (90.9%) and 2,656 (88.7%) experienced any AEs, after the first and second vaccine doses, respectively; however, their reporting rates were only 315 (11.6%) and 337 (12.7%), respectively . Of the total participants, 99 (3.3%) and 126 (4.2%) suffered serious AEs (requiring hospital visit/admission) after the first and second doses, respectively; their reporting rates were 50 (50.5%) and 63 (50.0%). Spontaneous AE reporting was more prevalent in females (aOR 1.54, 95% CI 1.31-1.81), those with serious AEs (5.47, 4.45-6.73), comorbidities (1.31, 1.09-1.57), a history of severe allergic reaction (2.02, 1.47-2.77), and those receiving mRNA-1273 and ChAdOx1 (1.25 [1.05-1.49] and 1.62 [1.15-2.30], respectively, versus BNT162b2).

Conclusions: Reporting rate of AEs after COVID-19 vaccination was highly low, at about 12% of any AEs and 50% of severe AEs. Female sex, those with severe AEs, comorbidities, history of allergic reactions, and vaccine types were associated with AE reporting.

Keywords: COVID-19, vaccine safety, pharmacovigilance

C.18

Development of a multivariable prediction model to assess potential drug-drug interactions in chronic kidney disease

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Aim/Objective: Drug-drug interactions are highly prevalent in chronic kidney disease (CKD) patients, owing to the progressive deterioration in renal function, the existence of various comorbidities, and the large number of drugs used to treat them. The objective of this study was to evaluate the number and types of potential drug-drug interactions (pDDIs) observed in the study population and to develop a pDDI prediction model based on various risk factors.

Methods: A retrospective study was conducted at a tertiary care teaching hospital with 392 CKD patients. The relevant patient demographics and clinical details were collected and documented in case record forms. Using different drug interaction detecting databases, the acquired data were screened to identify and classify pDDIs. Poisson regression was used to identify independent risk factors associated with the number of pDDIs. Data entry and analysis were done using IBM SPSS software v20.0.

Results: Mean age of the study population was 45.97 ± 10.32 years and almost 87% of the population belonged to stage 5 of CKD. A total of 2054 interacting drug pairs were found from the 392 patient files screened, out of which about 55.6% of the interactions were of moderate severity. Male gender, comorbid conditions like ischemic heart disease, hypertension, diabetes mellitus, and congestive heart failure, a higher number of therapeutic subgroups and drugs per prescription, were identified as independent risk factors associated with an increase in the number of pDDIs. The presence of liver disease was the only factor that reduced the number of pDDIs.

Conclusion: This study can play a significant role in the early prediction of pDDIs using prior information about the patient characteristics and attributes of various administered drugs in CKD patients.
Keywords: Chronic kidney disease, potential drug-drug interactions, prediction model, risk factors.

C.19

Hepatitis B virus screening and real life data in patients with rheumatoid arthritis receiving biological agents.

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Background: HBV reactivation may occur either during or after immunosuppressive therapy with chronic or occult HBV infection, sometimes causes fetal hepatitis. In 2010, Boxed Warning regarding HBV reactivation was added to the prescribing information for rituximab, and a hospital-based education and strategy was conducted from 2018 and 2021. NHI in Taiwan recommended prophylactic antiviral therapy at HBsAg+ patients when specific immunosuppressive therapy initiated from 2021. The purpose of this study was to identify HBV screening rates in rheumatoid arthritis (RA) patients underwent biological agents and to determine the outcomes of patients underwent HBV screening.

Methods: From January 2004 through December 2021, a total of 1059 patients were enrolled in this retrospective study. Screening was defined as HBV surface antigen (HBsAg), HBV core antibody (HBcAb) and HBV surface antibody (HBsAb) tests carried out within 2years prior immunosuppressive therapy. We calculated overall and annual HBV screening rates and the occurrence of HBV reactivation.

Results: HBsAg overall screening rate was 67%, and the annual screening rate increased from 28% (2004) to 57% (2010), 80 (2018) and 99% (2021). HBcAb overall screening rate was 38%, and the annual screening rate increased from 0% (2004) to 2% (2010), 69% (2018) and 96% (2021). HBsAb overall screening rate was 32%, and the annual screening rate increased from 6% (2004) to 5% (2010), 64 (2018) and 96% (2021). Antiviral prophylactic was started in 0% of HBsAg+ patients and increased to 30% when NHI reimbursed. HBV reactivation was identified in 41.7% of HBsAg+ patients and 4% in HBsAg-/ HBcAb+ patients, and occurred in 3 HBsAg+ patients receiving antiviral prophylaxis.

Conclusion: The HBV screening rate before biological agents was fair but increased overtime. Most common practice pattern of HBV screening was only HBsAg. These figures improved after education, especially implementing a hospital-based strategy.

C.20

Factors associated with repeated intravenous acetaminophen-induced hypotension

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Objective: Acetaminophen is often used for its antipyretic and analgesic effects. Recent studies suggest that intravenous (IV) administration of acetaminophen may cause hypotension. In this study, the factors that cause repeated hypotension were analyzed in patients who were receiving IV acetaminophen and propacetamol, a water-soluble prodrug form of acetaminophen.

Methods: Patients who were receiving IV acetaminophen or propacetamol in the critical care unit of Yongin Severance Hospital at 2020 were enrolled. In each case, the change in blood pressure within two hours of IV acetaminophen administration was investigated to confirm the occurrence of hypotension. Underlying disease, drug history, and blood test results were analyzed to determine the factors associated with the occurrence of hypotension. Hypotension was defined as a systolic blood pressure < 90 mm Hg, a systolic blood pressure decrease of 30 mm Hg, or a mean arterial pressure decrease of 15%.

Results: There were 1547 cases among 398 patients. Of these, 416 cases (26.9%) among 205 patients (51.5%) developed hypotension. The use of a beta blocker was significantly associated with the occurrence of hypotension (odds ratio [OR]: 2.117, p = 0.014). There were 1407 cases among 258 patients who received IV acetaminophen at least twice, among whom 159 developed hypotension. After repeated acetaminophen administration, hypotension occurred in ≤ 33% in 73 patients (45.9%), and in ≥ 66% in 28 patients. The significant risk factors for repeated hypotension on comparing these two groups were sepsis (OR: 11.431, p = 0.021) and the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) (OR: 20.523, p = 0.040).

Conclusion: Hypotension may occur frequently in some patients when IV acetaminophen or propacetamol is administered. When administering acetaminophen to patients with sepsis or to those taking ACE inhibitors or ARBs, attention should be paid to the possible occurrence of hypotension.

C.21

Association between antidepressants and sexual dysfunction: a systematic review and model-based network meta-analysis

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Background& Aim: This study aimed at comparing the risk of sexual dysfunction caused by different antidepressants, and try to capture the dose-response relationship between antidepressants and the risk of sexual dysfunctions.

Method: We systematically searched multiple databases for double-blinded randomized controlled trials (RCTs) that compared antidepressants with placebo, or different antidepressants, or different doses of antidepressants. Data were extracted using a predefined table. We first conducted a network meta-analysis (NMA) to compare antidepressants and placebo, and then performed a model-based network meta-analysis to describe the dose-response relationship between antidepressants and sexual dysfunction.

Result: Seventy-one RCTs are included in our network meta-analysis, with 23,302 patients observed. According to the result of NMA, agomelatine(OR=4.04; 95%CI:1.52-10.74), citalopram(OR=3.28; 95%CI: 1.39-7.76), duloxetine(OR=3.32; 95%CI: 2.22-4.97), escitalopram(OR=3.34; 95%CI: 2.17-5.15), fluoxetine(OR=3.53; 95%CI: 2.09-5.95), fluvoxamine(OR=3.04; 95%CI: 1.24-7.45), levomilcipran(OR=5.72; 95%CI: 1.84-17.78), paroxetine(OR=6.10; 95%CI: 4.25-8.76), reboxetine(OR=5.43; 95%CI: 2.72-10.81), sertraline(OR=4.09; 95%CI: 2.65-6.30) and venlafaxine(OR=6.29; 95%CI: 3.13-12.65) are indicated to increase the risk of sexual dysfunction significantly, comparing to placebo. According to the surface under the cumulative ranking curve (SUCRA), levomilcipran leads to the highest risk of sexual dysfunction. The dose-response curves of different antidepressants are captured using the restrictive cubic spine (RCS) model. The shapes of dose-response curves for different drugs are not identical. Curves of most drugs are captured as inverted U-shape curves or slowly rising diagonals, while venlafaxine is shown to be associated with a significantly increased risk of sexual dysfunction after 100mg/d, and the risk increases rapidly with dose increment.

Conclusion: Agomelatine, citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, levomilcipran, paroxetine, reboxetine, sertraline, and venlafaxine were indicated to be associated with the increment of the risk of sexual dysfunction. The risk of sexual dysfunction related to venlafaxine significantly increases at higher doses. The influence on sexual functions of antidepressants should be taken into account by clinicians when making decisions.

C.22

Temporal Trends in Drug-Related Severe Cutaneous Adverse Reactions in Taiwan: A Nationwide Study

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Objective: To investigate the temporal trends in drug-related severe cutaneous adverse reactions (SCARs) in Taiwan.

Methods: A retrospective study was conducted using Taiwan's National Health Insurance Database. SCAR-related admissions between 2001 and 2015 were identified, and the dates of admission were defined as the index date. For each SCAR case, drugs prescribed during -56 to -1 days before the index date but not prescribed during -365 to -57 days before the index date and +1 to +180 days after the index date were considered as potential culprit drugs. Each potential culprit dug was then assigned a score for causality based on the delay from initial drug intake to onset of SCARs (score 1-3) and the notoriety of the drug according to the literature (score 1-3). Characteristics and time trends of drug-related SCARs were assessed.

Results: Among 15608 cases of drug-related SCARs, 7911 cases had scores for causality ≥4. The number of drug-related SCARs decreased from 1206 cases in 2006 to 805 cases in 2015 (scores for causality ≥4: 604 cases in 2006 vs. 353 cases in 2015). Among cases with scores for causality ≥4, the severity of SCARs remained stable (e.g., median length of stay of 8-10 days, and 10-14% admitted to the ICU). The most frequent culprit drug classes were consistent throughout the study period, consisting primarily of antiepileptic drugs, anti-gout medications, and antibiotics. However, some individual culprit drugs changed remarkably over time. For example, carbamazepine (2001-2006) and allopurinol (2007-2014) were the top one culprit drug in the early years but ranked ninth and fourth, respectively, in 2015.

Conclusion: The number of drug-related SCAR cases in Taiwan declined in recent years, which may be related to several drug safety-related regulations on carbamazepine and allopurinol. Continuous monitoring is warranted to identify other culprit drugs as potential targets for future regulations.

C.23

Background Incidence Rates of Adverse Events of Special Interest for COVID-19 Vaccines in Taiwan: A Nationwide Cohort Study

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Objective: To estimate background incidence rates of adverse events of special interest (AESIs) that may be associated with COVID-19 vaccines in Taiwan.

Methods: A retrospective cohort study was conducted using the National Health Insurance (NHI) Database, the National Birth Certificate Application Database, and the National Death Registry in Taiwan. A total of 38 AESIs were selected, including five pregnancy outcomes. Enrollees in the NHI database who did not have a diagnosis of the AESI within a specific look-back period were included and were followed until the earliest of AESI occurrence, death, or end of the study period. Incidence rates of AESIs during 2016-2019 were estimated by calendar year, age and sex.

Results: Approximately 23 million people of all ages were included in the study. The incidence rates of AESIs remained stable from 2016 to 2019. In 2019, the incidence rates were 303.3 (per 100000 person-years) for stroke, 199.6 for arrhythmia, 99.9 for acute myocardial infarction, 23.2 for deep vein thrombosis, 12.3 for pulmonary embolism, 12.3 for immune thrombocytopenic purpura, 4.3 for myocarditis/pericarditis, 1.8 for Guillain-Barre syndrome, 0.3 for transverse myelitis, and 0.2 for cerebral venous sinus thrombosis. The incidence rates varied widely by age and sex. For example, the incidence rates of myocarditis/pericarditis (per 100000 person-years) were approximately 6-8 in men aged 12-24 years and 4-5 in men aged 25-69 years; in contrast, the incidence rates were 2-3 in women aged 12-69 years. As for pregnancy outcomes, the incidence rates were higher in the youngest and the oldest (e.g., preterm birth: 10.9%, 7.2%, 8.8%, 13.1% in pregnant women aged 12-19, 20-29, 30-39, and ≥40 years, respectively).

Conclusion: The background incidence rates of AESIs estimated using national databases could be utilized for safety surveillance of COVID-19 vaccines in Taiwan.

C.24

Association between Calcium Channel Blocker Use for Hypertensive Disorders in Pregnancy and Adverse Fetal Outcomes

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Objectives: Adverse fetal outcomes are the leading cause of neonatal mortality. Previous studies reported an association between calcium channel blocker (CCB) use and adverse fetal outcomes. However, the association was still uncertain. The first objective of this study was to determine the effect of CCB use on adverse fetal outcomes. Clinically, pregnant women with a need for antihypertensive drugs are commonly prescribed the first-line CCB, nifedipine, or the first-line beta-blocker, labetalol. The second objective of this study was to compare the effect of nifedipine use and labetalol use on adverse fetal outcomes.

Methods: This retrospective cohort study used data from a nationwide claims database. Pregnant women aged 18-49 years with their first known live singleton birth between 2009 and 2017 were enrolled. Women with hypertensive disorders during pregnancy were further included. Propensity score matching (PSM) and conditional logistic regression were performed to estimate the risk of several adverse fetal outcomes.

Results: After PSM, there are 6,740 pregnant women. Compared to CCB non-users, CCB users were significantly associated with increased risks of several adverse fetal outcomes, including preterm birth (aOR: 1.47; 95% CI: 1.21-1.79), small for gestational age (SGA) (aOR: 1.24; 95% CI: 1.11-1.38), and low birth weight (LBW) (aOR: 1.31; 95% CI: 1.15-1.48). However, compared to labetalol users, nifedipine users were not associated with increased risks of several adverse fetal outcomes, including preterm birth, congenital anomalies, SGA, LBW, and extremely low birth weight (ELBW).

Conclusion: CCB users were associated with higher risks of preterm birth, SGA, and LBW. If the medication treatment cannot be withheld, nifedipine and labetalol are alternatives for pregnant women with hypertensive disorders. When the medication is prescribed, health care providers should carefully monitor pregnancy conditions to prevent the incidence of adverse fetal outcomes.

Key Words: Hypertensive disorders, calcium channel blocker, adverse fetal outcomes, pregnancy

C.25

Reducing the anticholinergic burden in older outpatients by pharmacist-led anticholinergic burden risk management system

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Aim/Objective: Anticholinergic drugs have many adverse drug reactions and are inappropriate for the elderly.
The aim of this study was to evaluate the effectiveness of pharmacists using an intelligent system in reducing anticholinergic burden.

Methods: The "Outpatient Anticholinergic Burden Risk Management System" was implemented in January 2021.
Anticholinergic cognitive burden (ACB) and drug burden index (DBI) can be calculated at the same time to display the anticholinergic burden score.
According to the drug burden score, the pharmacist selects the patient into the "Interventional Patient Management System".
After the physician prescribes, the system automatically calculates and records a new drug burden score.

Results: A total of 1005 patients were included in 2021.
The mean age was 80.43±7.03 years, and 508(50.5%) were male.
After evaluation by pharmacists, 322(32.0%) had no intervention and 683(68.0%) had intervention to provide advice.
The ACB and DBI before and after the assessment were significantly different in each group (non-intervention group: ACB 3.11 ± 2.07, 2.82 ± 2.06, p<0.001; DBI 0.69 ± 0.44, 0.64 ± 0.44, p<0.001; intervention group: ACB 3.64 ± 1.61, 3.11 ± 1.90, p<0.001; DBI 0.72 ± 0.38, 0.61 ± 0.41, p<0.001).
However, in the pharmacist intervention group, the reduction of ACB or DBI was significantly better than that of the non-intervention group (ACB -0.53 ± 1.25, -0.29 ± 1.05, p<0.001; DBI -0.11 ± 0.21, -0.05 ± 0.19, p<0.001)
Measured the number of cases that the physician's prescription changed to lower the score (intervention group: 22.4% for ACB, 37.2% for DBI, p<0.001), the DBI can be more sensitive to display the effect of the pharmacist's suggestion.

Conclusion: The implementation of an outpatient anticholinergic burden risk management system can effectively assist pharmacists to screen patients with high drug burden, provide corresponding advice and reduce the drug burden of the elderly.

Keywords: Anticholinergic drug burden

C.26

Association between Risk of Clostridium Difficile Infection and Duration of Acid-Suppressive Medication Use in Taiwan Hospitalized Patients

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Objective: Previous studies reported the exposure to PPIs or H2RAs might increase risk of Clostridium difficile infection (CDI). Our aim is to evaluate the association of CDI and duration of PPIs or H2RAs in hospitalized patients between 2012 to 2018.

Methods: We conducted a nested case-control study to identify hospitalized patients prescribed PPIs or H2RAs in National Health Insurance Database (NHID) from 2012 to 2018. Patients were excluded if they aged <20, hospitalization over 90 days, had diagnosis of peptic ulcer, AIDS, pregnancy or records of PPIs or H2RAs during 180 days prior to admission. PPIs and H2RAs exposures were based on “as treated”, and the censoring was defined as occurrence of CDI, discontinuation, switch, death, or end of study period, whichever came first. The cases with prescription of metronidazole, fidaxomicin, or vancomycin over 7 days were defined as CDI. The controls were matched to a case at 1:1 ratio by age, sex, and entry years. Conditional logistic regression was used to estimate the adjusted odds ratios (aOR) and 95% confidence intervals (CI) associated with risk of CDI between PPIs and H2RAs. Youden's index was used to preform optimum cut-off days of PPIs and H2RAs use.

Results: A total of 6,933 cases and 6,933 controls were identified. The optimal cut-off days for PPIs and H2RAs use were around two weeks. Compared to H2RAs use ≤ 14 days, aOR were significantly higher when medication duration >14 days in either PPIs (OR, 5.38; 95%CI, 4.84-5.99) or H2RAs (OR, 4.19; 95%CI, 3.77-4.65).

Conclusions: Longer use of acid-suppressive medication was associated with higher risk of CDI, and the optimal length of medication use was within 14 days. Physicians are suggested to be aware of the risk of CDI in patients who required longer acid-suppressive treatment.

Keywords: acid-suppressive medication, PPIs, H2RAs, Clostridium difficile infection

C.27

Exploring patient preferred unlicensed indication of paracetamol in Saudi Arabia: A cross sectional study

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Aim and objectives: Paracetamol is the most used analgesics in Saudi Arabia. Its exposure leads to one fourth of the toxicity over all medication related toxicity in the country. This study aims to determine the patient preferred unlicensed use of paracetamol as well to understand the knowledge gap among the paracetamol users of all ages.

Methods: This cross-sectional study was conducted through Question PRO. Eligibility of the study was limited on Saudi Arabian citizens and residents, who use at least one paracetamol over last six months. Data will be summarized using descriptive statistics. Study has been approved by Institutional IRB (IRB-2022-05-125).

Results: Total of 584 individuals participated, of which 518 were using at least one paracetamol over six months and 113 were used it as off label indications (21.8%). Of the total 518 paracetamol users 13.5% received it as OTC medication. One fourth of the study participant use paracetamol in different combinations with caffeine, codeine, chlorpheniramine etc. Among the off labeled users one half them used paracetamol as sleep aid [n=52(46%)] and a quarter of them use it as prophylaxis for sick during travel [n=24(21.2%)]. Calming the baby and improve the energy were the other reported off label indications. Mixing paracetamol with smoking devises (3.5%) and energy drinks (1.8%) were also observed. One half (56%) our study population doubt that paracetamol and acetaminophen is not the same. However, 73% of the participant aware about the maximum dose.

Conclusion: This study highlights the amount of unlicensed use of paracetamol by the public, also communicate the level of knowledge gap exists in the society. Therefore, it may be an eye opener to HCP to need of adequately educate patients on most popular medication. Similarly, we are nearing the time to think about tightening the access to paracetamol.

C.28

Letermovir associated cytomegalovirus infection reactivation: a disproportionality analysis in a spontaneous reporting database

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Objective: To detect the possible safety signal of letermovir associated cytomegalovirus reactivation through disproportionality analysis in FDA Adverse Event Reporting System (FAERS) Database.

Methods: The case/non-case retrospective disproportionality analysis was performed in the publicly available FAERS database using Open Vigil 2.1(2017Q3-2022Q1). The preferred term used for the study was “cytomegalovirus infection reactivation” and the drug included in the analysis was letermovir. Proportional reporting ratio (PRR) and Reporting odds ratio (ROR) was used as the data mining algorithm for the analysis. A value of ROR-1.96SE>1 and PRR2 with an associated X2 value of 4 or more was considered as the threshold for a signal.

Results: FAERS database had a total of 481 reports associated with cytomegalovirus infection reactivation (CIR), out of which 40 reports were associated with letermovir. A significant signal was obtained for letermovir with a ROR value of 1737.98(95%CI=1243.24-2429.6) and PRR 1612.57(Chi-square:57599.8) associated CIR. The observed association revealed that females had a higher ROR value of about 5 times (ROR 4904.76) than males. On stratification of age groups, it was observed that the 19-64 age group had the highest association with ROR 2019.31(1319.68-3089.85). The major adverse outcome observed with letermovir-associated CIR was death(n=5).

Conclusion: In spite of letermovir being indicated as a treatment for cytomegalovirus infection, our analyses of the spontaneous reporting database identified a strong signal for letermovir to cause reactivation of cytomegalovirus infection. To validate these findings, more research with a superior epidemiological study design of a defined population is required.

Keywords: Letermovir, Cytomegalovirus reactivation, FAERS, disproportionality analysis,

C.29

Predicting potential inappropriate medication-related death: Real-world Data from Taiwan

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Objective: Potentially inappropriate medications (PIMs) are defined as medications whose risks outweigh the benefits for the elderly. Recently, the PIM-Taiwan 2018 and Beers Criteria 2019 have been renewed. However, these updated criteria for assessing the risk of adverse clinical outcomes have not been established. This study aimed to explore the PIMs patterns and predict the risk of adverse clinical outcomes.

Methods: We conduct a retrospective cohort study using the Longitudinal Health Insurance Database (LHID). Aged over 65 years old, patients who had at least one OPD visit with medication prescribed during 2015-2017 were enrolled. The outcome is death within 30 days of exposure to PIMs. The outcome risk was estimated as odds ratio (OR) by logistic regression, with adjusted covariates of gender, age group, and Charlson Comorbidity Index (CCI).

Results: A total of 47,782,283 medication records were analyzed from 240,014 outpatient elderly with a mean age of 75.43±7.32 years, and 53.72% of cases are females. The prevalence of PIMs prescribed was 14.03% and 12.68% for PIM-Taiwan 2018 and Beer's criteria 2019, respectively. The most frequent classification is the nervous system in both criteria; alprazolam is the most frequent drug. Among the top 20 prescribed PIMs defined by the PIM-Taiwan 2018, the associations for increased risk of death within 30 days were exposure to metoclopramide (OR=3.465, 95% CI: 3.334-3.601), spironolactone (OR=2.361, 95% CI:2.250-2.478), and amiodarone (OR=1.953, 95% CI:1.832-2.082).

Conclusions: This study shows the prevalence of PIMs in OPD prescriptions for the elderly in Taiwan ranged from 12.68% to 14.03%. The older age, male, higher comorbidities index, and exposure to partial PIM-Taiwan defined medications in the cardiovascular system (CV), and gastrointestinal system (GI) were associated with an increased risk of death within 30 days.

Keywords: PIM-Taiwan 2018, Beer's criteria 2019, adverse clinical outcomes.

C.30

Evaluation of Six Drug Information Resources for Recommendations on Drug Use in Lactation; A Systematic Comparison Study

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Aim/Objective: To evaluate the consistency of information among six drug information resources regarding drug use in lactation

Methods: We selected fifty commonly used drugs in lactating mothers and six drug information resources available at the study site. The recommendations documented in each drug information resource on drug use during lactation were carefully reviewed. The reviewed information was categorized as reassuring, cautionary, suggesting avoidance, inconclusive, and no specific recommendation. Additionally, Fleiss Kappa (k) score was estimated using SPSS (version 24.0, IBM, Armonk, New York, USA) to evaluate the reliability in documented information among drug information resources.

Results: Medscape.com, Medsafe. govt.nz, Brigg's Drugs in Pregnancy and Lactation; A Reference Guide to Fetal and Neonatal Risk, 12th edition (DPL), Drugs and lactation database (LactMed®), UpToDate®, and Portable Emergency Physician Information Database (PEPID©) were reviewed for the recommendation related to drug use during lactation. UpToDate® and PEPID© had the highest (100%), whereas Medsafe.govt.nz had the least (90%) scope score in providing information on drug use during lactation. Cautionary was the most frequent lactation risk category documented by Medsafe.govt.nz (21/45), Medscape.com (30/50), UpToDate® (35/50), and PEPID© (35/49). Whereas DPL and LactMed® categorized the majority of the drugs (34/48 and 20/48 respectively) as reassuring in the lactation risk category. The intersource reliability test revealed Fleiss' kappa score of 0.109, indicating poor consistency among the drug information resources concerning information on drug use during lactation.

Conclusion: Variations in the information provided among drug information resources pose challenges to the safe use of drugs during lactation. Therefore, developing an evidence-based list of lactation risk categories and re-categorizing the drugs accordingly by consolidating the information from the most commonly used drug information resources will help guide the safe and effective use of drugs in lactating mothers and infants.

Keywords: Consistency, Drug information resources, Lactation risk categories, Rational drug use

C.31

Safety monitoring of COVID-19 vaccine booster doses: an analysis of 80,266 VAERS reports

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Aim/Objective: In the U.S., three COVID-19 vaccines have been approved since December 2020. This study aimed to analyze the post-marketing safety (PMS) profiles of these booster doses of vaccines and their associated mortality levels in the USA.

Methods: Retrospective analysis of a database was conducted in this study. From the US Vaccine Adverse Event Reporting System (VAERS), we have retrieved details of US PMS reports for three vaccines (Pfizer-Biotech, Moderna, and Janssen Ad26.COV2.S) for the period June 11, 2021 to June 2, 2022. Adverse events (AEs) were characterized using a descriptive analysis.

Results: A total of 80,266 AE reports were retrieved (corresponding to the U.S. population who received at least third dose). Serious AEs were reported in only 3.8% of the reports with 1,858 hospitalizations. There were 986 deaths in total. After the vaccination with Pfizer-BioNTech, 524 (53.1%) were reported, 458 (46.5%) after Moderna, and 1 (0.1%) after Janssen Ad26.COV2.S.

Conclusion: According to our study, most adverse events observed at enhanced doses of COVID-19 in the USA are not severe, and no new severe AEs have been detected.

C.32

Incidence and Risk of Oxaliplatin-Induced Hypersensitivity in Patients with Colorectal Cancer at a Tertiary Care Hospital in Thailand.

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Objective: The aim of this study was to determine the incidence and risk factors associated with hypersensitivity reactions (HSR) in colorectal cancer patients treated with oxaliplatin-based regimen.

Methods: Data of patients who had received oxaliplatin between January 1, 2019, and December 31, 2021 were collected from hospital computer databases. The incidence and severity of HSR were analyzed retrospectively and demographic data, site of primary disease, cancer staging, treatment regimen and laboratory test data were reviewed to assess the risk factors.

Results: A total of 200 patients received oxaliplatin-based regimen (1,644 treatment cycles), with 25 (11.74%) experiencing HSR. Grade 1/2 and 3 events occurred in 9.86% and 1.88%, according to the NCI-CTCAE v4.03. Median cycle of the first hypersensitivity reaction was 8. HSR was associated with younger age (57.04±10.98 vs. 61.97±10.29 years with HSR vs. without HSR, p=0.027), treatment with FOLFOX regimen (p=0.009), total number of courses (p=0.049) and laboratory test data such as serum albumin (3.96±0.40 with HSR vs. 3.66±0.49 without HSR, p=0.004) and alanine aminotransferase (23(8-56) with HSR vs. 16(3-235) without HSR, p=0.020). Other factors were not significant.

Conclusion: The incidence of oxaliplatin-induced HSR found in this study was similar to the results of previous studies. Younger age, FOLFOX regimen, total number of courses, serum albumin and alanine aminotransferase were risk factors associated with an increased incidence of HSR. Therefore, the healthcare team's vigilance should be increased with these patients.

Keywords: Oxaliplatin, Hypersensitivity, Risk factors, Incidence

C.33

Signal Detection of Drug-Drug Interaction Focusing on QT Prolongation with Haloperidol Using Korea Adverse Event Reporting System (KAERS) Database, 2016-2020

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Objectives: To investigate the occurrence of QT prolongation after the use of haloperidol and concomitant drugs using the national spontaneous adverse event reports in Korea. To apply several statistical methods for detecting drug-drug interaction signals.

Methods: We mainly conducted disproportionality analysis using Korea Adverse Event Reporting System (KAERS) between 2016 and 2020. Cases were defined by Standardized MedDRA Queries (SMQ) 'Torsade de Points (TdP)/QT prolongation', and all reports other than TdP/QT prolongation were defined as non-cases. We selected the list of concomitant drugs known to QT prolonging with haloperidol. Unadjusted and adjusted reporting odds ratios (ROR) and 95% confidence intervals (CI) were calculated through logistic regression analyses. It was considered as a signal if ROR > 2 and the lower bound of 95% CI > 1 and at least three cases of interest reported. In addition, to test consistency of our findings, we also applied multiplicative, additive, Ω shrinkage measure, and chi-square statistics model.

Results: QT prolongation-related reports defined as cases have been consistently reported at an annual average of about 1,700 reports during the study period. Among cases including haloperidol, the use of haloperidol and concomitant QT prolonging drugs existed the most (23 out of 32). Among the 23 cases above, the most frequently reported combined use with haloperidol was levofloxacin (21 reports, 91%). The unadjusted and adjusted ROR (95% CI) of haloperidol-levofloxacin were 152.10 (79.35-291.56) and 120.88 (62.59-233.43), respectively. Results derived from the statistical model [value] for the concomitant use of haloperidol and levofloxacin were consistent with the ROR results and are as follows: additive [0.51], multiplicative [7.90], Ω shrinkage measure [Ω0.25(frequency)=2.41, Ω0.25(Bayesian)=2.38], and chi-square statistics model [χ=12.54].

Conclusions: The concomitant use of haloperidol-levofloxacin was detected as a signal. However, because other factors including demographics and comorbidities may affect AEs, cautious interpretation was required.

C.34

Providing Teratology Information Services in Nigeria: The viewpoints of Physicians in Obstetrics and Gynecology Specialty

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Background: Teratology Information Services (TIS) centre is necessary to provide information on safety and risk of exposures during pregnancy. This survey aimed to evaluate the knowledge of medical professionals in obstetrics and gynaecology in Lagos about teratogenic risk and to seek their opinions about the need for a teratology information service centre in Nigeria.

Materials and methods: A convenience sample of doctors in the field of obstetrics and gynaecology in private and public hospitals in Lagos were surveyed with a self-designed questionnaire. Information was sought on nine categories covering the demography of the participants, and their views on teratogens and teratology information service centre (TISC).

Results: Of the 174 respondents, 100(57.5%) were males. The majority of the respondents (171; 98.3%) believed that their trainings and/or exposures in obstetrics and gynaecology have adequately equipped them to provide good teratology counselling to pregnant women. Resources for teratology information mostly utilized by the respondents are internet (142; 81.6%) and medical journals (139; 79.9%). All the respondents (174; 100%) felt the need for a national teratology information service centre (TISC) in Nigeria and, if established, would consult the centre regularly (160; 92%). The respondents considered women planning pregnancy (174; 100%), breastfeeding (174; 100%), or already pregnant (174; 100%) as those who most need teratology counselling.

Conclusion: Medical professionals in the field of obstetrics and gynaecology in Lagos public and private hospitals felt the need for a national TISC in Nigeria and would consult regularly, if established. However, there is a need to improve their use of appropriate information resources on teratology.

C.35

Detecting signals for interaction between influenza vaccines and antiepileptic drugs using Korea Adverse Event Reporting System (KAERS)

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Aim/Objective: Clinical observations indicate that influenza vaccines may interact with specific drugs by affecting metabolism in a small number of susceptible patients. Published evidence for interactions between influenza vaccines and antiepileptics is scant and uncertain. We aim to describe and characterize the frequency of adverse events (AEs) ascribable to the concomitant use, and detect signals for interaction.

Methods: Data from Korea Adverse Event Reporting System (KAERS) from 2016 to 2020 was used. Reports based on exposure to influenza vaccines alone, antiepileptic drugs alone, and simultaneous administration of them were extracted. AEs derived from our analysis were confirmed by existing databases. Ω shrinkage measure model and χ2 statistics model were applied to calculate the criteria for detecting AEs signals. We defined as a signal when one or more of the following indices were satisfied: Ω025 (Bayesian) > 0, Ω025 (frequentist) > 0 and χ > 2.

Results: We identified 957,072 AE reports submitted to KAERS; which include 7,163 on influenza vaccines only, 30,924 on anticonvulsant drugs only, and 19 on their simultaneous administration. Of those 19 patients (8 male and 11 female) 2 were serious. The median age was 52.5 years. No data related to signal for interaction was detected. In a total of 42 vaccine–drug AE pairs, urinary tract infection was the most frequent with 4 reports. AE reported in prior studies regarding concomitant use such as paraesthesia, depression, pneumonia, asthenia, bronchitis, and condition aggravated were described in this study.

Conclusion: The total number of reports included in our study is significantly low compared to the number of doses given to the large number of recipients exposed to influenza vaccination yearly. However, the present AEs data are in line with previous cases. Further investigations using other databases and additional monitoring are needed.

Keywords: KAERS database, vaccine–drug interactions, influenza vaccination, antiepileptics

C.36

A Comparative Study of Morphine versus Tapentadol in the Treatment of Cancer Pain: A Longitudinal Study

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Aim: To assess the effectiveness of morphine and tapentadol in patients with cancer pain.

Methods: The study was a longitudinal observational study. After ethics approval, patients 18 years and above visiting outpatient department of palliative medicine of a tertiary care center and receiving oral tapentadol 50 mg or oral morphine 10 mg were recruited to the study. The severity of pain was assessed using the numerical rating scale (0-10). Categorical data in demographic parameters at baseline was analyzed by using 'Z' test for difference between two proportions. Continuous variables between the two treatment groups were analyzed by students t-test.

Results: A total of 94 patients participated in the study among whom, 51 patients received oral tapentadol and 43 received oral morphine. The mean age of the participants were 55.49(10.27) years in the morphine group and 58.45(10.98) in the tapentadol group. Morphine group consisted of 63% male whereas, tapentadol included 59% male. The median duration of follow-up in days was noted to be 15 and 11 in morphine and tapentadol group, respectively. Both the drugs were effective in reducing the intensity of pain during the end of follow-up with a mean difference of -1.24 [95% CI (-2.09, -3.86), p>0.05] in the morphine group and -0.75 [95%CI (-1.53, 0.053), p=0.06] in tapentadol group. The incidence of side effects such as nausea, disturbance in sleep and loss of appetite was higher in tapentadol group compared to morphine group.

Conclusions: The study showed that morphine was effective and well tolerated in cancer pain in routine medical practice in patients still in considerable pain despite treatment with less potent pain medications.

Keywords: Pain, Outpatients, NRS, Effectiveness

C.37

Guillain-Barre syndrome following COVID-19 vaccination: a systematic review of case reports to find the pandemic's unusual obstacle

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Background: COVID-19 vaccination has become a major prevention strategy for curbing the COVID-19 virus however, Guillain-Barre syndrome (GBS) has emerged as a rare but serious adverse event following immunization.

Objective: To systematically analyze, summarize, and assess causality and severity of the best available evidence on the occurrence of GBS after receiving the COVID-19 vaccination.

Methods: A systematic literature search was conducted on PubMed and Scopus databases using the MESH terms for Guillain-Barre Syndrome (GBS), COVID-19, vaccine, and filters were applied following PRISMA guidelines. Case reports (CR) and case series (CS) were included in the review, and the quality of evidence was assessed using the Oxford criteria, 2011. Causality assessment (Naranjo's scale) and Severity assessment (Hartwig et al.'s scale) of the Adverse reactions (ADR) were performed.

Results: 20 reports were included in our study (15 CR; 5 CS; 36 patients included). Vector-based vaccines showed a higher probability of causing GBS in comparison to the mRNA vaccines. Using Naranjo's scale for causality assessment, 32 patients were categorized in the probable ADR category, while four were placed in the possible ADR category. Using the Hartwig et al. scale for severity, 32 patients were classified as Level 4b, and 4 patients were classified as Level 5.

Conclusion: Patients and health care providers must remain vigilant and immediately notify any uncommon adverse reactions. Further research is required to establish a proper link between GBS and COVID-19 vaccines. Although such adverse events may occur, they will never outweigh the unsurmountable benefits of receiving the COVID-19 vaccines.

Keywords: Covid-19, Covid-19 vaccines, SARS-CoV-2, Guillain-Barre syndrome.

C.38

Risk based stratification of pronounced factors responsible for poor outcome in neonatal sepsis

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Aim: Risk factor-based approach is one of the best approaches employed by middle income countries which are not well facility driven for any disease management. Thus, we aim to identify the potential risk factors responsible for the poor outcome in both early and late onset neonatal sepsis.

Methods: A prospective cohort study was conducted in a tertiary care hospital where neonatal sepsis cases were identified and comprehended based on inclusion and exclusion criteria. Included cases were then segregated into early and late onset sepsis cases. Risk factors comprising of maternal, neonatal, and other laboratory and clinical parameters were taken and logistic regression was performed to identify the risk factors associated with mortality in both early and late neonatal sepsis.

Results: A total of 168 neonates were included in the study where, 78 cases were early onset, while the remaining 90 were of late onset. Primarily, maternal risk factors suchlike premature rupture of membrane (PROM) (OR-5.821, CI- 3.098-9.081), PV leaking (OR-3.679, CI-3.657-5.987), maternal fever (OR- 3.002, CI-0.297-2.431), maternal UTI (OR-4.301, CI-3.215-7.904) had shown promising result in early onset sepsis whereas invasive ventilation (OR-1.893, CI- 1.970-5.832), surgical intervention (OR- 13.893, CI- 1.006-4.058), delay in breast feeding initiation (OR- 2.164, CI-0.801-3.892) had shown significance in late onset. However, demographic features such as extreme low birth weight, very low birth weight, extreme preterm, very preterm had shown promising results in both the cases.

Conclusion: Risk- based approach applied was successful in determining plausible important predictors for assessing poor outcome in both early and late onset neonatal sepsis and thus can be considered as an effective tool for disease management in developing countries like India. However, comprehensive amount of research is still required to acknowledge, risk-based approach as only exclusive method for disease management.

Keywords: Neonatal sepsis, Risk stratification approach, Predictors, Logistic regression

C.39

Risk of age-related macular degeneration with 5-alpha reductases in benign prostatic hyperplasia

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Aim/Objective: To clarify the role of 5-alpha reductases on the incidence of new-onset age-related macular degeneration (AMD).

Methods: From the Taiwan National Health Insurance Database, we included individuals with benign prostatic hyperplasia (BPH) who used tamsulosin (T) or 5-reductase inhibitors (5ARI), including finasteride (F) and dutasteride (D), between 2010 and 2018. Incidence users on monotherapy of the studied drugs were included. Patients under the age of 50, or those with a history of AMD or prostate cancer, would be excluded. The major outcome was the analysis of AMD diagnoses using the Cox proportional hazard model with inverse probability treatment weighting (IPTW). The propensity scores (PS) were computed using baseline covariates and a logistic regression model. The subgroup analyses were based on age, a history of lens problem, diabetes, and chronic kidney disease (CKD). Sensitivity studies were performed by omitting patients who had prostate resection.

Results: The target cohort consisted of 661,311 patients (T: 647,487; F: 5,583; D: 8,241). Tamsulosin patients were younger (T:66.6; F:68.9; D:69.2) and had a lower proportion of hypertension (T:50.9%; F:57.7%; D:55.4%) than 5ARIs. There was no difference between finasteride and tamsulosin after IPTW (HRFT: 1.04, 0.91 - 1.17). Subgroup and sensitivity analyses yielded consistent results. However, dutasteride was associated with a greater risk of AMD than tamsulosin (HRDT: 1.16, 1.05 - 1.29). In subgroup analysis, the point estimates for dutasteride were still higher (HR: 1.09 - 1.26). However, after dividing into different age groups and those with the lens problem or CKD, there is no significant difference.

Conclusion: When compared to tamsulosin, we found that dutasteride users had a greater risk of AMD but not finasteride users. That might be because dutasteride has a higher level of 5-alpha reductase inhibition. Further research are needed to confirm the association.

Keywords: 5-reductase inhibitors, tamsulosin, age-related macular degeneration

C.40

Adverse Drug Reactions of Favipiravir in Pediatric Patients with COVID-19 Treated by Home Isolation

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Introduction: According to Thailand's National Treatment Guidelines 2022, Favipiravir is an antiviral medication recommended as an alternative treatment for COVID-19 patients who are at risk of severe symptoms or have moderate pneumonia. Nevertheless, there are few studies on the safety of favipiravir in pediatric under the age of 15.

Objective: This analytical cross-sectional study was conducted to determine the adverse reactions associated with favipiravir in patients under 15 years of age

Method: The participants were pediatric patients under 15 years of age who were diagnosed with COVID-19 and treated by home isolation under supervision of the Queen Sirikit National Institute of Child Health and was treated with favipiravir. Data were collected from telephone interviews with parents during January–February 2022. The data were analyzed by descriptive statistics and inferential statistic (logistic regression) at p-value < 0.05. Results: a total of 557 patients were included in this study. The majority of the cases were male (57.38 %), with an average age of 5.23±3.97 years. Favipiravir caused adverse reactions in 183 patients (32.85%). A total of 194 adverse events were reported (34.83%). The majority of adverse events reported (74.74 %) were predicted ADRs that could recover on their own. The most common adverse reactions were vomiting (47.94%), bluish discoloration of the cornea (24.74%), diarrhea (13.92%), nausea (12.89%), and one patient (0.52%) developed anaphylaxis requiring hospitalization. Factors associated with statistically significant ($p<0.05$) adverse reactions were age 11-15 years (OR: 0.34; 95% CI 0.20-0.59; $p<0.001$) (0-5 years old as reference group), whereas gender, underlying disease, and a history of medication allergy were not associated to the occurrence of adverse reactions.

Conclusion: Favipiravir is a relatively safe medicine for children under the age of 15 years. The ADRs discovered primarily affect the gastrointestinal system.

Keywords: Covid-19, Favipiravir, Adverse drug reactions, Pediatric

C.41

Analysis of COVID-19 vaccine-related cutaneous adverse drug reactions: reported from the largest healthcare system in Taiwan

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Aim/Objective: To analyze the clinical spectrums and outcomes of the COVID-19 vaccine-related cutaneous adverse drug reactions (cADRs).

Methods: We conducted a retrospective analysis of the spontaneous adverse drug reaction (ADR) reporting database from the largest healthcare system in Taiwan. The reported ADRs would be evaluated by physicians and pharmacists to ensure the data quality and drug causality. All COVID-19 vaccine-related cADRs, reporting between 1 March 2021 to 31 December 2021, were identified. We described the patients' demographics, suspected COVID-19 vaccines, clinical presentations, and outcomes.

Results: A total of 261 COVID-19 vaccine-related ADRs were identified, 74 (28.4%) of which were cADRs. The mean age of the patients with cADRs was 47.0 ± 16.9 years and maximum number of cADRs was reported in the age group of 36–65 years (56.8%), followed by 18–35 years (29.7%), older than 65 years (12.2%) and 1–17 years (1.3%). Women (68.9%) were more affected than men (31.1%). Most cases occurred cADRs after the first dose vaccine (76.0%), with the onset ranged from 1 to 72 days after vaccination (median 6 days). Among the brands of vaccine, 81.1% cases were related to AstraZeneca, followed by Moderna (12.2%), Pfizer-BioNTech (5.4%) and Medigen (1.3%). The most frequently reported types of cADRs included rash/eruption (27.0%), followed by itchiness/pruritus (15.1%), urticaria (15.1%), ecchymosis (11.1%), redness/erythema (6.4%), petechiae/petechial rash (5.6%) and so forth. Most cADRs would be resolved between 3 to 120 days (median 7 days) after symptom-relief treatments (e.g., topical/oral corticosteroids and/or oral antihistamines).

Conclusion: COVID-19 vaccine-related cADRs, developing within the median of 6 days after vaccination and resolving within the median of 7 days after treatments, accounted for one-fourth reported COVID-19 vaccine-related ADRs. Physicians should monitor the patients with vaccination in the first week for early detection and management of cADRs.

Keywords: COVID-19 vaccines, Cutaneous adverse drug reactions, Spontaneous reporting system

C.42

Efficacy and Safety of Amphotericin B and Miltefosine Combination in Patients with Visceral Leishmaniasis: A Systematic Review and Meta-Analysis

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Objective: To assess the efficacy and safety of Amphotericin B and oral Miltefosine combination in patients with Visceral Leishmaniasis.

Methodology: A thorough literature search was performed in PubMed, Cochrane CENTRAL, and Google Scholar from the inception to 31st May 2022. A combination of keywords, MeSH terms, and entry terms on Visceral Leishmaniasis, Amphotericin B, and Miltefosine was used in combination with Boolean operators. All randomized controlled trials (RCTs) investigating the efficacy (initial and definite cure, Reinfection, and Post Kala-Azar Dermal Leishmaniasis (PKDL)) and safety (adverse events and high creatinine) of Amphotericin B and oral Miltefosine combination on Visceral Leishmaniasis in comparison with placebo or active comparator were included in the study. The Fixed or Random-effects model was used based on the heterogeneity identified by using the I^2 statistic and Cochran's Q test.

Results: Out of 259 non-duplicate research articles identified through database searching, a total of eight high-quality studies (Jadad score ≥3), with 3,715 patients were included in this study. Amphotericin B and oral Miltefosine combination showed a significantly lesser incidence of PKDL (OR: 0.62; P=0.01) and high creatinine (OR;0.57 P=0.01) compared to the control group. There was no significant difference between groups in terms of definite cure (OR: 1.05; P=0.87), initial cure (OR:0.77; P=0.32), reinfection (OR:1.34; P=0.19) and adverse events (OR:1.21; P=0.40).

Conclusion: This systematic review and meta-analysis identified a significant association between Amphotericin B and oral Miltefosine combination and efficacy outcomes such as the incidence of PKDL and safety outcomes such as high creatinine. Non-significant results may be due to lower population size and a smaller number of outcomes; hence there is a need for large and long-term studies to address these issues further.

C.43

Post-discharge Use of Antipsychotics in Patients with Hospital-acquired Delirium and Associated Risk of Mortality – a population-based nested case-control study

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Aim/objective: To evaluate post-discharge use of antipsychotics in patients with incident hospital-acquired delirium and the associated risk of mortality.

Methods: A nested case-control study based on Taiwan's National Health Insurance Database (NHID) was conducted for the period from 2011 to 2018. We included patients who were newly diagnosed with hospital-acquired delirium and subsequently discharged from hospital. The case group included patients who died within 180 days after discharge, while the control group was selected using up to 1:5 matching by age, sex. The exposures were defined as specified antipsychotic medications received for patients with delirium. Conditional logistic regression models were used to derive odds ratios (OR) and 95% confidence intervals (CIs) for the mortality risk in patients with hospital-acquired delirium who received antipsychotics after discharge, compared to those who did not receive antipsychotics.

Results: We included a total of 13,219 cases and 56,301 matched controls. The mean age was 79.2 (SD 13.1) years and 55% were male. We found the use of antipsychotics after discharge did not increase the risk of mortality (adjusted OR: 1.03; 95% CI: 0.98-1.09). Specifically, compared to the controls, we found the crude mortality risks were higher for those receiving haloperidol or a combination of two or more antipsychotics; however, the risk differences were eliminated after taking into account the dosages of antipsychotics and the patients' baseline covariates.

Conclusion: Our findings did not support that the association between the use of antipsychotics and mortality post-discharge from hospitalization with hospital-acquired delirium.

Keywords: Hospital-acquired delirium, antipsychotics, mortality, haloperidol

C.44

Risk of Pancreatitis and Pancreatic Carcinoma for Anti-Diabetic Medications: Evidence Synthesis from a Disproportionality Analysis

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Objective: To identify the safety signals of anti-diabetic medications related to pancreatitis and pancreatic carcinoma.

Methods: A retrospective case/non-case study was carried out using spontaneous reports in the US FDA Adverse Event Reporting System (FAERS) and VigiBase. Reports on preferred terms 'pancreatitis' and 'pancreatic carcinoma' for all the anti-diabetic medications were retrieved up to 31st May 2022. Disproportionality analysis was performed by calculating the Proportional Reporting Ratio (PRR), Reporting Odds Ratio (ROR), and the Information Component (IC) to identify the signals on pancreatitis and pancreatic carcinoma for anti-diabetic medications (if PRR≥2, Lower Bound (LB) ROR>1 and IC025>0). Signal refinement analysis was performed by using OpenVigil 2.1.

Results: Among all anti-diabetic medications, incretin mimetics produced stronger signals for both pancreatitis and pancreatic carcinoma [Sitagliptin (PRR=24.2, LB ROR=24.5, IC025=4.4), (PRR=16.5, LB ROR=16.0, IC025=3.9], respectively; Saxagliptin (PRR=14.0, LB ROR=12.2, IC025=3.5), (PRR=3.4, LB ROR=2.4, IC025=1.2); Liraglutide (PRR=20.6, LB ROR=20.5, IC025=4.2); (PRR=9.1, LB ROR=8.4, IC025=3.0); Exenatide (PRR=12.3, LB ROR=12.0, IC025=3.5); (PRR=4.1, LB ROR=3.8, IC025=1.9)]. Sulfonylureas like Repaglinide (PRR=2.7, LB ROR=1.7, IC025=0.7) and Mitiglinide (PRR=11.1, LB ROR=4.2, IC025=0.7) were identified with pancreatitis and pancreatic carcinoma, respectively. A notable pancreatitis signals were identified for Sodium-glucose co-transporter-2 inhibitors (SGLT-2Is) like Empagliflozin (PRR=4.0, LB ROR=3.4, IC025=1.7), Canagliflozin (PRR=3.7, LB ROR=3.2, IC025=1.6) and Dapagliflozin (PRR=3.2, LB ROR=2.6, IC025=1.3). The VigiBase data analysis reiterated the findings of FAERS. The signal refinement analysis of FAERS data restated the original findings, and eliminated the false positive signals on Insulin analogs, Pioglitazone, Glimepiride and Glipizide induced pancreatitis; and Metformin, Pioglitazone and Repaglinide induced pancreatic carcinoma.

Conclusion: Up-to-date analysis of real-world post-marketing safety data on anti-diabetics revealed the significant risk of pancreatitis and pancreatic carcinoma for incretin mimetics, sulfonylureas and SGLT-2Is. It is important to carefully monitor and take the necessary steps by the regulatory authorities to reduce or prevent this risk.

C.45

KNOWLEDGE, ATTITUDE, AND ACCEPTANCE OF COMMUNITY REGARDING COVID-19 VACCINE: A CROSS-SECTIONAL STUDY IN VIETNAM

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Objectives: This study aimed to survey the knowledge, attitude and acceptance of Vietnamese community regarding COVID-19 vaccine and identify factors related to knowledge, attitude and acceptance of COVID-19 vaccine.

Methods: This cross-sectional study collected data by online survey in the Vietnamese community using Google Forms. The questionnaire comprised 8 questions about knowledge, 6 questions about attitudes, and 6 questions about acceptance of the COVID-19 vaccine. The descriptive statistical analysis was used to calculate frequency and percentage for each variable, using the Chi-square test to determine factors related to knowledge, attitude and acceptance of COVID-19 vaccine.

Results: 1485 valid responses were included in the analysis. Overall, the rate of good knowledge, positive attitude, and vaccine acceptance were 92.1%, 90.8% and 94.2%, respectively. Notably, more than half of the participants (56.5%) reported they were concerned about the risk of serious vaccine-related complications after COVID-19 vaccination. Related factors that positively and simultaneously affected knowledge, attitude and acceptance of vaccination include female, married, having university education or higher, living in Ho Chi Minh City, participating in the COVID-19 frontline, had been vaccinated against COVID-19, were not being infected and had never been infected with COVID-19 at the time of the survey, had no family member or friend infected with COVID-19 and/or died due to COVID-19. Study results also revealed that the acceptance rate of COVID-19 vaccine was higher in the group of people with good knowledge and positive attitude.

Conclusions: The study reflected that Vietnamese people had good knowledge, positive attitude and a high acceptance rate of the COVID-19 vaccine. However, the vaccine's safety was still the most concern of residents. Therefore, the authorities should implement vaccination communication programs with the participation of healthcare workers to relieve anxiety and hesitation, to maximize the rate of vaccination acceptance.

C.46

Use of Hydrochlorothiazide (HCTZ) and
Risk of Non-melanoma Skin Cancers:

A Population-Based Retrospective Cohort Study in Taiwan

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Aim/Objective: Previous studies, predominately from western countries, suggested hydrochlorothiazide (HCTZ) exposure may increase the risk of non-melanoma skin cancer (NMSC). This study aimed to evaluate the risk of HCTZ-associated skin cancer in the Asian population.

Methods: We conducted a population-based cohort study including patients aged 20+ years and newly received hypertensive drugs from Taiwan's National Health Insurance Database and Taiwan's Cancer Registry. We included patients with medication possess ratio of hypertensive drugs above 80% within two years to ensure they had sufficient exposure. We classified patients into 4 groups (i.e., HCTZ, other thiazide, non-thiazide diuretics and other hypertensive drugs (OHD)). We also randomly selected a-million patients as the control cohort from the database to evaluate background risk. The study endpoint was NMSC, and further classified into squamous cell carcinoma (SCC) and basal cell carcinoma (BCC). We performed multivariable Cox-proportional hazard model with adjustment of covariates, including age, sex, and comorbidities, to compare the risk of NMSC among groups.

Results: We identified a total of 41086 patients for HCTZ, 27402 for other thiazide, 19613 for non-thiazide diuretics, 812182 for OHD and 856782 for the controls. Comparing with control group, HCTZ was associated with NMSC (adjusted HR, 1.37; 95%, CI 1.06-1.77), especially for SCC (1.69; 1.16-2.46) but not BCC (1.18; 0.83-1.67). Comparing to HCTZ, we found no difference in the risk of NMSC for other thiazide (1.00; 0.71-1.40), non-thiazide diuretics (1.09; 0.70-1.69) and OHD (1.05; 0.83-1.33) groups, and the results were consistent in the analyses of SCC and BCC.

Conclusion: We found a higher risk of NMSC in patients receiving HCTZ compared to the control patients. However, it warrants attention to possible confounding by indication because the comparisons among hypertension groups showed no difference in the risk of NMSC.

Keywords: non-melanoma skin cancer, hydrochlorothiazide, hypertensive drugs

C.47

Predicting opioid-induced respiratory depression in hospitalized patients: a study protocol based on Yinzhou Regional Health Care Database in China

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Aims: Opioids are widely used to treat moderate to severe pain, opioid-induced respiratory depression is the most serious related adverse drug reactions. Recent guideline recommended that an integration of risk factor screening tools into the electronic health record (EHR) can facilitate clinicians in the comprehensive assessment of a patient's risk for OIRD. Therefore, we project to develop and validate a model for predicting the risk of OIRD in hospitalized patients.

Methods: Yinzhou Regional Health Care Database comprises health information from 1.5 million residents and all hospital in its jurisdiction. Adult patients who experienced opioid analgesia during hospitalization from 2010-2021 (index admission) and have ≥365 days of continuous observational data prior to the index admission date will be included. OIRD will be defined as the occurrence of either of the following two scenarios after administration of opioid: 1) a respiratory rate <10 breaths/minute or 2) any naloxone administration, tracheal intubation, or cardiopulmonary resuscitation. Candidate predictors included demographic, lifestyle, surgery events, opioid patterns, co-morbidity status (collected within 6 months prior to the index admission date) and concurrent administration medications. Opioid patterns and surgical events will be updated dynamically as time-dependent variables. Six machine-learning algorithms (Logistic Regression, Naïve Bayes, Gradient Boosting Machine, Random Forest, Elastic Net, and Neural Networks) will be developed and validated by k-fold cross-validation method.

Discussion: This is the first study in China to predict the risk of adverse drug reactions to opioids, clinician monitoring of OIRD will expectedly benefit from the integrated risk assessment tools. This study is limited by using retrospective data, but future evidence will be supplemented by prospective data collection or external validation. The study protocol was approved by the Ethics Committee of Peking University.

Key words: opioid-induced respiratory depression, machine learning, prediction model, regional health care database

D. Pharmacogenomics research and drug safety

D.1

The Associations of Two Common Polymorphisms in APOA1 Gene with Lipid-lowering Efficacy of Simvastatin

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Background and objective: Cardio-cerebrovascular disease is a major public health issue worldwide, and its complex pathogenesis has not been fully elucidated yet. This study was to evaluate the association between two common polymorphisms (rs670 and rs12721026) of APOA1 gene and the lipid-lowering efficacy of simvastatin in a Chinese population with dyslipidemia.

Methods: A total of 734 participants were enrolled from Anhui Province, China. By the extreme sampling method, we selected the low response group (n=108) and the high response group (n=106) based on the lipid-lowering response to simvastatin after consecutive 8-week medication. Both rs670 and rs12721026 loci were genotyped by MALDI-TOF MS platform. Serum total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels were measured at baseline and after 8-week treatment with oral 20 mg/d tablet of simvastatin.

Results: The frequency of rs670 polymorphism in the APOA1 gene had significantly different distribution between the low and high response groups (P=0.01). Compared with GG genotype, rs670 GA or GA+AA carriers had significantly higher change in HDL-C (ΔHDL-C) (GA: β=0.13, P=0.009; or GA+AA: β=0.12, P=0.015, respectively) and lower change in LDL-C (ΔLDL-C) (GA: β=-0.3, P=0.042; or GA+AA: β=-0.3, P=0.035, respectively). Alternatively, a statistical interaction between rs670 and gender was also observed. In females, patients with rs670 GA+AA had significantly higher ΔHDL-C (β=0.16, P=0.005) and lower ΔLDL-C (β=-0.39, P=0.032) levels than those with GG genotype. The A-T haplotype had significantly different ΔLDL-C (P=0.049) levels compared with the others.

Conclusions: Our findings indicate that the APOA1 rs670 and rs12721026 polymorphisms, especially for the rs670 locus, could be important genetic determinants of therapeutic response to simvastatin, and gender-specific associations are also observed with efficacy of simvastatin. It will be helpful for the understanding of the strategy of personalized medicine in Chinese patients with dyslipidemia.

D.2

The prevalence and factors associated with potentially inappropriate medication use in Chinese older outpatients with cancer with multimorbidity

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Background: Multimorbidity and polypharmacy is a general problem in older patients;, they increase the prevalence of potentially inappropriate medication (PIM) use. But the PIM use in patients with cancer is less clear. This study aimed to examine the prevalence and the predictors of PIM use in Chinese older outpatients with cancer with multimorbidity in Chengdu based on the 2019 Beers Criteria.

Methods: A cross-sectional study was conducted using electronic medical data from nine tertiary hospitals in Chengdu from January 2018 to December 2018. The 2019 AGS Beers Criteria were used to evaluate the PIM status of older outpatients with cancer (age ≥65 years), and multivariate logistic regression was used to identify the risk factors associated with PIM use.

Results: A total of 6,160 cancer outpatient prescriptions were included in the study. The prevalence of PIM use based on the 2019 AGS Beers Criteria was 32.65%. The most frequently used PIMs in outpatients with cancer were benzodiazepines and benzodiazepine receptor agonist hypnotics, diuretics, tramadol, non-steroidal anti-inflammatory drugs, and glimepiride. Logistic regression demonstrated that age≥80 (odds ratio [OR]: 1.238, 95% confidence interval [CI]: 1.071, 1.431, P=0.004), more diseases (OR: 1.193, 95% CI: 1.017, 1.399, P=0.03), polypharmacy (OR: 2.520, 95% CI: 2.169, 2.927, P < 0.001), and irrational use of drugs (OR: 1.762, 95% CI: 1.408, 2.205, P < 0.001) were positively associated with PIM use in older outpatients with cancer.

Conclusions: The prevalence of PIM use in Chinese older outpatients with cancer and multimorbidity is high in China. The increased prescription complexity caused by cancer will further increase the prevalence of PIM use. Research on interventions rationing PIM use in the older cancer population are necessary in the future.

E. Evidence-based medicine

E.1

Impact of Mobile Health Intervention on Glycemic Control and Quality of Life in Type 1 Diabetes Mellitus

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Objective: Good glycemic control and better quality of life (QoL) are known to reduce type 1 diabetes mellitus (T1DM) associated complications. In the era of advanced technology, the mobile app presents unique features for disease self-management. However, the impact of mobile health (mHealth) on glycemic control and QoL remains unclear. Therefore, the objective of this study was to carry out a systematic literature review and meta-analysis using published studies on mHealth interventions, determining glycemic control, and QoL.

Methods: A systematic search was performed on PubMed, Embase, and Cochrane Central Register of Controlled Trials to identify randomized controlled trials (RCTs). The outcome measure was glycemic control and QoL in the population with T1DM. QoL shows better treatment and satisfaction. Subgroup analysis was performed on the basis of mobile application users and text-messaging/feedback systems. Estimated the pooled mean difference (MD) and 95% confidence intervals (CIs) using a weighted random-effect model.

Results: Overall, nine studies were included in the meta-analysis. The results from the meta-analysis showed a significant reduction of mean HbA1c in intervention group compared to usual care. Subgroup analyses observed that mobile app intervention significantly reduced HbA1c levels by 0.27 percent, (Mean Difference, MD: -0.27; 95% CI: -0.49, -0.06; p< 0.05; heterogeneity, I2= 59%). While text-messaging/feedback systems have shown no significant reduction in HbA1c levels (MD: -0.19; 95% CI: -0.68, 0.30). mHealth did not improve QoL.

Conclusions: mHealth intervention may be effective for self-management and improvement of glycemic control. However, more RCTs and longitudinal studies are needed to be conducted worldwide to confirm the present findings.

E.2

Impact of Tuberculosis Disease on Human Gut Microbiota: A Systematic Review

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Objective: The aim of this study was to systematically identify and study the gut microbiota status in patients with TB and the changes associated with antitubercular therapy.

Methods: Systematic searches were conducted in Electronic bibliographic databases like PubMed, Embase, and Web of Science using keywords and MeSH terms for ‘gut microbiota’, ‘gut microbiome’, ‘tuberculosis’, and ‘anti-tubercular treatment’. All studies investigating the impact of TB disease or its treatment on GM were included. Studies, which did not have any healthy comparator group were excluded. The methodological quality of observational studies was appraised by using the Newcastle-Ottawa Scale (NOS) and Joanna Briggs Institute (JBI) critical appraisal checklist.

Results: A total of 11 studies were included in this review. A narrative synthesis was done, summarizing the current evidence for characteristics of the gut microbiota in the presence of Mycobacteria tuberculosis or its treatment. For evaluating gut microbiota out of 11 studies, eight studies have used 16S ribosomal gene sequencing, one study used short gun metagenomic sequencing and two studies have used both methods. For microbiota analysis, all the studies used stool as a biological sample. GM data was reported as taxa level status, alpha and beta diversity. The reported taxa level status from all the studies was summarized in tabular format and compared in terms of enrichment and depletion level between the TB group and the healthy comparator group.

Conclusion: From the reported GM data, majority of diversity indices were depleted in TB group. From the taxa level data, the overabundance of phylum Proteobacteria and depletion of some short-chain fatty acid-producing bacteria genera like Bifidobacteria, Roseburia, and Ruminococcus were found in the TB group.

Keywords: Tuberculosis, Gut Microbiota, Healthy comparator, Dysbiosis

E.3

Adjuvant use of Ribavirin with hepatitis C virus treatment in kidney transplant recipients: Systematic review and meta-analysis of real-world data

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Aim/Objective: Hepatitis C virus (HCV) infection among kidney transplant recipients (KTRs) is an important public health concern worldwide. Evidence on available treatments given shows a greater variability for safety and efficacy outcomes, thus we performed this large analysis to present the pooled findings.

Methods: PubMed/Medline, ScienceDirect, and Google Scholar were searched to identify observational studies of both Interferon based conventional treatment (CT) and recently approved direct-acting antivirals (DAAs). Newcastle–Ottawa Scale (NOS) was used for the quality assessment of studies. Meta-analysis of effectiveness outcome (SVR12) and safety data (adverse events and discontinuation rate) was performed using random-effect model. Subgroup analysis based on +/- Ribavirin with both treatment regimens was performed to assess its relevance in clinical practice. Chi-square and I2 tests were used to assess heterogeneity between the studies.

Results: Twenty-five and nine observational studies reporting on treatment with DAAs (n=943) and CT (n=125) respectively met the inclusion criteria for final data analysis. The overall pooled estimate of SVR12 rate was found as 95.3%, (range: 92.6%-97.0%) with DAAs in comparison to 46.4%, (range: 33.7%-59.6%) with CT. The pooled prevalence of adverse drug reactions (ADRs) in CT were higher as 47.8% than in DAAs as 23.8%, consequently showing a high discontinuation rate of 31.7% in CT as compared to 6.5% with DAAs. Subgroup analyses of both DAAs and Interferon based treatment +/- Ribavirin showed decreased effectiveness and increased ADR rates on adding Ribavirin. Significant heterogeneity ($p<0.05$) was found in all outcomes and was further handled by performing subgroup analyses.

Conclusion: The effectiveness of DDAs was found significantly higher than conventional treatment with a better safety profile in KTRs. Ribavirin did not provide any additional benefits while given in combination with either of the treatments available. Future research assessing genotype or regimen-specific outcomes with available treatment options is advised.

Keywords: HCV, KTRs, DAAs

E.4

Effectiveness of nonpharmacological interventions for the management of Fibromyalgia; A systematic Literature Review and Meta-analysis

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The objective of this study was to assess the mean change in VAS and FIQ scores using non-Pharmacological interventions in fibromyalgia.

Methods: We systematically searched on electronic databases like PubMed and Google Scholar from inception till March 2022. All English published comparing any nonpharmacological intervention to usual care, or placebo in people with fibromyalgia aged more than 18 years were included without any gender restriction. The change in Visual Analogue Scale (VAS) and Fibromyalgia Impact Questionnaire (FIQ) score was considered as primary outcome measures. Data was analysed and calculated using random effects model in R-Studio for standardised mean difference and 95% confidence interval. The risk of bias was evaluated using the Joanna Briggs Institute Critical Appraisal tool (JBI Scale).

Results: Of the 96 studies identified, 90 randomised controlled trials (n = 8734) and 6 cohort studies (n=307) assessing 37 nonpharmacological interventions were included. 2221 patients were given non-pharmacological intervention compared to placebo. Pharmacological intervention associated with significant improvements for both outcomes [FIQ (SMD= 2.89; 95% CI 0.41, 5.38) VAS (SMD= 1.82; 95% CI -0.19, 3.83)]

Conclusion: The findings of this study suggest that cognitive behavioural therapy aerobic exercise, multicomponent therapy and mindfulness were potential non-pharmacological interventions that enhances FIQ and VAS score significantly.

Keywords: Fibromyalgia, nonpharmacological interventions, Fibromyalgia Impact Questionnaire

E.5

Comparison of biologic and mechanical prostheses for aortic valve replacement in population aged 45-64 years

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Aim: To compare the long-term outcomes of aortic valve replacement (AVR) with mechanical or biologic prostheses in patients aged 45-64 years.

Methods: Patients aged 45-64 years who had undergone AVR between 2005 and 2018 were identified from a nationwide claims database. Risks of all-cause mortality and major adverse prosthesis-related events were compared between patients with a biologic or mechanical prosthesis, reported as restricted mean survival times (RMST) and hazard ratios (HR). Propensity score (PS) matching was used to balance the baseline characteristics of the study groups. Subgroups that could benefit more from a biologic or mechanical prosthesis were also identified. Sensitivity analyses were performed to assess the robustness of the results.

Results: There were 840 PS-matched pairs included, and the biologic and the mechanical prosthesis groups had similar mortality (mortality rate at 15 years, 42.4% vs. 43.6%; 10-year difference in RMST [95% CI], -0.21 years [-0.51 to 0.09]; HR [95% CI], 1.13 [0.91 to 1.41]). Patients with a biologic prosthesis had fewer major adverse prosthesis-related events than those with a mechanical prosthesis (cumulative incidence at 15 years, 35.0% vs. 53.5%; 10-year difference in RMST [95% CI], 0.79 years [0.44 to 1.15]; subdistribution HR [95% CI], 0.63 [0.52 to 0.77]). Subgroup analyses showed that mechanical prostheses were associated with better survival in patients aged 45-54 years, while biologic prostheses were associated with a lower risk of major adverse prosthesis-related events in patients aged 55-64 years. Sensitivity analyses showed similar results to the main analysis.

Conclusion: While patients aged 45-64 years with a biologic or mechanical prosthesis for AVR had similar survival, those with a mechanical prosthesis experienced more major adverse prosthesis-related events. These findings support a lower age cut-off point for choosing biologic prostheses over mechanical prostheses for AVR in Asian patients.

Keywords: aortic valve replacement, middle-aged, biologic prostheses, mechanical prostheses

E.6

Relationship between UGT1A1 polymorphisms and AT-DILI risk: evidence from a comprehensive systematic review and meta-analysis.

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Objective: UDP-glucuronosyltransferase enzyme 1A1 (UGT1A1) plays an important role in drug metabolism and detoxification through catalyzing the glucuronidation reaction, which is associated with the occurrence of anti-tuberculosis drug-induced liver injury (AT-DILI). The relationship between UGT1A1 polymorphisms and AT-DILI risk have been reported but with inconsistent results. We conducted a systematic review and a comprehensive meta-analysis to summarize the previous studies results and evaluate the relationship exactly.

Methods: Eligible studies were searched through English databases including PubMed, Medline, Web of Science, Embase, Cochrane Library, and Chinese databases including CNKI, WANFANG, VIP and SinoMed up to April 27, 2022. The study qualities were assessed by the revised Little's recommendations. Meta-analysis was conducted with a random-effects model using odds ratio (OR) with 95% confidence interval (95%CI) as the effect size.

Results: Totally, five case-control studies with 924 cases and 1642 controls were included, and 14 single nucleotide polymorphisms (SNPs) in the UGT1A1 gene have been reported. All studies were judged as high quality and the study subjects involved only Chinese and Koreans. The pooled results indicated that SNP rs3755319 might been associated with the risk of AT-DILI (AC vs. AA, OR=1.45, 95%CI: 1.10-1.92, P=0.009). However, SNP rs4148323, the most studied polymorphism, was no significant associations with AT-DILI risk for all genetic models (A vs. G, OR=0.98, 95% CI: 0.81-1.19, P=0.86; AG+AA vs. GG, OR=0.99, 95% CI: 0.82-1.19, P=0.91; AA vs. AG+GG, OR=0.78, 95% CI: 0.43-1.39, P=0.40). No statistically significant AT-DILI risks were observed for the other 12 SNPs.

Conclusions: UGT1A1 polymorphism rs3755319 was significantly associated with AT-DILI susceptibility, its potential use as a genetic risk marker in the population.

Keywords: anti-tuberculosis drug-induced liver injury, UGT1A1, genetic polymorphism, meta-analysis

E.7

Statin treatment and depression risk

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Aim/Objective: Statins are commonly prescribed cholesterol-lowering drugs. However, there were several contradictory reports describe the association between statin use and depression. In the present study, we conducted an updated meta-analysis of cohort studies and attempt to provide further empirical results in understanding the association between statin use and risk of depression. Our study also explored the role of class effect in this relationship.

Methods: A comprehensive literature search of the MEDLINE, PubMed and Cochrane Library was conducted through May 31, 2022. Searching for cohort studies evaluating statins as intervention and depression as outcome. A Pooled odds ratio (OR) with 95% confidence interval (CI) were calculated using the random-effects model and heterogeneity was assessed using Cochran's Q test and the I^2 statistic.

Results: A total of 10 cohort studies were qualified for this meta-analysis, involving 6,253,737 participants including 70,480 depression cases. Our data demonstrated that when compared with non-statin user, statin use was not significantly associated with the risk of depression under total analysis (OR, 0.99; 95% CI, 0.89–1.10) and statin class effect analysis (lipophilicity and potency). Similar results were also revealed in the subgroups analysis of depression history, following duration and match-design. However, a significant reduction of risk was found in the subgroup of age ≦60 years old (OR, 0.92; 95% CI, 0.88–0.97), but not in the subgroup of age > 60 years old. Furthermore, the significant heterogeneity in the overall analysis (I^2=92%, p<0.001) shows the diversity of study design of these cohort studies.

Conclusion: Except the subgroup of age ≦60 years old, our meta-analysis does not reveal significant results in supporting the potential role of statin use in the prevention of depression. Therefore, further double-blind, randomized and placebo-controlled trials are needed to confirm the magnitude of this association.

Keywords: Statins, Depression, Age, Meta-analysis

E.8

Hormonal therapies to treat infantile spasms in Asian children: A comparative analysis of 8 trials

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Objective: Evidence suggested that adrenocorticotropic hormone (ACTH) and oral corticosteroids fastly recover from infantile spasms (IS). Despite this, ACTH is most preferred first-line treatment for complete cessation of IS in children with West syndrome (WS). Hence this study was aimed to estimate the comparative efficacy and safety of hormonal therapies in children with WS.

Methods: Following a systematic literature search (PubMed and Embase from inception till April 2022), only Asian randomized controlled trials (RCTs) comparing the hormonal therapies (ACTH, methylprednisolone and prednisolone) with different doses or anti-seizure medications (ASMs) were included. Complete spasms cessation and proportion of adverse events (AEs) were the primary efficacy and safety outcomes respectively. A network meta-analysis was performed in Rstudio and reported as odd ratio (OR) with 95% confidence interval (CI). The hierarchy of competing interventions was defined using the surface under the cumulative ranking curve (SUCRA).

Results: Eight RCTs with 475 participants were evaluated for efficacy and safety of different hormonal therapies and ASMs. As compared with ACTH, a statistically significant number of participants achieved complete spasms cessation after two weeks treatment with prednisolone 40-60 mg/day (OR: 2.41; 95% CI: 1.1-5.5; p-score: 0.98). However, the results were not significant for direct and indirect comparison with the different ASMs or hormonal therapies except ACTH versus prednisolone 2 mg/kg/day (OR: 7.04; 95% CI: 1.21-41.0). During the treatment period, children had experienced hypertension, irritability, increased appetite, cushingoid facies, sleep disturbances and weight gain.

Conclusion: The findings suggested that high dose of prednisolone could be the best alternative option to be spasms free after two weeks of treatment than ACTH. In future, head-to-head trials comparing different doses of hormonal therapies are needed to better understand their comparative efficacy and safety.

E.9

Efficacy of Hyaluronic acid in the Management of Chronic Leg Ulcers: A Systematic Review and Meta-analysis

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Aim/objectives: Hyaluronic acid (HA) serves as an excellent tool in biomedical applications and has beneficial effects in tissue regeneration and wound healing. This meta-analysis is designed to evaluate the efficacy of HA in Venous leg ulcers and Diabetic foot ulcers.

Methods: Comprehensive literature search using PubMed and Google Scholar databases was performed for randomised controlled trials of both open labelled and blinded that have evaluated the efficacy of HA on adults with diabetic foot ulcers or venous leg ulcers and published in English language. Risk of bias for all included studies was performed using Cochrane Collaboration's risk of bias tool (ROB 2.0). Results are expressed as risk ratio (RR) and mean difference (MD) along with 95% confidence interval (CI).

Results: We analysed five trials with mixed arterial and venous ulcers, seven with venous leg ulcers and seven with diabetic foot ulcers involving 1495 participants. The combined RR revealed that the proportion of completely healed diabetic foot ulcers at 12 weeks was significantly higher for patients treated with HA therapy compared with non-HA therapy (RR=1.303, 95% CI = 1.128 - 1.505). HA or its derivatives have shown statistically significant benefits in improving pain intensity pooling the data from three trials measured pain using 100mm visual analogue scale (MD = -0.401, 95% CI: -0.650 to -0.152).

Conclusions: The meta-analysis strengthens the findings that HA is beneficial in treating diabetic foot by increasing the rate of wound healing, but still there is insufficient evidence to assist in decisions on the use of HA or its derivatives in the management of chronic leg ulcers.

Keywords: Efficacy, Hyaluronic acid, Leg ulcers, Meta analysis.

E.10

Analysis of the research status of Alzheimer's disease

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Globally, the disease burden of Alzheimer's disease (AD) is relatively heavy. The disease burden of AD in China is higher than the global average, and the situation is grim.

Objective: This paper aims to analyze the research status of AD at home and abroad, and provide guidance for AD prevention and treatment.

Methods: Pubmed was used to search related literatures about AD disease burden and prevention and treatment drugs in the past 5 years, and reviewed from the aspects of AD pathogenesis, current main drugs, new drug progress and risk factors.

Results: The neuropathological features of AD were mainly related to senile plaques and neurofibrillary tangles formed by the deposition of β-amyloid protein (Aβ) accompanied by neuronal cell loss. Related risk factors in addition to age, cardiovascular disease, diet, education, race, social status, stress, health status, and epilepsy also affect the prevalence of AD. New progress has been made in its prevention and treatment, such as the discovery of new formulations of Aducanumab and memantine hydrochloride.

Conclusion: With the emergence of new scientific research progress, the quality of life of AD patients can be effectively improved and the economic burden of the disease can be reduced.

Keywords: mechanism, risk factors, medication.

E.11

Effect of recombinant human endostatin injection on patients with colorectal cancer:a systematic review

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Objective: To systematically evaluate the efficacy and safety of endu combined with chemotherapy in the treatment of advanced colorectal cancer.

Methods: Cochrane Library， PubMed， EMBASE， CNKI， CBM， VIP and digital journals of Chinese Medical Association were searched by computer. The retrieval period is from the establishment of the database to June 2021. After evaluating the methodological quality of the included literature with the bias risk assessment tool recommended in Cochrane system evaluator manual 5.3， extract the data， conduct mesh meta-analysis with Stata 20.0 software， calculate the area under the cumulative probability curve （ Sucra） ， rank the probability of each intervention measure under different outcome indicators， and compare the advantages and disadvantages of each traditional Chinese medicine injection under different outcome indicators.

Results: a total of 20 randomized controlled trials were included， including 1147 cases. The results of mesh meta-analysis showed that compared with simple chemotherapy， the efficacy of endostar combined chemotherapy group was FOLFOX + endostar， XELOX + endostar， FOLFIRI + endostar， Xeloda single drug + endostar， oxaliplatin + endostar， and letitrexed + oxaliplatin + endostar. The main adverse reactions included nausea， vomiting， constipation， palpitation， ECG changes and so on.

Conclusion: endostar combined chemotherapy has more advantages than chemotherapy alone in the treatment of advanced colorectal cancer， among which FOLFIRI + endostar is the best treatment.

Keywords：Endostar， colorectal cancer， network meta-analysis， systematic review

E.12

HCV reinfection in HCV/HIV co-infected patients achieved sustained virologic response after direct-acting antiviral treatments: A systematic review and meta-analysis

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Background & Aims: The risk of hepatitis C virus (HCV) reinfection following successful direct-acting antiviral (DAA) treatment in HIV/HCV co-infected patients is a concern. The aim of this study was to discuss above issue, particularly among people who inject drugs (PWID) and men who have sex with men (MSM).

Methods: The PubMed, Cochrane library, and Embase databases were searched from inception until January 2021. Studies of HCV reinfection following successful DAA treatment among HIV/HCV-co-infected patients were included. A systematic review and meta-analysis was performed to calculate the relative risks and the pooled estimates of HCV reinfection. The time to occurrence of HCV reinfection in the MSM and PWID groups after achieving sustained virologic response (SVR) with DAA treatment was assessed.

Results: Six studies with 4426 HIV/HCV co-infected patients were included. The overall rate of HCV reinfection was 4.8 % (95% CI 1.0–11.2). The risk of HCV reinfection after achieving SVR with DAA treatment was significantly higher in MSM compared to PWID (10.8%, 95% CI 5.7–17.3, 477 patients; versus 0.7%, 95% CI 0.0–2.1, 1611 patients), with a summary risk ratio of 13.79 (95% CI 5.29–35.98, I2=0%). HIV-infected MSM developed HCV reinfection earlier than PWID, though not statistically significant, with a pooled mean difference time from post-SVR to HCV reinfection of -8.7 weeks (95% CI -28.7, 11.3).

Conclusions: HCV reinfection is higher in HIV-positive MSM treated with DAA. Risk counseling and regular HCV-RNA testing are crucial in this high-risk group following achieving SVR and successful treatment of HCV.

E.13

CATHETER INDUCED SPINAL EPIDURAL ABSCESS IN DIALYSIS PATIENTS: A SYSTEMATIC REVIEW OF DESCRIPTIVE STUDIES

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Background: Recently, there is an increased number of reports being published on catheter-induced spinal epidural abscesses (SEA).

Objective: This review aims to identify and critically evaluate all the descriptive studies that report the SEA due to catheterization and its presentation, diagnosis, management, and outcomes.

Methodology: A literature search was performed in the PubMed database using MeSH terms "epidural abscess" AND "renal dialysis" from inception to January 2021 without any language restriction. Google Scholar, grey literature databases (GreyNet. OpenGrey, Grey literature Report, BIOSIS Previews), and the bibliographic search of included studies were carried out to find the additional studies. Descriptive studies describing the SEA induced by catheter usage were included in the review. Study selection, data extraction, and quality assessment were conducted by two independent reviewers any disagreement was resolved by discussing it with the third reviewer.

Results: Data from 6 studies were retrieved for this review which includes 11 patients (5 females and 6 males) aged from 26 to 79 years old. The most common patient presentation was back pain, high-grade fever, quadriparesis, neck pain, drowsy, and altered mental status. The most common isolated microorganism from the blood and catheter tip was Methicillin-resistant Staphylococcus aureus. The most common findings in all the patients were elevated erythrocyte sedimentation rate and leucocyte count.

Conclusion: Clinicians must be aware of the possibilities of SEA initiated by catheter usage to prevent further consequences. Aggressive antibiotic therapy along with surgical intervention are the cornerstones in the management of SEA. Early diagnosis and initiation of treatment are important factors that decide the mortality and morbidity in patients with SEA.

E.14

Determination of burden of Hypovitaminosis D and Knowledge, Attitude and Practices of vitamin-D in Post Kala-azar Dermal Leishmaniasis patients

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Background: PKDL is a dermal manifestation caused by leishmania species. Micronutrients are essential instigate the immune defence against the foreign organisms. Vitamin D is an essential molecule which instigate both innate and adaptive immunity. Bihar is one of the endemic regions of leishmaniasis, and co incidentally it is also one of the most mal nutritious states in India. This study gives us a new insight in to the diagnosis, prognosis and treatment efficacy, relapse of leishmaniasis.

Objectives: Determination of hypovitaminosis D, and to determine the knowledge, Attitude, practices of vitamin D supplement in patients with post kala azar dermal leishmaniasis patients.

Methodology: The pathologically confirmed patients were included in the study. The written consent document is taken from the patients. Blood samples were collected, processed and stored as per protocol. Knowledge, Attitude, practices of PKDL patients was analysed by using D-KAP 38 questionnaire and the output is analysed by using the analytical scale given along with the D-KAP-38 questionnaire.

Results: In this study it was found that patients of PKDL, major population (n=15) were suffering from Vitamin D deficiency (<75nmol/L or 0-30 ng/ml) compared to healthy controls (n=12). The vitamin-D in sufficiency was found to be more in the PKDL group (n=6) compared to healthy controls (n=5) vitamin d sufficiency was only found in healthy controls (n=3). The PKDL patients were found to be Micronutrient deficient. The mean calcium levels were 8.462 ± 0.695 potassium 4.38 ± 0.32 sodium and alkaline phosphate was 142.9 ± 2.99 and 95.2 ± 42.36. The knowledge Attitude and practices towards micronutrient vitamin D was analysed by using D-KAP-38 Questionnaire. The general knowledge score was 240 (52.92%), nutritional knowledge was 73 (37.76%) Attitude was 787 (62.46%) and the practices of vitamin d was found to be 737 (70%) in PKDL patients.

E.15

Micronutrient status in diabetic foot ulcer patients: a systematic review and meta-analysis

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Objective: Is there an association between micronutrient status and risk of diabetic foot ulcers (DFUs)?

Method: This included all original research published in English that measured the status of any micronutrient in DFU patients. PubMed, Web of Science, Scopus, CINAHL Complete, and Embase were searched systematically to identify relevant studies. The last search was performed in October 2021. The risk of bias for all studies was assessed using either Cochrane risk-of-bias tool, Newcastle-Ottawa Scale, or Joanna-Briggs-Institute critical appraisal checklist for cross-sectional studies. Citations were retrieved into EndnoteX9.3.3 software, and data were extracted into Microsoft excel. The meta-analysis of selected studies was performed using RevMan5.4.1 software. The protocol has been registered with Prospero (CRD42021259817).

Results: Thirty-six studies were included in the systematic review, of which twenty-nine were included for meta-analysis. The number of DFU patients in the studies ranged from 19 to 387, including men and women. These studies reported levels of 12 nutrients: vitamin B9, B12, C, D, E, calcium, magnesium, phosphorous, iron, selenium, copper, and zinc. DFU compared to healthy controls (HC) showed significantly lower vitamin D [-10.82 (95%CI:-20.47, -1.16)], Magnesium [-0.45 (95%CI:-0.78, -0.12)] and selenium [-0.33 (95%CI:-0.34, -0.32)] levels. DFU compared to diabetic (DM) patients without DFU showed significantly lower vitamin D [-5.41 (95%CI:-8.06, -2.76)] and magnesium [-0.20 (95%CI:-0.25, -0.15)] levels. The overall analysis showed lower levels of vitamin D [15.51ng/ml (95%CI:13.40, 17.62)], vitamin C [4.99 µmol/L (95%CI:3.16, 6.83)], magnesium [1.53mg/dl (95%CI:1.28, 1.78)] and selenium [0.54 µmol/L (95%CI:0.45, 0.64)]. Subgroup analysis based on geographic location was performed.

Conclusion: Micronutrient levels are altered in DFU patients than HC and DM, suggesting an association between micronutrient status and risk of DFU. Hence requiring routine monitoring and supplementations as required. We further suggest that nutrient assessment and supplementation can be considered in the DFU management guidelines.

Keywords: Diabetic foot ulcers, Micronutrients.

E.16

Prophylactic Ivermectin for Prevention of COVID-19 infection: A Systematic Review and Meta-analysis

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Objective: We updated a systemic review to elucidate the effectiveness of ivermectin to prevent patients infected by COVID-19.

Methods: PubMed, Embase, Cochrane Library, and ClinicalTrials.gov were searched for eligible trials from inception to May 2022. We included randomized controlled trials (RCT) or observational studies comparing ivermectin to no treatment for COVID-19 prevention. Quality of studies was evaluated using the Cochrane Risk of Bias tool 2.0 and Newcastle-Ottawa scale for RCT and observational studies, respectively. A DerSimonian-Laird random-effects model was used to pool adjusted odds ratio (OR) and corresponding 95% CI. We also performed subgroup analyses to examine the effectiveness of ivermectin in either pre-exposure or post-exposure population.

Results: We identified 3 randomized controlled trials and 3 cohort studies involving 165,223 participants for analysis. Nearly all studies had high risk of bias in outcome assessment or population selection. Use of prophylactic ivermectin was significantly reduced incidence of COVID-19 infection (OR, 0.26; 95% CI, 0.12-0.54) compared with no treatment. For pre-exposure population, ivermectin user had lower risk of COVID-19 infection (OR, 0.25; 95% CI, 0.10-0.60); conversely, the protective effect did not exist in post-exposure population (OR, 0.28; 95% CI, 0.03-2.70).

Conclusion: Ivermectin was associated with lower infection rate of COVID-19, especially in pre-exposure population. Further well designed studies should be conducted in order to explore the efficacy of ivermectin for the prevention of COVID-19 due to the poor quality of currently available evidence.

Keywords: ivermectin, COVID-19, prophylaxis, meta-analysis

E.17

From Evidence-Based Medicine (EBM) to Share Decision Making (SDM): Whether to Continue the Antidepressant used to Achieve Remission or to Discontinue?

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Objective: We tried to confirm the relapse rate of depression and explore other factors that influencing patients' decisions through the evidence approach and implement with the interprofessional teamwork.

Methods: Setting patient, intervention, comparison and outcome (PICO) to form a question. In the Pubmed, Cochrane and Clinical Key databases, using MeSH term and Boolean logic combination (major depressive disorder AND antidepress* AND remission AND (discontinu* OR withdrawal OR stop OR quit)) for the literature search. Filters activated with meta-analysis, randomized controlled trial, systematic review, in the last 10 years, humans. 2 systematic reviews were finally selected to appraise. 1 quantitative research showed that the relapse rate was lower in the continue group than the discontinue group by about 20%. 1 qualitative research yielded 9 barriers and facilitators to discontinue use for patient perspectives. We created an interprofessional team and developed the patient decision aid (PDA) using evidence-based outcomes. We performed SDM via the SHARE approach (Seek, Help, Assess, Reach, Evaluate) and send questionnaires to patients to analyze.

Results: 10 patients with major depressive disorder were included in SDM between June and December 2021. 6 patients didn’t make decisions by themselves, but made decisions together with their relatives and friends. The interview time was shortened from 27.6 minutes to 16.8 minutes due to 12 PDA revisions. The anxiety level of patients about whether to discontinue the antidepressant after remission could be reduced by 40%. 2 patients were clearly aware of their options through SDM and 1 patient was allowed to regret the decision after one-month quitting the antidepressant.

Conclusion: Relapse rate was not the only one concern for patients and patients' inner voice should be heard. PDA was effective in facilitating SDM and could be helpful in the practice to support patient-centered care.

Keywords: share decision making、 antidepressant、 remission、 discontinue

E.18

The Use of Gamification in Evidence-Based Medicine Training

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Objective: To develop interactive games to reinforce Evidence-Based Medicine (EBM) concepts and literature searching skills.

Methods: We designed 3 interactive games through the use of “Wordwall” online templates: “Group sort” for “PICO (Patient/Problem, Intervention, Comparison and Outcome) structure”, “Find the match” for “EBM Definition” and “Quiz” for “Searching Skills”. The correct answer of each question could be shown automatically at the end of the game. The data about learning effect of pharmacy students and postgraduate pharmacists were collected during October 2021 to March 2022. The outcomes were evaluated with paired-sample Wilcoxon t-test by SPSS (Statistical Product and Service Solutions) 23.0.

Results: 13 pharmacy students and 7 postgraduate pharmacists were included in the pre- and post-assessment. The total correct rate of 3 interactive games were increased through EBM training: from 58.16±22.75 to 89.80±11.56 (p=0.006) in “PICO structure” game, from 74.73±18.69 to 93.41±8.22 (p=0.063) in “EBM Definition” game, from 50.00±10.80 to 98.46±3.76 (p=0.001) in “Searching Skills” game. The average satisfaction from the feedback with the Game-based Learning (GBL) design was 94.10%.

Conclusion: “Wordwall” was an easy-to-play and user-friendly game. Our results indicated that GBL was well accepted among Generation Z learners and had a positive influence on their motivation to learn.

Keywords: Game-based Learning、Gamification、Wordwall、Evidence-Based Medicine

E.19

Genetic variants in Nrf2/ARE signaling pathway and risk of anti-tuberculosis drug-induced liver injury: a pathway-based meta-analysis

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Objective: Reactive metabolites of anti-tuberculosis drugs can result in excessive reactive oxygen species (ROS), which are responsible for anti-tuberculosis drug-induced liver injury (AT-DILI). The nuclear factor erythroid 2-related factor 2 (Nrf2) /antioxidant response elements (ARE) signaling pathway plays a crucial role in protecting liver cells from ROS. The relationship between genetic variants in Nrf2/ARE signaling pathway and risk of AT-DILI have been reported previously, but the results are inconsistent. The present meta-analysis is conducted to obtain a more definitive conclusion about the effects of these variants on AT-DILI susceptibility.

Methods: We searched PubMed, Embase, Cochrane, Web of science, CNKI and WANFANG databases from inception to April, 2022 for genetic association studies following PICOS-based selection criteria. The effect sizes in the random effects model were calculated with odds ratios (ORs) with 95% confidence intervals (CIs). Newcastle-Ottawa Scale (NOS) was used to evaluate the methodological quality of case-control studies.

Results: Seven case-control studies with 1637 cases and 3039 controls were included, and the mean NOS scores was 6.87. A Total of 35 SNPs in the Nrf2/ARE signaling pathway have been reported, and 17 SNPs were reported in two or more studies. The pooled results indicated that MAFK rs3735656 (T>C) was significantly associated with a decreased risk for AT-DILI (allele model, OR=0.72, 95% CI: 0.62-0.84, P<0.001, I2=0%; dominant model, OR=0.64, 95%CI: 0.52-0.78, P<0.001, I2=0%). However, the most studied variants, rs2001350 and rs6726395 in NFE2L2 gene and rs2070401 in BACH1 gene reported in three studies, were no significant associations with AT-DILI risk under all genetic models (P>0.05). The remaining 13 SNPs were also not observed to be associated with AT-DILI.

Conclusions: The SNP rs3735656 of the MAFK gene in Nrf2/ARE signaling pathway may be associated with a decreased risk for AT-DILI.

Keywords: Nrf2/ARE pathway, genetic variants, anti-tuberculosis drug-induced liver injury, meta-analysis

E.20

Use of Antidementia Drugs and Risk of Nursing Home Placement: A Systematic Review and Meta-analysis

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Aim: The purpose of this study was to investigate the effect of antidementia drugs (ADD) including Acetylcholinesterase inhibitors (AChEIs) and memantine on nursing home placement (NPH) in dementia people.

Methods: PubMed, Embase, and Cochrane library were searched up to May 2022. Randomized controlled trials (RCTs) or observational studies investigating the effect of ADD were included. Two reviewers independently screened articles, extracted data, and assessed the quality of included studies. The effect estimates presented as risk ratios (RRs) with 95% confidence intervals (CIs) were pooled using the DerSimonian–Laird random effects models.

Results: Of the 1,152 studies identified, 4 RCTs and 12 observational studies met the inclusion criteria. The results from RCTs varied across studies, therefore, the meta-analysis could not be performed. For observational studies, ADD use was associated with a lower risk of NHP compared to non-ADD use [RR=0.60 (95% CI: 0.45 – 0.80), P<0.001, I2=78.2%]. When sub-group analysis based on geographical region, ADD use was associated with a lower risk of NHP compared to non-ADD use in both North America [RR=0.35 (95% CI: 0.17 – 0.75), P=0.006, I2=89.1%] and European region [RR=0.76 (95% CI: 0.60 – 0.96), P=0.019, I2=78.2%]. In addition, the finding from meta-analysis demonstrated that AChEIs use was associated with a lower risk of NHP compared to non-AChEIs use [RR=0.50 (95% CI: 0.36 – 0.71), P<0.001, I2=81.4%]. However, no significant difference was observed between a combination of AChEIs and memantine vs. AChEIs alone [RR=1.02 (95% CI: 0.96 – 1.09), P=0.484, I2=57.1%] with regards to NHP.

Conclusions: ADD use was associated with a lower risk of NHP compared to no treatment. However, the results relied on observational studies in which residual confounders could not be excluded. In addition, studies were based on small sample size and heterogeneity between studies. Rigorous studies with larger sample size are needed.

E.21

Comparative safety and efficacy of lactulose vs other conventional therapy in hepatic encephalopathy: A Systematic Review and Meta-analysis

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Aim/Objective: Hepatic encephalopathy (HE) is a type of brain dysfunction caused by acute liver failure or liver cirrhosis, and it is linked to a high rate of morbidity and mortality. This study aimed to provide the safety and efficacy of lactulose in hepatic encephalopathy.

Methods: Comprehensive literature search using electronic database like PubMed and manual search on Google Scholar from inception till January 2022. Randomized controlled trials (RCTs) reporting safety and efficacy of lactulose in any grade of hepatic encephalopathy regardless of gender, were included. Risk of bias was assessed using the Cochrane risk of bias assessment tool version 2.0. Blood ammonia level was considered as primary outcome. Data was analysed in Revmann 5.4 using fixed-effects models to give mean difference (MD) with 95% confidence intervals (CI).

Results: Eight trials with 499 patients were included. Lactulose is significantly superior in reducing ammonia levels in contrast with control (neomycin, lactitol, probiotic) (MD: -4.21, 95% CI: -5.14- -3.27). Compared with probiotics (MD: -31.68, 95% CI: -88.33-24.96) and antibiotics (MD: -7.01, 95% CI: -8.65- -5.37) lactulose demonstrated a significant lowering of blood ammonia level while lactitol was found to be superior in reducing the blood ammonia level when compared with lactulose (MD: 8.06, 95% CI: -7.47- 23.58). Adverse events such as abdominal discomfort, diarrhoea was associated with lactulose.

Conclusion: Lactulose is comparable to other oral treatments in terms of clinical efficacy for hepatic encephalopathy, and is linked with less adverse effects.

Keywords: Hepatic encephalopathy, lactulose, lactitol, meta-analysis

E.22

Hypnotic drug use and cardiovascular events in elderly patients with hypertension using Japanese health insurance database

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Aim/Objective: To investigate the association between the use of hypnotic drugs and incidence of cardiovascular diseases (CVDs) among elderly patients treated with antihypertensives using a large health insurance claims data in Japan.

Methods: This study was a retrospective cohort study using a claims database anonymized and provided from DeSC Inc. We included the patients who were 75-years or older and who had started antihypertensive drugs between April 2018 and November 2020 in this study. Patients who had a history of CVD were excluded from the study population. Patients exposed to hypnotic drugs were identified after starting antihypertensive drug treatment. CVDs included ischemic heart attack such as myocardial infarction and angina, heart failure, cerebrovascular infarction, strokes, and transient ischemic attack. The outcomes were defined with a record of diagnosis and medication and/or medical procedures such as surgery. A risk of CVDs adjusted by age, sex, and comorbidities was analyzed using a Cox proportional-hazards regression model.

Results: The mean age of eligible patients (n=152,962) was 82.8 years, 63.0% were women, and the mean follow-up was 2.2 years. Overall CVD incidence rate was 19.4 [18.9-19.9] (/1,000 person-years); compared to the group using hypnotic drugs, non-exposed individuals had an increased risk (1.2 [1.2-1.3] of incidence rate ratio [IRR]). The incidence of CVD increased by age group, and the use of hypnotic drugs slightly increased the risk; IRR 1.3 [1.2-1.5] for those aged 75-79 years,1.1 [1.0-1.2] for those aged 80-89 years, and 1.1 [1.0-1.2] for those aged 90 years or older). The adjusted hazard ratio for hypnotic drug use was 1.2 [1.1-1.3], and men were found to be at higher risk (1.5 [1.4-1.6]).

Conclusion: There was a significant association between the use of hypnotic drugs and CVDs in elderly patients treated with antihypertensives. Further research is required to estimate the risk adjusting lifestyle-related factors.

E.23

Efficacy and safety of zoledronic acid as an adjuvant therapy in patients with breast cancer: A systematic review and meta-analysis.

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Aim/Objective: Zoledronic acid is widely used as adjuvant chemotherapy for the treatment of breast cancer. This study aims to evaluate the efficacy and safety of zoledronic acid in patients with Breast Cancer.

Methods: Comprehensive literature search using electronic database like PubMed and manual search using Google scholar for relevant studies till February 2022. Randomized controlled trials that investigated the efficacy or safety or both of zoledronic acid were eligible for inclusion in our research. Risk of bias was assessed using revised Cochrane Risk of Bias Tool (ROB 2.0). The primary endpoints included disease free survival (DFS), overall survival (OS) while the secondary endpoints included fracture rate, bone metastasis, death rate, distant recurrence, safety outcome. The survival outcomes were represented as hazards ratio (HR) and dichotomous outcome were measured using risk ratio (RR) along with 95% Confidence Intervals (CI).

Results: A total of 22 studies including 12,419 subjects met inclusion criteria were evaluated. The use of zoledronic acid found to improve DFS (HR, 0.83, 95% CI, 0.72–0.96; p-value = 0.0114) and there was no significant difference in OS with the application of zoledronic acid (HR, 0.97, 95% CI, 0.91-1.04; p-value = 0.3723) compared with non-zoledronic acid. Furthermore, statistically significant benefits were associated with fracture rate (RR = 0.64; 95% CI, 0.46-0.90), bone metastasis (RR= 0.83;95% CI, 0.71-0.96). Adverse events such as arthralgia and bone pain were more common with zoledronic acid.

Conclusion: Zoledronic acid not only reduces the fracture risk but also appears to offer a substantial survival benefit over the non-zoledronic acid.
Keywords: Breast cancer, zoledronic acid, disease free survival, overall survival

E.24

Quality Assessment of the Latest Oncology Guidelines and Systematic Reviews Referenced in these Guidelines

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Objective: To assess the quality of oncology guidelines published by the National Comprehensive Cancer Network (NCCN) and assess the quality of systematic reviews referenced in the latest oncology guidelines by NCCN.

Methods: We evaluated the NCCN guidelines with two famous quality assessment tools: the Appraisal of Guidelines for Research & Evaluation (AGREE-II) and Reporting Items for Practice Guidelines in Health Care statement (RIGHT). Quality of the systematic reviews assessed using the two tools Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) and Assessment of Multiple Systematic Reviews (AMSTAR-2). Based on the scores reviews were categorized into high-, moderate-, and low-quality studies. All the domains and items were represented in mean percentage (MP%).

Results: A total of 59 CPGs were included in the study. Using the AGREE II criteria, The domains 4 and 6 (Clarity of presentation and Editorial independence) scored high (81.4% and 95.8%, respectively) and the domain “Stakeholder involvement” scored the lowest (49%). Using the RIGHT statement, the domain “Funding and interest” reported the highest (100%) and the domains “Evidence” and “Recommendations” were the lowest for all CPGs (30% and 49.8%, respectively). The overall assessment for all CPGs shows “Recommended with modifications”. Among 549 Systematic reviews (SRs) referenced, 50 (9.1%) high quality, 252 (45.9%) moderate quality, and 247 (44.9%) rated with low quality according to the PRISMA checklist. Item 9 scored highest among all items (92.4%), and Item 7 and 12 scored least (8.9 and 9.4%, respectively), according to the AMSTAR-2 tool.

Conclusion: Our findings suggest that the overall quality of the NCCN guidelines is moderate and recommended with some modifications to guide oncologists in patient care. Each guideline contains strengths and limitations, and improving these limitations (e.g., improvements in stakeholder involvement, recommendations, and evidence domains) will enhance the relevance of the NCCN recommendations.

E.25

Dementia and domestic violence/abuse – a population-based cohort study of the United Kingdom

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Aim/objective: To evaluate the prevalence of domestic violence/abuse (DVA) among 1) adults with dementia, and 2) people living with adults with dementia.

Methods: A population-based cohort study based on the IQVIA Medical Research Data (IMRD-UK, formerly known as The Health Improvement Network database) was conducted for the period from 2004 to 2018. We identified patients aged 18 years and older who were diagnosed with DVA. We further classified individuals with dementia and individuals living in the same household with those with dementia. The prevalence rate of DVA was calculated by total number of patients with at least one record related to DVA dividing by total number of persons for the calendar year.

Results: We included a total of 27,366 DVA cases. The mean age was 34.8 (SD 14.2) years and 84.1% were female. The prevalence rate of DVA increased from 161.1 to 608.8 per 100,000 persons over the 15-year period. Specifically, the prevalence rate of DVA among patients with dementia fluctuated from 1.9-8.5 per 100,000 persons and peaked in 2018. Moreover, the prevalence rate of DVA among people living with those diagnosed with dementia showed similar results, ranging from 1.2 to 8.9 per 100,000 persons.

Conclusion: Our results demonstrated the increased prevalence of DVA in the UK, especially in households which had at least one individual with dementia. The finding warrants further investigation for the risk factors of dementia-related DVA to inform effective prevention strategies and reduce harmful outcomes.

Keywords: domestic violence/abuse, dementia

E.26

Systematic review and meta-analysis of the effectiveness and safety of Janus kinase inhibitors in treating COVID-19 patients

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Background: The “cytokine storm,” the most renowned underlying pathophysiologic mechanism of Coronavirus disease-2019 (COVID-19), can be targeted at several stages theoretically and may contribute to the mortality of COVID-19. Janus kinase (JAK) inhibitors constitute a drug class that could interfere cytokine receptor signal transduction and therefore ameliorate the inflammatory response. Hence, we aimed to evaluate the efficacy of JAK inhibitors in patients with COVID-19.

Methods: Eligible studies from Medline, Cochrane Library, and Web of Science database were identified by November 16th, 2021. Randomized and nonrandomized trials that compared the treatment outcomes among JAK inhibitors or placebo in combination with standard of care in the hospitalized or severe COVID-19 patients were included. Primary outcomes was all-cause mortality, while secondary outcomes were clinical recovery, and severe adverse events. Systematic review and meta-analysis were conducted. Subsequent subgroup analysis was carried out by JAK inhibitors including baricitinib, tofacitinib, ruxolitinib, and nezulcitinib.

Results: Of 654 identified studies, 8 studies were included for meta-analysis. When JAK inhibitors were compared with placebo, the risk of all-cause mortality (OR: 0.55; 95% CI: 0.43-0.71) and severe adverse events (OR: 0.71; 95%CI: 0.51-0.98) were significantly reduced, while clinical recovery rate (OR: 1.58; 95%CI: 0.29-8.63) was comparable. Subgroup analysis for all-cause mortality showed baricitinib (OR: 0.58; 95% CI: 0.45-0.76) and ruxolitinib (OR: 0.29; 95% CI: 0.09-0.90) were significant effective. When concerning serious adverse events, only baricitinib outranked placebo (OR: 0.72; 95% CI: 0.58-0.90).

Conclusions: In the hospitalized or severe COVID-19 patients, JAK inhibitors were more effective in reducing all-cause mortality and severe adverse events compared with placebo. In subgroup analysis, baricitinib and ruxolitinib used for treatment has revealed benefits in decreasing the mortality rate. Accordingly, more rigorous, large-scale, and long follow-up period studies in patients with COVID-19 are needed.

F. Evidence-based pharmacy

F.1

Development and validation of patient information leaflet for management of dyslipidemia

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Aim: The primary aim of this study was to prepare, validate & translate patient information leaflet (PIL) for dyslipidemia patients.

Methods: The study is divided into three phases. In the first phase, a patient information leaflet was developed using primary, secondary and tertiary literature. In the second phase, the prepared patient information leaflet was validated, and in the third phase, the PIL was translated into local languages. The leaflet was validated for its readability (Flesch reading scale). The content of the PIL was validated by the expert committee using evaluative linguistic framework criteria. Then the validated English version of the PIL was translated into two local languages, namely Kannada and Marathi. The English PIL was forward translated into two languages and then backward translated in English to check the correctness of the translation.

Results: The patient information leaflet contains information about cholesterol, dyslipidemia & its risk factors, and management. Non-pharmacological management includes aerobic exercise, smoking cessation, and heart-healthy foods. It also provides information about lipid screening. The Flesch Reading Ease scale and FK-GL scores for the English version of the patient information were 90.9 and 2.3, respectively. The patients can easily understand the PIL as per the Flesch Reading Ease scale. The Committee members were asked to read the patient information leaflet on dyslipidemia. Then asked to give feedback by placing agree and disagree on each question in the evaluating linguistic framework criteria. Later they were interviewed to find the reasons why it has been placed agree and disagree with each question, after which corrections were made in the PIL as per suggestions.

Conclusion: Patient information leaflet on dyslipidemia in English was prepared, validated, and then translated into two different local languages, namely Kannada & Marathi, for user testing in patients.
Keywords: PIL, dyslipidemia, Hyperlipidemia, Validation

F.2

Comparison of standard-dose with reduced-dose of non-vitamin k antagonist oral anticoagulant in atrial fibrillation patients by risk of bleeding

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Background: In Taiwan, the reduced dosage of non-Vitamin-K antagonist oral anticoagulant (NOAC) is prevalent due to the concern of bleeding. However, whether a reduced dosage on Asian patients with high bleeding risk can lead to better outcomes remains elusive.

Aim/Objective: We aim to evaluate optimal NOAC dosage in Asian patients with high bleeding risk.

Methods: We conducted a retrospective cohort study using National Health Insurance Research Database. The study population was atrial fibrillation (AF) patients who were incident users of NOACs. The CHA2DS2-VASc score and the HAS-BLED score were applied to quantify the thrombotic and bleeding risk, respectively. We cross-stratified the patients into four groups (low-thrombotic with low-bleeding risk, low-thrombotic with high-bleeding risk, high-thrombotic with low-bleeding risk, and high- thrombotic with high-bleeding risk). Within each group, patients were assigned to two dosage arms according to their initiated dosage. The standard dose refers to dabigatran 300mg, rivaroxaban 15-20mg, apixaban 10mg, edoxaban 60mg per day. Any dosage below the standard dose was regarded as a reduced dose. Between the two dosage arms, the inverse probability treatment weight was used to balance the baseline characteristics, and the Cox proportional hazards model was used to generate the hazard ratios.

Results: In low-thrombotic with high-bleeding risk patients, a reduced dose tended to decrease the risk of major bleeding (HR =0.06; 95%CI =0.00-1.16) while increasing the risk of thromboembolism (HR =1.48; 95%CI = 0.39-5.62). Furthermore, a reduced increased risk of cardiovascular-related death (HR =1.07; 95%CI = 1.02-1.13) in general population.

Conclusion: Reducing NOAC dosage in AF patients with high bleeding risk is not likely to lead to better outcomes. The on-label use of NOAC is of great importance.

Keywords: Atrial fibrillation, NOAC, CHA2DS2-VASc score, HAS-BLED score

F.3

The value of CRP in COPD exacerbations: a meta-analysis

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Objective: To investigate the clinical significance of C-reactive protein (CRP), partial pressure of arterial blood carbon dioxide (PaCO2), and forced expiratory volume in one second as a percentage of predicted (FEV1% PRED) levels in acute exacerbations of chronic obstructive pulmonary disease (COPD) using meta-analysis.

Methods: The databases of CNKI, VIP, Wanfang, PubMed, EBSCO, Web of Science, and Elsevier were searched for relevant literature from their inception to April 2022, and the literature was screened and relevant information was extracted according to the criteria of narrow, and Stata 16.0 was used for statistical analysis.

Results: A total of 10 studies were included, 489 patients in the death group, 2798 in the survival group CRP and PaCO2 were significantly higher in the death group than in the survival group, FEV1% PRED was significantly lower in the death group than in the survival group, and the differences were all statistically significant.

Conclusions: CRP and PaCO2 were positively correlated with death and negatively correlated with FEV1% PRED in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).
Keywords AECOPD, C-reactive protein, meta-analysis

F.4

Comparison of the curative effect of bone cement and non-bone cement in femoral head replacement: a systematic review and meta-analysis

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Objective: To systematically evaluate the curative effect of cemented and non-cemented femoral head replacement.

Methods: Search the databases of CNKI, Weipu, Wanfang, PubMed, Cochrane Library, and Embase, and collect relevant randomized controlled trials (RCT) published from January 2010 to January 2021. Meta-analysis using RevMan5.3 software.

Results: 10 RCTs meeting the requirements were finally included, and 1564 patients underwent hip replacement were collected. The operation time of the bone cement group was longer [MD=6.78, 95% CI (5.61, 7.94), P<0.00001], and the intraoperative blood loss was more in the bone cement group [MD=18.52, 95% CI (9.56,27.40), P <0.0001], the bone cement group had fewer total complications [RR=0.42, 95% CI (0.33, 0.54), P<0.00001], the bone cement group had lower mortality [RR=0.42, 95% CI (0.29, 0.61)), P<0.00001]. Subgroup analysis was performed after the included studies were divided into subgroups according to publication time, and the results showed that the potential factor for heterogeneity among studies was publication time.

Conclusion: In patients undergoing femoral head replacement, although the amount of bleeding during the operation with bone cement is greater and the operation time is longer, the postoperative mortality and overall complication rate of the patients are reduced. It is recommended that the bone cement type be used for femoral head replacement in clinic.

Keywords: bone cement, non-cement, femoral head replacement, artificial hip replacement

F.5

Safety evaluation of metformin and acarbose in the treatment of diabetic patients

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Objective: To systematically evaluate the efficacy and adverse reactions of metformin and acarbose in the treatment of diabetic patients.

Methods: PubMed, Cochrane Library, EMBASE, CNKI, VIP database and Wanfang database were searched by computer, and all randomized controlled trials (RCTs) of metformin combined with acarbose in the treatment of type 2 diabetes were screened out. Meta-analysis was conducted by RevMan software, and the effects of metformin combined with acarbose (experimental group) and metformin alone (control group) in the treatment of type 2 diabetes were compared, and dizziness, hypoglycemia and hypoglycemia were compared.

Results: A total of 1057 articles in Chinese and English were detected, and 20 RCTs studies were selected, with a total of 1691 patients. In terms of therapeutic effect, the experimental group (metformin+acarbose) was significantly better than the control group (metformin alone) {RR=1.21, 95% Cl (1.17 ~ 1.26), P < 0.00001}. The subgroup analysis according to age showed the same results. In terms of safety, Meta-analysis showed that the total adverse reaction rate of the experimental group was lower than that of the control group {RR=0.44, 95% Cl (0.30 ~ 0.63), P < 0.00001}. Sub-group analysis according to age showed the same results.

Conclusion: Metformin combined with acarbose can effectively improve the therapeutic effect of patients with type 2 diabetes, and it is safe.

Key words: metformin, acarbose, Meta-analysis, diabetes

F.6

Systematic Evaluation of the Efficacy and Safety of Cetuximab in patients with Colorectal Cancer

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Objective: To systematically evaluate the efficacy and adverse reactions of cetuximab in patients with colorectal cancer, and to provide further reference for clinical.

Methods: CnKI, VIP, Wanfang, PubMed, The Cochrane Library, Embase and Web of Science were searched to collect published data on cetuximab, an EGFR antibody, in the treatment of patients with advanced colon tumor. A randomized controlled study was conducted on the treatment effect and adverse reactions of patients. The retrieval time was from database construction to April 2021, according to the inclusion and exclusion criteria, literatures were screened. Meta-analysis was performed using RevMan5.3 software, and forest plot and funnel plot were drawn.

Results: A total of 11 studies with 2447 patients were included. The results of meta-analysis showed that the disease response rate and partial response rate of the experimental group were significantly higher than those of the control group, the disease stabilization rate and disease progression rate of the experimental group were lower than the disease stabilization rate of the control group, and the objective response rate of the experimental group was also significantly higher than that of the control group, with statistically significant differences. Cetuximab use was also associated with an increased risk of severe adverse events, including grade 3 rash (13.4%) versus 0.9% in the control group, with a statistically significant difference. The incidence of rash of any grade was 38.8% compared with 8.2% in the control group, and the difference was statistically significant.

Conclusion: In patients with advanced colorectal cancer, the addition of cetuximab can significantly improve the disease response rate and partial response rate, reduce the disease stabilization rate and disease progression rate, and significantly improve the objective response rate.

Keywords: Cetuximab, colorectal cancer, combined chemotherapy, meta-analysis

F.7

Perioperative brain protection of dexmedetomidine in children with congenital heart disease: a meta-analysis

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Objective: To systematically evaluate the cerebral protective effect of dexmedetomidine on the perioperative period of children with congenital heart disease.

Methods: All relevant Chinese and English literatures in Cochrane, PubMed, Embase, CNKI, VIP, and Wanfang databases were searched. The search time was from the establishment of the database to February 2021, and literatures were selected according to the inclusion and exclusion criteria. Meta-analysis was performed using Stata 12.0 software.

Results: A total of 20 studies were included, involving a total of 1363 children with congenital heart disease undergoing cardiopulmonary bypass surgery. Dexmedetomidine significantly decreased TNF-α [SMD = -1.14, 95% Cl (-1.91, -0.37), P = 0.004] and IL-6 [SMD = -2.09, 95% Cl (-4.12, - 0.06), P=0.044]; inhibition of NSE [SMD = -4.27, 95% Cl (-6.28, -2.25), P = 0.000] and S100-β [SMD = -2.47, 95% Cl (-3.57 , -1.37), P=0.000] secretion; reduced cortisol [SMD = -2.72, 95% Cl (-4.64, -0.81), P=0.005] and glucose [SMD = -1.09, 95% Cl, (- 1.33, -0.85), P=0.000] release. In response to stress, dexmedetomidine achieved hemodynamic stabilization and attenuated the stress-related increase in cerebral oxygen metabolism.

Conclusion: Dexmedetomidine can effectively protect the brain during perioperative period in children with congenital heart disease.

Key words: adrenergic alpha agonists; congenital heart disease; infants and young children; cardiopulmonary bypass

F.8

Analysis of current situation and influencing factors of children's immunization

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Objective: To analyze the situation of parents receiving health education, participating in medical insurance and children's immunization, so as to provide a theoretical basis for vaccination units to formulate countermeasures.

Methods: Based on the data from 2017 national special survey on dynamic monitoring of health and family planning of floating population in China-the survey on epidemic factors of urban key diseases, the χ2 test and multiple Logistic regression were used to analyze the effects of social and demographic factors of parents, health education index and medical insurance index on children's immunization.

Results: The differences of nationality(χ2=59.40, P=0.000) and educational level(χ2=81.17, P=0.000) of parents were statistically significant. When the parents were in the following conditions: Han nationality(P=0.036), high educational background(P=0.008), young(P=0.000), receiving more health education(P=0.018) and actively participating in medical insurance(P=0.049), the timeliness of children's immunization was higher. Moreover, the younger the parents were, the more they received health education and the better they participated in medical insurance, the better the children's immunization situation would be.

Conclusion: The socio-demographic factors (ethnicity, educational level and age) and health care factors (health education and medical insurance) of parents can affect children's immunization. Immunization units should actively carry out parents' health education and medical insurance popularization work, to improve the timeliness of children's immunization.

Keywords: parents' health education; medical insurance; children's immunization; influencing factors

F.9

A meta-analysis of recurrence and adverse reactions after infusion of gemcitabine and pirarubicin in NMIBC patients after TURBT

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Objective: To compare the efficacy and safety of gemcitabine and pirarubicin after transurethral resection of bladder tumor (TURBT) for bladder cancer.

Methods: Six electronic databases, including Cochrane Library, PubMed, EMBASE, CNKI, VIP database and Wanfang database, were searched as of May 13, 2022 to determine the randomized controlled trial of gemcitabine and pirarubicin after TURBT for non-muscular invasive bladder cancer(NMIBC). The main results were the number of postoperative recurrence and overall adverse reactions. Study selection was based on predetermined inclusion and exclusion criteria. Data such as literature title, first author, publication years, general situation of research objects, intervention measures and observation indicators were collected. The quality assessment was conducted according to the Cochran manual. Q test and I-squared statistics were used to test the heterogeneity of results among studies, and sensitivity analysis was used to solve the problem of high heterogeneity.

Results: A total of 1681 participants in 20 trials were determined to be eligible and included in the meta-analysis. The results showed that gemcitabine could significantly reduce the recurrence level within 2 years (OR=0.47, 95% CI [0.36,0.63], P<0.00001) compared with pirarubicin. There was no heterogeneity between them (I2=0%, P=0.98). In terms of adverse events, the results showed that gemcitabine had fewer adverse reactions than pirarubicin (OR=0.37, 95% CI [0.24,0.57], P < 0.00001). However, there was great heterogeneity between groups (I2=57%, P=0.002). And sensitivity analysis was performed without heterogeneity after removing one study (I2=32%, OR=0.43, 95% CI [0.30,0.61]).

Conclusion: Compared with pirarubicin chemotherapy, gemcitabine chemotherapy can effectively improve the clinical efficacy, and gemcitabine chemotherapy is safer than pirarubicin.

Keyword： Gemcitabine, Pirarubicin, Bladder cancer, Meta-analysis

F.10

Network Meta-analysis of five Chinese herbal injections combined with FOLFOX chemotherapy regimen in treating advanced gastric cancer

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Objective: To systemically evaluate the efficacy and safety of Chinese herbal injections combined with FOLFOX chemotherapy regimen in treating advanced gastric cancer.

Methods: All of randomized controlled trials were retrieved in PubMed, Embase, Cochrane Library, CNKI, VIP and Wanfang databases from database inception to November 31, 2021. Screening based on preset inclusion and exclusion criteria, and quality evaluation of the included RCTs. Review Manager 5.3 for heterogeneity test and Stata 16.0 for network meta-analysis.

Results: A total of 25 RCTs involving 1921 cases of advanced gastric cancer patients were included. ①Efficacy, CKS+ FOLFOX and KA+ FOLFOX are significantly better than FOLFOX alone, and significantly better than LE+FOLFOX; ②Life quality and leukopenia, KA+FOLFOX is significantly better than FOLFOX alone; ③Gastrointestinal toxicity, AD+FOLFOX is significantly better than FOLFOX alone; ④Hepatic injury, AD+FOLFOX is significantly better than FOLFOX alone, and significantly better than KA+FOLFOX; ⑥Peripheral neurotoxicity, AD+FOLFOX is significantly better than FOLFOX alone, and is significantly better than KA; The results also showed that the incidence of peripheral neurotoxicity that KA+FOLFOX is significantly higher than FOLFOX alone, and significantly higher than SQFZ+FOLFOX.

Conclusion: The application of CKS+FOLFOX for advanced gastric cancer has shown obvious advantages in improving the total clinical effective rate and quality of life of patients and reducing the incidence of adverse reactions, and it is most likely to become the best Chinese herbal injections; AD+ FOLFOX will be higher in safety.

Keywords: Chinese herbal injections; FOLFOX; advanced gastric cancer; network meta-analysis; adverse reactions

F.11

The value of procalcitonin in guiding anti-infective therapy in acute exacerbation of chronic obstructive pulmonary disease: Meta-analysis and systematic review

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Objective: Systematic evaluation of the clinical value of serum procalcitonin in anti-infective therapy in AECOPD.

Methods: Search PubMed, EMBASE, The Cochrane Library for relevant Randomized controlled trials, (RCTs). Two researchers independently screened the literature according to the inclusion and exclusion criteria, and extracted relevant information. The quality of the included studies was assessed using the Cochrane Collaboration's risk of bias assessment tool, and a risk-of-bias map was obtained using Review Manager 5.3. Meta-analysis using STATA 12.0.Outcomes from pooled analyses of random-effects models were tested using Galbraith plots. Sensitivity analysis was used to find sources of heterogeneity and judge the robustness of the results. The results of 5 literatures showed that the antibiotic prescription rate in the PCT group was 27% lower than that in the control group (RR=0.73, 95%CI:0.58-0.92, I2=65.3%). The results of 2 literatures showed that the PCT group needed to be admitted to the Intensive Care Unit (ICU), and the treatment time was shorter than that of the control group (SMD=0.26, 95%CI:-0.43~-0.08, I2 = 0%).

Conclusion: Monitoring PCT can reduce the rate of antibiotic prescriptions in patients with AECOPD and shorten the duration of treatment in patients requiring ICU admission. Large-scale, high-quality literature is still needed for meta-analysis and systematic review to provide a reliable basis for PCT-guided anti-infective treatment of AECOPD.

Key words: procalcitonin, COPD, meta-analysis

F.12

Systematic evaluation of the efficacy and safety of dobutamine in the treatment of sepsis

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Objective: To evaluate the efficacy and safety of dobutamine in the treatment of sepsis.

Methods: By searching PubMed, Cochrane, CNKI and other databases, the literature was collected, the literature was screened according to the inclusion and exclusion criteria, the relevant information in the study was extracted, and the quality of the included studies was evaluated according to the Cochrane bias risk assessment method. The research results were statistically analyzed by Rev man5.3 software.

Results: A total of 6 literatures were included. The results showed that compared with the control group, dobutamine group was more effective [OR= 9.46,95% CI (2.96,30.21), P = 0.0001]; Fewer deaths [OR= 0.09,95% CI (0.02,0.35), P = 0.0004]; The number of organ failure was less [OR= 0.23,95% CI (0.12,0.43), P < 0.00001]; The disappearance time of dyspnea was shorter [MD = -4.48, 95% CI (- 4.92, - 4.03), P < 0.00001]; The recovery time of blood pressure was shorter [MD = -4.75, 95% CI (- 5.18, - 4.32), P < 0.00001]; The length of hospitalization was shorter [MD = -6.72, 95% CI (- 7.67, - 5.76), P < 0.00001].

Conclusion: Compared with the control group, the dobutamine group has higher effective rate, fewer deaths, fewer organ failure, shorter disappearance time of dyspnea, shorter recovery time of blood pressure and shorter length of hospitalization.

Keywords: Dobutamine; Sepsis; Curative effect; Meta analysis

F.13

First-line Therapies in Recurrent or Metastatic Head and Neck Cancer: A Systematic Review and Network Meta-analysis

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Aim/Objective: More than half of head and neck cancer patients develop locoregional recurrence within two years, and 20 to 30% develop metastases. Even though multiple treatment regimens for recurrent or metastatic head and neck cancer (R/M HNC) were listed in the treatment guideline, the optimal first-line treatment was still unknown. This systematic review and network meta-analysis aimed to evaluate the efficacy and safety of first-line therapies in patients with R/M HNC.

Methods: The PubMed, EMBASE, Web of Science databases, and ClinicalTrials.gov website were systematically searched for phase II and III randomized controlled trials (RCTs) comparing the first-line treatments in patients with R/M HNC up to May 2021 without language restriction. The comparing treatments included single or combined immunotherapy, targeted therapy and chemotherapy. The sub-analysis of other RCTs were excluded. One-year rate of overall survival (OS), progression-free survival (PFS), and grade ≥3 adverse events (AEs) were the outcomes of interest. The random effects model was used to assess the surface under the cumulative ranking curve (SUCRA) by WinBUGS 1.4.3.

Results: Nine studies involving eight treatments were included. There was a high probability that cisplatin plus cetuximab was the best for improving OS (SUCRA 0.88), followed by pembrolizumab plus cisplatin plus 5-fluorouracil (SUCRA 0.78). Considering PFS, cisplatin plus cetuximab ranked first, with the SUCRA value of 0.93. Besides, pembrolizumab was the highest-ranked treatment for grade ≥3 AEs (SUCRA 0.95).

Conclusion: In patients with R/M HNC, cisplatin plus cetuximab seemed to be the best first-line treatment when considering drug efficacy. On the other hand, pembrolizumab was suggested to be the safest drug for grade ≥3 AEs. Further high-quality RCTs comparing cisplatin plus cetuximab versus the pembrolizumab-based regimen are warranted to validate the results.

Keywords: recurrent or metastatic head and neck cancer, first-line therapy, network meta-analysis.

F.14

Comparative drug persistence of brand and biosimilar biologics in rheumatoid arthritis patients in real-world practice: A systematic review and meta-analysis

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Aim/Objective: Biologic agents was widely used for rheumatoid arthritis (RA) patients. However, drug persistence rates between brand and biosimilar biologics in RA patients remained unclear. The aim of study was to compare the effectiveness of brand and biosimilar biologics in the patients with RA.

Methods: We conducted a systematic review by searching retrospective design studies in English that assessed the effectiveness between brand and biosimilar biologic in RA patients. Medline (via PubMed) and EMBASE were screened for relevant publications with last updated February 2022. The outcomes included retention rates with a follow-up between 6 months to 4 year were extracted for meta-analyses.

Results: A total of seven studies were included, involving 3,412 patients with RA. Four studies reported data of infliximab and infliximab biosimilar and two studies involved data of etanercept and etanercept biosimilar. One study evaluated data of rituximab and rituximab biosimilar. The retention rates of brand and biosimilar biologics were 63.6% and 66.3% (risk ratio: 0.89, 95% confidence interval: 0.83 – 0.95), respectively.

Conclusion: The rate of drug persistence between brand and biosimilar products was comparable. Further investigation is needed to consolidate the result.

Keywords: Rheumatoid arthritis, drug survival, biosimilar, biologics

F.15

The Quality of Reporting Methods and Results of Cost-Effectiveness Analyses Conducted in India: A Methodological Systematic Review

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Objectives: To identify and report the characteristics of cost-effectiveness studies conducted in India and to assess quality of these studies.

Methods: A systematic search was performed using PubMed, Cochrane CENTRAL, and Google Scholar from inception to 30th May 2022 to identify cost-effectiveness studies conducted in India. A combination of keywords, MeSH terms on cost-effectiveness, and India were used with Boolean operators. The quality of studies was evaluated using the Consensus on Health Economic Criteria (CHEC) and Quality of health economic studies (QHES) checklists.

Results: A total of 48 studies were included. Only seven (14.5%) studies reported working with the protocol. 85% of the studies were model-based, of which the Markov model was frequently reported. Most study interventions were categorized as therapeutic (45.8%), and some studies (35.4%) considered an active alternative as the comparator. The effectiveness of the data was derived from a single study in 19 (39.58%) reports, and only 15 (31.25%) used evidence-based estimates. Two (4.1%) studies reported a complete description of the QALY calculation methods. Most of the studies (34, 70.8%) reported that the study intervention produced "most costs and more QALYs" than the comparator. 39 (81.25%) studies reported favorable conclusions. The majority of articles showed moderate-quality when assessed with the CHEC (68.75%) and QHES (45.83%) checklists. In CHEC, 39 (81.3%) studies did not mention the costs of physical units, and 27(56.3%) were not valued appropriately. In contrast, in the QHES, 26(54.2%) and 32 (66.7%) studies did not mention the study objective or data abstraction, respectively, leading to a decline in the quality of the studies.

Conclusions: Several crucial components of techniques and outcomes were commonly lacking in published cost-effectiveness analyses from India. It is difficult to ascertain the validity of research findings and conclusions without complete and comprehensive description of how the studies were organized and executed.

F.16

Accessing biosimilar adherence following a switch from reference to biosimilar in rheumatoid arthritis patients: A systematic review and meta-analysis

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Aim/Objective: Drug persistence rate in the rheumatoid arthritis (RA) patient who switched from reference to biosimilars in real-world switching studies were evaluated in present study.

Methods: This systematic review screened database including PubMed, EMBASE, and Cochrane Library for reports of monoclonal antibody (mAb) switching from their inception. The last date of screening published studies was February 2022. We included biosimilar studies if they reported an observational study comparing a biosimilar for RA treatment and its brand-name reference product. All available information on drug persistence was assessed. Meta-analysis was performed with the inverse variance method using R software.

Results: A total of 34studies were identified and seven studies met all screening criteria. 1,098 RA patients were included. After extracting studies' characteristics, published studies varied greatly in experimental design, data sources, studied population studied, follow-up time, monoclonal antibodies and endpoint definitions. The drug persistence after switching from originator to biosimilar was 74% (95% confidence interval: 49% - 89%).

Conclusion: Drug persistence rates following a switch to a biosimilar in patients with RA was consistent over time.

Keywords: Rheumatoid arthritis, Biosimilar, Drug adherence, Drug persistence

F.17

The effectiveness of Denosumab versus Bisphosphonates in The Treatment of Osteoporosis: A Systematic Review and Meta-analysis of cohort studies

Qingxia Xue[1,2], The effectiveness of Denosumab versus Bisphosphonates in The Treatment of Osteoporosis: A Systematic Review and Meta-analysis of cohort studies Na He[1], The effectiveness of Denosumab versus Bisphosphonates in The Treatment of Osteoporosis: A Systematic Review and Meta-analysis of cohort studies Quan Zhao[2], The effectiveness of Denosumab versus Bisphosphonates in The Treatment of Osteoporosis: A Systematic Review and Meta-analysis of cohort studies Suodi Zhai[1]
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Objective: Denosumab (DMab), a fully human monoclonal antibody that inhibits receptor activator of nuclear factor kappa-B ligand, is one of the first-line options for osteoporosis. This study aims to compare the effectiveness of DMab versus bisphosphonates (BP) in the treatment of osteoporosis based on real-world studies.

Methods: We searched PubMed, Embase, the Cochrane Library, Wanfang Data, CNKI, and SINOMED databases from inception to April 2022. Active-comparative cohort studies among osteoporotic patients with the comparison of DMab and BP were included. Accounting for the confounding bias, we excluded studies without adjusted effect estimates. Moreover, studies were required to report fracture or bone mineral density (BMD). We calculated the overall effect estimate of DMab versus BP in preventing fracture by pooling RR or HR separately.

Results: A total of 16 cohort studies with 132,955 patients were included, and the follow-up time ranged from 6 to 36 months. Pooling analysis showed that DMab was associated with a lower risk of vertebral fracture [RR 0.32 (0.14, 0.76)] compared with BP. However, there was no statistical difference between DMab and BP in preventing composite [HR 0.97 (0.89, 1.05)], hip [HR 1.05 (0.79, 1.41)], and non-vertebral [RR 0.81 (0.26, 2.48)] fracture. Concerning the improvement of BMD, DMab was more effective than BP. Notably, we found that the advantage of DMab in improving BMD compared with BP was more obvious as the follow-up time prolonged.

Conclusions: Based on real-world evidence, DMab is superior to BP in improving BMD, but the difference in other fracture risk is not statistically significant except vertebral fracture. Further real-world studies are needed to elucidate the difference in long-term fracture risk.

Keywords: Osteoporosis; Denosumab; Bisphosphonates; Systematic Review; Meta-Analysis; Real-world evidence

F.18
Association of direct oral anticoagulants with risk of dementia in atrial fibrillation patients: a meta-analysis for observational studies

Objectives: Some evidences indicated that direct oral anticoagulants (DOACs) were associated with a significantly lower risk of dementia. The purpose of this meta-analysis is to evaluate the association between DOACs and risk of dementia in atrial fibrillation patients (AF).

Methods: The information is obtained mainly from the following sources: PubMed, Embase, Wiley Online Library, ClinicalKey, Google Scholar, WANFANG MED ONLINE and Airiti Library for all-language publications till May 2022. There are total four studies recruited between 2018 and 2021. Sample size ranged from 4657 to 46483. All participants were from United States of America and Asia with follow-up duration of 1.7 year to 18 years. The main outcome is overall AF-related dementia. We used random effect models to calculate pooled relative risks (RRs) and to estimate statistical heterogeneity. All data were analyzed using STATA 14.0 statistical analysis software.

Results: The pooled relative risk of AF-related dementia in DOACs users as compared with warfarin users were 0.72 (95% CI: 0.55-0.95) estimated by random effect model, with evidence of heterogeneity (I^2=92.8%, P<0.001).

Conclusion: This meta-analysis showed that, DOACs use was associated with lower risk of overall dementia in AF patients.

G. Drug utilization evaluation studies

G.1

Medicine Utilisation in Malaysia: Data from the Malaysian Statistics on Medicines 2017

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Aim/Objective: National medicines utilisation statistics provide insights into the healthcare burden when it comes to the pattern of disease epidemiology. It is also essential for monitoring and predicting the financial allocations and procurement of drugs, as well as evaluation of policy interventions. The annual reporting of medicines utilisation study is published as the Malaysian Statistics on Medicines (MSOM) with its main objective to quantify the total medicines utilised in the Malaysian healthcare system in accordance with the WHO Anatomical Therapeutic Chemical (ATC) classification system.

Methods: Medicines procurement data for the year 2017 segregated by the public and private healthcare sectors and categorised according to the ATC codes was analysed and described to estimate the total national medicines utilisation.

Results: Total estimated medicines utilisation in 2017 increased by 13.5% compared to 2016, at 717.85 DDDs per every 1,000 inhabitants per day, with the public sector accounting for 66% of the total utilisation. The total expenditure on medicines was MYR 5.9 billion (USD 1.3 billion), which reported an 11.3% increase from the previous year. The private sector reported the highest expenditure on antibacterials for systemic use. Drugs used in diabetes were the most utilised group of drugs overall, while amlodipine remained as the most utilised medicine in Malaysia.

Conclusion: The utilisation of medicines documented was in line with the prevalence of non-communicable diseases which accounted for over 73% of deaths in the country. The information obtained from this study is crucial to enable informed decision-making pertaining to pharmaceutical products and pharmacotherapy, as well as supporting the local policies and interventions.

Keywords: medicine utilisation, national statistics on medicines, drug procurement

G.2

Analysis of special approval medicines used among children in a Malaysian tertiary care hospital

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Aim/Objective: Special approval medicines (SAM) are medicines used with approval from the Director General of Health Malaysia when the therapeutic options within regulatory and formulary boundaries appear unsuitable or ineffective to treat the patients. This study was conducted to examine and characterize the use of SAM among children in a Malaysian tertiary care hospital.

Methods: The retrospective study reviewed the named-patient basis SAM application forms, cover letter, pharmacist review summary and patient monitoring forms available at the Pharmacy Department between 1st January 2019 and 31st December 2020. Unprocessed, unapproved and stock-basis applications were excluded. The outcome measures were categories, scope, off-label use and cost of SAM. Per-patient data were analyzed descriptively.

Results: Overall, 328 SAM applications for 1010 patients (mean age of 8.7±1.0 years) were analyzed. Top three SAM were melatonin (11.5%), scopolamine (7.6%) and cholecalciferol (7.1%). The most common pharmacological group was nervous system (n=371, 36.7%) and antineoplastic and immunomodulating agents (n=332, 32.9%). A total of 513 (50.8%) and 837 (82.9%) patients were involved in the SAM applications for unregistered and non-formulary medicines, respectively. Unregistered, non-formulary medicines were applied for 47.3% (n=478) of the patients. The majority of the scope for SAM (64.7%) were to substitute the available alternatives in the national formulary which were ineffective or sub-optimal for the patients. Among the 262 patients with repeat applications, 93.8% reported disease or symptom improvement while 1.9% experienced side effects. About 28% of the patients received SAM for an off-label indication. The total cost of the SAM was MYR8,748,358.38 (USD 2,090,408.87).

Conclusion: The use of SAM among children in this hospital involved unregistered, non-formulary medicines used to substitute the available alternatives in the formulary. A concerted effort is warranted in exploring supplementary mechanisms to enhance the medicine registration process and formulary system towards facilitating enhanced provision of treatment for children.

G.3

Measurement of antibiotic utilization pattern before and during COVID-19 in a tertiary care hospital in India

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Aim: COVID-19 infection is promoting irrational use of antibiotics in several countries. Inappropriate use of antibiotics within the hospital is among the contributing factors for antimicrobial resistance. This study evaluates antibiotic utilization patterns in in-patients in India's 2032 bedded tertiary care hospital.

Methods: A point prevalence study was performed in in-patients using antibiotics from May 2019 to October 2021. ATC/DDDs index (the standard method by WHO) was used to evaluate AMR risk.
The susceptibility pattern of the bacteria was also studied.

Results: Broad-spectrum antibiotics such as penicillins and cephalosporins combinations, fluoroquinolones were most widely used but with a decreasing trend. The 'Watch group' antibiotics were prescribed more than the 'Access group'. Utilization of last-resort or 'Reserve group' antibiotics such as carbapenems, polymyxins, tigecycline and linezolid were kept low. Carbapenem-resistant Enterobacteriaceae were found high even as the carbapenem usage was low. Klebsiella spp. followed by E.coli and Acinetobacter spp. were the most common causes of superinfections occurring in COVID-19 patients.

Conclusion: Restricted use of antibiotics was encouraged in our hospital during the pandemic. Nonetheless, judicious antibiotic use, preparing and implementing in-house guidelines, and prompt submission of culture reports can ameliorate AMR.

G.4

A survey of HLA-B*1502 genotype testing on carbamazepine

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Background: Carbamazepine is associated with life-threatening cutaneous disorders, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Carbamazepine-induced SJS/TEN is strongly associated with the HLA-B*1502 allele in Han Chinese populations. The National Health Insurance Bureau has included HLA-B*1502 genetic testing into the NHI benefits package since June 1, 2000. The purpose of this study was to survey the HLA-B*1502 genetic testing rate in cases using Carbamazepine.

Methods: In this retrospective study, 78 patients who received carbamazepine were recruited between January 2021 and December 2021, and HLA-B*1502 genotype testing on carbamazepine was evaluated to understand utilization appropriately.

Results: In this retrospective study, 42 males and 36 females were recruited. There were 38 seizure disorders patients, 18 trigeminal neuralgia patients, 8 bipolar disorder patients, and 14 patients with another diagnosis. 7(9%) cases had been tested for the HLA-B*1502 gene and the report was negative, and 71 cases haven't processed HLA-B*1502 genotype testing. Among the 71 patients who have never been tested for HLA-B*1502, 38 patients have used carbamazepine in other medical institutions and cannot confirm whether they are tested or not, and as many as 33 patients (42.3%) used carbamazepine first time without the HLA-B*1502 genetic testing.

Conclusion: In the study, as many as 33 patients (42.3%) had not received genetic testing prior to their first use of carbamazepine. According to the statistics of the Taiwan Drug Relief Foundation, SJS ranks first in the adverse reactions of drug injury relief payment cases, accounting for about40% of the total cases. The National Health Insurance Administration recommends genotyping all patients for the allele before carbamazepine therapy. Pharmacogenetic testing enables physicians to screen out high-risk groups prone to severe allergic reactions before prescribing carbamazepine, which not only maintains the safety of patients' medication but also reduces the waste of medical and social resources.

G.5

Utilization review of Total parenteral Nutrition (TPN): A Prospective Study

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Aim/Objective: To review the utilization of parenteral nutritional services of neonates at NICU.
Methodology: A prospective observational study was conducted at NICU of Tertiary care Hospital for a duration of 9 months. Neonates requiring parenteral nutrition were included in the study. All the relevant data were collected from the case sheet. All the neonates were followed until the discharge to assess the utilization of TPNs

Result: A total of 375 preterm neonates were enrolled for the study, 207 were male. 223(59.46%) neonates were very preterm (28 -32 weeks) who received parenteral nutrition for a longer duration followed by 17 (4.53%) neonates were born as extremely preterm neonates (lesser than 28 weeks) rest 135 (36%) neonates were born as moderate preterm. Study population had average gestation age of 31± 5 weeks and birth weight of 1320 ± 680g. 196 preterm neonates were delivered via Lower segment cesarean section (LSCS). Neonates received TPN with a mean of 5± 3 days during their hospital stay. Correction of Electrolytes was done on daily bases. A total of 1259 bags of parenteral nutrition were prepared out of which 465 bags were neomaintaence and this was dispensed. There were no major problems identified for the prepared TPNs. Preterm neonates received TPN got discharged from NICU faster than others.
Conclusion: parenteral Nutritional care for preterm neonates is very well established at our Tertiary care unit. Therefore the study concluded that the parenteral nutrition support is more required for Very preterm neonates.

Keyword: Neonates, Total parenteral nutrition, Neonatal intensive care unit, Clinical Pharmacist.

G.6

Assessment of Individualized Dosing method for amikacin and vancomycin in hospitalized patients

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Objectives: To assess the individualized dosing method for amikacin and vancomycin in hospitalized patients

Methodology: This prospective study was conducted in a tertiary care hospital that included patients admitted to any ward and received either physician prescribed doses or calculated individualized doses of amikacin and/or vancomycin. The dose was calculated based on patient's body weight and renal function. Efficacy was assessed by time for resolution of infection, normalization of body temperature, cell counts and, length of hospital stay. Safety was assessed by actively monitoring for the occurrence of drug-related problems.

Results: A total of 70 subjects were enrolled for study. The average prescribed dose for amikacin and vancomycin were 916.66 ± 248.32 mg and 1518.18 ± 648.95 mg respectively, whereas the calculated doses were 873.41±159.9 mg and 1850.81 ± 709.08 mg respectively. About 35.7% of calculated doses were accepted and used. In prescribed-dose group for amikacin, overdose was higher 25 (67.5%) as compared to calculated-dose group. In prescribed-dose group for vancomycin sub-therapeutic doses were higher 6 (75%) than the calculated-dose group. In amikacin group, major interactions were identified with loop diuretics and piperacillin whereas in vancomycin group it was with amikacin, gentamicin, and piperacillin. In patients who received amikacin and vancomycin calculated doses, measured serum creatinine after therapy was significantly lower than those who received prescribed doses (p=0.0091 and p=0.049, respectively). The drug-related problems were higher in prescribed-dose group of both amikacin (75, 64.1%) and vancomycin (53, 76.8%) as compared to their respective calculated-dose groups [amikacin (42, 35.8%) and vancomycin (16, 23.1%)]. Electrolyte disturbances were the commonly observed adverse drug reaction in amikacin (33%) and vancomycin group (25%).

Conclusion: The safety and efficacy among the calculated-dose groups of both amikacin and vancomycin was high as compared to their prescribed-dose groups, however larger studies are required to validate the findings.

G.7

Evaluate the use of inhaled aminoglycosides by the criteria established from evidence based

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Aim/Objective: Aminoglycosides is a type of antibiotics for treating gram negative bacteria. There are some clinical researches showed some treatment benefit about inhaled antibiotics for ventilator-association pneumonia and reducing systemic adverse effects, but lack of clinical experiencing. The aim of this study is to establish a evidenced-base criteria and evaluate the use of inhaled aminoglycosides.

Methods: First, establish criteria for inhaled aminoglycosides. Second, conduct a retrospective study based on a hospital clinical database from 2016 to 2021. Any patients who were prescribed inhaled amikacin or gentamicin were included. Analysis of indications, bacterial culture results, concomitant use of other antibiotics, diagnosis, patient demographic variables. Finally, the self-defined criteria were used to evaluate whether the prescribing of inhaled aminoglycosides is reasonable.

Results: The self-defined criteria of inhaled aminoglycosides included the following:
1. Appropriate indications: pneumonia or respiratory infections with ventilator used.
2. The result of bacterial culture is P. aeruginosa or multi-drug-resistant (MDR) gram negative strains.
3. Inhaled aminoglycosides should be used as a adjunctive therapy.

There are 27 times (23 patients) inhaled aminoglycosides prescribed. 14.8% combine IV aminoglycosides and 66.7% combine other systemic antibiotics. The average usage is 8.8days. The average age of the 23 patients was 76, and 69.6% were male. 74.1% cases are diagnosed pneumonia. 18.5% has respiratory-associated infection. There are 25.9% with ventilator. As a result of bacterial culture, 74.1% are infected with Pseudomonas aeruginosa, and MDR strains was 66.7%. According to clinical self-defined criteria, 70.4% are evaluated as appropriate. Among the inappropriate use, 87.5% are used inhaled aminoglycosides alone, and the rest was not indicated or no bacterial growth.

Conclusion: Clinical evidence suggests that inhaled aminoglycosides are prescribed for respiratory-related infections, and more effective with gram negative strains infections. Inhaled aminoglycosides alone are not recommended. Pharmacists can evaluate the use of inhaled aminoglycosides based on this principle.

G.8

Comparative Effectiveness of Concurrent Radiotherapy with Cisplatin versus Cetuximab in Locally Advanced Head and Neck Cancer: A Population-based Cohort Study

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Aim/Objective: Locally advanced head and neck cancer is usually treated with concurrent systemic therapy and radiotherapy for functional preservation. The efficacy of concurrent radiotherapy with cisplatin (CRT) comparing cetuximab (BRT) was seldom demonstrated in clinical trials. We aimed to evaluate the effectiveness of CRT versus BRT among patients with locally advanced squamous cell carcinoma (LASCC) of the oropharynx, hypopharynx, and larynx.

Methods: A population-based retrospective cohort study was conducted using Taiwan's National Health Insurance Research Database. Patients newly diagnosed with oropharynx, hypopharynx, and larynx LASCC during 2011-2015 and received CRT or BRT within six months were included. We performed propensity score fine stratification (PSFS) and multivariate Cox proportional hazards model to evaluate the outcomes of interest, overall mortality, cancer-specific mortality (CSM), and time-to-treatment-failure (TTF). The hazard ratio (HR) and 95% confidence interval (95% CI) were shown, and a p-value less than 0.05 was considered statistically significant. The follow-up endpoint was when the outcome or the study end date (December 31, 2019) came first.

Results: The cohort consisted of 3,288 patients. Among them, 3,013 patients received CRT and 275 patients received BRT. After PSFS, 2,780 and 223 patients were in the CRT and BRT groups, respectively. The mean age was 67.7 years old, and males accounted for the majority (96%). The median follow-up time was separately 2.23 and 1.29 years in the CRT and BRT groups. For the overall mortality, the HR[95% CI] of BRT was 1.19[0.96-1.48] versus the CRT group, with a p-value of 0.12. The HR[95% CI] was 1.43[1.08-1.88] (p=0.012) and 1.30[1.11-1.52] (p=0.001) for CSM and TTF when comparing BRT group to CRT group, respectively.

Conclusion: Most patients received CRT in this situation. It indicated no significant differences in the effectiveness of overall mortality, but not CSM and TTF.

Keywords: locally advanced head and neck cancer; chemoradiotherapy; cetuximab.

G.9

Drug Utilization Evaluation of Entecavir

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Background: Hepatoma is the top ten cancer in Taiwan. In 2020, the number of people who died of liver cancer took second place. Seventy percent of these people had a history of hepatitis B. With the advance of drugs, treatment for HBV has been perfectly improved. According to the latest guideline published by the American Association for the Study of Liver Diseases (AASLD) in 2018, entecavir was superior to the traditional HBV drugs because of its lower rate of resistance and became one of the first line drugs.

Objectives: Entecavir is primarily excreted by the kidney, so the dose should be adjusted based on renal function. We analysed the patients who took entecavir in our hospital to evaluate the utilization of entecavir.

Methods: Screen all patients on entecavir from January to December 2021 to analyze the indication and if their renal function is monitored regularly and the dose of entecavir be adjusted based on renal function.

Results: In total, there are 350 patients were included. In this population, 196 (56%) patients took entecavir for treating active HBV, and 154 (44%) for prophylaxis of HBV reactivation because they were doing chemotherapy. There are 50 (14.3%) patients who did not make dose adjustment based on renal function, 24 of them was treating active HBV, and 26 of them was for prophylaxis of reactivation of HBV. Thirty-four (9.7%) patients had not monitored renal function for at least a year, 24 of them were treating active HBV, and 10 of them were for prophylaxis of reactivation of HBV.

Conclusions: According to the result, the number of patients who did not regularly follow up renal function or make dose adjustments was approximately 24%. Though there is no adverse drug reaction reported in these patients, healthcare professionals should notice that monitoring renal function and making dose adjustments is necessary to make sure medication safety of patients.

G.10

Treatment Persistence with Lipid-Modifying Agents after Percutaneous Coronary Intervention in Acute Coronary Syndrome Patient as a Predictor of Clinical Outcomes

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Background: Patients experiencing acute coronary syndrome (ACS) who went to their first Percutaneous Coronary Intervention (PCI) represent a high-risk population. Lipid management post-PCI is an important strategy for preventing complications and improving long-term clinical outcomes.

Aim/Objective: To assess the association between treatment persistence with lipid-modifying agents and clinical outcomes after PCI in Acute Coronary Syndrome (ACS) patients, adjusted by various patient characteristics at baseline.

Methods: A retrospective cohort study was conducted using medical record data from five hospitals with PCI facilities in Indonesia. Treatment persistence was evaluated for lipid-modifying agents (WHO ATC Code: C10). The primary clinical outcomes were major adverse cardiovascular and cerebrovascular events (MACCE) defined as a composite of all-cause death, myocardial infarction, stroke, and repeat PCI. Secondary clinical outcomes were cardiovascular death and hospitalization.

Results: In total, 367 patients were analyzed (85% male). The mean and standard deviation (SD) of the low-density lipoprotein cholesterol (LDL-C) level in all patients was 125.0 mg/dl (SD: 36.3). There was a significant association between non-persistence with lipid-modifying agents and the incidence of MACCE (RR 2.07, 95%CI = 1.04-4.10), recurrent PCI (RR 2.99, 95%CI = 1 .14-7.85), and hospitalization (RR 1.78, 95%CI = 1.01-3.15). The association of non-persistence with lipid-modifying agents and the incidence of MACCE was modified by active cigarette smoking (RR 5.11; 95%CI = 1.22-21.44), body mass index ≤ 25 kg/m2 (RR 3.21; 95%CI = 1.37-7.52), and diastolic blood pressure ≥ 80 mmHg (RR 2.56; 95%CI = 1.08-6.03).

Conclusion: Non-persistence of lipid-modifying agents predicts poor clinical outcomes after PCI in ACS patients with increased risk of MACCE, recurrent PCI, and hospitalization. Several factors that significantly increased the adjusted relative risk for MACCE were active cigarette smoking, body mass index, and diastolic blood pressure.

Keywords: treatment persistence, lipid-modifying agents, hypolipidemic, acute coronary syndrome

G.11

Drug utilization patterns during delivery and abortion episodes in women with systemic lupus erythematosus

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The appropriate disease control during pregnancy in women with systemic lupus erythematosus (SLE) is a key to a successful pregnancy outcome. At the same time, the medication with the possible teratogenicity should be carefully monitored. Therefore, this study assessed and compared the drug utilization patterns of delivery and abortion episodes for better understanding of the successful pregnancy in SLE patients.

A drug utilization study was conducted using the National Health Insurance Service database of Korea between 2002 and 2018. The pregnancy episodes were included in the study if 1) women of childbearing age (15-49 years), 2) records of HIRA procedure codes for delivery or ICD-10 codes for abortion, 3) the conception between 2010 and 2017, 4) at least two years of SLE diagnosis before the conception date. The frequency of SLE medications for disease control as hydroxychloroquine (HCQ), methotrexate (MTX), mycophenolate mofetil (MMF), and cyclophosphamide (CYC) was mainly examined during the pre-conception period (12 months before conception) and pregnancy period. We compared and assessed the trend of medications from pre-conception (PC) to pregnancy period (PP) for delivery and abortion episodes.

A total of 2,752 pregnancy episodes of SLE patients were included in this study. The increase in HCQ use was observed from PC to PP in delivery episodes. However, it decreased in abortion episodes. All other immunosuppressants were maintained or discontinued in delivery and abortion episodes. MTX and MMF prescriptions were more prevalent in delivery episodes than abortion episodes. A higher prevalence of intravenous and oral steroids during both PC and PP was noted in the abortion episodes than in delivery episodes.

The prevalence of MTX and MMF was higher, and steroid use was lower in abortion episodes. It implies that abortion episodes require more steroids for uncontrolled SLE. Further studies are needed on disease activity and successful pregnancy outcomes.

G.12

Factors affecting outcomes in patients with Multidrug-resistant gram-negative sepsis

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Background: The prevalence of infections due to multi-drug resistant bacteria especially in low and middle-income countries is on a surge.

Aim: To assess the clinical profile, treatment pattern, and outcomes in MDR gram-negative sepsis and assess the factors affecting mortality among this cohort of patients.

Methodology: This retrospective observational study evaluated the outcomes of all consecutive patients hospitalized for gram-negative sepsis from January 2016 to December 2020. Univariate and multivariate linear and logistic regression analyses were conducted in SPSS v20 to identify significant predictors of outcomes.

Results: A total of 589 patients (387 males and 202 females) with a mean age of 55.55±15 years were included in the study. Fever (56%), leucocytosis (56%), and tachycardia (41.3%) were the common clinical presentations. Comorbidities observed were Type II diabetes mellitus (41.4%) and hypertension (35.8%) followed by liver diseases (14.8%) and malignancy (14.9%). Liver complication (77.2%) and acute respiratory distress syndrome (76.4%) were major complications followed by cardiac (69.8%) and septic shock (51.1%). Mortality rate was 68.3% in our study group. The mean number of hospitalization and mechanical ventilation days was 14.02±11.34 and 2.88±1.08 days. Albumin levels [OR:4.748(1.135-19.851)] was an independent predictor of mortality in sepsis patient. Factors such as fever (p=0.0230), tachycardia (p=0.004), multiple or extensive drug antibiotic resistance (p=0.007), and immunocompromised nature of patients (p=0.008) were significant factors affecting ICU-free days. Serum creatinine (p=0.000), creatinine clearance (0.001), urine protein (0.045), tachycardia (p=0.032) and intermediate-acting steroids (p=0.000) were significant factors affecting mechanical ventilation free days.

Conclusion: A comparably high mortality rate in sepsis patients was observed in our study. Albumin was an independent predictor of mortality. Other factors such as the immunocompromised nature of the patient and multiple or extensive antibiotic resistance were significantly affecting ICU-free days whereas renal function parameters and intermediately acting steroids were significantly affecting mechanical ventilation-free days.

G.13

Assessment of empirical antibiotic therapy and determinants for its initiation in hospitalised COVID- 19 patients: a retrospective study

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Objectives: To study the patterns and identify the predictors for initiation of empirical antibiotic therapy in hospitalised moderate to severe COVID-19 patients.

Methods: A single-center retrospective study was conducted by enrolling all hospitalised moderate to severe COVID-19 patients. The patients were classified into two groups, one initiated on antibiotics empirically (<48hrs) and other who were not initiated or given antibiotics later on(>48hrs). Those initiated on antibiotics were further subclassified based on the severity of COVID-19. The independent and dependent variables were identified to develop a prediction model for initiating empirical therapy in hospitalized patients. The predictors were analysed using multivariate logistic regression.

Results: The majority [n= 371 (83.2%)] of hospitalized patients with COVID-19 were prescribed early empiric antibiotic therapy, with 23.5% having an unknown indication for initiation. Clinical manifestations of bacterial infection/pneumonia was the major factor for initiation of anti-bacterial therapy in moderate [n=44 (45.3%)] and severe Covid [n=153 (55.8%)] cases. Ceftriaxone was the most prescribed empiric antibiotic in the moderate group [n=65 (67.01%)], while piperacillin-tazobactam was for the severe group [n=136 (49.64%)]. Descriptive statistics and risk estimation were performed for factors that could predict the use of empirical antibacterial therapy. On multivariable analysis, severity of the disease [2.475(1.385-4.424), p=0.002], abnormal x-ray manifestations [3.516(1.881-6.572), p<.001], positive procalcitonin [5.930(2.254-15.596), p<.001] and higher CRP levels [1.006(1.001-1.011), p=.0025] were found to be statistically significant predictors for initiation of empirical antibiotics.

Conclusions: The study gives insight into the early empiric antibiotic usage pattern amoung hospitalised COVID-19 patients. The prediction model could help in identifying patients in whom empirical therapy is likely to be initiated. Thus, help in designing a protocol for the management of hospitalised COVID-19 patients.

G.14

Irregular Blood Glucose Control Status Alter the Risk of Low Awareness of Diabetes Mellitus Medication in Indonesia

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Introduction: Low awareness of medication is common among patients with diabetes mellitus due to their lack of understanding of the disease. Therefore, it is essential to determine the underlying risks influencing low awareness to design effective intervention strategies. This study aims to evaluate the association between modifiable factors and non-modifiable factors to low awareness of diabetes mellitus medication in Indonesia.

Method: Retrospective data were obtained from the Indonesian Family Life Survey (IFLS-5), the national cross-sectional population-based survey among respondents with diabetes mellitus aged ≥15 years. Diabetes mellitus status was confirmed by HbA1c testing, while sociodemographic and other health-related information was obtained from self-reported data. Gender, age, education level, marital status, economic status, comorbidity, religiosity, residence, and health insurance status are considered as non-modifiable factors. While smoking habits, blood glucose control, sleeping problems, depression status, having a general medical check-up, satisfaction with health care needs, and happiness status were considered as modifiable factors. Logistic regression analysis was used to evaluate the association between low awareness of diabetes mellitus medication to modifiable and non-modifiable factors adjusting for confounders. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported.

Result: Most of the 706 respondents were women (58.8%) and aged 55-65 years (28.8%). Most of them showed low awareness of diabetes medication (87.7%). Irregular blood glucose control (adjusted OR: 29.6, 95%CI 15.20—57.75; p-value<0.001) and having 1-3 comorbidity (adjusted OR 3.00, 95%CI 1.59—5.48; p-value 0.001) were significantly associated with low awareness of diabetes medication.

Conclusion: Irregular blood glucose control status alter the risk of low awareness of diabetes mellitus medication. Therefore, our findings reveal a need to develop intervention strategies targeting those who irregularly control their blood glucose level and those with multiple comorbidity.

Keywords: low awareness medication, diabetes mellitus, blood glucose control

G.15

Trends in incidence of ischemic stroke and antiepileptic drug use after a stroke admission

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Aim/objectives: Post-stroke epilepsy is an important complication which may increase the risk of recurrent stroke and mortality. However, there are no clinical guidelines on the appropriate use of antiepileptic medications in post-stroke cohorts. This study aimed to investigate trends in incidence rates of ischemic stroke and examine the patterns of antiepileptic drugs (AED) in people with ischemic stroke in Victoria, Australia.

Methods: Retrospective cohort study was conducted using the victorian linked health database. Patients aged ≥30 years old and discharged from Victorian hospitals following ischemic stroke between July 2012 and June 2018 were included. Age-standardised incidence rates of ischemic stroke between 2012/13 and 2017/18 were estimated and the annual trend was assessed using log linear regression model. The average Daily Defined Dose (DDD) of AED dispensed per person per day during one year follow-up after discharge was also estimated. Generalised linear model was used to analyse factors associated with DDD of AED.

Results: Trend in the incidence of ischemic stroke was relatively constant over time in Victoria (Annual percentage change (APC) -0.02; 95% confidence interval (CI) -0.84 – 0.80). A statistically significant decrease in the incidence was observed in females (APC -0.64; 95% CI -1.22 – -0.004) whereas a no changes were observed in males over time (APC 0.42; 95% CI -1.03 – 1.90). Overall, the average DDD per day declined from 0.63 DDD per day per person in 2012/13 to 0.54 DDD per day per person in 2016/17. After adjusting for other factors, having neurological diseases was positively associated with DDD of AED. Female and types of AED were negatively associated with DDD of AED.

Conclusion: Overall, no significant change in the incidence of ischemic stroke was observed whereas the stroke incidence significantly declined in females. The amount of AED dispensed after stroke has declined over time.

G.16

Evaluation of The Drug Rational Use for Tenofovir

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Background: In 2019, WHO reported hepatitis B resulted in an estimated 820,000 deaths. Treatment chronic hepatitis B infection can slow theprogression of cirrhosis, reduce the incidence of liver cancer and improve long-term survival. TreatedHepatitis B oral agents, including Tenofovir disoproxil fumarate (TDF, Viread®), Tenofovir alafenamide (TAF,Vemlidy®). With the side effects of nephrotoxicity and bone loss,

Objectives: TDF (Viread®) according to package insert's suggest Clcr ≥50 ml.min: 300 mg every day; Clcr 30-49ml/min: 300 mg every 48 hours; ClCr 10-29 mL/min: 300 mg every 72-96 hours; CrCl < 10 mL/min: shouldavoid use. TAF (Vemlidy®) is based on package inserts's suggest CrCl < 15 mL/min: Use is notrecommended. The purpose of this study is to evaluate renal function and drug use.

Methods: This study recruited patients who have prescribed Tenofovir between January 2021 and December 2021with written informed consent in the Taichung Tzu Chi Hospital. Analysis on the data whether adjusts thedose of drugs according to the renal function of the individual case, and evaluates the safety of Tenofovir.

Results: This study recruited 344 patients, whose average age was 57.09± 10.92. Thedisease progressed to cirrhosis in 73 patients (21.2%) and liver cancer in 55 patients (16.0%). Prescribed Tenofovir (93 used TDF (Viread®), 251 used TAF (Vemlidy®), of which 334 patients (97.1%) had goodrenal function didn't adjust was required, while 12 patients (3.4%) should be adjusted Tenofovir's dosageaccording to the renal function of cases. Among 12 patients, 4 patients (1.2%) adjusted the frequency ofdrug use correctly, 6 patients (1.7%) didn't adjust the drug dose according to renal function, and 2patients (0.5%) used Tenofovir inappropriately.

Conclusions: According to the renal function of individual cases and package insert's suggestion, had 2.2%inappropriate use Tenofovir. In the future, we recommend that clinicians must consider the patient'srenal function when prescribing Tenofovir to protect the patient's medication safety.

G.17

Use of Drugs Among Pregnant Women: A Nationwide Database Linkage Study in Taiwan

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Objective: To assess utilization patterns of all drugs among pregnant women in Taiwan.

Methods: By linking Taiwan's National Birth Certificate Application Database with National Health Insurance Database, 2,322,274 pregnancies resulting in live births or stillbirths between 2005 and 2017 were identified. All drugs except those for topical use were assessed and classified according to the Anatomical Therapeutic Chemical (ATC) classification. The prevalence of drug use and the most frequently prescribed drugs among pregnant women were assessed, and drug utilization patterns between different calendar years and different pregnancy periods (84 days before pregnancy, each trimester during pregnancy, and 84 days after delivery) were compared.

Results: In 2017, 95.9% of the pregnant women received at least one drug during pregnancy, and the prevalence of drug use was highest during the 1st trimester (83.8%), followed by the 2nd (78.0%) and the 3rd trimesters (71.7%). In addition, increasing trends in drug use during the 2nd and 3rd trimesters were observed from 2005 to 2017. Compared to their prevalence in the 84 days before pregnancy, the prevalence of use of several drug classes increased during pregnancy (e.g., antianemic preparations in all trimesters, sex hormones in the 1st trimester, and gynecologicals and calcium channel blockers in the 2nd and 3rd trimesters), whereas the prevalence of use of some drug classes (e.g., anti-inflammatory agents) decreased during pregnancy. The most commonly prescribed drugs during pregnancy were paracetamol, progesterone, and ritodrine. However, among the top 10 most commonly prescribed drugs in pregnancies, several drugs were found to be classified as "human data suggest risk during pregnancy" or "limited human data" by the literature, such as pseudoephedrine and domperidone.

Conclusion: The use of drugs during pregnancy was very common among pregnant women in Taiwan. Several drugs warranted future investigation to ensure safe and rational use of drugs during pregnancy.

G.18

Utilization Patterns of Intravenous Immunoglobulin under National Health Insurance System in Taiwan

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Aim/Objective: Intravenous immunoglobulin (IVIG) has been covered by National Health Insurance (NHI) scheme in Taiwan for decades, with the indication for infectious and inflammatory diseases. In recent years, the reimbursed indication of IVIG has been expanded to neurology diseases such as Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy. The study aims to investigate the clinical usages and patterns of IVIG.

Methods: Patients with incident IVIG prescriptions (Anatomical Therapeutic Chemical code: J06BA02) during hospitalization in 2018-2019 were identified from the National Health Insurance Research Database (NHIRD). One-year wash out period was applied. IVIG-related indication was defined by diagnosis with the International Classification of Disease codes, tenth revision. Patients were further categorized into adults (>18 y/o) and children (<=18 y/o) groups. Study findings were summarized using descriptive statistics to investigate the indications for first IVIG use and the clinical patterns of IVIG use.

Results: During 2018 to 2019, a total of 3,929 incident IVIG users were identified, with 71.2% (n=2,798) of children. Among children, the common indications for IVIG were Kawasaki disease (n=1,694, 60.5%), idiopathic thrombocytopenic purpura (ITP; n=160, 5.7%) and enterovirus complications (n=125, 4.47%). The indications for IVIG use varied in adults. Hematological malignancy (n=156, 13.8%), ITP (n=108, 9.6%) and primary or secondary immune deficiency (n=40, 3.5%) were three commonly used indications, while 58.7% of adults were likely to be off-label use.

Conclusion: The patterns of IVIG use were different between adults and children. Autoimmune disease was the main indication for IVIG use in children group. With regards of high cost of IVIG and the dosage may vary with different indications, the clinical use of IVIG should be further investigated and monitored to assist the control of NHI expenditures.

Keywords: Intravenous immunoglobulin, Treatment Patterns, National Health Insurance Research Database

G.19

Findings from the National Health Interview Survey on Online Prescription Filling Behavior Among American Adults with Chronic Conditions, 2009-2018

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Aim/Objective: This study investigated (1) the trend, prevalence, and utilization rate of online prescription filling among patients with chronic conditions (by the number of chronic conditions and the specific condition) and (2) to evaluate the association of participants' characteristics and online prescription filling behavior.

Methods: Data from the 2009 to 2018 National Health Interview Survey were used for this study. The online prescription filling behavior was defined as respondents who self-reported to fill a prescription using the Internet during the survey year. We analyzed the prevalence of online filling behavior by multiple chronic conditions (MCC), one chronic condition (OCC), and no chronic condition (NCC) groups. Prevalence and trend differences in 10 different chronic conditions were reported. The association between online prescription filling behavior and sociodemographic characteristics (i.e., age, gender, race/ethnicity, education, region, family income, health insurance coverage, and perceived health status) was analyzed using chi-square tests. Multivariable logistic regression models were conducted to identify factors associated with online prescription filling behavior.

Results: In the U.S., the prevalence of online prescription filling had significantly increased in all three groups: NCC (4.3% to 8.5%), OCC (7.5% to 13.2%), and MCCs (8.1% to 15.5%) (P<.001). People with asthma (14.3 %) were most likely to fill prescriptions online compared to patients with the nine other chronic diseases. Stroke patients, on the other hand, were less likely to fill prescriptions online (7.7%). MCC patients, aged 50-64 years old, female, white, married or lived with a partner, had higher education, job, higher income, and insurance coverage were significantly more likely to report to fill a prescription online.

Conclusion: Patients with chronic conditions increasingly rely on online filling services. Healthcare providers should be aware of the growing popularity of online prescription filling and ensure drug safety in patients with chronic diseases.

G.20

Factors Associated with Requirement of Non-steroid Anti-inflammatory Drugs as Add-on Therapy with Oral Sumatriptan for Migraine Attacks and Effectiveness Analysis

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Migraine is a common disabling headache disorder widely prescribed triptans as acute treatment medications. However, previous studies demonstrated that 30 to 40% of triptan users did not reach a sufficient response. Physicians attempt to overcome it by adding non-steroidal anti-inflammatory drugs (NSAIDs). Though, it is worth noting the excessive usage of analgesics may rise medication-overuse headaches, primarily in migraineurs. This study was to investigate the associated factors regarding the requirement of NSAIDs as add-on therapy with oral sumatriptan and of the attack frequency after combinations.

This is a retrospective cohort research via data collections from the outpatient of the Taipei Veterans General Hospital. Migraineurs who were with oral sumatriptan prescriptions from neurologists as sole acute medication from 2018/7/1 through 2020/12/31 were recruited. Factors associated to the requirements of NSAIDs as an add-on therapy of oral sumatriptan within 6 months were recognized through logistic regression. Generalized linear model was applied to examine the discrepancies in the average monthly migraine attacks after the combination therapy.

Among the 859 patients analyzed for associated factors, 160 of them required NSAIDs as combination therapy. Result showed that patients with acute medication overuse (OR 1.565,95% CI 1.040, 2.354) and proton-pump inhibitors (PPIs) utilization (OR 2.060, 95% CI 1.024, 4.143) were the significant associated factors. With every 1-attack increase before combination therapy, reflecting on the 0.6-attack increase after combination therapy; female would get more 1.2 attacks than male, and every 1-day postpone to initiate the combination therapy, would result in more 0.01 attack.

Migraineurs using oral sumatriptan with acute medication overuse and PPIs utilization were at higher risk for the requirement of NSAIDs as add-on therapy for acute migraine attacks. Attack frequency after combination therapy was significantly affected by the attack frequency before combination, gender, and the timing about initiation of combination therapy.

keyword; migraine, sumatriptan, NSAIDs

G.21

Prescription pattern of nonsteroidal anti-inflammatory drugs among patients with CKD stage 3-5 in a district hospital

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Aim/Objective: The main goal of chronic kidney disease (CKD) management is to prevent progression to end-stage renal disease. Non-steroidal anti-inflammatory drugs (NSAIDs) may lead to kidney injury. Therefore, current guidelines do not recommend long-term use of NSAIDs for these patients. Our study aimed to elucidate the prescriptions patterns of NSAIDs among patients with CKD stage 3-5 in a district hospital over a 2-year period.

Methods: A cross-sectional study was conducted from May 2020 to April 2022 using a database that consisted of electronic medical records. Outpatients with an estimated glomerular filtration rate <60 ml/min/1.73m² were enrolled and classified by CKD stages. We defined prolonged NSAIDs use as inappropriate prescription according to consensus criteria from Taiwan Society of Nephrology and Health Insurance Administration. We estimated the prevalence of NSAIDs prescriptions as an outcome. Among patients receiving inappropriate prescriptions, we evaluated the prescription prevalence in CKD stages and different clinical departments.

Results: During the study period, 16,335 outpatients (CKD stage 3a: 44.3%, 3b: 23.8%, 4: 13.0%, 5: 18.9%) were included and 1,134 (6.9%) patients received NSAIDs with a mean age of 71.1 (±11.8). As for NSAIDs prescriptions, 903 (79.6%) were considered potentially inappropriate. Of these 903 prescriptions, 39.8% were prescribed by orthopedics, followed by rheumatologists (20.8%). The prescription prevalence of NSAIDs was 5.7%, 6.8%, 5.0% and 4.0% in CKD stage 3a, 3b, 4 and 5, respectively. The most common NSAIDs were celecoxib (48.0%), followed by etoricoxib (18.4%) and diclofenac (8.6%).

Conclusion: We evaluated the patterns of NSAID prescriptions to CKD patients. In high-risk patients, especially in older CKD patients, prolonged NSAID use should be avoided. Pharmacists need to notify their physicians of potentially inappropriate prescriptions. Further alerts system embedded in hospital information system would be an option to remind the health care providers.

Keywords: prescription pattern, NSAID, chronic kidney disease, prescription prevalence

G.22

Metformin use and associated clinical outcomes in COVID-19 patients with diabetes: a retrospective cohort study

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Objective: To assess the effect of metformin on clinical outcomes including in-hospital mortality in diabetics with COVID-19.

Methods: A retrospective cohort study was conducted with 261 diabetic patients who have COVID-19 hospitalized between 1st April 2020 and 31st March 2022 in a tertiary healthcare facility. Patients with metformin or its combination were selected as the study cohort (SC; n= 141), and other antidiabetic drugs were the reference cohort (RC; n=120). Odds ratio (OR) were calculated for the risk estimation and chi-square test and unpaired t-tests were performed to associate metformin use with the severity of COVID-19 and mortality.

Results: The average age of SC and RC were 53.11 ± 8.1 and 54.3 ± 8.0 years, respectively. The majority (70.4%) of the subjects were men and the mean hospital stay of the study and the reference cohorts were 12.7± 5.9 days and 12.6± 5.9 days, respectively. Individuals with severe disease have a higher risk of death than individuals with mild/moderate disease (OR: 59.18, 95% CI: 7.8891- 443.9107; p <0.01). A significant association was found between metformin use and duration of hospitalization (p<0.01); and between metformin use and reduced mortality rate (χ^2: 23.685; p=0.009). A lower occurrence of death was found in SC (2.1%) than RC (20.8%). The risk estimation shows that metformin is a protective factor against mortality in diabetics with COVID-19 (OR: 0.0826, 1/OR: 12.11, 95% CI: 0.0242 – 0.2814). The calculated number needed to treat (NNT) for metformin was 5.3.

Conclusion: We found a lower incidence of death in SC than in RC, indicating a lower mortality rate among metformin users. The study concluded that metformin has a protective effect against mortality in diabetics with COVID-19. Therefore, the study warrants using metformin in all diabetics with COVID-19 when tolerable.

Keywords: Metformin; Mortality; Diabetes; SARS-CoV-2

G.23

The efficacy of two different doses of dexamethasone in COVID-19 patients: A systematic review and meta-analysis

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Objective: To evaluate the efficacy of dexamethasone in moderate to severe and critically ill COVID-19 patients and to compare the efficacy of the low dose versus the high dose of dexamethasone in this population.

Methods: We searched PubMed, Embase, Scopus, and Web of Science for articles published from December 2019 to September 2021 to identify randomized controlled trials (RCTs) that evaluated the efficacy of dexamethasone in moderate to severe and critically ill COVID-19 patients. Outcomes of interest were mortality and medical ventilation requirements. Subgroup analyses of different doses were performed in this meta-analysis to compare the efficacy of low-dose versus high-dose of dexamethasone.

Results: Four studies were included with a total of 7,824 patients. Dexamethasone significantly reduced the rate of mortality (RR 0.85, 95% CI: 0.78–0.93, p = 0.0004). The number of days alive and free from mechanical ventilation in patients treated with dexamethasone was significantly higher than that of the control group (6.6 vs 4.0 days, p = 0.04). Mortality rates were not significantly different between patients treated with high-dose dexamethasone (12-16mg) and those with the low-dose (6mg) (28.3% vs 32.9%, RR = 1.16, 95% CI: 0.96–1.38, p = 0.12).

Conclusion: In moderate to severe and critically ill COVID-19 patients, dexamethasone substantially reduced mortality and medical ventilation requirements. High-dose of dexamethasone was not superior to the low-dose in reducing mortality. More studies which comprehensively investigate the efficacy and safety of high-dose versus low-dose of dexamethasone are needed to optimise the use of dexamethasone in COVID-19 patients.

Keywords: dexamethasone, COVID-19, efficacy

G.24

Prevention of venous thromboembolism in patients undergoing lower limb orthopedic surgery in a Vietnamese hospital

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Objective: To investigate the risk of VTE, the appropriateness of VTE prophylaxis and its associated factors in patients undergoing lower limb orthopedic surgery.

Methods: A cross-sectional study was conducted at Gia Dinh People's Hospital. Data was collected from medical records of patients aged 18 years or older undergoing lower limb orthopedic surgery between March 1st 2020 and June 30th 2020. VTE risk was stratified using the Caprini Risk Assessment Model, contraindications to anticoagulation and the appropriateness of thromboprophylaxis were evaluated according to current guidelines. Multivariate logistic regression analysis was used to determine factors associated with the appropriateness of VTE prophylaxis.

Results: A total of 217 patients was included, the median age was 54 (37 - 66) and 57.6% of patients were male. There were 80.2% of patients at risk of VTE. Pharmacological prophylaxis was properly indicated in 43.4% of patients. Overall rate of appropriate VTE prophylaxis was 35.0%. Patients with age ≥ 41, BMI > 25 kg/m2, surgical duration > 45 minutes, plaster cast or screw splint were less likely to receive appropriate VTE prophylaxis; patients with hospital stay greater than four days after surgery got more chances to have proper VTE prophylaxis ($p < 0.05$).

Conclusion: The majority of patients undergoing lower limb orthopedic surgery were at risk of VTE, but the overall rate of appropriate VTE prophylaxis was low. Suitable interventions are needed to improve the appropriateness of VTE prophylaxis.

Keywords: venous thromboembolism (VTE), orthopedic surgery, thromboprophylaxis.

G.25

Clinical Pharmacists Interventions in Neonatal Intensive Care Unit of a Tertiary Care Hospital: A prospective Interventional study

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Background: The neonatal drug therapy is rapidly changing. In addition, the risk of drug-related problems (DRPs) and medication incidents (MIs) is high among neonates.

Aim: To review the drug use pattern, assess the incidence and determine the predictors of DRPs and MIs in neonatal intensive care unit.

Methods: The prospective interventional study was conducted in the neonatal intensive care unit of a south Indian hospital for a period of 9 months by enrolling neonates admitted over there based on the study criteria. Treatment chart of the study population was reviewed on daily basis to identify the DRPs and MIs. The utilisation review was performed as per the WHO core drug use indicators. Comparing the drug use with standard drug information resources identified the DRPs and / or MIs and appropriate intervention was initiated. The predictors for DRPs and MIs were identified following logistic regression analysis.

Results: A total of 200 neonates were included. The median (IQR) number of drugs per encounter was 4 (3-7). The incidence of off-label drug use was 28.2%. The incidence of DRPs and MIs was 67% and 39% respectively. Neonates delivered by lower segment caesarean section, APGAR score less than 7 at 5th minute, extremely preterm (P value 0.0001), extremely low birth weight (P value 0.0001), upper middle, upper lower & lower middle socio-economic class (P value 0.0001), NICU stay for more than 15 days (P value 0.0001), more than two diagnoses (P value 0.0001), use of more than 5 medications (P value 0.0001), were the predictors of DRPs and MIs.

Conclusion: The individual drug use indicators suggest that there is a need to improve the drug prescribing by generic names. Almost one-third of the drugs used were off-label and there is a need to evaluate the rationality before using off-label drugs among this special population.

G.26

Drug Utilization Evaluation of Opioid Analgesics in a Tertiary Care Cancer Centre

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Objective: To assess the prescription pattern of opioid analgesics at the time of hospitalization in a cancer care center.

Methodology: The study was conducted after ethics approval in a tertiary care cancer center. Electronic medical records were reviewed retrospectively for opioid prescriptions. The prescriptions of opioids were comparatively assessed for their drug utilization pattern. The test for the association between continuous and categorical data was assessed using the student t-test and chi-square test.

Results: Among 828 patient records audited, 428 (52%) were female patients. Overall mean (SD) age was 54.2 (13.6) years, and hospital length of stay was 6.98 (5.94) days. 49% of the patients were prescribed with more than one opioid. The primary cancer was found in gastrointestinal (41%), gynecological (14%) and in breast (12%). Among the included patients 40% were diagnosed with advanced cancer. More than 49% of the prescriptions had more than one opioid. 21% of the patients had two opioids included in their prescription. The commonly prescribed analgesics were tapentadol (55%), followed by fentanyl (45%) in patients with advanced cancer whereas, the overall preferred analgesics were fentanyl (37%) and tapentadol (35%) among the included patients. The highest prescribed concomitant drug along with opioids was found to be pantoprazole (12.4%). In this study analysis, almost 50% of the patients either received fentanyl citrate or tapentadol during the overall treatment.

Conclusion: The most prescribed opioids were identified to be Fentanyl (37%), Tapentadol (35%), and Morphine (18%). The frequent choice of concomitant medications was pantoprazole (12%), paracetamol (8%), and glycopyrrolate (6%). The mean length of stay was 6.98 days among the cancer patients. Future assessment of the prescription pattern of opioids in specific cancer populations is required to identify the outcomes based on the type of cancer.

Keywords: Opioid analgesic, Cancer, Prescription, Palliative care

G.27

Adherence of Methadone Medication Treatment and the Association with Risk of Re-offense Among Patients with Opioid Use Disorder

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Aim/Objective: To compare the risk of re-offense in patients with opioid use disorder with different adherences to methadone medication treatment.

Methods: We conducted a retrospective cohort study by analyzing data from Drug Abuse Case Management System. We included patients who were newly enrolled in methadone maintenance treatment (MMT) program for opioid use disorder (OUD) with a least one record of offense. The new MMT was defined as no record of MMT for 6 months before the first MMT. We calculated patients' adherence by the proportion of the number of days with MMT within 90-day after the first MMT, and classified patients into adherent group (≥ 80%) or non- adherent group (<80 %). We performed intention-to-treat analysis and followed up patients from the 91st date after the first MMT to the re-offending, dead or the end of the study (on December 31, 2020). We performed Cox proportional hazards regression to compared the risk of re-offense between the two groups. We changed the 90-day to 180-day windows and the cut point of 80% to 70% for adherence and respectively repeated the analyses to examine the robustness of results.

Results: We identified 643 patients with average age 46.4 (SD 6.98) years and 90% were male. Comparing with adherent group, the non-adherent group had higher risk of re-offense (HR, 1.29; 95% CI, 0.88-1.87), although no statistical significance. We found consistent results when we changed to 180-day window (1.32; 0.85-2.05) or changed the cut point to 70% (1.25; 0.84-1.85) for the classification of adherent group.

Conclusion: We found patients with better adherence MMT may associate reduced risk of re-offense. Future study with large sample size is required to obtain more definitive conclusion.

G.28

The anticholinergic drug utilization pattern among adult patients with cirrhosis in Taiwan

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Objective: To describe trends in the use of anticholinergic drugs among adult patients with liver cirrhosis in Taiwan.

Methods: This retrospective cohort study was conducted for cirrhotic patients aged 20 and over between January 2008 and December 2014 by using Health and Welfare Database. The main analysis would describe the overall drug utilization and the trends of anticholinergic drug use in each drug class including antiarrhythmic drugs, antihistamines, antidepressants, antiepileptics, antivertigo/antiemetic agents, antiparkinson agents, antipsychotics, bladder antimuscarinics, skeletal muscle relaxants, gastrointestinal antispasmodics, and antimuscarinic bronchodilator drugs. The joinpoint regression analyses were adopted to analyze the average annual percent change of anticholinergic drug use.

Results: This cohort study included 185,084 cirrhotic patients (≥ 20 years), and 93.2% of them had at least one prescription of any anticholinergic drug between 2008 and 2014. The prevalence of anticholinergic use among these patients increased over time, with 1.1% of average annual percent change (p-value < 0.001). Among drug users, antihistamines were the dominant drug class, especially diphenhydramine. We further analyzed the utilization pattern in each drug class among users. We found that there was a statistically significant rise in the percentage of the use of antipsychotics (p<0.001), bladder antimuscarinics (p=0.033), and antimuscarinic bronchodilator drugs (p<0.001) among drug users across 7 years.

Conclusion: The current findings of this study showed that most of the patients with cirrhosis took at least one anticholinergic drug between 2008 and 2014. The percentage of drug utilization among cirrhotic patients rose during the 7-year period. Antipsychotics, bladder antimuscarinics, and antimuscarinic bronchodilator drugs had increasing proportions in the user population. Therefore, we should pay attention to the subsequent drug effects of anticholinergic drugs with an increasing trend.

Keywords: anticholinergic drug, cirrhosis, utilization, trend analysis

G.29

MONO, DUAL VERSUS TRIPLE THERAPY AND 1-YEAR OUTCOMES IN HEART FAILURE PATIENTS FROM MANIPAL HEART FAILURE REGISTRY

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Background: Drugs are the mainstay of heart failure (HF) therapy. Although several guidelines are available in this regard, optimal implementation of guideline-directed medical therapy (GDMT) still remains a challenge.

Purpose: Assessment of drug prescription patterns and their effect on clinical outcomes among patients with heart failure enrolled in Manipal Heart Failure Registry (MHFR).

Methods: MHFR is a prospective, observational cohort of patients with heart failure in a tertiary health center in southern India. From this registry, we analyzed drug utilization patterns over a period of one year from index admission and correlated them with clinical outcomes.

Results: A total of 1354 patients with a mean age of 65 ± 13.6 years were enrolled in MHFR from September 2015 to September 2017. The average duration of index hospitalization was 5.3 days and 40.2% were females. Heart failure with reduced ejection fraction (<40%) was seen in 51.1% of patients.
Patients received disease-modifying drugs like beta-blockers (BBs), angiotensin-converting enzyme inhibitors (ACEIs), or angiotensin receptor blockers (ARBs) and aldosterone receptor antagonists (ARAs) at rates of 43.6%, 49.3%, and 34.3% respectively. Dual therapy (BB and ACE or ARB) was used in 36.7 % and triple therapy (BB, ACE or ARB and ARA) in 31.2%.
Unscheduled visits and re-hospitalization rates were 34.8% and 11.2% respectively. All-cause mortality during index hospitalization and at one-year mortality was 8.8% and 16.5% respectively. The composite clinical outcome occurred in 32.1%.
Patients who received monotherapy (BB or ACEI/ARB or ARA) had a better outcome compared to those who did not (p=0.021). Dual and triple therapy was associated with better outcomes compared to monotherapy (p=0.002).

Conclusion: GDMT improves outcomes in patients with HF but is underutilized in patients with HF. Steps to improve the use of GDMT need to address the factors associated with underutilization.

G.30

Burden of pneumococcal disease in adults – A retrospective database study in South Korea

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To examine hospitalized incidence, case fatality rate (CFR), healthcare resource utilization and costs associated with pneumococcal diseases including invasive pneumococcal disease (IPD) and pneumonia in adults before and after introduction of 13-valent pneumococcal conjugate vaccine (PCV13) into childhood immunization program (CIP) in 2014.

Data of eligible adults (≥18 years) was extracted from the National Health Insurance Database during 2010-2019 in Korea. The Korean version of International Classification of Diseases codes were used for case identification. Bacteremia without identifiable focus, bacteremic pneumonia and meningitis were considered as IPD. Study findings were summarized using descriptive statistics, and compared pre- (2010-2013) and post-introduction of PCV13 (2015-2019). Incidence time trends were assessed with interrupted time series analyses (ITSA).

Overall, 1,682 IPD and 8,635 pneumonia episodes were included. Annual hospitalized incidence rates of IPD and pneumonia were 0.4 and 2.1 episodes per 100,000 person-years, respectively. Incidence rates were higher in patients ≥65 years than those 18 to <65 years (IPD: 1.9 vs. 0.1; pneumonia: 8.2 vs. 0.9 episodes per 100,000 person-years). For IPD, ITSA showed no significant difference in incidence rate between pre- and post-PCV13 periods. However, incidence rate was significantly higher in the post-PCV13 period for pneumonia. CFR of IPD and pneumonia were 14.9% and 3.0%, respectively. For IPD, the median length of hospitalization per inpatient visit appeared lower in the post-PCV13 period (range 13.5-14.0 days), compared with pre-PCV13 period (range 17.0-20.0 days). However, for pneumonia, no significant difference was observed. The average total (inpatient and outpatient) costs per episode ranged from 5.5-8.0 million (pre-PCV13) and 5.7-8.5 million (post-PCV13) South Korean Won (KRW) for IPD, and 2.7-3.6 million (pre-PCV13) and 3.1-5.2 million (post-PCV13) KRW for pneumonia. Disease burden was generally higher in older patients ≥65 years.

After PCV13 introduction into CIP, incidence of IPD remained stable, while incidence of pneumonia had increased in Korea.

G.31

Title: Estimation of healthcare costs among Japanese patients with terminal cancer using the national database sampling dataset

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Aim/Objective: Terminal care of cancer is an alternative to life-prolonging treatment. In the case that cure of cancer is difficult, many patients choose palliative treatment to improve their quality of life, rather than choose continuing treatments that are not well tolerated. Although the duration of terminal care is relatively long and sometime be carried out over several months, only limited Japanese evidence of explaining actual healthcare costs in terminal care. In this study, we estimated terminal care costs for cancer in Japan using national database (NDB) sampling data.

Methods: We used medical receipts from the NDB sampling dataset (April and October in 2015-2019, for ten months). The analysis included patients aged 65 years or older with at least one confirmed diagnosis of cancer, not undergoing active treatment for cancer (surgical treatment, radiotherapy, and chemotherapy), and who had not died during the study periods. Only medical direct costs were included. Endpoints were cumulative medical costs per month and week, with respective descriptive statistics. As a stratified analysis, we assessed the sub-population of palliative care units as well as type of cancer tumors to identify patients receiving terminal care.

Results: We selected 70,672 people for analysis. Among them, 13,662 (19.3%) were aged 65-74 years and 57,010 (80.7%) were aged 75 years or older, and the main cancer types were stomach cancer 12,271 (17.4%) and colon cancer 12,007 (17.0%). The mean (SD) monthly and weekly medical costs were $5,317 ($2,328) and $1,436 ($646), respectively. The results suggest that changes in medical costs are largely influenced by cancer tumor, type of hospitalization and whether a palliative care unit is available.

Conclusion: The actual costs of terminal care for cancer in Japan were revealed. It was suggested that costs vary depending on the cancer tumor, type of hospitalization and other factors.

G.32

Anti-dyslipidemic Agent Use in Japanese Patients Aged 55 Years or Older Starting Treatment

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Objectives: To analyze the actual use of the anti-dyslipidemic agents, statins (S), ezetimibe (E), and fibrates (F) in Japanese patients aged ≥55 years starting treatment.

Methods: This retrospective cohort study used the National Database of Health Insurance Claims and Specific Health Checkups of Japan to identify patients aged ≥55 years who started S, E, or F treatment between April 2014 to March 2018. The patients were followed to either death or the study end-date (March 2020). The discontinuation (defined as the individual variation in median dosing days from treatment initiation of each agent) and resumption dates of the agents were investigated. Adherence from initiation to the last dispensing date prior to discontinuation of each agent was calculated for patients with 2 dispensing records as the proportion of days covered (PDC), with non-adherence defined as PDC <0.8. Kaplan-Meier curves were used to evaluate the cumulative persistence rate per agent.

Results: Of the 3,675,949, 564,868, and 565,011 patients starting S, E, or F treatment, 43.7%, 41.6%, and 56.3%, were male, respectively, indicating a higher proportion of males who received F. Almost one-quarter of patients were aged ≥75 years for the three agents. The proportion of patients discontinuing treatment within 364 days was slightly higher for F (S, E, and F, 41.7%, 43.4%, and 49.9%, respectively), while the proportion who resumed treatment within 2 years of initiation was higher for S (61.5%, 40.7%, and 44.0%, respectively). The proportions of non-adherent patients were 8.0%, 7.6% and 9.0% for S, E, and F, respectively, showing slightly higher non-adherence for F. The cumulative persistence rate was significantly higher for S.

Conclusions: The use of three kinds of anti-dyslipidemic agents differed slightly in Japanese patients aged ≥55 years starting treatment. These results provide useful information for patient follow-up.

Keywords: hypolipidemic agents, persistence, adherence

G.33

Effectiveness and Prescription Pattern of Tapentadol in the Treatment of Cancer Pain

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Aim: To evaluate the effectiveness and prescription pattern of tapentadol in patients with cancer pain

Methods: The study was a longitudinal observational study. Patients above 18 years of age visiting out-patient department of palliative medicine and supportive care of a tertiary care center receiving oral tapentadol 50 mg were included in the study. The study was initiated after the approval of the institutional ethics committee. The severity of pain was assessed using the numerical rating scale (0-10). Wilcoxon ranked test was used to test for significance during the initial and final visit. A p-value <0.05 was considered to be statistically significant.

Results: A total of 51 patients visiting the outpatient department participated in the study. The mean age of the participants was 58.5 (11) years. The participants included 59% male and 41% female. The median duration of follow-up in days was noted to be 11 days. Among the participants, 11 were diagnosed with advanced cancer. The majority of the participants were prescribed tapentadol for gastrointestinal cancer (39%) followed by head and neck (16%), gynecology (16%), and lung (16%) respectively. At least one analgesic was prescribed in addition to tapentadol. The most prescribed analgesic was paracetamol (16%) followed by pregabalin (14%). Tapentadol significantly reduced pain in patients with cancer at the end of follow-up (p>0.05). The incidence of side effects such as nausea, disturbance in sleep, and loss of appetite was identified during the course of treatment.

Conclusions: Tapentadol showed a significant reduction in the intensity of pain in routine medical practice. It can serve as the choice of opioid in patients with considerable pain despite treatment with less potent medications.

Keywords: Pain, NRS, Tapentadol, Outpatient

G.34

Analysis of clinical pharmacist interventions in adult COVID-19 patients admitted to an Intensive Care Center in Vietnam

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Objective: The global coronavirus disease 2019 (COVID-19) pandemic has created unprecedented strains on healthcare systems around the world. The overwhelming surge of COVID-19 patient admissions, high demand of medication administration, and excessive utilization of antibiotics necessitate the proactive involvement of clinical pharmacists in the critical care team to optimize the efficacy and safety of pharmacological treatments. The objective of this study is to describe our institution's strategy to deploy pharmacy resources and to standardize pharmacy processes to optimize the management of patients with COVID-19.

Methods: A retrospective, descriptive study was conducted on all COVID-19 positive patients admitted to the Intensive Care Center of a teaching hospital in Vietnam between August 2021 and February 2022. All the documented pharmaceutical interventions (PIs) have been electronically extracted, reviewed, and analyzed by senior clinical pharmacists. For each PI, the name and therapeutic classification of related medications was recorded, and the drug related problems and interventions were classified according to French Society of Clinical Pharmacy (SFPC). The potential impact of each PI was assessed independently by two clinical pharmacists using the Clinical, Economic and Organizational (CLEO) tool, developed by experts of the SFPC. When there was disagreement, the case was discussed until reaching consensus.

Results: A total of 2,780 PIs were included in the final analysis. The average number of PIs per patient was five. The most common interventions were dosing adjustment (37.4%) and drug therapeutic monitoring (30.4%). Antibiotics were the most reported class of medication, constituting 81,9% of the total interventions. The physicians' acceptance rate was 80.4%.

Conclusion: Pharmacists intervened to address a wide range of medication-related issues, contributing to the improvement of COVID-19 patient management. The results demonstrate the vital role of clinical pharmacists as members of multidisciplinary team during times of crisis.

Keywords: antibiotics, COVID-19, clinical pharmacist, pharmaceutical intervention

G.35

Burden of pneumococcal disease in adults – A retrospective database study in Taiwan

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To examine hospitalized incidence, case fatality rate (CFR), healthcare resource utilization (HCRU) and costs associated with pneumococcal disease including invasive pneumococcal disease (IPD) and pneumonia in adults before and after introduction of 13-valent pneumococcal conjugate vaccine (PCV13) into national childhood immunization program (CIP) in 2015.

Data of eligible adults (≥18 years) was retrospectively extracted from Taiwan National Health Insurance Research Database. The International Classification of Disease codes were used for case identification. Bacteremia without identifiable focus, bacteremic pneumonia and meningitis were considered as IPD. Study findings were summarized using descriptive statistics and compared pre- (2011-2014) and post-introduction of PCV13 (2016-2019). Incidence time trends were assessed with interrupted time series analyses (ITSA).

3,001 IPD and 7,574 pneumonia episodes were identified from 2011-2019. Annual hospitalized incidence rates of IPD and pneumonia were 1.5 and 3.9 episodes per 100,000 person-years, respectively. Incidence rates were higher in patients ≥65 years than those 18 to <65 years (IPD: 4.5 vs. 0.8; pneumonia: 11.3 vs. 1.9 episodes per 100,000 person-years). For both conditions, ITSA showed significantly lower incidence rates in post-PCV13 period compared with pre-PCV13 period. CFR was almost 2.5 times higher in IPD (17.2%) than pneumonia (7.0%), with higher rates in patients ≥65 years. For IPD and pneumonia, no significant differences in length of hospitalization per inpatient visit were observed (pre- vs. post-PCV13). The average total (inpatient and outpatient) costs per episode were 127,555 (pre-PCV13) and 122,406 (post-PCV13) New Taiwan Dollars (NTD) for IPD, and 86,061 (pre-PCV13) and 83,420 (post-PCV13) NTD for pneumonia. HCRU and costs were also generally higher in patients ≥65 years, compared with those aged 18 to <65 years.

Incidence rates of hospitalized IPD and pneumonia decreased in Taiwan after PCV was introduced into the CIP. However, disease burden (clinical and economic) remains substantial, particularly in the elderly ≥65 years.

G.36

Burden of pneumococcal disease in adults – A retrospective database study in Hong Kong

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This study aims to assess pneumococcal disease burden among adults in Hong Kong by estimating the hospitalized incidence rate, trend and case fatality rate (CFR).

The Clinical Data Analysis and Reporting System was used in this retrospective observational study. Data was extracted from eligible adults (≥18 years) hospitalized with pneumococcal diseases including invasive pneumococcal disease (IPD) and pneumonia from 2005-2019. Bacteremia without focus, bacteremic pneumonia and meningitis were considered as IPD. Incidence rate and CFR were estimated. Interrupted time series analysis (ITSA) on incidence rates was performed to evaluate the impact of 13-valent pneumococcal conjugate vaccine (PCV13) introduction into the childhood immunization program (CIP) in 2011.

The overall hospitalized incidence rate of IPD and pneumonia in adults was 0.8 (range between 0.2-1.4) and 5.3 (range between 3.3-6.5) episodes per 100,000 person-years, respectively. Incidence rates were higher in patients ≥65 years than those 18 to <65 years (IPD: 2.7 vs. 0.4; pneumonia: 22.3 vs. 1.9 episodes per 100,000 person-years). The ITSA showed no significant changes in IPD incidence rate and trend after PCV13 introduction. For pneumonia, there was no significant change in incidence rate, but a marginal significant decrease in trend was observed in the post-PCV13 period. Similar results were obtained when ITSA was conducted separately in adults aged 18 to <65 and ≥65 years. The CFR of hospitalized IPD was 24.1%, while pneumonia was higher at 30.1%. For both conditions, mortality was higher in patients ≥65 years, compared with those 18 to <65 years.

The hospitalized incidence rates of IPD and pneumonia fluctuated over the study period. After introduction of PCV13 in CIP, there was only a marginal reduction in trend of pneumonia among adults. The CFR of hospitalized pneumococcal disease was high (>20%). Disease burden remains substantial. Future studies are warranted to examine the effectiveness of PCV immunization.

H. Rational drug use

H.1

Patients' perspective on medicines information

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Aim/Objective: Patients are mainly interested to receive information about medicines. It helps them to achieve safe and effective use of medicines. The objective of this study was to evaluate the value of medicines information for patients in Armenia.

Methods: Survey was conducted in 10 regions of Armenia and Yerevan. Visitors of pharmacy outlets were interviewed (n=1059) using a previously developed questionnaire. The results were analysed with SPSS statistical software, version 22.0.

Results: The majority (68.9%) of respondents reported that they use medicines if the necessary information is available. 45.9% do it always, 23.0% - often. When participants were asked to assess importance of having information on specific topics of medicines information (MI), the great majority of them acknowledged the importance of knowing the therapeutic indications of pharmaceuticals to be used (91.8%), their dosage and method of administration (91.1%), contraindications (82.4%), adverse reactions (81.9%) and interaction with other medicines (76.5%). 58.9% of consumers indicated that they value having information on medicine's price. 63.9% participants reported that they need information to achieve better treatment outcomes, 53.4% noted that they want to be assured whether they do not have contraindications for use the medication, 53.1% indicated that they believe that knowledge of possible side effects could prevent adverse reactions.

Conclusion: Patients need medicines information, and the majority of them use it for achieving better treatment outcomes. They are interested in having knowledge on many specific topics of medicines information. Community pharmacists can serve as an important source for providing wide range of medicines information needed by patient.

Keywords: Medicines information, patients

H.2

Consumer's Understanding and Satisfaction of Patient Information Leaflet: A Case Study of Amoxicillin

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Objective: To evaluate consumer's understanding and satisfaction of patient information leaflet (PIL) for amoxycillin. In addition, to evaluate the factors associate with consumer's understanding and satisfaction of amoxycillin PIL

Method: This research was cross-sectional analytical study. Study participants were Thai adults aged over 18 years old who lived in Muang District, Chiang Mai. Data were collected using stratified random sampling during August 1st 2016 to September 30th 2016. Samples were asked to read amoxycillin PIL developed from the 2013 Thai Patient Information Leaflet guideline. Then, the study participants' understanding were evaluated using interview, while PIL satisfaction was assessed using a questionnaire. Descriptive statistic, Independent t-test, ANOVA, Mann-Whitney U test and Kruskal Wallis test were used to analyze the data.

Results: From 180 participants, the average age was 44±4.11, most and graduated high school or vocational school. The average amoxycillin PIL score was 69.61±9.02%.. The average satisfaction score of amoxycillin PIL was 3.84±0.46, from5). The factors affecting overall consumer's understanding of amoxycillin PIL were education, career and experience of using antibiotic ($P < 0.001$). Age was significantly associated with satisfaction of amoxycillin PIL ($P = 0.039$).

Conclusion: Thai adults presented low level of understanding of amoxycillin PIL, but high satisfaction of the PIL. Educations, career and an experience were associated with amoxycillin PIL, while only age were understanding were and factors associated with PIL satisfaction. It is suggested that amoxycillin PIL should be modified to use language and terminology appropriated with medicine users to improve understanding of medicine recommendations that leads to effective and safe use of amoxycillin.

Keywords: Understanding, Satisfaction, Amoxicillin, Patient Information Leaflet

H.3

Knowledge video and wired broadcasting improve community knowledge and practice of antibiotics use in COVID-19 ERA.

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Objective: Overuse of antibiotics is a serious health issue worsened of rational drug use. Inadequate knowledge has been related to the improper use of antibiotics. In COVID-19 ERA, it is critical to provide accessible and safe interventions to promote antibiotics smart use. This study aims to evaluate effect of educational program on antibiotics knowledge and practice.

Methods: A prospective cohort study was conducted in Dok Kham Tai District, Phayao Province located in North Thailand between October 2021 and March 2022. Adults over 20 years of age were recruited using multistage sampling. 369 representatives of households, divided into 2 groups: 185 samples in the control group received academic poster, and 184 samples in the intervention group received academic poster, knowledge video, and wired broadcasting. The data was collected twice by trained community health workers, before and after the educational program on antibiotics use. Descriptive and inferential statistics was used to analyze.

Results: All of 369 representatives of households. The mean age of participants was 56.36 ± 0.62 years old. Most of the respondents were female (264, 71.54 %) and had primary education (186, 50.41%). A mean difference score was generated for control group and intervention group. After educational program, both groups had a statistically significant increase with knowledge (3.42±0.31, $p<0.001$ and 5.42±0.37, $p<0.001$ respectively). A mean difference score was generated for control group and intervention group, with practice (1.78±0.25, $p<0.001$ and 2.77±0.25, $p<0.001$, respectively). Moreover, the mean scores of knowledge and practice after educational program in intervention group were higher than control group ($p < 0.001$).

Conclusions: An educational program including academic poster, knowledge video, and wired broadcasting was effective to increase knowledge and practice scores. This program should be continued and encouraged into future antibiotics awareness campaigns to achieve rational antibiotics use.

Keywords: Educational program, Knowledge, Practice, Rational drug use

H.4

Pharmacodynamic Target and Treatment Outcome of Vancomycin in Hemodialysis Patients with Oxacillin-resistant Staphylococcus aureus Bloodstream Infection

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Objective: Vancomycin, a glycopeptide antimicrobial agent, is the first-line therapy for hemodialysis (HD) patients due to high prevalence of oxacillin-resistant Staphylococcus aureus (ORSA) infections. However, the outcome studies investigating the pharmacodynamic targets of vancomycin in HD patients with ORSA bloodstream infection (BSI) are scarce. This study was designed to establish a population pharmacokinetic (PPK) model and to explore pharmacodynamic targets of vancomycin in these population.

Methods: A retrospective study was conducted in a medical center. We selected admitted HD patients who had ORSA bloodstream infection and received at least three dosage of vancomycin from July 1, 2014 to June 30, 2021. Patient clinical outcome, drug level and relevant data were retrieved from electronic medical record. Vancomycin PPK model was built using Monolix software. Treatment failure was defined as either 30-day mortality or persistent BSI >7 days. The cut-off points of trough and mean AUC24h/MIC ratio associated with treatment failure were identified by classification and regression tree (CART) analysis. We performed multivariable logistic regression to identify risk factors for treatment failure.

Results: A total of 95 patients and 230 vancomycin concentration data were included. The mean age and body weight were 67.3 years old and 58.2 kg. Treatment failure rate was 32%. The PPK of vancomycin was best described by two-compartment model. The clearance of vancomycin estimated from model in non-HD and HD status were 0.23 L/h and 1.88 L/h, respectively. The median trough and AUC24h analyzed from PPK model were 16.83 mg/L and 514 mg*hr/L. CART analysis found cut-off points of trough <15.4 (accuracy rate= 58.9%) and AUC24h/MIC <436 (accuracy rate= 70.5%) for treatment failure. In logistic regression, AUC24h/MIC <436, septic shock and infective endocarditis related BSI were significant risk factors for treatment failure.

Conclusion: AUC24h/MIC could be used as a pharmacodynamic target in HD patients with ORSA bloodstream infection.

H.5

Deprescribing of oral hypoglycemic medications for diabetes reversal through integrative medicine approach

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Aim/Objective: Deprescribing is a systematic process of withdrawal, dose reduction, frequency reduction, switching to appropriate medications and cessation of potentially inappropriate medications (PIMs) to reduce polypharmacy, medication related adverse reactions and maintain the quality of life. The aim of our study is to analyze the appropriateness of deprescription of oral hypoglycemics and the remission rate of type 2 diabetes mellitus after diabetes reversal program.

Methods: This is a retrospective observational study carried out for a period of 6 months in the Wellbeeing Integrative Medicine and Healthcare Center among patients enrolled for diabetes reversal program (DRP). The study was approved by institutional ethics committee of Ramaiah Medical College. A total of 101 type 2 diabetes mellitus patients were included in the study. The glycemic control was monitored by analyzing the initial and final FBS, PPBS and HbA1c levels. We studied the pattern of oral hypoglycemics deprescription among the patients. A telephonic interview was conducted to analyze the relapse rate of type 2 DM in the patients after completion of DRP. The statistical analysis was done using paired Student T test, repeated measures ANOVA and descriptive statistics.

Results: Among the 101 patients included in the study, significant difference was observed among initial and final FBS, PPBS and HbA1c values depicting good glycemic control with p value 0.000 (<0.05) for all the three laboratory parameters by paired student t test. Almost 78(77%) patients were deprescribed in which 20(20%) had complete cessation of oral hypoglycemic medications. The relapse rate of type 2 diabetes mellitus was found to be 26(26%).

Conclusion: Effective deprescription can be achieved in type 2 diabetes mellitus patients by integrative medicine and lifestyle modifications under the supervision of diabetologist, ayurvedic physicians, pharmacist, dietician and yoga instructor.

Keywords: Deprescribing, diabetes reversal, oral hypoglycemics, Integrative medicine

H.6

Assessment of knowledge, attitude, and practice of disposing and storing of unused and expired medicines among the communities of Nepal.

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Background: Unused medicines can be stored by people at their places of residence and houses for later use. The study explored the status of medicine disposal and storage practices and evaluated knowledge, attitude, and practice of medicine storage and disposal techniques among households of three districts of the Kathmandu valley, Nepal.

Method: A cross sectional study with a two-stage cluster survey design was done using a semi-structured questionnaire from April 2021 to October 2021. The sample size (total households) after adjusting for design effect and non-response rate was 210 and the study population were the household heads. Simple random sampling was done to select clusters during the first stage and systematic random sampling to select households in the second stage. Descriptive statistics and t-test/One-way ANOVA were used to compare the respondents' average knowledge scores. Practice variables were presented using frequency distribution.

Results: Around half the respondents were from the Kathmandu district whereas nearly 20% were from Bhaktapur and 30% were from Lalitpur. Nearly two thirds were male and about 25% had a bachelor's degree. Nearly 90% respondents agreed that storage of excess medicines at home may promote self-medication. Similarly, 97.6% of respondents agreed that there is a lack of adequate information that safe disposal of unused medicines. The majority [125 (59.5%)] of participants always checked the expiry date of medicines. The safe methods of medicine disposal were not known by 137 (65.2%) participants. Throwing in a dustbin was the preferred method of expired medicine disposal.

Conclusion: There is good level of knowledge and practice of disposing the unused medicines among the public of Kathmandu Valley. Various educational intervention programs may help improve awareness further. Creating a chart summarizing disposal procedures of common medicines is important. Similar studies in other regions are required.

Keywords: Medicine storage, medicine disposal, Kathmandu, Nepal, self-medication

H.7

Point Prevalence Survey of antibiotics use in six private hospitals in Kathmandu.

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Introduction: Point prevalence survey (PPS) on antibiotic use developed by WHO is used globally This study was done to obtain information on prescribing of antibiotics using PPS methodology in six private hospitals in Kathmandu.

Method: This cross sectional descriptive study was done from 20th July to 28th July 2021 among inpatients admitted at or before 8:00AM on the day of survey in various wards of hospitals. Patient sampling was done as per the PPS methodology. The institutional capacity was measured by indicators for infrastructure, policy and practice and monitoring and feedback. Data were presented as frequencies and percentages.

Results: Patients above 60 years were 34 (18.7%). There were equal number of males and females, 91 (50%). Maximum patients were from the surgery ward 38 (20.8%) followed by Obstetrics and Gynecology ward 25 (13.5%).
Only one antibiotic was used in 81 patients (44.5%) followed by two antibiotics in 71 (39%) patients. Duration of antibiotic prophylactic use was one day in 66 (63.7%) patients. The culture result was positive for 17 (24.7%) samples. The organisms isolated were E. Coli, Pseudomonas aeruginosa and Klebsiella pneumoniae. Ceftriaxone was the most used antibiotic.
Drug and therapeutics and pharmacovigilance activities were present in 3/6 (50%) study sites. About 38.9% antibiotics were from access and watch groups, and 11.1% from reserve and not recommended groups. Antibiotic formulary and antibiotic guideline was present in 4/6 sites, and facilities to audit surgical antibiotic prophylaxis choice in 2/6 (33.3%) sites and cumulative antibiotic susceptibility reports in 2/6 (33.3%) sites.

Conclusion: Not all infrastructure, policy and practice and monitoring and feedback parameters were present in the study sites. PPS studies should be done periodically to study AMR and monitor the impact of antimicrobial stewardship and infection control programs.

Keywords: Point prevalence survey, antibiotics, private hospitals, tertiary care centers, Nepal

H.8

Development and Validation of Rational Drug Use Literacy Tool for Thai Adults

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Rational Drug Use Literacy (RDUL) is considered medication literacy described as the degree to which individuals can obtain, comprehend, communicate, calculate and process patient-specific information about their medications to make informed medication and health decisions in order to safely and effectively use their medications, regardless of the mode by which the content is delivered.

To develop RDUL tool and investigate RDUL tool's validity and reliability in screening for RDUL in Thai adults.

This study developed a new instrument, RDUL tool, based on 6 abilities; access, comprehend, converse, analyze, decide, and communicate. A cross-sectional study was conducted in Thailand between 2021. Demographic data, RDUL scores were collected using RDUL tool. Health Literacy scores (HLS) and Thai Health Literacy Assessment Instrument: Nutrition label scores (THLA-N) were used as gold standards. Participants were ≥ 15 years old using purposing sampling from 8 provinces. The diagnostic sensitivity and specificity of the RDUL tool compared with HLS and THAL-N were determined to indicate the cut-off score. The Receiver Operating Characteristics (ROC) was analyzed to evaluate its diagnostic accuracy.

The study included 761 Thai adults, 55.4% was 21–60 years old, 61.1% was female, 77.1% had education lower than bachelor's degree, and 45.3% had chronic disease(s). The cut-off score of the RDUL was 41.5 with a sensitivity of 72.4% and a specificity of 60.9%. Positive predictive value was 93.2% and negative predictive value 23.0%. The area under the ROC curve being 0.704. Cronbach's alpha for the RDUL tool was 0.891, indicating acceptable internal consistency. The RDUL score was positively correlated to HLS and THAL-N scores ($r = 0.352$ and $r = 0.399$, $p < 0.001$, respectively). The prevalence of adequate RDUL in Thai samples was 54.8%.

The RDUL tool demonstrated good reliability and validity for screening RDUL in Thai adults.

H.9

Patterns of Use of Antibiotics in Hospitalized COVID-19 Patients in a Tertiary Care Centre in Lalitpur District, Nepal.

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Objectives: The objective of this study is to explored the patterns of use of antibiotics in the management of hospitalized Coronavirus Disease 2019 (COVID-19) patients.

Methods: A cross-sectional study was conducted at KIST medical college and teaching hospital among hospitalized COVID-19 patients after taking ethical approval from institutional review committee. The study period was from 6 August 2021 to 6 October 2021 during which COVID-19 patients admitted from April 2021 to June 2021 were studied. All the COVID-19 cases confirmed by reverse transcriptase polymerase chain reaction test were studied. A sample size of 73 was calculated at 95% confidence interval (CI) with 5% margin of error. A total of 106 patient were enrolled by convenience sampling method. Demographical, clinical and antibacterial profile of the patients were recorded in profoma retrospectively by reviewing the patient's medical records from medical records section. The data was analyzed using Statistical Package for the Social Sciences version 21. Descriptive statistical tests and chi-square test were used.

Results: The prevalence of use of antibiotics among COVID-19 patients was 104 (98.11%) (95.12-100 at 95% CI). About 74 (71.15%) of patients received two or more antibiotics. The most common class of antibiotics used were cephalosporin 85 (81.73%) and macrolides 57 (54.81%). Meropenem and cefepime were exclusively used in patients on ventilator support. The number of antibiotics used, and the estimated cost of antibiotics was significantly associated with the patients in the intensive care unit and patients on ventilatory support.

Conclusions: The prevalence and number of antibiotics used among hospitalized COVID-19 patients were higher when compared to studies from other countries. Higher classes of antibiotics were mostly used in critical patients. Judicial use of antibiotics should be promoted and practiced even during COVID-19 pandemic to prevent antimicrobial resistance.
Keywords: antibiotics; antibiotic resistance; COVID19; hospitalized patients

H.10

Availability of Paediatric Essential Medicines in Armenia

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Background: Availability of essential medicines for children is an important precondition for effective treatment of priority diseases and saving lives. However, access to essential medicines for children remains low, especially in low- and middle-income countries. The objective of this study was to examine the situation with availability of essential medicines for children in Armenia.

Methods: The Armenian List of Essential Medicines (AEML), the Lists of medicines authorized in Armenia, pricelists of main wholesalers and national clinical guidelines for pneumonia treatment in children were analyzed.

Results: The percentage of medicines from the World Health Organization Model List of Essential Medicines for Children (WHO EMLc) (with taking into account pharmaceutical forms and doses recommended by WHO), which were included in the current AEML was only 57.7%; and only 68.5% of essential medicines for children were authorized in the country. 81.2% of all the active ingredients from WHO EMLc were included in the AEML. However, only 61.5% of them were authorized in the country. Only 56.1% of active ingredients from WHO EMLc were available on the pharmaceutical market. Analysis of recommendations on prescribing medicines for pneumonia treatment included in clinical guidelines, approved in Armenia during the past ten years, has revealed that these recommendations slightly differ in terms of recommended medicines and other treatment details. The latest draft of clinical guideline for pneumonia treatment in outpatient children developed in 2017 is still not approved.

Conclusions: Essential medicines for children recommended by WHO, are covered by a medicines supply system for children in Armenia, yet not in full. There is a need in improving the situation. Development and approval of Armenian EMLc can be the first step in improving access to medicines for children. Draft of Armenian EMLc has been developed and submitted to the Ministry of Health.

Keywords: essential medicines, treatment of children

H.11

Identification of Drug Interactions and Potentially Inappropriate Medications in Geriatrics

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Introduction: Healthcare organizations focus on patient safety monitoring to improve health delivery. Prevalence of Potential Drug-Drug Interactions (pDDIs) and Potentially Inappropriate Medications (PIMs) contribute to an increased rate of morbidity and mortality. Therefore, it is essential to monitor patients and prevent associated morbidities.

Aim and Objectives: The study aimed to determine the prevalence of PIMs and PDDIs among geriatrics.

Methodology: A hospital-based prospective observational study was carried out for a period of six months in the Department of Geriatrics, M.S. Ramaiah Teaching Hospital, Bangalore. Potential drug-drug interactions were analyzed using Micromedex database 2.2 and potentially inappropriate medications were analyzed using Beer's criteria.

Results: Among 395 patients included, 226(57.2%) were males and 169(42.8%) were females. Out of 395 prescriptions, 221 (56%) prescriptions showed pDDIs and 41 (10.4%) prescriptions showed PIMs. From 221 prescriptions, 559 pDDIs were observed; 281 (50.3%), 260 (46.5%), 16 (2.7%) and 2 (0.3%) were major, moderate, minor and contraindicated respectively. Based on duration of onset of drug interaction 62 (11.0%) were rapid and 97 (17.4%) were found to be delayed. Almost 321 (57.5%) were synergistic and 196 (35.0%) were antagonistic drug interactions.

Conclusion: This study creates awareness on commonly occurring drug interactions among geriatrics and helps the practitioners to prescribe drugs with a low risk of pDDIs. The authors suggest PIM monitoring in geriatrics to avoid harmful drug effects and improve patients' quality of life.

Keywords: PIMs, pDDIs, Micromedex 2.2 and Beer's criteria.

I. Pharmacoepidemiology and traditional medicines

I.1

Camellia sinensis tea and risk of anxiety disorder for medical students at Universitas Lambung Mangkurat Indonesia

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Background: Anxiety is a response for inability to overcome problems that commonly occurs in medical students. It is thus able to affect their academic performances. The content of L-theanine in Camellia sinensis (C. sinensis) tea is allegedly able to generate a relaxing effect to reduce anxiety.

Objectives: to determine the association between C. sinensis tea consumption and a decreased risk of anxiety disorder for medical students.

Method: An analytic observational study with cross-sectional approach was conducted within 332 undergraduate medical students at Universitas Lambung Mangkurat in December 2021. They were selected using simple random sampling technique. An online questionnaire was applied to figure out the characteristics of respondents including tea consumption status, while The Zung Self-rating Anxiety Scale was used to determine the anxiety status. Collected data were then analyzed using a multinomial logistic regression test to estimate odds ratios (OR)s and 95% confidence interval (95%CI).

Results: Drinking tea occasionally (≥1 glass per week) showed a lower risk of mild-moderate anxiety by 9% (adj. OR 0.91, 95%CI: 0.47-1.77) and of marked-severe anxiety by 45% (adj. OR 0.55, 95%CI: 0.12-2.43) compared to non-tea drinkers. Meanwhile, consuming 1 glass and 2-3 glasses of tea per day showed a 20% (adj. OR 0.80, 95%CI: 0.36-1.79) and a 54% (adj. OR 0.46, 95%CI: 0.15-1.37) lower risk of mild-moderate anxiety, respectively compared to non-tea drinkers. However, this association was not statistically significant (p>0.05).

Conclusions: There is a tendency of a decreased risk of anxiety disorder for the increased consumption of C. sinensis tea.

Keywords: Anxiety, Camellia sinensis, tea, students, medical faculty

I.2

Does Camellia sinensis tea reduce the risk of anxiety disorder for Covid-19 survivors? A cross-sectional study among medical students

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Introduction: Covid-19 survivors are not uncommon to be seen as a source of the infection. This negative stigma might induce anxiety. To treat anxiety disorders, Camellia sinensis (C. sinensis) tea has been used. However, no studies evaluate the effect of the tea on the risk of anxiety disorder specifically among medical students who were Covid-19 survivors.

Objective: to evaluate the risk of anxiety disorder for C. sinensis tea drinkers compared to non-tea drinkers among medical students who were Covid-19 survivors

Methods: A cross sectional study was conducted among students from four undergraduate schools at Medical Faculty Universitas Lambung Mangkurat Banjarmasin-Banjarbaru, Indonesia in December 2021. Information about tea consumption and demographic data were collected from a questionnaire. Anxiety disorder was determined by using an online questionnaire, i.e., Zung Self-rating Anxiety Scale. Binomial logistic regression analysis was used to calculate Odds Ratios (ORs) and 95% confidence intervals (CIs).

Results: Of 129 respondents, 55 students (42.64%) had anxiety disorder and 74 students (57.36%) did not. Forty-three students (33.33%) did not drink the tea, while 71 students (55.04%) and 15 students (11.63%) drank the tea up to 1 glass and at least 2 glasses per day, respectively. Students who drank tea at least 2 glasses per day had a lower risk of anxiety disorder by 90.4% (Adj. OR 0.096, 95%CI; 0.015-0.615) than non-tea drinkers.

Conclusions C. sinensis tea was significantly associated with a lower risk of anxiety disorder by about 90% started from at least 2 glasses per day compared to non-drinkers among medical students who were Covid-19 survivors.

Keywords: Camellia sinensis, tea, anxiety disorder, Covid-19 survivors, medical students

I.3

Treatment-resistant depression and risk of autoimmune diseases: a seven-year population-based cohort study

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Aim/Objectives: Recent literature increasingly suggests the predictive role of depression in autoimmune diseases (AID) due to increased immune activation among affected patients, but the role of treatment-resistant depression (TRD) is lesser-known in AID development despite the proneness to long-term dysregulated inflammation. In this retrospective cohort study, we examined the association between TRD and subsequent risk of AID.

Methods: Using the territory-wide electronic medical records in the public healthcare setting of Hong Kong, we identified 24,566 incident depression patients between 2014 and 2016 without autoimmune history and followed up from diagnosis of depression to death or December 2020 to identify TRD development and AID incidence. TRD was defined as having received at least two antidepressant regimens for adequate duration and the third regimen to confirm previous treatment failures. We matched TRD group 1:4 to non-TRD group based on age, sex and year of first depression diagnosis, then conducted survival analyses for AID hazard estimation, adjusting for history of physical and psychiatric conditions. Index dates were the prescription dates of the third regimen for TRD group, whilst the same index dates were assigned for the matched non-TRD control.

Results: Grouping 22 types of AID with 71,232 person-years of follow-up, the cumulative incidence in the TRD group was generally higher compared with the non-TRD group (21.5 vs 14.4 per 10,000 person-years). Proportional hazard model suggested a marginally significant association between TRD status and AID (HR:1.45, 95%CI: 0.98–2.23, p=0.059). Subgroup analysis showed that the risk magnitudes were generally higher among men compared with women.

Conclusion: In line with the inflammation theory, our study observed a marginally increased risk of AID in patients with TRD. Further validation for the association and potential sex-specific disparities is encouraged. Clinical attention should be paid to screen and monitor potential AID to avoid unsatisfactory consequence from both conditions.

I.4

Risk of developing fractures in adult patients with atopic dermatitis, allergic rhinitis, and asthma: A Nationwide Population-based Cohort Study

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Background: The risk of osteoporosis has been explored in atopic disorders included atopic dermatitis, allergic rhinitis, and asthma. The long-term risk of fractures in adult patients with various atopic disorders and the effects of two or three combined atopic disorders on bone health remain to be elucidated.
Objective: To evaluate the long-term risk of fractures in adult patients with asthma, atopic dermatitis, or allergic rhinitis.

Methods: This nationwide population-based retrospective cohort study was conducted using Taiwan National Health Insurance Research Database for the period 2000 to 2013. A total of 105,828 patients with atopic disorders and 104,258 reference subjects without atopic disorders were identified. Demographic characteristics and comorbidities were compared, and incidence of fractures was evaluated. Adjusted hazard ratios for fracture risks of various atopic disorders and two or three combined atopic disorders were calculated using the Cox proportional-hazards model.

Results: During the mean 8.6-year follow-up, a total of 9332 newly diagnosed fractures patients (8.8%) were included in the atopic diseases cohort and 6864 patients (6.6%) in the reference cohort. The results indicated that atopic patients exhibited a significant higher risk of subsequent fractures than reference cohort (aHR: 1.29, 95% confidence interval [CI]: 1.25–1.34, P <0.001).
Subgroup analyses confirmed that two or three combined atopic diseases exhibited a markedly higher fracture risk (aHR: 1.74, 1.40-1.73, respectively) compared with controls. Furthermore, Cox proportional-hazards analysis revealed that aged, female atopic patients had a higher risk of fractures (aHR: 1.07, 2.0, respectively). These patients with diabetes mellitus, and osteoporosis, and used systemic glucocorticoids also exhibited a higher fractures risk (aHR: 1.31, 1.34, 1.49, respectively).

Conclusions: Various adult atopic patients and combined two or three atopic disorders were associated with a higher risk of developing fractures than reference cohort patients.

I.5

Diversity in epidemiology and risk profiles between hospital-acquired and community-acquired methicillin-resistant Staphylococcus aureus infection: A systematic review and meta-analysis

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Aim: To determine diversity between prevalence and risk profiles of hospital-acquired (HA) and community-acquired (CA) methicillin-resistant Staphylococcus aureus (MRSA) infection.

Methods: A comprehensive search strategy was prepared and executed in PubMed/MEDLINE and EMBASE databases. The case-control and cohort studies, irrespective of publication year, which reported hospital/community-acquired MRSA risk factors were included. Non-English and animal studies were excluded. New-castle Ottawa scale was used to appraise quality of included studies. Based on heterogeneity, a random/fixed model was utilized to conduct a meta-analysis. Additionally, a t-test was carried out to evaluate significant difference (P<0.05) between risk profiles of HA-MRSA and CA-MRSA. Publication bias was assessed using Egger's test and funnel plots. Furthermore, sensitivity analysis was performed to analyze robustness of evidence. This meta-analysis is registered with PROSPERO (CRD42022326508).

Results: Primary (900) and full-text screening (70) resulted in 30 citations with a sample size of 37407 (case 6881; control 30526) were selected for quantitative analysis. A total of 56 risk factors were found for HA-MRSA (34) and CA-MRSA (22).
The prevalence rate of HA-MRSA was [35.7%, 95% CI:0.265-0.461] higher than CA-MRSA [28.0%, 95% CI:0.162-0.440].
The most strongly associated predictors for HA-MRSA were use of nasogastric tube [OR 9.23], prior MRSA infection [OR 7.63] and previous antibiotic use [OR 4.52]. In the patients with CA-MRSA, previous MRSA infection [OR 5.88], malignancy status [OR 2.03], HIV infection [OR 1.76] and smoking status [OR 1.76] were top four risk factors.
Of 13 common risk factors between HA-MRSA and CA-MRSA, only two factors namely malignancy [Difference in ORs;0.66, P=0.003] and presence of a liver disorder [Difference in ORs;1.12, P=0.014] demonstrated a statistically significant difference.

Conclusion: These findings demonstrate that HA-MRSA is more prevalent compared to CA-MRSA. Further, there are multiple risk factors of MRSA infection. And, therefore, individual monitoring of risk profiles is recommended for effective infection control

I.6

Analysis of key factors and risk prediction of diabetic nephropathy

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Objective: by constructing a logistic regression model to analyze the association factors and predicting the risk of 2 diabetes mellitus nephropathy, and to provide scientific evidence for screening and intervention in patients with type 2 diabetes mellitus nephropathy.

Methods: diabetic patients diagnosed and treated in a National Clinical Medical Science Data Cente were selected and screened according to the diagnostic data of the patients electronic medical records. They were randomly divided by 7:3 ratio. There are 1594 males and 283 femalesin the modeling group,and 717 males and 381 females in the validation group.The data were collected from urine routine data, diabetes biochemical examination data and glycated data of diabetes, and the significant variables were obtained from univariate Logistic regression analysis. The Logistic regression analysis of these variables was used to get Logistic regression model. According to the area under the ROC curve, the sensitivity and specificity of the prediction model are tested in order to achieve an ideal prediction effect.

Results: 1.Logistic single factor regression analysis showed fibrinogen (P=0.012, OR=1.012), 24h urinary microalbumin (P<0.001, or=0.49), serum creatinine (P<0.001, or=1.025), prothrombin activity (P=0.02, OR=1.025), C-reactive protein (P=0.004, OR=0.806), urine albumin creatine ratio (P<0.001, OR=1.005) was significantly associated with type 2 diabetes nephropathy.2.The variables with P<0.02 in the single factor were included in Logistic multivariate regression analysis, and X18:24h urine microprotein (P=0.004, OR=0.726), X19: serumcreatinine (p<0.01, OR=1.030), X37:urine albumin creatine ratio (P < 0.01, OR=1.006), urine red blood cells (P=0.006, OR=0.533) were obtained.

Conclusion: This study found that gender, age, urinary biliary tract, urinary red blood cells, alkaline phosphatase, lactate dehydrogenase and patients with type 2 diabetes were significantly different in patients with type 2 diabetes mellitus and coronary heart disease. Cardiovascular disease in diabetic patients should be strengthened.

I.7

Targeted Therapy and Treatment Trends in Locally Advanced Head and Neck Cancer in Taiwan: A Population-Based Retrospective Study

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Aim/Objective: Taiwan's National Health Insurance has covered targeted therapy, namely cetuximab, for locally advanced head and neck cancers (LAHNC) since July 2009. This study aimed to estimate the trends of first-course treatment modalities before and after cetuximab was reimbursed in Taiwan and examine treatment selection factors and survival effects among patients with LAHNC.

Methods: A population-based retrospective study was conducted using Taiwan's National Health Insurance Research Database. Patients over 20 years old who were newly diagnosed with LAHNC during 2008-2016 and received treatments within six months were included. They were divided into targeted therapy and nontargeted therapy groups. The treatment trends were estimated using the Cochran-Armitage trend test. Multiple logistic regression and Cox proportional hazards model were performed to evaluate treatment selection factors and survival effects after 2009, respectively.

Results: A total of 22,969 patients were included in the study, with 21,765 in the nontargeted therapy group and 1,204 in the targeted therapy group. Around 151 (5.7%) patients received targeted therapy each year, increasing annually from 2009 to 2016 (p-value <0.001). Most (99.4%) patients also received radiotherapy while few (33.1%) of them were given surgery, showing significant differences from nontargeted therapy group (surgery: 58.0%; radiotherapy: 82.6%; p-value < 0.001). Patients with hypopharynx and oropharynx cancers were more likely to receive targeted therapy compared to oral cavity cancer (odds ratio [95% confidence interval]: 2.76 [2.40-3.18]; p-value < 0.001). The targeted therapy group had a higher long-term mortality rate than the nontargeted one (68.0% vs. 53.3%).

Conclusion: The treatment patterns between targeted and nontargeted therapy groups differed significantly. Most patients did not receive targeted therapy even after cetuximab was reimbursed. It was also shown that patients in the targeted therapy group had a higher mortality rate than the nontargeted therapy group.

Keywords: locally advanced head and neck cancer; targeted therapy; cetuximab; chemoradiotherapy.

I.8

Birth outcomes after preconception paternal exposure to tyrosine kinase inhibitor for chronic myeloid leukemia: A nationwide cohort study

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Aim/Objective: Tyrosine kinase inhibitors (TKI) significantly improve the survival of chronic myeloid leukemia (CML), which patients often require long-term medication. Large studies for effects of TKI on offspring of CML patients in childbearing age are limited. This aim of study is to investigate the health status of offspring from male CML patients with usage of TKIs.

Methods: The study cohort was constructed from Taiwan Maternal and Child Health Database, Taiwan Birth Certificate Application, Cancer Registry, and National Health Insurance Research Database between 2010 and 2020. Children whose father had history of CML and TKI treatment were identified. They were further divided into exposed and reference groups according to fathers' TKI exposure being within 3 months before conception or not. The outcome measures include any type of congenital abnormalities (CAs), preterm birth, low birth weight (LBW), large for gestation age (LGA) and small for gestational age (SGA). We used multivariable logistic regression with adjustment of parents' age at deliver, and year of children's birth.

Results:Eighty-one children whose fathers with CML and receiving TKIs in preconception period, and 109 children composed the reference cohort. The adjusted odds ratio of CAs of the circulatory system and of the digestive system were 3.42 (95% CI: 0.97–11.99) and 14.22 (95%CI: 1.21–166.45), respectively. There was no statistical significance between paternal TKI exposure and preterm (0.60, 95% CI: 0.20–1.80), LBW (0.62, 95% CI: 0.15–2.52), LGA (1.58, 95% CI: 0.65–3.84) and SGA (1.21, 95% CI: 0.37–3.90).

Conclusion: Our findings suggest that paternal exposure to TKI within 3 months before conception seems to have a trend towards higher risk in CAs within cardiovascular and digestive organs. Despite using a nationwide database, small sample size remains the main limitation. The findings warrant further validation with large-scale international collaborative studies.

Keywords: Tyrosine kinase inhibitor; Chronic myeloid leukemia; Birth outcomes; Offspring

I.9

Signals of Drugs Affecting Urinary Dysfunction: A Case/ Non-case Study using Nationwide Spontaneous Reporting Database

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Aim: Urinary dysfunction induced by medications may lower patients' quality of life and may lead to prescribing cascade. Several medications are known to affect urinary dysfunction or overactive bladder symptoms via effects on bladder contractility, etc. We conducted a case/non-case study using a spontaneous reporting database to detect signals of urinary dysfunction following medication use.

Methods: We analyzed individual case safety reports (ICSRs) in Korea Adverse Events Reporting System (KAERS) between 2016 and 2020. As cases of urinary dysfunction, we included urinary incontinence, urinary retention, micturition frequency, nocturia, and micturition urgency (WHO-ART No. 156, 157, 606, 611, and 1497, respectively). Non-cases were defined as all reports with other AEs. Each case was matched to four non-cases with age and sex. To detect safety signals, we analyzed individual drugs and therapeutic classes with specific target drugs using World Health Organization's Anatomical Therapeutic Class (WHO-ATC) code. As the target therapeutic classes, we included alpha-receptor antagonists (C02C, G04CA), calcium channel blockers (C08G, C08GA), opioids (N02A), sedative-hypnotics (N05C), antipsychotic agents (N05A), anticholinergics (N04A), tricyclic antidepressants (N06A), alcohol (N07B), and ACEIs (C09D). Logistic regression analysis was conducted to estimate reporting odds ratios (RORs) and their 95% confidence intervals (CIs).

Results: Among 3,722,834 ICSRs in the KAERS database, a total of 2,699 cases of urinary dysfunction and 10,796 non-cases were identified. The number of aged over 65 years old for cases and non-cases was 1,337 (9.9%) and 5,348 (39.63%), respectively. The logistic regression result shows large significant differences in 'narcotic analgesics opioids (ROR=0.484, 95% CI=0.415-0.563), 'antidepressant tricyclic (ROR=2.811, 95% CI=2.176-3.633) and 'aceis (ROR=3.911, 95% CI=3.149-4.857).

Conclusion: Signals of urinary dysfunction were detected for narcotic analgesics opioids, antidepressant tricyclic, and aceis. Monitoring of urinary dysfunctions among patients using these medications is required.

I.10

Safety of the COVID-19 vaccine in Kidney Transplant Recipients: the experience of a single medical center

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Aim/Objective: Kidney transplant recipients are considered at high risk for critical coronavirus disease 2019 (COVID-19) illness due to chronic use of immunosuppressive medications. The association of COVID-19 Vaccine with kidney allograft outcomes remains controversial. We aimed to assess the safety of COVID-19 vaccine in post-renal transplant recipients, focusing on evaluating the chances of contracting COVID-19 and recovery of allograft renal function.

Methods: A single-center retrospective study tracking kidney transplant patients (n=52, 35 males and 17 females) vaccinated against COVID-19 from May 2019 to April 2022. Safety outcomes following administration of the COVID-19 vaccine in transplant patients were assessed. Descriptive statistics were used for patient demographics, adverse events, patient and renal allograft survival.

Results: Fifty two patients were included in this study. The median age was 49.15 years (interquartile range, [IQR] 41.4-58.8), with a predominance of males (67.3%). Kidney transplantation vintage was 8.6 (0.6-21.3) years, and 65.4 % of patients were on triple COVID-19 vaccine. After the vaccine was administered, 70.3% of the patients had symptoms of pain at the injection site, and one of them had acute rejection, renal function changes that reduced the dose of immunosuppressants, experienced irreversible graft failure, respectively. Five kidney transplant recipients tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by polymerase chain reaction, and 1 were admitted. Nobody are reported to have died from COVID-19 after being vaccinated.

Conclusion: 2.5% of patients received the COVID-19 vaccine had unpredictable responses and even impaired renal function, but the COVID-19 vaccine can reduce mortality in transplant patients. The results of this study indicated that no post-transplantation recipients have died due to COVID-19, but the renal function changes of confirmed patients should be continuously tracked in the future.

Keywords: COVID-19 vaccine, Renal transplant recipients, Safety

I.11

Evaluation of medication adherence in hypertension and dyslipidemia: population-based cohort study in Japan

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Aim/Objective: Lifestyle diseases（dyslipidemia: DL, hypertension: HT, and diabetes） are major risk factors for cardiovascular disease. Despite the use of numerous medications to reduce the cardiovascular risk, poor adherence to medications remains. The aim of this study is to evaluate medication adherence in DL and/or HT by using insurance claims. Individual-related and medication-related determinants on adherence were also examined.

Methods: Of 7,645 beneficiaries of the National Health Insurance from the participants of Tsuruoka Metabolomics Cohort Study, 1,985 had any of lifestyle diseases and took medications regularly. Information on lifestyle was collected through a questionnaire. Proportion of days covered （PDC） was calculated for 1-year after the survey and a PDC of ≥80% was considered adherent. Predictors of non-adherence were determined by performing multivariable logistic regression, adjusting for sex, age, BMI, drinking status, regular exercise habit, eating speed, sleep status, attitude toward lifestyle change, perception of the medications, the number of tablets and the instructions when to take the medication.

Results: Of 1,985 participants （DL-only: 512, HT-only: 755, DL and HT: 487), the rates of adherent were the lowest for those with DL-only [86%], followed by HT-only [91%], and DL and HT [93%]. Due to a small number of diabetes participants, only those with DL and/or HT were included in the analysis. As predictors of non-adherence, aged≥ 65, not exercising regularly and fast eating were found to be associated with DL-only and taking medications after dinner was found to be a predictor of adherence. As predictors of non-adherence, lack of motivation to improve the lifestyle and a small number of tablets were found to be associated with HT-only.

Conclusion: Although high adherence was found for those with DL and/or HT, differences were seen among medication groups. Predictors of non-adherence could help the target those who need adherence supports.

Keywords: Adherence, medications, insurance claims, cohort-study

I.12

Trends in Hozai, Kampo medicine, prescription for different age groups in Japan from 2015 to 2019

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Aim/Objective: Basic and clinical studies on Hozai, tonic formulas of Kampo medicine (traditional Japanese medicine), have drawn attention to its use in the treatment of aging-related symptoms such as sarcopenia and frailty. This study aimed to investigate the recent trends in prescription of Hozai using nationwide data in Japan.

Methods: We used publicly available aggregated data in the national claims database for the period from fiscal year 2015 to 2019. The data contained the 100 most frequently prescribed Kampo extract products by age and gender. Of these, Hochuekkito (HET), Juzentaihoto (JTT), and Ninjin'yoeito (NYT) as major Hozai were investigated, and only products for which 5-year data were available were included in the study. Furthermore, taking into account the changes in population sizes, we evaluated the trends in prescription of the three Hozai per 100,000 individuals for the following age groups: 40–64, 65–79, and ≥80 years.

Results: Over time, the total number of Hozai prescriptions increased. Throughout the study period, HET was the most commonly prescribed medication in all age groups, with a 25% increase in 40–64 year age group. NYT prescription has increased the most in the last five years (+145% in 40–64, +157% in the 65–79 year age group, and +253% in ≥80 year age group), whereas JTT prescription decreased by 19% in the 65–79 and 18% in ≥80 years. Prescription the 40–64 years and HET in the ≥65 years age groups was almost unchanged.

Conclusion: During the last five years in Japan, there has been an increase in the prescription rate of NYT, with the largest relative increase observed in those aged ≥80 years. Further studies using individual data are needed to determine whether the increase is attributable to the greater use of NYT for sarcopenia and frailty.

Keywords: Japan, Kampo medicine, NDB Open Data, Older adults

I.13

The epidemiology and treatment patterns of refractory chronic lymphocytic leukemia in Taiwan

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Aim/objective: Chronic lymphocytic leukemia (CLL) is one of the most common leukemia in Western countries and Australia, where incidence of CLL is higher (4-6.5/100,000 persons/year) than in Asia (1.5/100,000 persons/year). In this study, we employed both the Taiwan Cancer Registry (TCR) and National Health Insurance Database (NHID) to estimate the incidence of CLL, relapsed and refractory CLL patient numbers, and to identify the treatment patterns.

Method: We collected the information of the newly diagnosed CLL cases between 2013 and 2017 from the TCR and the NHID to estimate CLL incidence, relapsed and refractory CLL patient numbers, and treatment patterns. Relapsed and refractory CLL patients was defined as those who had received at least 2 cycles of alkylating agents combined with rituximab, yet the disease status remained progressing.

Results: We totally included 2267 patients aged 20 years or above with newly-diagnosed CLL during 2013-2017. The number of patients with CLL increased from 137 increased to 232, while the incidence rates from 0.59 to 0.98 per 100,000 persons in Taiwan. Most of incident CLL patients were older than 60 years-old, mainly distributed within 60-69 years. Around 6.13% (99/1617) of CLL patients were relapsed or refractory disease (incidence rates: 0.047 per 100,000 persons in 2013 and 0.13 per 100,000 persons in 2017). The treatment pattern of all CLL patients was diverse with various agents and regimens. Totally 1617 (71.28%) patients were included in our analysis for analysis of treatment pattern. Overall, around 45% patients received monotherapy with chlorambucil or cyclophosphamide, and 25% patients were treated with alkylating agent combined with rituximab.

Conclusion: The incidence rate of CLL was much lower to be compared with that in Western countries in Taiwan and the rate of relapsed and refractory CLL was lower among CLL patients in Taiwan. Further investigations on treatment effectiveness were warranted.

I.14

The risk assessment of tuberculosis in patients with severe renal dysfunction in Taiwan: a population-based cohort study

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Objectives: Patients with severe renal dysfunction have significantly higher risks of developing tuberculosis (TB) thus WHO recommends routine latent TB infection (LTBI) screening. However, this policy was not performed in Taiwan. We aimed to evaluate the TB risk and the potential risk factors for TB in severe renal dysfunction patients in Taiwan.

Methods: This study retrospectively enrolled adult patients with newly receiving maintenance dialysis or kidney transplant, from January 1, 2006, to December 31, 2015. The TB outcome was defined as the diagnostic TB code and at least three first-line anti-TB drugs for more than seven days. All patients were followed until TB development, death, or December 31, 2018. The Cox proportional hazard model was used to identified the risk factors for TB in maintenance dialysis and kidney transplant groups, respectively.

Results: During the average follow-up period of 7.30 and 7.56 years, we enrolled 98937 maintenance dialysis and 2341 domestic kidney transplant patients. Of them, the incidence rate of TB was 274.40/100,000 person-years and 254.37/100,000 person-years, and the median of TB onset was 0.37 years (mean, 2.25 years) and 0.66 years (mean, 3.19 years), respectively. Patients with comedication of short-acting steroids had a significantly higher risk for TB development in dialysis group (adjusted hazard ratio, aHR 1.79, 95% confidence interval 1.23-2.60). Prescribing comedication with calcineurin inhibitors (CNIs) or mammalian target of rapamycin (mTOR) inhibitors was associated with TB development, but not significant, and the aHR was 2.23 (95%CI 0.83-6.00) and 0.84 (95%CI 0.29-2.47) respectively in kidney transplant group.

Conclusion: The TB risk in severe renal dysfunction patients in Taiwan was similar to the previous and foreign studies. Patients with comedication of short-acting steroids is a significant risk factor in dialysis patients. Routine screenting for LTBI may be considered in the future.

Keyword: dialysis, kidney transplant, tuberculosis, risk assessment

I.15

Ethnic Disparities in Treatment Patterns of Prostate Cancer Patients in Inner Mongolia Autonomous Region, China: A Real-world Study

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Background: There is scant real-world evidence on the ethnic disparities of treatment patterns in prostate cancer (PC) patients in China. We aimed to compare treatment patterns of PC patients between Han and Minority ethnicities from Inner Mongolia Autonomous Region.

Methods: We conducted a retrospective study in three databases from Inner Mongolia Autonomous Region, China: Basic Medical Insurance Database for Urban and Rural Residents, Medical Insurance Database for Urban Workers, and Death Monitoring System. The patients diagnosed with PC from January 1st, 2010 to December 31st, 2021 were included in the analysis. PC patients were identified with diagnosis characters and ICD-10 code.

Results: A total of 4752 PC patients were included, and 563 (11.8%) were minority ethnicities. The PC patients of minority ethnicities had younger diagnosis age (71.8±8.8 vs 73.3±8.6, P<0.001) and more death (31.1% vs 26.0%, P=0.012) than Han ethnicity. Waiting for observation (40.1%) and androgen deprivation therapy (46.5%) were the two mainly treatment patterns. LHRH agonist (42.0%), androgen-receptor antagonist (21.9%), and androgen-receptor antagonist combined with 5-alpha reductase inhibitors (15.1%) were the three most frequently used medication patterns. A total of 719 (15.1%) PC patients received surgery treatment. Compared with Han ethnicity, less minority ethnicities waited for observation (32.15% vs 41.2%, P<0.001) or accepted androgen deprivation therapy (35.2% vs 42.9%, P=0.001). Chemotherapy, targeted therapy, immunotherapy, and palliative treatment were similar among two ethnicities. Minority ethnicities accepted less LHRH agonist medication (35.2% vs 42.9%, P=0.001), and more androgen-receptor antagonist (29.1% vs 21.0%, P<0.001) than Han ethnicity. For surgeries, more minority ethnicities accepted radical prostatectomy (6.4% vs 3.8%, P=0.005) or transurethral prostatectomy (12.6% vs 8.5%, P =0.002).

Conclusion: Among PC patients, minority ethnicities accepted less waiting for observation or androgen deprivation therapy, and more surgeries. The ethnic disparities in treatment patterns ought to be further considered in clinical practice.

I.16

Epidemiology of atherosclerotic cardiovascular disease in public hospitals in Hong Kong: A territory-wide study in Hong Kong, 2010-2020

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Aim: There are limited population-wide data on the disease burden for secondary prevention of atherosclerotic cardiovascular disease (ASCVD). We aim to describe the epidemiological trends and treatment patterns of ASCVD in Hong Kong.

Methods: All patients with incident ASCVD from 2010 to 2020 in a territory-wide clinical database in Hong Kong were identified. We studied the incidence trends, the prevalence of recurrent events, mortality rates, duration of hospitalization, low-density lipoprotein (LDL) cholesterol trends, and treatment patterns stratified by each ASCVD, age and sex group.

Results: A total of 243,201 patients with a mean age of 69.98 years and 59.6% males were identified. The majority of patients had coronary heart disease with 122,947 cases followed by 86,251 cases of ischemic stroke. The incidence of all ASCVD decreased from 326 to 266 per 100,000 individuals from 2010 to 2020. Myocardial infarction, angina and other acute coronary syndromes had the highest prevalence of recurrent hospitalization due to ASCVD. Peripheral vascular disease, myocardial infarction, other acute coronary syndrome and ischemic stroke had the highest mortality rate during follow-up and ischemic stroke had the longest duration of hospitalization. The majority of patients with ASCVD received simvastatin in Hong Kong and the uptake of non-statin lipid-lowering agents was very low. Although 80.42% of patients received statins during follow-up and most of them started prescription directly after ASCVD diagnosis for over a year, half of the patients still had an LDL cholesterol level over 1.8 mmol/L after one year of follow-up.

Conclusion: The overall incidence of ASCVD has decreased from 2010 to 2020. Despite high coverage of statin prescriptions in Hong Kong, a big proportion of patients still did not meet the target LDL cholesterol level.

I.17

Insights into pharmacoepidemiologic burden of esophageal cancer patients: actionable evidence from the regional claims database and death registry in China

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Aim: Generating cost-effective evidence from real world data (RWD) has become a boosting paradigm in pharmacoepidemiologic studies, especially for cancer-related health managements. We utilize RWD for pharmacoepidemiologic burdens on esophageal cancer (ECa) in China.

Methods: Between 2008 and 2021, full-cycle records on diseases diagnoses and prescriptions were captured for ECa patients using the claims database in inner Mongolia, China. The first admission date of diagnosis related to ECa was identified as their cancer onsetting date. ECa patients were subsequently linked to death registry for their survival information, including death date and cause of death. Data linkage and integration is conducted using de-identified personal identify number for privacy protection.

Results: 16635 new-onsetting ECa patients with 5141697 pieces of prescription records (accorded to 73.4% patients) were identified from claims. ECa patients' age at first diagnoses was 64[IQR = 14]. 9036 patients died with 237 days of median survival [IQR = 382.5] after first diagnoses. Shorter survival time was found in female (median survival = 217 [IQR = 377] days), while male was reported an earlier age at diagnosis but higher incidence and mortality rates, 8.96 and 9.53 to female. Among 2377552 pieces of prescriptions after ECa diagnoses, only 48.5% patients (n = 8068) were captured during median interval of 491[IQR = 807] days between dates of first diagnoses and last prescriptions. 144771 pieces of prescriptions were on antineoplastic agents and 149272 on alleviators of side effects due to ECa therapies.

Conclusion: Low drug prescriptions and treated population were found during ECa therapies after diagnoses. This relates to short survival in both sex after diagnoses, as patients with prescription records showed longer survival. Our findings highlight the priority of earlier detection (i.e., screening) and ECa treatments, especially for high risky male ECa patients.

Keywords: administrative claims database, death registry, esophageal cancer, cancer therapy

I.18

Disparities in treatment patterns between male and female breast cancer: a 9-year real-world study in China

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Objective: Treatments recommendations for male breast cancer (MBC) were extrapolated from guidelines for female breast cancer (FBC), little is known about disparities of treatment patterns between MBC and FBC. We aimed to describe this disparities in China.

Methods: A retrospective population-based cohort was established based on Medical Insurance data of Inner Mongolia (2012-2021), the largest Mongolian gathering zone in the northern China. Patients diagnosed with breast cancer were identified with diagnosis characters and ICD-10 code. Treatments of interest included surgery, lymph node dissection and antitumor drug.

Results: Of 636 MBC and 34 823 FBC identified, MBC were diagnosed at older age (58.88±13.97 vs 52.35±10.99, P<0.001). More MBC died during follow-up (20.60% vs 11.99%, P<0.001). In total, only 21.86% of MBC and 45.43% of FBC received any anti-tumor treatment (P<0.001). Specifically, MBC received less surgery (11.16% vs 29.17, P<0.001), including 5.82% mastectomy and 0.16% breast-conserving surgery, compared to 18.30% (P<0.001) and 1.91% (P<0.001) in FBC. Marginal significant differences were discovered in patients who delivered sentinel lymph node biopsy and axillary lymph node dissection between MBC and FBC (0.94% vs 2.10%, P=0.047; 0.94% vs 1.93%, P=0.078). Furthermore, MBC received less antitumor drugs (13.68% vs 27.52%, P<0.001) including only 6.13% taxane (vs 13.09%, P<0.001), 0.47% trastuzumab (vs 2.47%, P=0.002) and 0.16% anthracyclines (vs 2.02%, P=0.001). Besides, MBC visited less (1.95±3.01 vs 5.43±6.30, P<0.001) and stayed shorter in hospital (9.29±23.43 days vs 10.77±29.22 days, P=0.027) but spent more per visit ($1691.18±2346.44 vs $1526.98±2038.82, P=0.014).

Conclusion: MBC patients tended to receive less treatments but spent more per visit, as well as worse prognosis. More advanced investigations about MBC targeted efficient treatments and management are urgently needed to improve the prognosis. Meanwhile, treatment proportions for FBC should also be at least doubled.

Keywords: Treatment patterns disparities, male breast cancer, real-world study, antitumor drug, surgical treatment

J. Prevention of medication errors and drug misuse/abuse

J.1

Assessment of drug interactions in CKD patients and identification of the associated independent risk factors - a retrospective study

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Aim/Objective: To evaluate the number and types of potential drug-drug interactions (pDDIs) and to identify the independent risk factors associated with its occurrence by binary logistic regression.

Methods: A retrospective study was conducted at a tertiary care teaching hospital with 392 CKD patients. The relevant patient demographics and clinical details were collected and documented in case record forms. Using different drug interaction detecting databases, the acquired data were screened to identify and classify pDDIs. Binary logistic regression was used to identify independent risk factors associated with the occurrence of pDDIs. Data entry and analysis were done using IBM SPSS software v20.0. The results were reported as odds ratios with a 95% confidence interval.

Results: Mean age of the study population was 45.97 ± 10.32 years and almost 87% of the population belonged to stage 5 of CKD. A total of 2054 interacting drug pairs were found from the 392 patient files screened, out of which about 55.6% of the interactions were of moderate severity. Insulin and oral antidiabetics with furosemide was found to be the most commonly interacting drug pair. Multivariate logistic regression showed that CKD stages 3a and 3b and the number of prescribed medications were significantly associated with the occurrence of pDDIs.

Conclusion: This study could play a significant role in the early prediction of pDDIs as well as the assessment of frequent interactions using prior information about the attributes of various administered drugs. This can assist the clinicians to prevent undesirable interactions, choose therapeutic alternatives, and provide necessary interventions in case of any adverse events, which will ultimately improve the therapeutic outcome for CKD patients.

Keywords: chronic kidney disease, potential drug-drug interactions, risk factors

J.2

Information provided on OTC medicines at community pharmacies in Armenia

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Aim/Objective: Patients can make mistakes when using medicines. Pharmacists and pharmacy technicians working at community pharmacies play an important role in ensuring safe and effective use of medicines by patients through providing necessary medicines information (MI). The aim of this study was to identify specific topics of MI provided by pharmacy professionals to patients when dispensing over-the-counter (OTC) medicines at community pharmacies in Armenia.

Methods: 348 professionals (pharmacists and pharmacy technicians) working at randomly selected community pharmacies in all the 11 regions of Armenia including Yerevan were interviewed. Previously developed and tested questionnaire was used for interviewing respondents. Statistical analysis was carried out using SPSS statistical software, version 22.0.

Results: More than three quarters of all the respondents reported that when dispensing OTC medicines to patients they provide information on dosage (98.0% of professionals), method of administration (96.6%), therapeutic indications of pharmaceuticals (95.1%), storage conditions (83.0%), contraindications (82.5%) and adverse reactions (77.9%). 60.3% of all the participated professionals mentioned that they provide data on interaction with other medicines or foodstuffs. Pharmacists more often than pharmacy assistants gave information on medicine storage conditions at home ($p<0.001$) when they dispense OTC medicines at community pharmacies.

Conclusion: Most of professionals when dispensing OTC medicines provide necessary information on medicines to patients. For providing appropriate MI to patients, the pharmacy staff needs access to sources of independent, objective, comprehensive and up-to-date information.

Keywords: medicines information, community pharmacists

J.3

Real-world effectiveness of follow-up care on the reduction of suicidal attempts in patients with opioid use disorder.

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Aim/Objective: To evaluate the effectiveness of follow-up care on the reduction of risk of suicidal attempts.

Methods: We conducted a case-crossover study by analyzing the data from Suicide Prevention System (SPS) and Drug Abuse Case Management System (DACMS). We included patients who were enrolled in DACMS program for opioid use disorder (OUD) with a record of suicide attempt from 2013 and 2020 in Tainan metropolitan city. We defined the date of suicide attempt as index date. We defined the 1-45 days, 46-75 days and 76-120 days before the index date as the event, washout and reference windows, respectively. We performed conditional logistic regression to compare the rate of follow-up care in event window comparing with reference window. To address the temporal trends of follow-up care, we conducted a case-time-control analyses by selecting control patients without suicide attempt 1:1 matching by age and sex. We redefined the event and reference window from 45-day to 30-day or 90-days intervals to test the result robustness.

Results: We identified a total of 268 cases. The average age was 42.7 (SD 8.7) and 65.3% were male. The case-crossover analysis showed patients had lower rate of follow-up care in event window comparing with reference window (OR, 0.86; 95% CI, 0.50-1.48). The control-crossover analysis showed a higher rate of follow-up care in event window than reference window (1.45; 0.99-2.14), suggesting a corrected case-time-control OR of 0.59 (0.50-0.69). The results were consistent when we refined event and reference windows to 30-day (0.44; 0.56-0.86) or 90-days (0.68; 0.56-0.83) intervals.

Conclusion: We finding suggested follow-up care was associated with 41% reduced risk of suicide attempts in patients with OUD. The finding could be a fundamental ground for policy making to avoid suicide risk in patients with OUD.

J.4

Inappropriate medication use in 26,151 school aged children in Jiangsu of China

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Objective: Inappropriate medication use in school aged children can result in adverse health and social outcomes. Previous studies estimated that 26.4%-51.8% of school aged children had experienced inappropriate medication use in America, 17.6% in Canada, and 3.8% in Japan. In this study, we aimed to examine the prevalence of inappropriate medication use in school aged children in Jiangsu of China and to explore potential multilevel factors associated with inappropriate medication use in children.

Methods: We used data for 26,151 school aged children from the Surveillance for Common Disease and Health Risk Factors among Students during the 2020-21 academic year in Jiangsu province. We performed multilevel logistic regression to evaluate the association of individual-, school-, and district-levels factors with inappropriate medication use in children.

Results: The prevalence of inappropriate medication use in school aged children in Jiangsu of China was 16.5% (95%CI: 16.0%-17.0%). Inappropriate medication use in children was more common in rural areas than their urban counterparts (RR:1.35, 95%CI:1.27-1.44). Individual-level factors (including smoking, drinking, internet addiction, sleep insufficiency, and lack of exercise) and school-level factors (including boarding school) were associated with inappropriate medication use in children.

Conclusion: Inappropriate medication use in school aged children in Jiangsu of China demonstrates an unrecognized problem that requires immediate countermeasures. Potential intervention strategies should target rural children and those with unhealthy lifestyles, especially in boarding schools where medication safety initiatives should be established.

Keywords: Inappropriate medication use, Children, Prevalence, China

K. Rare disease and orphan medicines

K.1

Health state utility values in glioblastoma multiforme: A systematic literature review

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Objective: Glioblastoma multiforme (GBM) is an aggressive form of brain cancer with grade-IV malignancy. Health state utilities values (HSUVs) are required to conduct economic evaluations to make informed healthcare decisions. The current systematic literature review (SLR) assessed the HSUVs in GBM patients.

Methods: Medline, Embase and Cochrane databases (via-Ovid) were searched comprehensively from inception to May-13-2022. Web searches and bibliography of included studies were also conducted for additional publications. Studies (in-English) reporting HSUVs in GBM were included. Two-reviewers independently performed all steps followed by third reconciler wherever required. Quality-assessment was conducted using Newcastle-Ottawa-Scale.

Results: Eight observational were included after screening 244 studies. All included studies used EuroQol-five-dimension scale to evaluate HSUVs. GBM patients had poor mean HSUVs (0.51). Progressed patients had significantly lower (worse health-state) mean HSUVs (0.26) than stable disease (0.53, p<0.001) and those responding to treatment (0.61, p<0.001). The mean/median HSUVs for GBM patients receiving Tumor-Treating Fields (TTFields) therapy were 0.836/0.913. GBM patients receiving TTFields therapy with disease progression and no disease progression reported mean/median HSUVs 0.748/0.855 and 0.882/0.929, respectively. GBM patients receiving first-line treatment had poor mean HSUVs (0.57). The mean HSUVs were 0.67 preoperatively and 0.62 postoperatively. In primary-surgery group, HSUVs were slightly improved from pre-operation (0.760) to post-operation (0.796) but inverse results were reported in recurrent-surgery group (0.796 vs. 0.760, respectively). Functionally dependent (Karnofsky-performance-status, KPS <70) GBM patients showed non-significant improvement in mean HSUVs from preoperative (0.34) to postoperative (0.45). Functionally independent patients (KPS ≥70) had significantly better HSUVs than functionally dependent patients at post-operation (mean: 0.71 vs. 0.45, p=0.009).

Conclusion: GBM patients showed poor HSUVs indicating deteriorated quality of life. Progressed patients had worse HSUVs than patients with stable disease and responding to treatment. This SLR provides essential inputs for conducting economic analysis and policy making.

Keywords: Glioblastoma; Health state utility values

K.2

Repurposing of anti-rheumatic drugs for cystic fibrosis: a disproportionality inverse signal analysis in spontaneous reporting database

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Objective: To identify potential drug-repositioning by inverse associations revealed through disproportionality analysis in FDA Adverse Event Reporting System (FAERS) database

Methods: Using OpenVigil 2.1, a case/non-case retrospective disproportionality study was done in the publicly available FAERS database (2004Q1-2022Q1). OpenVigil is a pharmacovigilance based tool for extraction of drug safety reports and generation of new hypotheses. The preferred term used for the study was “cystic fibrosis” and the drugs included in the analysis were ones used in the treatment of Rheumatoid Arthritis(RA) . Reporting odds ratio(ROR) was used as a measure for disproportionality. A value of ROR+1.96SE<1 and ≥5 cases was considered as a threshold for inverse signal.

Results: FAERS database had a total of 2733 reports associated with cystic fibrosis, of which 53 reports had significant inverse signals of drugs used in treatment of RA. The number of case reports for methotrexate, hydroxychloroquine, adalimumab, abatacept, etanercept
and tofacitinib associated cystic fibrosis were 16,5,14,6,6 and 6 respectively. Significant inverse signals were obtained for methotrexate[ROR 0.275(95%CI:0.168-0.449)], hydroxychloroquine[ROR 0.349(0.145-0.839)], adalimumab[ROR 0.191(0.113-0.323)], abatacept[ROR 0.433(0.194-0.965)], etanercept[ROR 0.055(0.024-0.122)] and tofacitinib[ROR 0.234(0.105-0.522)].

Conclusion: The discovery of an inverse relationship of drugs used in the treatment of RA with cystic fibrosis was a notable result of our study. Scanning pharmacovigilance data for inverse signals can aid in the development of novel drug repurposing hypotheses, theoretically for all indications. In silico, in vitro, and in vivo research must be undertaken to validate these findings, and these discoveries translated to the clinics.

Keywords: Cystic Fibrosis, Neglected disease, FAERS, Anti-rheumatic drugs

L. Post-marketing drug effectiveness and safety evaluation

L.1

Investigation of depression and suicidality of glucagon-like peptide-1 receptor agonist in patients with antipsychotic-induced weight gain

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Aim/Objective: Some biological evidence suggests that concomitant use of atypical antipsychotics with glucagon-like peptide-1 receptor agonist (GLP-1ra) may accompany depressive symptoms. We aimed to investigate whether GLP-1ra attribute to antipsychotic-associated depression or suicidality.

Methods: We conducted a case/non-case analysis using WHO-VigiBase from Jan 2008 to Apr 2022. We included two classes of drugs, antipsychotics (clozapine, olanzapine, risperidone, paliperidone, aripiprazole, and quetiapine) and GLP-1ra (albiglutide, dulaglutide, liraglutide, semaglutide, exenatide, and lixisenatide). Cases were defined by reports in which AEs included depression and self-injury/suicide using SMQ terms. Non-cases were defined by other AE reports. We extracted all consecutive AE reports of antipsychotics and classified them into two groups, antipsychotics with GLP-1ra and antipsychotics only. Subsequently, we calculated the adjusted reporting odds ratio (aROR) by multivariable logistic regression to investigate the potential association between the use of antipsychotics with GLP-1ra and depression or suicidality. Additionally, we performed sensitivity analyses by restricting the database reported by physicians and reported as serious AE (SAE) to validate the robustness of our findings.

Results: We identified 302 reports of antipsychotics with GLP-1ra (195 [65%] female; 242 [80%] aged 18-64 years; 164 [54%] and 110 [36%] reported from America and Europe). Compared with reports in patients who received antipsychotics only, concomitant use of antipsychotics with GLP-1ra was associated with lower reporting of depression or suicidality (38 reports for antipsychotics with GLP-1ra versus 113,469 reports for antipsychotics only, aROR 0.42 [95% CI 0.30-0.58]). Sensitivity analyses also showed the significantly lower reporting of depression or suicidality in patients who received antipsychotics with GLP-1ra (aROR 0.34 [95% CI 0.13-0.86] and 0.47 [0.31-0.72] when restricting the database reported by physicians and reported as SAE, respectively).

Conclusions: Our findings supported the acceptability of using GLP-1ras in the management of antipsychotic-induced weight gain from a psychiatric safety perspective.

Keywords: Antipsychotics, GLP-1ra, Depression, Self-injury/Suicidality

L.2

Kidney outcomes with sodium-glucose cotransporter-2 inhibitors in type 2 diabetes: Does background treatment with metformin matter?

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Aim/Objective: This study aimed to investigate whether sodium-glucose cotransporter-2 inhibitors (SGLT-2is)-associated kidney effects would be modified by background treatment of metformin.

Methods: Individual-level data of patients with type 2 diabetes between May 2016 and June 2018 were collected from three healthcare delivery systems separately and transformed into a common data model for multi-database analysis. New users of SGLT-2is with and without metformin background treatment were identified and matched in each healthcare delivery system using a propensity score matching procedure (up to 4:1) to balance baseline patient characteristics (e.g., HbA1c and eGFR). Cox regression models were used to compare the times to 30%, 40%, and 50% estimated glomerular filtration rate (eGFR) reduction following SGLT-2i initiation. The change of eGFR over time was also measured and compared. A sensitivity analysis was conducted using background treatment with sulfonylureas as a negative control exposure to confirm study robustness.

Results: After matching, there were 6,646 and 3,282 new users of SGLT-2is with and without metformin included, respectively. The baseline eGFR was 86.06 and 83.79 mL/min per 1.73 m2 in the two treatment arms. An eGFR dip was observed around one month after SGLT-2i initiation in those with and without metformin, with the mean relative changes of -3.23% and -2.93%, respectively. Subsequently, the eGFR improved and sustained until the end of the 12-month follow-up in both treatment groups, with no significant between-group difference in slowing eGFR declines (i.e., hazard ratios [95% CIs] for 30%, 40% and 50% eGFR reductions: 0.94 [0.81-1.08], 0.88 [0.71-1.09], 0.90 [0.66-1.22], respectively). Similarly, the background treatment with sulfonylurea did not change SGLT-2is-associated kidney effects.

Conclusion: Background treatment with metformin did not affect the level of eGFR change following SGLT-2is initiation.

Keywords: kidney outcomes, SGLT-2 inhibitors, metformin, combination therapy

L.3

Effectiveness and Safety of Direct Oral Anticoagulants versus Warfarin in Patients with Atrial Fibrillation and Advanced Kidney Disease

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Aim/Objectives: To evaluate the effectiveness and safety between direct oral anticoagulants (DOACs) and warfarin in Taiwanese patients with atrial fibrillation (AF) and advanced kidney disease.

Methods: Patients with AF and advanced kidney disease were selected at a medical center in Taiwan between July 2011 and December 2020. The primary outcomes were admissions due to ischemic stroke or systemic embolism and major bleedings. Survival analyses were performed to estimate Kaplan-Meier curves and hazard ratios (HRs) with 95% confidence intervals (CIs) using inverse-probability-of-treatment weighted Cox proportional hazards models. In secondary DOAC-specific analyses, we examined HRs with 95% CIs for the association of each DOAC.

Results: A total of 1011 patients with atrial fibrillation and creatinine clearance less than 30 mL/min were enrolled, of whom 809 (80.0%) were in the DOACs group (15.3% dabigatran, 25.4% rivaroxaban, 25.2% apixaban, 14.1% edoxaban), and 202 (20.0%) in the warfarin group. In weighted cohorts compared to warfarin, after adjusting for age, sex, comorbidities, and co-medications, the DOACs group had significantly lower risks of ischemic stroke or systemic embolism (adjusted hazard ratio [aHR] 0.29; 95% CI, 0.09-0.97; P=0.0439), and any ischemic events (aHR: 0.42; 95% CI, 0.22-0.79; P=0.0067), but had similar risks of major bleeding (aHR: 0.99; 95% CI, 0.34-2.92; P=0.9851) and any bleeding event (aHR: 0.74; 95% CI, 0.50-1.09; P=0.1236). In secondary analyzes, apixaban was associated with significantly lower risks of any ischemic event (aHR: 0.13; 95% CI, 0.04-0.48; P=0.0021) and any bleeding event (aHR: 0.53; 95% CI, 0.28-0.99; P=0.047) than warfarin.

Conclusion: Among patients with AF and advanced kidney disease, DOACs may be associated with a lower risk of ischemic events compared to warfarin, and apixaban appears to be a safe and effective alternative to warfarin in this population.

L.4

Comparative Cardiovascular Safety of Fixed-dose Combinations of LABA/LAMA versus LABA/ICS in Patients with COPD

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Background: Combinations of long-acting β2 agonist/long-acting muscarinic antagonist (LABA/LAMA) and long-acting β2 agonist/inhaled corticosteroid (LABA/ICS) are recommended for COPD patients with persistent symptoms and high risk of acute exacerbation. There has been increasing use of both combination therapies after the reimbursement of the fixed-dose combination (FDC) dosage form. However, real-world evidence that focused on the cardiovascular (CV) safety of LABA/LAMA in comparison with LABA/ICS remains limited.

Objective: This cohort study aimed to investigate the CV safety of LABA/LAMA FDC versus LABA/ICS FDC in patients with COPD in real-world settings.

Methods: We identified patients with COPD who initiated LABA/LAMA or LABA/ICS FDCs from a nationwide Taiwanese database between 2017 and 2020. The outcomes of interest were hospitalized composite CV events, including acute myocardial infarction, unstable angina, heart failure, cardiac dysrhythmia, and ischemic stroke. We estimated propensity scores (PS) for each patient based on their baseline demographics, comorbidities, concurrent medications, and resource utilizations. The Cox proportional regression model was applied to estimate the hazard ratios (HR) and the 95% confidence intervals (CI) for composite and individual CV outcomes comparing LABA/LAMA versus LABA/ICS after PS matching.

Results: The study population consisted of 61,221 LABA/LAMA FDC initiators and 38,285 LABA/ICS FDC initiators. After 1:1 PS matching, 54,104 patients were included in the analysis. The HR of composite CV events comparing LABA/LAMA and LABA/ICS was 0.96 (95% CI, 0.80-1.09). The results did not materially change for individual CV outcomes. In subgroup analyses, the results were similar although LABA/LAMA seemed to have a lower risk of composite CV events in patients aged ≥65 years, male patients, and those with COPD duration <1 year compared to LABA/ICS.

Conclusion: In this population-based cohort study, we observed a comparable CV safety profile between LABA/LAMA and LABA/ICS in patients with COPD.

Keywords: Chronic obstructive pulmonary disease, LABA/LAMA, LABA/ICS, cardiovascular safety

L.5

Long Term Use and Major Adverse Cardiac Events between Abiraterone and Enzalutmide in Chemotherapy-naive patients with Metastatic Castration-Resistant Prostate Cancer

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Aim/Objective: This is a retrospective cohort study by analyzing a multi-institutional electronic medical records database in Taiwan to compare long-term effectiveness and risk of major adverse cardiac events (MACE) in chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC) patients treated with enzalutamide (ENZ) or abiraterone (AA).

Methods: Patients aged 20 years and older and newly receiving androgen receptor targeted therapies ENZ or AA from September 2016 to December 2019 were included. We followed patients from initiation of therapies to the occurrence of outcomes (prostate-specific antigen (PSA) response rate, PSA progression free survival (PFS), overall survival (OS), and MACE), death, the last clinical visit, or December 31, 2020. We performed multivariable Cox proportional hazard models to compare ENZ and AA groups for the measured outcomes.

Results: A total of 363 patients treated with either ENZ (n=157) or AA (n=206) were identified. The analysis found a significantly higher proportion of patients with a PSA response rate higher than 50% among those receiving ENZ than among those receiving AA (ENZ vs. AA: 75.80% vs. 63.59%, p=0.01). However, there was no significant difference in PSA PFS (adjusted hazard ratio: 0.89; 95% CI 0.65–1.22) and OS (0.65: 0.40–1.07) between the use of ENZ and AA in chemotherapy-naïve mCRPC patients. Regarding the cardiovascular (CV) safety outcome, there was a significantly lower risk of MACE in patients receiving ENZ, compared to patients receiving AA (0.28: 0.10–0.75).

Conclusion: The findings suggest that enzalutamide may be more efficacious for PSA response and suitable for chemotherapy-naïve mCRPC patients with high CV risk profile.

L.6

Evaluation of confounding by indication in cohort study of Crohn's disease patients exposed biologics

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Aim/Objective: To estimate sub-optimal outcomes of biological use in Crohn's disease (CD) patients using different comparison group.

Method: This study was a retrospective cohort study using Taiwan's National Health Insurance data (NHID) from 2003-2018. We identified CD patients with biologic treatment in the post-biological era (POB, 2011-2018). We selected two comparison groups: an external control group as biologics-naïve CD patients in pre-biological era (PRB, 2003-2010) and a parallel control group as non-biologics users in the post-biological era (PNOB, 2011-2018). The index date was the 1st biological prescription date in POB group. In PRB/PNOB group the index date was assigned by computer based upon the distribution of duration between the 1st CD-related medication and 1st biologics date in POB group. Followed 1-year and study outcome was sub-optimal outcomes defined as CD-related hospitalization, emergency room visit and surgeries. We applied stabilized inverse probability of treatment weighting (sIPTW) estimation to adjust confounding factors and performed Cox regression model to estimate hazard ratio (HR) and 95% confidence interval (CI) within intention-to-treat (ITT) and as-treated (AT) analysis.

Result: We enrolled 735 CD patients (PRB: 286; POB: 220, PNOB: 229). There was no statistical difference for sub-optimal outcomes between 2 era groups (HR, 0.98; 95%CI, 0.65-1.46) in ITT analysis. A consistent finding was observed in AT analysis (HR, 089; 95%CI, 0.59-1.35). However, we found a significant decreased suboptimal outcome (HR, 0.65; 95%CI,0.44-0.95) in PNOB compared to PRB group and POB had a significant increased sub-optimal outcome in comparison with PNOB, HR=2.29, 95%CI, 1.58-3.31).

Conclusion: Confounding by indication presented in this cohort study by using IPTW approach. Further research on reducing this bias or residual unmeasured confounding factors is needed.

Keywords: Crohn's disease, biologics, sub-optimal outcomes

L.7

The Result of Post Marketing Surveillance of Remdesivir in COVID-19 Patients: Safety Profile in Indonesia

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Introduction: Remdesivir has obtained Emergency Use Authorization (EUA) for COVID-19 in many countries, including Indonesia. However, the massive use of remdesivir for COVID-19 patients in Indonesia needs a safety evaluation through a post-EUA surveillance study.

Methods: This post-EUA surveillance was designed in a prospective cohort study to compare remdesivir with other standard therapy in COVID-19 patients admitted to the three referral hospitals (private, academic, or public referral hospitals) in Indonesia between June – November 2021. The data were analyzed descriptively to estimate the proportion of adverse events (AEs), including serious adverse events (SAE).

Results: There were 402 COVID-19 patients hospitalized at the respective three referral hospitals between the study period, 394 patients (327 of them received remdesivir, 67 were controls) were analyzed. There were no significant differences between remdesivir and controls, respectively, in gender (female, 40.7% vs 47.8%), pregnancy status (3.0% vs 3.1%), elderly status (41.0% vs 31.3%), and comorbidities (71.3% vs 77.6%). Among top 10 non-serious adverse events, breathlessness and fever are significantly higher in remdesivir than in control group. There was no statistically difference in Serious Adverse Event (SAE) and no hypersensitivity / anaphylactic reaction case in both groups. Furthermore, there were no statistically differences in hyperuricemia, psychoneurotic, acute respiratory failure, hypotension, hypertension, and gastrointestinal events in both groups.

Conclusion: Based on this pharmacovigilance study, there are no additional safety concerns related to the use of 100 mg remdesivir indicated for patients with COVID-19. No evidence emerged of previously unknown side effects.

Keywords: remdesivir, COVID-19, post-marketing, pharmacovigilance

L.8

Cardiovascular outcomes of discontinuing statins prescribed for primary prevention in elderly Asian population

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Objective: To assess whether discontinuation of statins for primary prevention is associated with higher risks of cardiovascular events in patients aged 75 years and older.

Methods: This retrospective cohort study was conducted with a nationwide claims database. Patients who turned 75 years old (i.e., cohort entry) between January 2006 and December 2017 with continuous statin use for primary prevention in the previous year were first enrolled. Subjects who stopped statin therapy after 75 years old were identified as discontinuers. Statin discontinuers were compared with continuers who were matched with propensity score and the year of cohort entry. The primary outcome was 3-point major cardiac adverse events (3P-MACE, including nonfatal myocardial infarction, stroke, and cardiovascular death), and the secondary outcomes included all-cause mortality, 6P-MACE, and the individual components of 3P-MACE. A series of sensitivity analyses were performed to assess the study's robustness.

Results: There were 32,149 patients included in both the discontinuer and continuer groups after matching. Overall, 64% were female and the mean age at the index date was 77.5 years. Most of the patients used moderate-intensity statins and were in a fit frailty condition. Hypertension (74%), diabetes mellitus (56%), and hyperlipidemia (70%) were the frequent comorbidities. Patients who discontinued statin had a significantly higher risk of 3P-MACE (HR 1.35, 95% CI 1.20-1.52), stroke (HR 1.23, 95% CI 1.03-1.46), cardiovascular death (HR 1.39, 95% CI 1.17-1.64), all-cause mortality (HR 1.42, 95% CI 1.31-1.55) and 6P-MACE (HR 1.38, 95% CI 1.25-1.53). In general, the sensitivity analyses showed consistent results.

Conclusion: Our study revealed that discontinuation of statin for primary prevention was associated with increased risks of cardiovascular events in those aged 75 years and older. Further studies are needed to evaluate whether the risk is different among subgroups with different characteristics.

Keywords: Cardiovascular outcomes; Statin discontinuation; Primary prevention; Elderly.

L.9

Clinical Outcomes of Ticagrelor-and Clopidogrel-based Dual Antiplatelet Therapy in Acute Myocardial Infarction Patients with a History of Ischemic Stroke

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Objective: This study aimed to compare the effectiveness and safety between ticagrelor or clopidogrel based dual antiplatelet therapy (with aspirin) among patients having acute myocardial infarction (AMI) with a prior history of ischemic stroke.

Methods: This retrospective cohort study was conducted using a nationwide claims database. Patients with a history of ischemic stroke who were prescribed with ticagrelor plus aspirin or clopidogrel plus aspirin after the primary AMI hospitalization between July 1, 2013 and December 31, 2018 were included. Inverse probability of treatment weighting was applied to balance the covariates between groups. We assessed outcomes including AMI, ischemic stroke, composite major cardiovascular events (i.e., the composite of ischemic stroke and AMI), intracranial hemorrhage (ICH), major gastrointestinal (GI) bleeding, and composite major bleeding events (i.e., the composite of either ICH or GI bleeding).

Results: A total of 1,691 eligible patients were enrolled in our study, of which 734 (43.4 %) patients received ticagrelor plus aspirin treatment and 957 patients received clopidogrel plus aspirin treatment. Ticagrelor group was associated with a lower risk of composite major cardiovascular events (HR=0.78 [0.62-0.97]), but a higher risk of ICH (HR=3.34 [1.27-8.81]), as compared with the clopidogrel group. There were no significant differences regarding the risks of AMI (HR=0.79 [0.59-1.07]), ischemic stroke (HR=0.77 [0.55-1.06]), major GI bleeding (HR=0.82 [0.45-1.49]), or composite major bleeding events (HR=1.26 [0.78-2.04]) between the two groups.

Conclusion: In AMI patients with a history of ischemic stroke, ticagrelor-based dual antiplatelet therapy reduced the risk of cardiovascular events, but increased the risk of ICH. Patients using this combination therapy should be carefully monitored, especially among patients who carry additional risk factors for ICH.

Keywords: acute myocardial infarction, ischemic stroke, ticagrelor, clopidogrel

L.10

Stevens-Johnson syndrome in a patient receiving cetuximab and nivolumab for sigmoid colon cancer.

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Objective: Cetuximab and nivolumab were approved for several advanced malignancies. However, cetuximab and nivolumab could lead to life-threatening severe cutaneous adverse reactions (SCARs). If SCARs could be quickly recognized, the patient's mortality risk could be significantly decreased.

Methods: This case report described a patient with metastatic sigmoid colon carcinoma suffering from cetuximab and nivolumab-induced SJS.

Results: An otherwise healthy 67years old man was diagnosed with sigmoid colon cancer with liver metastases, stage 4B, BRAF V600E (+), presented diffuse erythematous plaques with dusky red centers on trunk and extremities after treatment with cetuximab and nivolumab for 2 weeks.
The patient shifted to the combination therapy (cetuximab, dabrafenib, trametinib, nivolumab) on day 0. Small rashes appeared on the distal extremities (bottoms of feet, lower legs, and ankles) on day 15. The rash progressed to extremities and trunk, with no discomfort complained to the eyes and the genitourinary tract, but slight ulcers in the mouth were found and the palms showed swelling. The therapy was suspended, a steroid was prescribed, and conducted a skin biopsy on day 20.
There were sub epidermal blisters with confluent macules and a few lesions with epidermal central necrosis and erosion over extremities of more than 20% of the body surface area. The microscopic finding showed the atrophic of the epidermis, cell necrosis, and a focal vacuolar interface alteration.
The rash was relieved after being suspended for two weeks. After rechallenged the dabrafenib and trametinib, the patient underwent a cetuximab rechallenge test with recurrence, confirming the cetuximab-related SJS.

Conclusion: It is important to recognize Stevens-Johnson syndrome earlier, distinguish SJS from other nonfatal dermatologic toxicities, and discontinue causative agents rapidly. This is relevant and important considering that the use of cetuximab and nivolumab in oncology is increasing in multiple cancer types.

Keywords: cetuximab, nivolumab, Stevens-Johnson syndrome

L.11

Regional Differences in Propacetamol-related Adverse Events: A World Health Organization Pharmacovigilance Study To Support Decision-Making

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Aim/Objective: Propacetamol, an injectable formulation of the paracetamol prodrug, has been widely utilized to manage fever in Asia. However, in accordance with the withdrawal of propacetamol in Europe due to safety concerns of injection site reaction (ISR) and thrombosis, the South Korea's regulatory body requested a post-marketing surveillance study, as part of the risk management plan, exploring the safety profile of propacetamol across Asia and Europe. We therefore aimed to characterize regional disparities in adverse events (AE) associated with propacetamol between Asia and Europe.

Methods: By using the World Health Organization's pharmacovigilance database, VigiBase, we performed a disproportionality analysis using reporting odds ratios (ROR) and information component (IC) to determine whether five AEs of interest (anaphylaxis, Stevens-Johnson Syndrome [SJS], thrombosis, contact dermatitis/eczema, injection site reaction [ISR]) were associated with propacetamol compared to non-propacetamol injectable antipyretics in Asia and Europe, separately.

Results: In Asia, there was a high reporting ratio of propacetamol-related ISR (ROR 5.72, 95% CI 5.19-6.31; IC025 1.27), which satisfied the criteria as a signal (e.g., ROR≥2, IC025>0); however, there were no reports of thrombosis and contact dermatitis/eczema. Meanwhile, two signals were identified in Europe, with higher reporting ratios for thrombosis (7.45, 5.19-10.71; 1.92) and contact dermatitis/eczema (16.73, 12.48-22.42; 2.85); only one criterion of a signal were met for SJS (1.78, 1.29-2.47; 0.23) and ISR (1.65, 1.30-2.10; 0.27). Reporting ratios of propacetamol-related anaphylaxis were low for both Asia (0.13, 0.10-0.16; -2.97) and Europe (0.65, 0.48-0.88; -1.07). Results of the sensitivity analysis that compared propacetamol to paracetamol were consistent with main findings.

Conclusion: While signals were found for thrombosis and contact dermatitis/eczema in Europe, these were not detected in Asia. Our findings on propacetamol-related AEs in an Asian population suggest potential ethnic differences in propacetamol related AEs between Asia and Europe, which could serve as supportive data for future decision-making.

L.12

Association between Bone-Targeted Agents and Skeletal-Related Events in Breast Cancer Patients with Bone Metastasis

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Aim/Objective: Bone metastasis is common (70%) in breast cancer (BC) patients. Majority of them (50%) may develop skeletal-related events (SREs). The efficacy of denosumab has been demonstrated in previous clinical trials, evidence from Asian or from real-world data are still limited. The aim of this study is to compare the effectiveness between denosumab and bisphosphonates on skeletal-related events in BC patients with bone metastasis.

Methods: This study used databases including Cancer Registry (CR) and National Health Insurance Research Database (NHIRD) from 2006 to 2018. The BC patients were identified from CR (ICD-O-3: C50). The bone metastasis diagnosis and prescriptions of denosumab or bisphosphonates were identified by using ICD-10 and order codes from NHIRD. SREs were defined as having records of pathological fracture, spinal cord compression, and surgery or radiotherapy related to bone. The propensity score (PS) weighting was applied to balance baseline characteristics between groups. Kaplan-Meier estimates, Cox regression and Poisson regression were used to compute median time-to-event, hazard ratios (HR) and incidence rate ratio (IRR).

Results: There were 4437 BC patients with bone metastasis identified, in which 1724 patients were in denosumab group (mean age: 54.84 ± 11.67) and 2713 were in bisphosphonates group (mean age: 53.59 ± 11.54). PS was computed using logistic regression with covariates at baseline. After PS overlap weighting, the median time to the first SRE event was 17.4 months for denosumab and 13.8 months for bisphosphonates (Log-rank p=0.12). The HR of denosumab vs. bisphosphonates in time-to-SRE was 0.88 (95% CI, 0.70-1.10; p=0.26). A lower SREs incidence rate was observed in denosumab (IRR=0.78; 95% CI, 0.65-0.93; p=0.006). The results were similar regardless patients with or without SREs history.

Conclusions: Our results indicate that denosumab users have significantly lower SREs incidence rate as comparing with users of bisphosphonates.

Keywords: bone metastasis, bisphosphonates, denosumab, skeletal-related events

L.13

Exacerbation of chronic obstructive pulmonary disease and timing of paracetamol (acetaminophen) use in older Australians

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Aim/Objective: This study investigated whether the dose and timing of paracetamol (acetaminophen) exposure was associated with exacerbations of chronic obstructive pulmonary disease (COPD) in older Australian veterans.

Methods: The study population was 3523 Australian Government Department of Veterans' Affairs full entitlement holders who had existing COPD on 1 January 2011, who were dispensed at least one prescription of paracetamol between 1 January 2011 and 30 September 2015, and had no paracetamol dispensed in the six months prior to 1 January 2011. The outcome was time to first hospitalisation for COPD exacerbation after initiation of paracetamol. A weighted cumulative exposure approach was used.

Results: The association between paracetamol exposure and COPD exacerbation was protective or harmful depending on the dose, duration, and recency of exposure. Compared to non-use, current use at the maximum dose of 4g daily for 7 days was associated with a lower risk (HR=0·78, 95% CI = 0·67-0·92) and a higher risk after 30 days (HR=1·27, 95% CI = 1·06-1·52). Risk declined to baseline after two months. For past use, there was a short-term increase in risk on discontinuation depending of dose, duration and time since stopping.

Conclusion: Patients and doctors should be aware of the possible risk of COPD exacerbation with higher dose paracetamol one to six weeks after initiation or discontinuation, but no increased risk after two months.

L.14

Acute Renal Injury and Vascular Endothelial Growth Factors Inhibitors in Patients with Diabetic Retinal Edema– a population-based retrospective cohort study

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Background: Diabetic macular edema (DME) leads to visual loss in diabetic patients. Intravitreal anti-vascular endothelial growth factor (anti-VEGF) agent is the mainstream treatment for DME. Renal toxicity has been reported in patients receiving systemic anti-VEGF therapy but unknown to intravitreal use.

Method: We conducted a retrospective cohort study by analyzing the data from National Health Insurance database (NHID) in Taiwan. We selected a cohort of patients newly diagnosed of DME from 2011 to 2017 and newly receiving intravitreal aflibercept or ranibizumab. We defined the date of first prescription of either anti-VEGF as index date. The study primary endpoint were composite outcomes of acute renal injury (AKI), death from renal causes, hospitalized or emergency visits due to renal events. Patients were followed from the drug initiation date until the occurrence of outcome events, death, or the end of the study period. Covariates included patients' age at index date, sex, comorbidities and co-medications. We used stabilized inverse probability of treatment weighting (sIPTW) with propensity score to create more homogeneous groups for companions. The propensity score was derived from logistic regression conditioning on the all covariates.

Results: We identified a total of 6330 patients in ranibizumab group and 1258 patients in aflibercept group with the mean age of 61.50±10.38 and 62.07±11.19 years respectively. The hazard ratio of composite outcome for aflibercept was 1.36 (95% CI, 1.18-1.55) compared to ranibizumab. Specifically, the hazard ratios of AKI, death from renal causes, hospitalized or emergency visits due to renal events for aflibercept were 1.11 (0.90-1.37), 1.37 (1.20-1.57), 0.85 (0.54-1.32) when compared to ranibizumab, respectively.

Conclusion: The findings suggested that aflibercept had higher risk of composite renal events than ranibizumab when treating DME. Future study with larger sample size is required to provide sufficient statistical power to reassure the analyses for individual outcomes.

L.15

Real-world use of Paxlovid in hospitalized patients with mild and moderate COVID-19

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Aim/Objective: Nirmatrelvir plus ritonavir (Paxlovid) showed a significant reduction in the risk of hospitalization and death among people with coronavirus disease (COVID-19) in the clinical trial. It received the U.S. Food and Drug Administration emergency use authorization (EUA) for COVID-19 oral antiviral treatment on December 22, 2021. Paxlovid was approved in Taiwan on January 15, 2022. With the outbreak of COVID-19 in Taiwan, we aim to report our real-world experience with the use of Paxlovid in a regional hospital in Taiwan.

Methods: We conducted a single-center retrospective observational study. Records reviewed during this study were of patients who were hospitalized for mild or moderate COVID-19 and received Paxlovid between January 15, 2022 and April 30, 2022.

Results: A total of 14 patients were enrolled. All patients started their treatment of Paxlovid within 5 days of a confirmation of COVID-19 infection. The mean age of the patients was 56.5±18.8 years and 6 of the 14 (42.9%) were male. Four patients were asymptomatic and thirteen had received at least one dose of a COVID-19 vaccine. The mean baselines of serum creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were 0.9±0.35mg/dL, 30.4± 21.93 U/L, and 21.3±8.96 U/L, respectively. The most common coexisting conditions associated with high risk of progression to severe COVID-19 were having a body mass index (BMI) of 25 or above (9 patients [64.3%]) and cardiovascular disease (7 patients [50%]); 8 patients (57.1%) had two or more coexisting conditions. All patients were discharged after a 10-day isolation period. No adverse events requiring discontinuation of Paxlovid were reported.

Conclusion: Although the clinical trials were conducted with unvaccinated people, our trial contained mainly vaccinated patients. Our results demonstrated good efficacy of Paxlovid among people with COVID-19 who are at high risk of severe illness without serious adverse events.

Keywords: Paxlovid, real-world, COVID-19

L.16

Effects of DPP-4 inhibitors on renal outcomes in adults with type 2 diabetes and chronic kidney disease

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Aim/Objective: The efficacy and safety of dipeptidyl peptidase-4 inhibitors (DPP-4i) are well established in type 2 diabetes mellitus (T2DM) patients. Current evidence about the renal outcomes of DPP-4i have shown neutral effects. However, these results had short follow-up duration or possessed limited generalizability to chronic kidney disease (CKD) patients. This study aimed to evaluate the effects of DPP-4i on kidney and CV outcomes in patients with T2DM and CKD stages 3-5.

Methods: This retrospective cohort study utilized data from Taipei Veterans General Hospital Big Data Center in Taiwan. Patients with T2DM, who were new users of DPP-4i or other glucose-lowering drugs (oGLD), and with eGFR <60 ml/min/1.73m2 were identified during 2012-2019. Patients initiated with SGLT2i or GLP-1 RA were active control group. Baseline patient characteristics were matched using 1:1 nearest neighbor propensity score matching. The primary and secondary outcomes were composite kidney outcomes and composite CV outcomes. Other outcomes include progression in albuminuria category and severe hypoglycemia. Cox proportional hazards model was employed to assess the association between study drugs and outcomes.

Results: A total of 2,465 matched pairs of DPP-4i and oGLD users were analyzed. Higher risk of DPP-4i in composite kidney outcomes (HR 1.129 (1.012-1.260), p=0.0302), lower risk in albuminuria progression (HR 0.833 (0.718-0.967), p=0.0162), similar risk in composite CV outcomes (HR 0.981 (0.857-1.121), p=0.7747) and severe hypoglycemia (HR 0.972 (0.769-1.229), p=0.8145) were observed. As-treated analysis showed neutral results. Risk of composite kidney outcomes was higher when DPP-4i was compared with active control group (HR 1.753 (1.190-2.582), p=0.0045).

Conclusion: Use of DPP-4i compared with oGLD in patients with T2DM and CKD stages 3-5 was associated with higher risk of kidney outcomes, lower risk of albuminuria progression, and similar risk of CV outcomes and severe hypoglycemia.

Keywords: Type 2 diabetes, dipeptidyl peptidase-4 inhibitors, chronic kidney disease

L.17

Effectiveness of Vascular Endothelial Growth Factor Receptor Tyrosine Kinase Inhibitors in Renal Cell Carcinoma Patients

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Aim/Objective: Clear cell renal cell carcinoma (ccRCC) is the most common histological subtype of renal cell carcinoma. Patients in the metastatic stage have a 5-year survival rate of 12%. The aim of this study is to evaluate the VEGFR-TKIs (Vascular Endothelial Growth Factor Receptor-Tyrosine Kinase Inhibitors) usage patterns and compare the effectiveness between sunitinib and pazopanib.

Methods: This retrospective population-based cohort study was conducted by Taiwan Cancer Registry (TCR), Death Registry (DR), and National Health Insurance Research Database (NHIRD) from 2009 to 2018. The ICD-O-3 and order codes were used to identify ccRCC patients and VEGFR-TKI users. We computed rates of overall survival (OS) and time to second-line treatment (TT2T) as outcome measures. Propensity score (PS) weighting was applied to balance the baseline distributions between two groups. Kaplan-Meier estimates and Cox regression were conducted to compare effectiveness.

Results: A total of 1577 ccRCC VEGFR-TKI new users (1191 males and 386 females) were identified. The mean (±sd) age was 64.29 (±12.46) years old, and there were 1378 (87.38%) patients in sunitinib, 199 (12.62%) in pazopanib, and 51.49 % of patients who switched to second-line therapies, in which everolimus accounted the most. PS was computed using logistic regression with covariates at baseline. After PS overlap weighting, the median OS was 19.4 months in the pazopanib group and 14.2 months in the sunitinib group (Log-rank p-value=0.1242). The hazard ratio (HR) was 0.86 (95% CI, 0.65-1.14). The median TT2T was 10.3 and 7.4 months (p-value=0.0008) for two groups, and HR was 0.74 (95% CI, 0.57-0.96).

Conclusions: Our findings showed that the pazopanib group had longer OS and TT2T median time than the sunitinib group. However, only TT2T reached statistical significance. These results indicated that pazopanib has better effectiveness than sunitinib in ccRCC patients.

Keywords: clear cell renal cell carcinoma, sunitinib, pazopanib, propensity score weighting

L.18

Machine-Learning Approaches to Predict Major Bleeding Events in Patients with Non-valvular Atrial Fibrillation Treated with Direct Oral Anticoagulants

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Purpose: This study aimed to identify the possible predictors of major bleeding, in addition to the variables from HAS-BLED scores, by machine learning models in the cohort of direct oral anticoagulants (DOACs) users.

Material and Methods: We included patients with non-valvular atrial fibrillation (NVAF) newly initiating DOACs during 2011-2019 in the largest multi-institutional electronic medical records (EMRs) database in Taiwan. We followed these patients from the first prescription date to major bleeding event occurrences, death, loss to follow-up or 1 year post DOACs treatment. We identified the most 3 important predictor variables for major bleeding from 79 candidates using EMRs data from 90 days prior to each DOACs prescriptions by the machine learning of random forest methods. Finally, we compared the predicted performance between the HAS-BLED scores added on our identified predictor variables and the original HAS-BLED scores.

Results: We inlcuded a total of 14,574 patients (mean age: 74.0 ± 10.4 years; female: 57.9%) with NVAF newly initiating DOACs in this study. We identified a total of, 2,112 patients with incident major bleeding events. After the machine learning approaches, we identified the uses of insulins (HR: 5.27, 95% CI: 4.74-5.87), antifungals (HR: 3.69, 95% CI: 2.813-4.849) and anemia (HR: 3.59, 95% CI: 3.22-4.00) were the important predictors for major bleeding events after DOACs treatment. Compared to the original HAS-BLED scores (AUROC: 0.73, 95% CI: 0.70-0.75), the predicted performances for major bleeding events were better in the HAS-BLED scores added on our identified three predictor variables (AUROC: 0.79, 95% CI: 0.76-0.81).

Conclusions: Our findings suggested the baseline uses of insulins, antifungals and anemia associated with for major bleeding events in patients under DOACs treatment, and additions of these predictors into the original HAS-BLED scores may increase the predicted performance for major bleeding events. Further external validation of our findings is suggested.

L.19

Association Between Sodium Glucose Co-transporter 2 Inhibitor Use and Incidence of Dry Eye Disease in Patients with Type 2 Diabetes

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Aim/Objective: To investigate whether sodium-glucose co-transporter 2 (SGLT2) inhibitor use was associated with a lower dry eye disease (DED) incidence in type 2 diabetes mellitus (T2DM) patients.

Methods: We retrospectively analyzed the largest multi-institutional electronic medical records database in Taiwan to include T2DM patients newly receiving SGLT2 inhibitors or glucagon-like peptide-1 receptor agonists (GLP-1 RAs) from 2016 to 2018. We generated propensity scores with inverse probability of treatment weighting (IPTW) to enable homogeneous comparisons between the two groups. The study outcome was incident DED, defined by clinical diagnoses, plus the related drug prescription. We followed study patients from initiation of SGLT2 inhibitors or GLP-1 RAs to December 31st, 2021, and performed Cox proportional hazards regression models to estimate hazard ratios (HR) with 95% CI for the risk of DED.

Results: We included 9,964 SGLT2 inhibitor [mean age: 59.5yrs (SD: 12.1), HbA1c: 8.6% (IQR: 7.7-9.7), estimated glomerular filtration rate; eGFR: 89.2ml/min/1.73m2 (IQR: 71.3-108.8)] and 1,068 GLP-1 RA new users [mean age: 58.3yrs (SD: 41.1), HbA1c: 8.9% (IQR: 8.0-9.8), eGFR: 91.6ml/min/1.73m2 (IQR: 68.3-114.5)]. The baseline characteristics between the two groups were well balanced after propensity score with IPTW adjustment. The incidence of DED was lower in patients receiving SGLT2 inhibitors (8.5 events per 1,000 person-years), compared to those receiving GLP-1RAs (11.1 events per 1,000 person-years), yielding an HR of 0.77 (95% CI: 0.67-0.89). Subgroup analyses indicated the lowered DED risks from SGLT2 inhibitors in patients with T2DM were similar across different age-, sex-, blood sugar level- and renal function groups. The results from the sensitivity analyses, including on-treatment analyses and different follow-up periods of 1 year, 2 years and 3 years, were similar to the main analyses.

Conclusions: T2DM patients newly receiving SGLT2 inhibitors were associated with a lower risk for DED, compared to those receiving GLP-1 RAs.

L.20

Lower risks of cirrhosis and hepatocarcinoma with use of GLP-1RAs versus long-acting insulins among real-world patients with type 2 diabetes

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Aim/objective: The use of glucagon-like peptide-1 receptor agonists (GLP-1RAs), a new class of injectable glucose-lowering agents for type 2 diabetes (T2D), has been shown to significantly improve liver disease-related biomarkers, reduce liver inflammatory lesions, and slow the progress of hepatic steatosis to fibrosis. However, whether these short-term effects translate to a long-term benefit on the development of chronic liver diseases, including cirrhosis and hepatocarcinoma, remains unclear. This study therefore evaluated the association of chronic liver disease outcomes with using GLP-1RAs versus long-acting insulins (LAIs) in a real-world clinical practice setting.

Methods: An incident new-user and active-comparator cohort study was designed to identify stable users of GLP-1RAs and LAIs during 2013-2018 from Taiwan's National Health Insurance Research Database. The propensity score matching (PSM) procedures were applied to ensure between-treatment group comparability in baseline patient characteristics. Study outcomes included a composite of incident cirrhosis or hepatocarcinoma and each liver disease in the composite outcome. Each patient was followed until the occurrence of a study outcome, death, or the end of 2019, whichever came first. Subdistribution hazard models which account for competing risks of death were employed to assess the association of liver outcomes with treatments.

Results: We included 7,171 PSM pairs of GLP-1RA and LAI users with no significant between-group difference in baseline patient characteristics. Compared with LAI users, GLP-1RA users had significantly decreased risks of the composite liver outcome (subdistribution hazard ratio [95% CI]: 0.56 [0.42-0.76]), cirrhosis (0.59 [0.43-0.81]), and hepatocarcinoma (0.47 [0.24-0.93]). These findings were generally consistent with the results from sensitivity and subgroup analyses (e.g., as-treated analysis, patients with obesity or viral hepatitis history).

Conclusion: The use of GLP-1RAs versus LAIs was associated with a lower risk of chronic liver diseases, and this finding could inform real-world treatment decision-making for T2D patients at a risk of chronic liver diseases.

L.21

Real-world cardiovascular and renal outcomes with use of glucagon-like peptide-1 receptor agonists versus long-acting insulins among type 2 diabetes patients

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Aim/Objective: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) and long-acting insulins (LAIs) are the two most prescribed injectable glucose-lowering agents (GLAs) for type 2 diabetes (T2D) patients who failed to oral GLA therapy. Few real-world studies revealed that GLP-1RA versus LAI therapy yielded a lower risk of cardiovascular diseases (CVDs), and evidence about the comparative renal outcomes remains limited. Moreover, most previous studies did not perform stratification analyses by patient characteristics to assess whether heterogeneous treatment effects existed. This study aimed to assess the comparative cardiovascular and renal outcomes of GLP-1RAs versus LAIs and further explore whether the treatment effects varied among patient subgroups.

Methods: Taiwan's Health and Welfare Databases were utilized for this cohort study. Incident new users of GLP-1RAs and LAIs during 2013-2018 were identified and followed until the end of 2019. Propensity score matching (PSM) was applied to ensure the between-group comparability. Study outcomes included CVDs (myocardial infarction [MI], stroke, heart failure [HF], and cardiovascular death) and renal diseases (chronic dialysis and renal death). Subdistribution hazard ratios (SDHRs) with 95% confidence intervals (CIs) were used to estimate the relative treatment effects on study outcomes.

Results: A total of 7,357 PSM pairs of GLP-1RA and LAI users were included, and there were no significant between-group differences in baseline patient characteristics. Compared with LAIs, the use of GLP-1RAs was associated with significantly lower risks of MI (SDHR [95% CI]: 0.73 [0.54-0.99]), stroke (0.76 [0.60-0.95]), HF (0.69 [0.57-0.84]), and cardiovascular death (0.49 [0.34-0.69]). For renal outcomes, GLP-1RA versus LAI users had significantly decreased risks of chronic dialysis (0.29 [0.20-0.43]) and renal death (0.28 [0.15-0.51]). As-treated and subgroup analyses (e.g., patients with a history of CVDs or nephropathy) showed consistent results with the primary analyses.

Conclusion: Compared with LAIs, the use of GLP-1RAs yielded favorable cardiovascular and renal outcomes among real-world T2D patients.

M. Prevention and treatment of drug-induced diseases

M.1

Patterns of LTBI screening and treatment before JAKi or TNFi therapy among patients with rheumatoid arthritis (RA)

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Patients with rheumatoid arthritis (RA) undergoing targeted therapy have a higher risk of developing tuberculosis (TB). This requires diagnosis and treatment of latent tuberculosis infection (LTBI). In this study, we aimed to describe treatment patterns and completion rate of three LTBI treatment regimens for patients receiving Janus kinase (JAK) or tumor necrosis factor (TNF) inhibitor.

A descriptive study was conducted using the National Health Insurance Service(NHIS) database between 2009 and 2019 to investigate the LTBI detection and treatment among RA patients treated with JAKi or TNF inhibitor. We investigated the RA population treated with JAKi or TNF inhibitor. LTBI screening was detected on the basis of tuberculin skin test (TST) results and interferon-gamma release assay (IGRA). We assessed patterns of LTBI treatment and completion rate from 1 year before and after the start of the targeted drugs. Treatment completion rate was defined as over 80% of prescriptions for each 9-month isoniazid (9H), 4-month rifampicin (4H), and 3-month isoniazid/rifampicin (3HR) drug.

A total of 11,936 patients with RA were included. The mean age was 55.40 years and 77.9% were female. The proportion of LTBI screening was observed as a decrease in TST and an increase in IGRA. In the TNF inhibitor group, the 9H, 4R, and 3HR treatment regimens were prescribed to 1,775 (91.7%), 660 (34.1%), and 31 (1.6%) patients, respectively. In the JAK inhibitor group, the 9H, 4R, and 3HR treatment regimens were prescribed to 298 (85.6%), 84 (24.1%), and 34 (9.7%) patients, respectively. Among LTBI treatment regimens, completion rate was the highest in the patients who received 3HR (93.9%).

In patients receiving JAKi or TNF inhibitors, LTBI treatment showed a high rate of treatment completion. However, because of the limitation of claim data, the diagnostic accuracy of LTBI cannot be guaranteed. Therefore, our findings should be interpreted with caution.

M.2

Signal detection of Myopathy due to Drug-Drug Interaction Statin using KAERS Database

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Background: Early detection of Drug-Drug interaction (DDI) is important in both a public health and individual patient safety point of view. In addition, it is necessary to identify not only known adverse events (AEs), but also potential drug interactions that may occur following co-administration. Polypharmacy is common for cardiovascular treatment, and there has been no study in Korea focusing on contraindications for concomitant use with statins.

Objectives: The aim of this study was to detect signals of myopathy related to the DDI of statins with contraindicated drugs using spontaneous reporting database.

Methods: This study used the Korea Adverse Events Reporting System (KAERS) database from 2016 to 2020. The combinations of statin and contraindicated drug were extracted from drug utilization review (DUR) criteria in Korea and the targeted AE was myopathy. For signal detection, five frequency statistical models were applied: the Ω shrinkage measure, additive (risk difference, RD), multiplicative (risk ratio), combination risk ratio, and chi-square statistics models. Additionally, a disproportionality analysis (cases/noncase) were performed. The indices were used to define signals: Ω025 >0, p11 − p10 − p01 + p00 > 0 , p11 × p10 / p01 × p00 > 1, CRR>2, Chi >2.

Results: The database contains 1,011,234 individual case safety reports (ICSRs) and there were 25,720 ICSRs of concomitant statins. As a results of analyzing the combination drugs by effect group, the ‘statin and cyclosporine’ combination was the most common with 124 cases (ROR, 7.289; 95%CI, 4.254-12.488). Three combinations of signals were detected through the additive model: ‘Simvastatin and antiviral drug’ (RD, 0.236), ‘Rosuvastatin and immunosuppressant’ (RD, 0.053), ‘Atorvastatin and antifungals’ (RD, 0.005).

Conclusions: We identified signals for DDI of statins and concomitant drugs. Further pharmacoepidemiological studies of DDI should be needed to detect signals associated with concomitant use of statins.

M.3

Thiamine Responsive Pulmonary Hypertension in Pediatrics: An Under-Reported Adversity

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Introduction: Early infancy has been considered a rare period for the emergence of new-onset PH. However, multiple cases of severe PH caused by thiamine deficiency in early childhood have lately been recorded across the globe. TD is frequently misdiagnosed due to the vast range of symptoms and can lead to adverse outcomes if not diagnosed and managed at an early stage.

Methods: An electronic search was conducted using PubMed, Scopus, and incorporated forward and backward research methods on case series, and case studies and the keywords included: thiamine, thiamine deficiency, pediatrics, pulmonary hypertension. Data was collected and analyzed to stay current with the most recent evidence and guidelines for the best care for children.

Results: The common manifestations included fever, vomiting, respiratory distress, and dyspnea with dilation of either right atrium or ventricle or both with moderate to severe tricuspid regurgitation and alteration of the interventricular septum being the most common diagnostic findings of PH. The therapy of choice was i.v thiamine 100 mg/day. Most patients demonstrated a substantial clinical improvement and complete recovery with thiamine therapy. However, 13 instances of fatalities were reported amongst the 346 patients included in this review.

Conclusion: Early infancy has been considered to be an unusual phase for the onset of new-onset PH. However, in recent years, several cases of severe PH caused by thiamine deficiency in early childhood have been reported all over the world. Despite the introduction of new pharmacological therapies, patients with severe PH continue to suffer from poor long-term outcomes.

Key words: Pulmonary hypertension, pediatrics, thiamine, thiamine deficiency

M.4

Treatment comparisons for gastrointestinal adverse events of interventions for preventing chemotherapy induced oral mucositis in adult cancer patients: network meta-analysis

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Background: Treatment comparisons for gastrointestinal adverse events of oral mucositis (OM) in patients with cancer receiving chemotherapy is largely unknown, mainly because of an absence of head-to-head trials.

Methods: We searched PubMed, Embase, and the Cochrane Central systematically for the randomized control trials (RCTs) of interventions for preventing CIOM. Network meta-analysis (NMA) was performed to estimate risk ratio (RR) and 95% confidence interval (CI) from both direct and indirect evidence. Primary outcome was any grade of OM. Secondary outcomes were moderate-severe OM and adverse events, such as taste disturbance and gastrointestinal adverse events.

Results: A total of 29 RCTs with 2348 patients (median age, 56.1 years; 57.5% male) were included. Cryotherapy was associated with a significantly lower risk of OM than control (Risk Ratio [RR] 0.51, 95% Confidence interval [CI] 0.38 to 0.68), and zinc sulfate (RR 0.47, 95% CI 0.23 to 0.97), no significant differences were observed between cryotherapy and control for taste disturbance and gastrointestinal adverse events.

Conclusion: Amifostine was found to cause the most gastrointestinal adverse events. (Risk Ratio [RR] 0.89, 95% Confidence interval [CI] 0.22 to 3.66) and then Misoprostol (Risk Ratio [RR] 1.15, 95% Confidence interval [CI] 0.06 to 22.36). However, further large RCTs are needed to confirm these finding.

Keyword: mucositis, gastrointestinal adverse events, chemotherapy, cancer, network meta-analysis

N. Other related fields

N.1

Economic Burden of Oral Cancer in Asian Low Middle- Income Countries: A targeted literature review

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Objectives: In low middle-income countries (LMICs) oral cancer (OC) is common cancer with low five-year survival rate. OC incidence was highest in South Asia (Age Standardized: 9.65/100,000) in 2019. Current targeted literature review (TLR) summarizes economic burden in OC across Asian LMICs.

Methods: Extensive literature search was conducted on Medline, Embase and Cochrane databases (via-Ovid) by combination of Emtree/ MeSH and other keywords from 01-January-2012 to 27-May-2022. It was supplemented by grey literature search. Economic burden studies in adult OC patients were included. Quality assessment was performed by Newcastle-Ottawa-Scale.

Results: Twenty Asian studies were identified with 6 good quality studies reporting data for LMIC (World Bank criteria), out of 778 studies (4 from India, and 1 each from Pakistan and Sri Lanka).
For India, total direct healthcare costs to treat 100 OC patients was Indian rupee (INR)160,01,368 (United States Dollar (USD)2,14,237). Unit cost of treating advanced stages was USD2,717, 42% greater than early stages (USD1,568). In early-stage OC, surgery constituted 30% (INR35,436; USD475) of overall costs followed by 19% for in-patient department (INR22,823; USD306) and 17% diagnostics (INR19,827; USD265). In advanced stage OC, radiotherapy constituted 30% (INR58,302; USD781) of costs followed by 26% surgery (INR49,727; USD666). Mean expenditure in OC patient for hospitalization and surgery was INR1,46,093 and INR82,626, respectively in 2014. Total productivity loss (lip and oral cavity cancers) was USD0.74 billion in 2012.
In Pakistan (2019), treatment expenditure ranged from Pakistan Rupee (PKR) 6,00,000–12,00,000 (USD 5,000-10,000). In Sri Lanka, annual mean cost/patient for managing Stage II and Stage III/ IV patients was Sri Lankan Rupees (SLR)1,36,628 and SLR3,75,551, respectively in 2019.

Conclusion: This TLR provides insights on various enormous costs associated with OC leading to high economic and overall burden in Asian LMICs. Certain strategies are required to minimize financial burden on patient and health system.

N.2

Substance use among pregnant women in a tertiary teaching hospital in Jimma, Ethiopia: a cross-sectional study

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Objective: This study determined the prevalence, types, and determinants of substance use during pregnancy in Jimma university medical center (JUMC), Ethiopia.

Methods: A hospital-based cross sectional study was conducted on 1117 hospitalized pregnant women or postpartum women at the maternity and gynaecology wards at JUMC between February and June 2017. Data were collected using an interviewer-administered structured questionnaire and analyzed using descriptive statistics and logistic regression.

Results: This study found that 108 (9.7%) women used at least one type of substance during pregnancy. Concerning specific substance type, 65 (5.8%) of the women chewed khat and 46 (4.1%) of the women consumed alcohol during pregnancy. Of those pregnant women who used substances, 32 (26.9%) had concomitantly used conventional medicines, and 51 (47.2%) had concomitantly used medicinal plants. Medicinal plants use during pregnancy (adjusted OR 2.75; 95% CI 1.79, 4.24), and Orthodox Christian (adjusted OR 4.08; 1.19, 13.99) or Islam religion (adjusted OR 3.79; 1.13, 12.76), and admission to the gynaecology ward (adjusted OR 2.81; 1.31, 6.04) were significant associated with substance use. On the other hand, shorter duration of hospital admission was inversely associated with substance use during pregnancy (adjusted OR 0.63; 95% CI 0.41, 0.95).

Conclusion: One out of ten women reported taking at least one type of substance during pregnancy in JUMC. There is need to increase awareness of pregnant women on the potential negative consequences of substance use during pregnancy to prevent neonatal and maternal hazards.
Key words: Substance use; Pregnancy; Prevalence; Ethiopia

Disclosure: Some part of the results has been published as a secondary objective under the title ‘‘Self-Medication and Safety Profile of Medicines Used among Pregnant Women in a Tertiary Teaching Hospital in Jimma, Ethiopia: A Cross-Sectional Study’’ in the Int J Environ Res Public Health, 2020; 17(11):3993

N.3

Nation-wide analysis of determinants of vaccine hesitancy: A qualitative study.

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Background: Public health is at risk from refusals and delays in vaccination. The aftereffect of vaccine hesitancy will trigger massive outbreaks of preventable diseases.

Aim: To evaluate the determinants of vaccine hesitancy among the population in India.

Method: A qualitative study was conducted from 2020 to 2022 in a tertiary care teaching hospital. Eligible study participants enrolled after taking informed consent exclusively designed as per the requirements of the Indian Council of Medical Research guidelines for biomedical research on human subjects. The study used a Vaccine Hesitancy Open-Ended Survey Questions developed by WHO SAGE WG and A qualitative thematic analysis (QTA) was performed to analyze participants' answers to open questions. A deductive approach was chosen i.e., the codes and themes development was guided by existing concepts and ideas, including, in this instance, the WG Matrix of Determinants (MxDt) of vaccine hesitancy.
Results: Out of 28 states and 8 Union territories, 673 participants were interviewed by a research team from 14 states. A total of 1355 statements were obtained, and 34 statements were not codable. The 53.67% (n=709), interactions were coded to the "individual and Group influences", and 34.29% (n=453) interactions were coded to "Vaccine and Vaccination Specific Issues."
Conclusion: Vaccine-hesitant individuals come from a mixed group with many different types of concerns about vaccines. As a result of the many different concerns, it is difficult to draw conclusive conclusions about the effect of certain factors or factors in combination on vaccine-hesitant behavior. To improve understanding of decision-making processes and influences on vaccination behavior, qualitative studies in all regions will be preferred in the future.

Keywords: Acceptance, Hesitancy, Refusal, Vaccine

N.4

Tracking public attitude towards COVID-19 Vaccine: A nation-wide study

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Background: Safe and effective COVID-19 vaccines have been approved for emergency use in India by January 2021. Country-wide vaccination has crossed beyond one billion doses. Even so, vaccines are refused /hesitated in the country.

Aim: To determine the prevalence, socio-demographic differences, the predictors associated with COVID-19 vaccine refusal and to ascertain the determinants of vaccine refusal among the study population.

Method: A web-based, observational study was conducted from 2020 to 2022 in a tertiary care teaching hospital. Eligible study participants enrolled after taking informed consent exclusively designed as per the requirements of the Indian Council of Medical Research guidelines for biomedical research on human subjects. The study used a validated questionnaire and data collection was done according to the checklist for reporting results of internet e-surveys guidelines.

Results: Out of 353 individual participants, 34.68% (n=137) were accepting, and surprisingly 52.15%(n=206) were hesitant/refusers of COVID-19 Vaccines. The general public hesitated/ refused vaccination with the concerns of losing the work hours [20.25% (n=80)] and negative influence on COVID-19 Vaccine safety [16.70%(n=66)].

Conclusion: As for now, the COVID-19 Vaccines are given to the age group above 12, the refusal tendency is more because of the concerns about missing work hours and income either due to immunization or adverse events of immunization. Effective interventional strategies such as Dialogue-based and reminder/ recall-based interventions need to be implemented to overcome the hesitancy and refusal attitude of the public. Otherwise, lower herd immunity will lead to multiple waves of COVID-19 spread in the community. In the present situation of fast-spreading and genetically modifying COVID-19 virus attack, vaccination is the only way to bring us back to the previous normalcy.

Keywords: Acceptance, Hesitancy, Refusal, Vaccine

N.5

A billion people's attitude to vaccines: hesitancy and safety concerns.

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Background: Vaccines are considered to be primary health services to ensure the health and well-being of all age groups and a huge population can reach out for vaccination than any other health service all around the world. Unfortunately, World Health Organization (WHO) has identified Vaccine Hesitancy (VH) as the most problematic threat in 2019.

Aim: To determine the prevalence, socio-demographic differences, the predictors associated with vaccine hesitancy.

Method: A web-based, observational study was conducted form 2020-2022 in a tertiary care teaching hospital. Eligible study participants enrolled after taking informed consent exclusively designed as per the requirements of the Indian Council of Medical Research guidelines for biomedical research on human subjects. The study used questionnaire The Potential Vaccine Hesitancy Survey Questions: Version 1.0 and Vaccine Hesitancy 5point Likert scale questions developed by the WHO SAGE WG (2015) and data collection were done according to the checklist for reporting results of internet e-surveys guidelines.
Results: Out of 673 participants, 30.76% (n=207) have directly admitted / openly expressed the fact that they are vaccine-hesitant, while 21.84% (n=147) have accepted that they are vaccine refusers by responding “Yes” to questions number 3 &4. Out of that, 9.36% (n=63) exhibited an anti-vaxxer mentality by answering "No" to question number 1. And also, 6.09% (n=41) by answering “Yes” to question number 8. Participants [7.58% (n=51)] have indirectly accepted the fact that they are vaccine-hesitant by answering “Yes” to question number 6.

Conclusion: There are no specific methods and tools available yet to address the identified concerns with vaccine hesitancy, a problem facing the health care system. An opportunity exists for the researcher to investigate concerns about vaccinations and vaccination-related issues, as well as identify possible management/intervention approaches that might meet these concerns.

Keywords: Acceptance, Hesitancy, Refusal, Vaccine

N.6

Healthcare delay and clinical outcomes among patients with tuberculosis: a large-linked database study

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Aim/Objective: While many resources are contributed to eradicating tuberculosis (TB), a substantial number of patients with TB are still unlikely to receive timely treatment. We aimed to measure healthcare delay and its association with clinical outcomes in TB patients from 2013 to 2018.

Methods: We conducted a retrospective cohort study using linked data of the Korean National Tuberculosis Surveillance System Registry and the National Health Insurance Database. All individuals with new-onset TB were included, and healthcare delay was defined as the period between the first medical visit related to TB symptoms and the initiation of anti-TB regimen. We described the distribution of healthcare delay, and the study population was classified into two groups with mean as a cutoff. The association between healthcare delay and treatment outcomes (all-cause mortality, hospitalization for pneumonia, progression to multi/extensively drug-resistant, intensive care unit admission, and mechanical ventilation use) were evaluated using Cox proportional hazard model. Several stratified and sensitivity analyses were conducted.

Results: We observed the average of healthcare delay was 42.3 days, and healthcare-delayed and non-delayed groups were 10,680 (26.9%) and 29.067 (73.1%), respectively. Healthcare delay was associated with an increased risk of all-cause mortality (HR 1.10, 95% CI 1.17), hospitalization for pneumonia (1.13, 1.09–1.18), and mechanical ventilation use (1.15, 1.01–1.32). We also observed monotonic increased risks for these outcomes according to the duration of healthcare-delay. Stratified analyses showed patients with pre-existing respiratory diseases were at higher risk, and the consistent results to the main results were observed in the sensitivity analyses.

Conclusion: In this nationwide cohort study, the healthcare delay was observed from the substantial number of patients. Moreover, healthcare delay was associated with deterioration of clinical outcomes. Our findings suggest that attention from authorities and healthcare professionals is needed to attenuate the preventable burden caused by TB through timely treatment.

N.7

Incidence of post radiotherapy Hypothyroidism in Head, Neck and Breast Cancers- A prospective observational study

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Thyroid gland being one of the radiosensitive endocrine glands get affected during radiotherapy that is given as part of Multi-Modality treatment in breast, head, neck cancers as thyroid gland comes into radiation field due to its anatomical position.

Aim and objectives:
To determine the Percentage of population developing
Post radiotherapy hypothyroidism in head ,neck and breast cancers
To determine the significance of Clinical factors and patient related factors that may precipitate post radiotherapy hypothyroidism.

Problem Studied: ICD-10 E03.2: Hypothyroidism due to medicaments and other exogenous substances
Study design: A prospective observational study.
Parameter studied: Levels of Thyroid Stimulating Hormone post radiotherapy
Study site: The Study is conducted in Good Samaritan Cancer Hospital, Vangayagudem.
Binominal Z -TEST is used to establish the statistical significance employing MS excel software.

Inclusion criteria
Adult patients who are greater than 18 years of age and less than 80 years with non metastatic Head and neck carcinoma, Breast carcinoma
Patients who received Radiotherapy as part of their treatment after 2017.
Patients receiving radiotherapy at a dose of >40 GY OR 40
GY as part of their treatment.

Exclusion criteria
The history of hypothyroidism in the past for which he/she is currently on supplement.
Patients above 80 years of age

Conclusion
In India, Generally the prevalence of hypothyroidism was 3.9%. The prevalence of subclinical hypothyroidism 9.4%.
In our study, the incidence of post radiotherapy hypothyroidism is found to be 45.8% in the study population. Female population (63.9%) is more prone to post radiotherapy hypothyroidism compared to male population (37.03%)
The incidence of post radiotherapy hypothyroidism is significant in people who received radiotherapy to the head and neck region for head and cancers compared to left chest wall or right chest wall for breast cancers

N.8

Incubation periods of the 3 major COVID-19 variants in XXX

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Objective: One of XXX's strategies for controlling the COVID-19 pandemic was containment, which included a fourteen-day quarantine of close contacts, who were subjected to an entry and exit SARS-CoV-2 PCR test done 11-14 days post exposure. Additionally, symptomatic contacts were tested for SARS-CoV-2. We aim to compare the incubation periods of the 3 major SARS-CoV-2 variants in XXX.

Method: Information was collected for patients under quarantine from the YYY COVID-19 Registry. The start date of the quarantine period was assumed to be the last date of exposure to the index case. Incubation period was defined as the duration between date of exposure and date of the first positive SARS-CoV-2 PCR test. The prevalent strain in circulation was identified from the XXX database in the GISAID collection. Only variants of concern, as categorized by WHO, Alpha (23rd Jan 2020 – 1st Mar 2021), Delta (5th May 2021 – 31st Oct 2021) and Omicron (1st Jan 2022 – Present) were considered. For the Omicron variant, quarantine was discontinued, hence only those with preceding international travel were included and the last date of arrival was assumed to be the date of exposure.

Results: From January 2020 to March 2022, there were 19,905 patients in the COVID-19 registry, of whom 11,235 were under quarantine and 8,612 had preceding international travel. Of the 11,235 patients under quarantine, 8,189 and 3,046 patients were infected during the Alpha and Delta waves, respectively. 6,503 of the patients with preceding international travel were infected during the Omicron wave. The median incubation periods for the Alpha, Delta and Omicron variants were 11 days (IQR: 7-14 days), 3 days (IQR: 2-4 days), and 3 days (IQR: 0-5 days), respectively ($p<0.001$).

Conclusions: The Delta and Omicron variants had significantly shorter incubation periods compared to the Alpha variant.

N.9

Effectiveness of Minimally Invasive Hepatectomy in Patients with Early or Intermediate-stage Hepatocellular Carcinoma: A Multi-institutional Cohort Study

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Aim/Objective: To compare the effectiveness of MIH with standard curative treatments (open hepatectomy, OH, and radiofrequency ablation, RFA) in patients with early or resectable intermediate-stage HCC.

Methods: This retrospective cohort study analyzed multiple databases including a large multi-institutional electronic health records database with 1.3 million individuals, the Taiwan Cancer Registry and the Taiwan Cause of Death Registry. We included patients aged 20 years and older, newly receiving MIH for HCC with Barcelona Clinic Liver Cancer (BCLC) classification stage 0, A or B from 2010 to 2019. Two 1:1 propensity score-matched cohorts of those receiving OH and those receiving RFA were selected as comparison groups. As a control analysis we compared patients receiving OH with those receiving RFA under the hypothesis that the OH group had better survival outcomes than the RFA group. Hazard ratios (HR) of overall survival (OS) and progression free survival (PFS) for the three curative treatments were estimated by Cox regression models.

Results: We included a total of 555 matched patients receiving MIH or OH, and 382 matched patients receiving MIH or RFA. Compared to the OH group, the MIH group was associated with better OS (HR: 0.62; 95% CI: 0.43-0.88) and similar PFS (HR: 0.92; 95% CI: 0.74-1.16). Compared to the RFA group, we found the MIH group was associated with better OS (HR: 0.46; 95% CI: 0.32-0.67) and better PFS (HR: 0.48; 95% CI: 0.38-0.61). We found consistent results from a series of subgroup analyses (e.g., age groups, BCLC stages and hospital levels) and sensitivity analyses (e.g., study period restricted to the most recent 5 years (2015-2019)). The control analysis (OH group vs. RFA group) confirmed the robustness of the main analysis.

Conclusions: Our study suggested that MIH had better survival outcomes for patients with early or resectable intermediate-stage HCC, compared to RFA or OH.

N.10

SJS and TEN in Taiwan Drug Injury Relief System: New Trends in Culprit Drugs from 2017 to 2021

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Aim/Objective: To identify new trends in culprit drugs inducing SJS/TEN in Taiwan Drug Injury Relief System from 2017 to 2021.

Methods: The approved applications associated with SJS, TEN (including SJS-TEN overlap) in Taiwan Drug Injury Relief System from 2017 to 2021 were retrospectively analyzed. Culprit drugs and adverse drug reactions (ADRs) were categorized according to their ATC and MedDRA codes respectively.

Results: From 2017 to 2021, a total of 273 approved applications associated with SJS and TEN were identified. The top-ranked culprit drugs were allopurinol (n=25), piperacillin/tazobactam (n=18), diclofenac(n=17), levofloxacin(n=16), ibuprofen(n=15), esomeprazole(n=14), amoxicillin/clavulanate (n=14), vancomycin(n=12), sulfasalazine(n=12), co-trimoxazole(n=12) and celecoxib (n=11). SJS and TEN induced by PD-1/PDL-1 inhibitors (pembrolizumab [n=3] and nivolumab [n=3]) and the abovementioned AED, zonisamide (n=1), were also identified.

Conclusion: In addition to allopurinol and diclofenac, the new trends in culprit drugs inducing SJS and TEN were penicillins/beta-lactamase-inhibitors combinations (such as piperacillin/tazobactam and amoxicillin/clavulanate), fluoroquinolones (such as levofloxacin), proton pump inhibitors (such as esomeprazole), NSAIDs (such as ibuprofen and celecoxib) and sulfasalazine. SJS and TEN associated with ICIs (pembrolizumab and nivolumab) and a novel AED (zonisamide) were also identified in Taiwan Drug Injury Relief System. Safety measures should be implemented to mitigate the risks of SJS and TEN when prescribing those commonly or newly-identified culprit drugs.

Keywords: SJS, TEN, culprit drugs, Drug Injury Relief.

N.11

Air Pollution and Cardiovascular and Thromboembolic Events in Older Adults with High-Risk Conditions in Taiwan: Assessing Drug-Environment Interactions

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Background: Older adults with chronic diseases are vulnerable to the health effects of air pollution, not only due to particular low adaptive capacity, but also because of the multiple medications they often take. Therefore, the role of drug-environment interactions in health effects of air pollution needs to be further explored.

Objective: Assess patterns of Cardiovascular and Thromboembolic Events (CTEs)hospitalizations and PM2.5 exposures in different seasons as the first step toward assessing PM2.5 and drug interactions.

Methods: We used data from 2009-2018 National Health Insurance Database (NHID), identifying patients >= 65 years with high-risk conditions for CTEs, i.e., cardiovascular disease, venous thromboembolism and post joint replacements. Seasonal average PM2.5 concentration estimated from Data Bank for Atmospheric and Hydrologic Research were merged to NHID by postcodes. Seasons were defined as December-February, March-May, June-August, and September-November. CTE hospitalizations were defined as time to first hospitalization for venous thromboembolism, heart failure, transient ischemic attack, ischemic stroke, acute coronary syndrome, myocardial infarction, or atrial fibrillation.

Results: Among 291,320 patients with high-risk conditions for CTE (mean age 74.3, 62% female). The overall mean PM2.5 in Dec-Feb, Mar-May, Jun-Aug and Oct-Nov was 30.8µg/m3, 27.1µg/m3, 14.1µg/m3 and 24.4µg/m3 respectively. The seasonal average PM2.5 concentration in each year showed consistent variations with peaks appearing in Dec-Feb (21.6µg/m3 to 40.2µg/m3) and trough in Jun-Aug (8.2µg/m3 to 21.9µg/m3). Seasonal incidences of myocardial infarction, heart failure, and atrial fibrillation were associated with PM2.5 exposure. The correlation coefficient was 0.67 for myocardial infarction and 0.56 for heart failure and atrial fibrillation. Our results show a trend of decreasing year-by-year PM2.5 exposure and decreasing incidence of CTE outcomes.

Conclusion: Both the risk of myocardial infarction, ischemic stroke and heart failure and PM2.5 showed corresponding seasonal patterns. Further analyses understanding the interaction between PM2.5 and medications are underway.

N.12

Estimated glomerular filtration rate on hospital admission and mortality prognosis in stroke patients: The Shiga Stroke and Heart Attack Registry

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Aim: The relationship between estimated glomerular filtration rate (eGFR) levels and mortality prognosis after stroke incidence remains inconsistent. This study aimed to investigate the effect of eGFR level at hospital admission on survival outcome in patients with first-ever stroke incidence.

Methods: A retrospective cohort study was conducted based on the Shiga Stroke and Heart Attack Registry (SSHR) in Japan. Patients were classified according to their eGFR value at hospital admission into 7 following levels as <15 or dialysis, 15–29, 30–44, 45–59, 60–89, 90–124 and ≥125, with 60–89 mL/min/1.73m2 being the reference group. Cox proportional hazards models were used to evaluate the association between eGFR levels and mortality.

Results: A total of 11,017 patients who were residents of Shiga Prefecture were followed up for 2.81±1.59 years, with the mean (±SD) age was 73.60±13.68 years; and 46.48% of patients were women. Among patients with all strokes, considering the 60–89 mL/min/1.73m2 of eGFR as the reference group, the gradually increasing of adjusted hazard ratio (95% confidence interval) for mortality occurs on both sides of the reference group [2.13 (1.67-2.72), 1.21 (1.06-1.38), versus 1.10 (0.99-1.22), 1.52 (1.36-1.70), 2.32 (1.99-2.70), 3.52 (2.94-4.22)], relevant to eGFR levels ≥125, 90–124 versus 45–59, 30–44, 15–29 and <15 or dialysis. The “U-shapes” of adjusted HRs of mortality are found for ischemic and hemorrhagic stroke as well.

Conclusion: The findings suggest that first-ever stroke patients with lower eGFR and with higher eGFR exhibited a higher risk of all-cause mortality than patients with eGFR from 60 to 89 mL/min/1.73m2. Thus, the management of treatment for stroke and renal function should be considered not only for patient with decreased renal function but also for higher glomerular filtration rate group for all stroke patients.

Keywords: eGFR, stroke patients, mortality

N.13

Analysis of key factors and risk prediction of diabetic nephropathy

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Objective: by constructing a logistic regression model to analyze the association factors and predicting the risk of 2 diabetes mellitus nephropathy, and to provide scientific evidence for screening and intervention in patients with type 2 diabetes mellitus nephropathy.

Methods: diabetic patients diagnosed and treated in a National Clinical Medical Science Data Cente were selected and screened according to the diagnostic data of the patients electronic medical records. They were randomly divided by 7:3 ratio. There are 1594 males and 283 femalesin the modeling group,and 717 males and 381 females in the validation group.The data were collected from urine routine data, diabetes biochemical examination data and glycated data of diabetes, and the significant variables were obtained from univariate Logistic regression analysis. The Logistic regression analysis of these variables was used to get Logistic regression model. According to the area under the ROC curve, the sensitivity and specificity of the prediction model are tested in order to achieve an ideal prediction effect.

Results: 1.Logistic single factor regression analysis showed fibrinogen (P=0.012, or=1.012), 24h urinary microalbumin (P<0.001, or=0.49), serum creatinine (P<0.001, or=1.025), prothrombin activity (P=0.023, or=1.025), C-reactive protein (P=0.004, or=0.806), urine albumin creatine ratio (P<0.001, or=1.005) was significantly associated with type 2 diabetes nephropathy.2.The variables with P<0.02 in the single factor were included in Logistic multivariate regression analysis, and X18:24h urine microprotein (P=0.004, OR=0.726), X19: serumcreatinine (p<0.001, OR=1.030), X37:urine albumin creatine ratio (P < 0.001, OR=1.006), urine red blood cells (P=0.006, OR=0.533) were obtained.

Conclusion: This study found that gender, age, urinary biliary tract, urinary red blood cells, alkaline phosphatase, lactate dehydrogenase and patients with type 2 diabetes were significantly different in patients with type 2 diabetes mellitus and coronary heart disease. Cardiovascular disease in diabetic patients should be strengthened.

N.14

Correlation between country-level numbers of COVID-19 cases and mortalities, and country-level characteristics: A global study.

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Aim/Objective: We aimed to assess the relationship between country-level characteristics and COVID-19 infection/mortality.

Methods: We conducted an ecological study utilizing publicly available country-level COVID-19 data and other data from the World Health Organization, and other publicly available country-level data from the United Nations, the United States Central Intelligence Agency (CIA) and the World Bank. The study period was from January 2020 to August 2021. We summarized country-level COVID-19 case and mortality counts per 100,000 population and case fatality rate. We conducted adjusted linear regression analysis to assess relationships between these counts/rate and certain country-level characteristics, and we reported adjusted regression coefficients, β and associated 95% confidence intervals (CI).

Results: We included 130 countries in the analyses. The mean number of COVID-19 cases and mortalities per 100,000 population were 5,148 (CI 4,405 – 5,891) and 94 (CI 78 – 110). There was a positive correlation between the number of cases and country-level male/female ratio; and positive correlations between the numbers of cases and mortalities, and country-level proportion of 60+ year-olds, Universal Health Coverage index of service coverage (UHC) and tourism. Country economic status correlated negatively with the numbers of cases and mortalities. COVID-19 case fatality rate was highest in Peru, South American region (9.2%), and lowest in Singapore, Western Pacific region (0.1%). A negative correlation was observed between case fatality rate and country-level male/female ratio, population density, and economic status. These observations remained mostly among mid/low-income countries; particularly, a positive correlation between the number of cases and male/female ratio and proportion of 60+ year olds.

Conclusions: Various country-level characteristics appear to be correlated with country-level number of COVID-19 cases and/or mortalities. It may be necessary to consider these country-level characteristics when designing country-level COVID-19 epidemiological studies and comparing COVID-19 data between countries.

Keywords: COVID-19; Country-level characteristics; Correlation

N.15

Community-based activities to empower chronic disease patients for improving drug use behavior and managing leftover medicines

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Objectives: 1) to explore drug use behaviors among chronic disease patients living in a community in Northern Thailand 2) to develop community-based activities to improve their drug use behaviors, and to assess the outcomes

Methods: The study was conducted at a community in Northern Thailand. Participants were 17 diabetes and hypertensive patients receiving care from a district hospital. In phase I, the researchers explored the participants' drug use behaviors and leftover medicines problems using a structured interview. In phase II, the findings were used for developing community-based participating activities using a concept of communication for development (C4D) developed by the UNICEF. Outcomes were the patients' drug use behaviors. The study was conducted in 2015.

Result: The chronic patients had several inappropriate drug use behaviors, such as forgetting, stop using medicines, and sharing medicines with others. In addition, 15 out of 17 patients had leftover medicines at home. With the concept of C4D, 4 community-based activities were developed. The activities included informing the patients about chronic disease, learning about drug use behaviors, finding the cause and management of drug use and leftover medicines, and discussing on questions and concerns. After 2 weeks, researchers assessed the results of activities during home visit. Almost (5 of 7 participants) knew about the results of unsuitable drug use behaviors for chronic disease. They were aware of leftover medicines problems but they concerned effect of budgetary more than health perspective. However, 4 participants continued their inappropriate behaviors.

Conclusion: Participating the community-based activities, chronic patients gained knowledge about chronic disease and appropriate drug use behaviors. Some of them improved their drug use behaviors.

Keywords: community-based activity, leftover medicines, drug use behavior, chronic disease

N.16

FACTORS AFFECTING TOTAL HOSPITALIZATION COST AND COST-EFFECTIVENESS ANALYSIS OF CORTICOSTEROID MANAGEMENT IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME

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Background: There is currently a dearth of information in India on the factors that affect total hospitalization cost; and the cost-effectiveness of corticosteroid management in patients with acute respiratory distress syndrome (ARDS)

Methodology: A retrospective observational study was conducted in a south Indian tertiary care hospital among patients diagnosed with ARDS for a period of 5 years. The total hospitalization cost (INR [₹]) was used as the cost; while, ICU-free days (IFD), oxygen-free days (OFD), and ventilator-free days (VFD) were considered as outcomes to perform the cost-effective analysis. Additionally, factors affecting total hospitalization costs were also analyzed through univariate and multivariate linear regression.

Results: A total of 578 patients were included in the study. The factors such as sepsis, septic shock, use and course of antibiotics, ICU, oxygenation, and ventilation days have all been identified as significant independent predictors of higher hospitalization costs in ARDS patients. A total of 305 patients were included in the cost-effective analysis, with 151 receiving corticosteroids and 154 not. Among the steroid group, 69 received intravenous (IV) steroid [IV steroid with or without nebulization/oral], and 82 received another steroid [nebulization/oral without IV]. Steroid treatment is more cost-effective than non-steroid treatment, with an incremental cost of 305 per VFD and 1645 per IFD. Additionally, steroid treatment had better OFD (12.8vs10.3) with lower cost (₹7815 vs ₹7883). Subgroup analysis indicated that another steroid was cost-effective with a lower cost and better outcomes in terms of VFD (11.8vs9.6; 8681 vs 10001), IFD (6.7vs5.3; 15393 vs 18114), and OFD (13.8vs11.7; 7473 vs 8206).

Conclusion: According to this retrospective cost-effectiveness analysis based on direct medical costs, corticosteroid management had a beneficial effect on ARDS patients. Furthermore, these findings should be supported by prospective studies that include direct non-medical costs and indirect cost components.

N.17

Economic Evaluation of Riluzole Treatment in Amyotrophic Lateral Sclerosis: A Systematic Review

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Objection: To systematically review of the economic evaluation of riluzole treatment

Methods: Relevant studies published from inception to April 2022 were searched from PubMed, Scopus, Embase, The National Health Service Economic Evaluation Database and The Cost-Effectiveness Analysis Registry. Studies were eligible if they included amyotrophic lateral sclerosis (ALS) patients, riluzole usage and reported economic evaluation outcomes. Data were extracted on study type, comparator, input parameters, modelling methods, cost-effectiveness results and conclusion. Quality assessment was performed.

Results: The search produced a total of 299 articles, but only six met inclusion and exclusion criteria. Of those six studies, five were conducted in Europe and America. Supportive care was used as a comparator in all studies. Almost all (5/6) were cost-effectiveness analysis, which used Markov model for four studies. Another study was cost-benefit analysis. Five studies considered healthcare system perspective. One study considered both healthcare system and societal perspective. The treatment effects were based on randomized controlled trial (4/6) while the remaining studies obtained from the real-world data. Direct medical costs such as hospitalization, medications, laboratory were included. The discount rate used was between 3% and 6%. A hundred percent (2/2) from societal perspective and 20% (1/5) from healthcare system perspective concluded that riluzole was cost-effective. Based on ECOBIAS checklists, no bias related to perspective, cost measurement and invalid valuation were found.

Conclusion: Only half of all studies reported that riluzole was cost-effective compared with supportive care for treating patients with ALS. The majority was from the societal perspective. This indicates that costs incurred by patients are very important when conducting cost-effectiveness study.

Keywords: Amyotrophic lateral sclerosis, economic evaluation, riluzole, systematic review

N.18

Incidence and Risk Factors of New-onset Diabetes Mellitus in Heart Transplantation Patients: A Systematic Review and Meta-analysis

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Objective: The aim of this study is to assess the incidence and risk factors of new-onset diabetes mellitus in heart transplantation patients.

Methods: This review is registered in PROSPERO with registration number; CRD42022331969.
A comprehensive search was performed in the MEDLINE and Embase databases to retrieve relevant case-control and cohort studies. Quality of the included studies was assessed using New-castle Ottawa scale (NOS). A meta-analysis was conducted using Comprehensive Meta-Analysis (CMA) software. Incidence and risk factors were identified using event rate and pooled odds ratio respectively.
Due to the inclusion of observational studies and high heterogeneity, a random effect model was used. Publication bias was examined through the eggers test (significant; p-value <0.05).

Results: Combinedly, two database searches yielded 830 studies with a total number of 10508 participants which includes cases (2613) and controls (7895). From these, 711 were eliminated in title and abstract screening. After secondary screening, 13 articles were considered adequate for meta-analysis. This analysis identified a total of 21 risk factors. Among, highly significant were as follows; Obesity [OR 5.92; 95% CI 4.39, 7.98], Hypertension [OR 2.61; 95% CI 1.49, 4.58] and Black race [OR 2.28; 95% CI 1.75, 2.97]. In addition, Incidence rate of new-onset diabetes mellitus after heart transplantation was found to be 23% [Event rate 0.23; 95% CI 0.14, 0.35]. Moreover, the NOS scale unveiled only high-quality studies were implicated except two; moderate quality. Furthermore, publication bias was shown to be symmetric using funnel plot and sensitivity analysis revealed no variation among the results of included studies.

Conclusion: Patients with obesity, hypertension, black race and steroid use; are at higher risk of developing diabetes. Hence, monitoring these traits may be helpful to prevent and reduce the incidence of the new-onset diabetes mellitus after heart transplantation.

Keywords: New-onset diabetes mellitus, Heart transplantation, Risk factors, Incidence

N.19

Comparison of safety of original and generic lansoprazole in Japanese patients in the real world

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Objective: The use of generic drugs has been promoted in Japan, but their safety in the real world has not been fully evaluated. In this study, we compared the incidence of two clinically important adverse reactions of lansoprazole, an antiulcer drug, between the original and the four generic products in Japanese patients.

Methods: Using a medical information database (Medical Data Vision Co., Ltd.), a total of 48,887 patients who received lansoprazole OD tablets dispensed in the hospital up to 60 days between April 2008 to November 2020 were selected and classified into five groups (one original and four generic groups). Outcomes were defined as new onset of gastrointestinal disorders (using ICD-10) and incidence of pancytopenia (using laboratory data) during the final dispensing phase. Adjusted odds ratios (95% CI) of each generic to the original were determined by multivariate logistic regression models using patient characteristics (age, sex, medical history, comorbidities, and laboratory data, etc.) as covariates.

Results: The overall incidence of new gastrointestinal disorders was 0.28% (137/48,887) in all patients, and that of pancytopenia was 0.58% （206/35,800）. There were no significant differences in adjusted odds ratios for both adverse reactions, except for one generic product, which showed a significantly lower risk of pancytopenia. Several risk factors were identified including primary diseases/comorbidities for gastrointestinal disorders and myelosuppression and hepatic dysfunction for pancytopenia.

Conclusion: Generic lansoprazole products were found to have no higher risk of the two clinically important adverse reactions compared to the original product. This study also suggests that it is important to consider the risk factors at baseline for appropriate use of this drug in the real world.

N.20

Development of a Non-invasive Topical Photodynamic Therapy Delivery Approach

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Objective: Photodynamic therapy (PDT) is a process of applying light to a photosensitizer ultimately leading to the production of reactive oxygen species (ROS). PDT has been used to treat several different forms of cancer via ROS mediated killing, vasculature damage, and induced immunogenic defense. Using PDT it is possible to bypass some of the adverse effects that commonly occur with cytotoxic agents, such as hair loss, nausea, vomiting, and overall fatigue. PDT is usually injected into a tumor leading to a more localized effect.

Methods: By using a layer-by-layer (LbL) multilayering technique it is possible to construct a nanofilm, which have the potential of being a drug delivery system. By loading a photosensitizer into multilayered films, it can subsequently leach out and accumulate within cancer cells. The quantity, release rate, and adhesion properties of the loaded nanofilms can be modified by altering the fabrication conditions. Thus, photosensitizer can be absorbed through the skin topically, followed by irradiation such that a non-invasive approach, to treat surface level cancers, such as melanomas could be obtainable.

Results: We utilized the 1st generation photosensitizer, Photofrin® and 2nd-generation agents, such as Rose Bengal and Methylene Blue. We have successfully multilayered, poly-L-lysine (PLL) and hyaluronic acid (HA) at a variety of different solution pH's, loaded the three aforementioned photosensitizers, and demonstrated their release rates at a pH environment resembling the skin. The loading of the photosensitizer is more closely related to the solution pH, while the release profile is associated to the assembly pH conditions.

Conclusion: It is possible to fabricate a nanofilm consistency of PLL/HA that is tunable to allow for the loading of a variety of photosensitizers. Reloading/releasing profiles of these photosensitizers, that has the potential to be used in PDT for melanoma, is related to both the assembly and loading solution pH values.

N.21

Nationwide exploratory survey assessing perception, practice, and barriers toward pharmaceutical care provision among hospital pharmacists in Nepal

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Introduction: Pharmaceutical care (PC) services in low-middle-income countries (LMICs) settings like Nepal are not commonly provided in hospital pharmacies. Therefore, we conducted to determine PC status in hospital pharmacies and explore the perception, practice, and barriers (and their determinants) encountered by hospital pharmacists while providing PC.

Methods: We conducted a cross-sectional study from 25th March-25th October 2021 among pharmacists in hospital pharmacies using non-probability quota sampling. We developed a questionnaire which addressed perception and practice regarding PC, and barriers encountered. Experts and pre-tested validated the developed questionnaires. Kendall's correlation was used to explore the correlations among various perception and practice constructs. To compare the scores among subgroups of respondents, the Mann-Whitney test for subgroups with two categories and Kruskal-Wallis test for greater than two categories was used.

Results: Total number of 144 pharmacists participated. Majority (50%) of participants had received no training in PC. Patients did not request PC services, and supportive practice guidelines were lacking. Scores of perception were higher among those with more work experience and the practice scores among those who had received PC training. Participants agreed that there were significant barriers to providing PC, including lack of support from other professionals, lack of demand from patients, absence of guidelines, inadequate training, lack of skills in communication, lack of compensation, problems with access to the patient medical record, lack of remuneration and problems with accessing objective medicine information sources. A correlation was noted between certain perceptions and practice-related constructs.

Conclusion: Hospital pharmacists who participated had a positive perception of providing pharmaceutical care. However, PC is not commonly practiced in hospital pharmacies. Significant barriers were identified in providing PC, such as adequate space, proper layout and adequate human resources. Further studies, especially in LMICs, are required.

N.22

Geographic Linkage of Environmental Factors and Taiwan National Health Insurance Database for Pharmacoepidemiologic Studies

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Objectives: Geographic patterns and regional differences play an important role in epidemiological research. Researchers may assess the clustering effect of health outcomes through spatial distribution profiles. In this study, we demonstrate an algorithm to estimate a person's place of residence in Taiwan National Health Insurance Database (NHID), which can then be linked with environmental factors, such as PM2.5, PM10, temperature, etc., to permit drug-environment interaction analyses.

Methods: The NHID and Data Bank for Atmospheric and Hydrologic Research from 2009-2018 were used. We conducted a retrospective cohort study to identify an elderly cohort with cardiovascular diseases from NHID. The principle of estimating residence was based on beneficiary category and location of clinic/hospital visits. Because not every township has stations observing air quality, neighboring areas around the station shared the same PM2.5 exposure. The estimated place of residence and air quality information were linked with ZIP code.

Results: the average of PM2.5 concentration was 24.1 μg/m3 from 2009-2018. The PM2.5 concentration showed a seasonal effect, the lowest concentration in summer, gradually increasing in the fall, and highest in winter. The pattern was similar to results from The Environmental Protection Administration.

Conclusions: The algorithm we demonstrate is a feasible method to estimate a person's place of residence. This permits extended data to investigate associations between air pollution exposure and health outcomes for drug-environment interaction studies.

N.23

Adherence to immunosuppressive drugs in kidney transplant recipients

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Objectives: To evaluate adherence to immunosuppressive drugs in kidney transplant (KT) recipients and determine factors associated with adherence.

Methods: A cross-sectional study was conducted between December 2018 to January 2019 at a university hospital kidney transplant outpatient clinic. Kidney transplant recipients were interviewed by clinical pharmacists, and their adherence was measured using an immunosuppressant therapy adherence instrument (ITAS).

Results: In total, 224 KT recipients participated in the study. The mean age was 47.89±14.69 years, 146 (65.2%) were male, 180 (80.4%) had a partner or caregiver, and 128 (57.1%) had a high school education or below. The sample was very closely divided between those who received living donor transplants and those who received deceased donor transplants and the median post-transplant time was 48 months (IQR 20-90.75). A range of immunosuppressive drugs were prescribed to participants: tacrolimus (3.20 (±1.51) mg/day), mycophenolate sodium (900.43 (±328.60) mg/day), mycophenolate mofetil (1250.78 (±509.86) mg/day), and prednisolone (4.88 (±0.54) mg/day). Thirty-five participants (15.6%) were taking at least 10 different medications. Based on the ITAS scores, 210 (93.8%) patients had good adherence to the immunosuppressive drugs and had ITAS scores greater than or equal to 10. Patient factors, treatment factors and disease factors were not associated with adherence.

Conclusion: Most kidney transplant recipients had good adherence to immunosuppressive drugs and specific characteristics related to adherence could not be identified among the factors studied.
Key words: Adherence of immunosuppressive drugs, kidney transplant, ITAS

N.24

Assessment of medication adherence and belief about medicines amongst the elderly: A developing country scenario

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Aim: To assess the medication adherence and belief about medicines amongst the elderly and their association.

Methods: A prospective cross-sectional study was conducted to assess the medication adherence level, and the beliefs about medicines using the simplified medication adherence questionnaire, and belief about medicines questionnaire, respectively amongst the geriatric patients admitted to the department of geriatrics with at least one chronic disease condition. Data thus collected were categorically analysed. Association between age, gender, level of education, area of domicile, socio-economic status and level of adherence was tested using chi-square test. T-test was used to find the relation between the adherent and non-adherent groups and their beliefs about medicines.

Results: A total of 30 patients were interviewed during December 2021, of which 70% were males and the mean age was found to be 72 ± 4.73 years. The average length of hospital stay was found to be 10 days. The medication adherence amongst the study participants was found to be 50%. The majority of the study participants endorsed the belief that their current health depended on their medications [24 (80%)] and that their medications kept them from getting worse [22 (73.33%)]. The concerns regarding medications were also reported. The majority reported having worries about the long-term effects of their medications [26 (86.67%)]. Also, doctors using too many medicines [7 (23.33%)] and medications are addictive [9 (30%)], were commonly reported. Chi-square analysis indicated significant variation in medication adherence by age ($p = 0.0223$) and gender ($p=0.0464$), and there was no statistically significant difference found between the two groups with regards to their beliefs about medicines (t-ratio = 0.14, $p = 0.88$).

Conclusion: A clinical pharmacist can play a vital role in identifying the medication adherence behaviour through such surrogate markers and provide the necessary counselling, thereby promoting medication adherence.

Keywords: Medication-adherence, Clinical-pharmacist

N.25

Initiating GLP-1 RA therapy to improve renal outcomes for persons with uncontrolled diabetes: hypothetical intervention using parametric g-formula modeling

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Aim/Objective: Several clinical trials have shown that glucagon-like peptide-1 receptor agonists (GLP-1 RAs) may have a renoprotective effect in persons with type 2 diabetes mellitus (T2DM). Whether this effect is replicatable in the routine care setting is unclear.

Methods: This is the sub-analysis of our study published recently, an observational study analyzed under a counterfactual framework. We used the electronic healthcare database in Japan, comprising data from approximately 20 million patients at approximately 160 medical institutions. Persons with T2DM with an estimated glomerular filtration rate (eGFR) ≥ 30 mL/minute/1.73 m2 in April 2014 were eligible. Excluded were prevalent users of GLP-1 RAs. The primary endpoint was the composite of renal deterioration (>40% decline in eGFR) and the development of eGFR<30 mL/minute/1.73 m2. We estimated the risk of the composite endpoint occurring over 77 months. Because it was challenging to define “uncontrolled” diabetes uniformly, different thresholds for intervening GLP-1 RA treatment were tested based on the hemoglobin A1c (HbA1c) level and its sustained duration. The parametric g-formula was used to estimate the risk of the composite endpoint, adjusting for time-fixed and time-varying confounders.

Results: We tested 12 scenarios using data from 35,438 persons (145,862 person-years of observation), of whom 1261 started GLP-1 RA therapy (5946 person-years of observation). Overall, there observed no differences in the outcome occurrence from the very early introduction scenario (HbA1c ≥6,5% for 3 months: 77-months risk difference of 0.82 % [95% CI: -5.9% to 7.7%]) to the deffred introduction scenario (HbA1c ≥7.5% for 12 months: risk difference of 0.96 % [95% CI: -2.6% to 4.9%]).

Conclusion: In all scenarios examined, GLP-1 RAs showed no clear benefits in delaying the renal function decline within 77 months of observation. However, we might miss a small but clinically relevant difference due to the small number of GLP-1 RA initiators.

N.26

Polypharmacy was associated with declines in intrinsic capacity of community dwelling elderly in rural area in Taiwan

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Aim: In 2017, W0rld Health Organization launched the Integrated care for older people (ICOPE) guidelines on community-level interventions to manage declines in intrinsic capacity (IC). This study aimed at evaluate IC of community dwelling elderly in rural area of Taiwan and the association between declines in ICs and the polypharmacy.

Methods: It was a cross-sectional research and community dwelling elderly in Yunlin County who participating in community-base long-tern care services or activities were invited and evaluated from 2021.09 to 2022.04. Mian IC domain evaluated in this study included mobility, vitality (nutrition), sensory capacity (visual impairment and hearing loss), cognitive capacity, psychological capacity. The definition of declined in mobility was five chair rises test longer than 14s. Declined in vitality was weight loss more than 3 kg over the last 3 months or appetite loss. Visual impairment and hearing loss was evaluated by weather the elderly has difficulties in reading or whisper test, respectively. Cognitive and psychological capacity were evaluated by Mini-Cog and EQ-5D-5L, respectively. The definition of polypharmacy was concomitant use of more than 10 drugs, included nutrition supplement and Chinese herb medicine. The association between polypharmacy and decline in the intrinsic capacity was tested by using age and sex adjusted logistic regression.

Results: 567 elderly completed the WHO-ICOPE evaluation. Polypharmacy was significantly associated with decline in mobility ability (Odd Ratio (OR)=2.01, 95% Confident Interval (CI):1.04-4.23, p=0.038) and visual impairment (OR=1.80, 95%CI:1.04-3.13, p=0.036). Polypharmacy was also associated with increased in risk of the declines in hearing, cognitive and psychological capacity, although there was no statistically significant difference.

Conclusion: Polypharmacy was associated with many domains of intrinsic capacity decline. Strategies for managing declines in intrinsic capacity should include pharmaceutical services which aimed at improving polypharmacy associated drug-related problems.

N.27

Association between prenatal antipsychotic exposure and the risk of attention-deficit/hyperactivity disorder and autism spectrum disorder: a systematic review and meta-analysis

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Background: The risk of attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) in children with prenatal antipsychotic exposure is unclear.
Objective: To evaluate whether prenatal exposure to antipsychotics is at increased risk of ADHD and ASD in children.

Methods: A systematic literature search was conducted in PubMed, EMBASE, APA PsycINFO and Cochrane Library databases up to March 29, 2022, for data from observational studies assessing the association between prenatal antipsychotic use and ADHD/ASD in children. Non-English studies, animal studies, case reports/series, cross-sectional studies, conference abstracts, book chapters, reviews and summaries were excluded. The primary outcome was ADHD/ASD reported with prenatal antipsychotic use. The Newcastle–Ottawa Scale (NOS) was used to assess the methodological quality of included studies. Estimates were pooled using a random effect model, with the I2 statistic used to estimate heterogeneity of results.

Results: In total, six studies fulfilled our systematic review inclusion criteria with more than eight million pregnancy episodes in nine different countries/regions. Three studies were included in the primary meta-analysis for ADHD or ASD, which provided a pooled adjusted relative risk (aRR) of 1.11 (95% confidence interval [CI]: 1.03-1.19, I2=0.0%, p=0.956) for ADHD and 1.10 (95% CI: 0.98-1.24, I2=0.0%, p=0.930) for ASD. However, when compared past exposed with never exposed, the pooled aRRs for ADHD and ASD were 1.96 (95% CI: 1.05-3.66, I2=95.8%, p=0.000) and 1.38 (95% CI: 1.20-1.60, I2=0.0%, p=0.890), respectively. The pooled aRRs for sibling-matched analyses were 1.11 (95% CI: 0.78-1.60, I2=0.0%, p=0.410) for ADHD and 1.17 (95% CI: 0.73-1.87, I2=0.0%, p=0.432) for ASD.

Conclusions: The findings did not suggest a causal relationship for the risk of ADHD or ASD with maternal prenatal antipsychotic exposures. Women should discuss their individual cases with clinicians to decide whether use of antipsychotic in pregnancy is indicated and that potential benefits outweigh the risks.

N.28

Incidence Rate and Risk of Subsequent Dyslipidemia after Diagnosed with Hypertension in Newly Diagnosed Diabetic Patients in Three Generation Cohorts

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Objective: To measure temporal incidence rate of dyslipidemia, hypertension in newly diagnosed diabetic (NDDM) patients and identify risk of subsequent dyslipidemia after diagnosed with hypertension in NDDM patients. Methods: We used data from 2014-2021 from national health security office region 10 Thailand to identify NDDM patients with ICD10 code (E10-E14) during 2014-2018 and were followed up for diagnosis of hypertension with ICD10 code (I10), then followed up for subsequent dyslipidemia (E78X). NDDM patients were categorized by year of birth (Baby Boomers II, Gen X, Millennials). Hazard ratios (HR) of hypertension and subsequent dyslipidemia were compared between sex in three cohorts. Results: Of 97,904 NDDM patients identified, 60,345 were subsequently diagnosed with hypertension. Incidence rate of hypertension was 225.88 cases per 1,000 person-years. For all three cohorts, males were more likely to be significantly diagnosed with hypertension than females. The hazard ratio for Baby Boomers II, Gen X, and Millennials were 1.12 (95%CI=1.10-1.15), 1.09 (95%CI=1.05-1.13), and 1.19 (95%CI=1.06-1.33). After diagnosed with hypertension, statistical significance of developing hyperlipidemia in NDDM patients was not observed between sex for two cohorts (95%CI of HR=0.99-1.07 for Baby Boomers II, 95%CI of HR=0.96-1.10 for Gen X). The incidence rate of dyslipidemia in three cohorts were 100.44, 96.99 and 83.13 cases per 1,000 person-years for three cohorts respectively. Only the Millennials, males were statistically less likely to be diagnosed with dyslipidemia than females (HR=0.75 with 95%CI of HR=0.57-0.98). Conclusion: Male NDDM patients had higher risk of hypertension compared with females for all three cohorts. However, females in the Millennial group were at higher risk for subsequent dyslipidemia than male after diagnose with hypertension and diabetes.

Keywords: subsequent dyslipidemia, hypertension, diabetes

N.29

Incidence and characteristics of small for gestational age in Taiwan, 2007-2017

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Objective: 1) to update birth weight percentiles for gestational age in Taiwan, 2) to report the incidence trend of small for gestational age (SGA), and 3) to evaluate demographic characteristics associated with SGA.

Methods: Data were collected from the Health and Welfare Database and Birth Certificate Application. Live, singleton, known sex, and gestational age between 20 to 42 weeks infants were included to build the birth weight percentiles curves. Infants whose birth weights were out of the range of median ± 2 x interquartile range were excluded. Infants were further divided into SGA (birth weight below the 10th percentile for gestational age) and non-SGA. Characteristics including gender, gestational age, preterm birth, delivery type, maternal age, and maternal nationality, were presented by groups. Simple T-test and Chi-square tests were used to examine the differences. Odds ratios were estimated by multivariable logistic regression models.

Results: There were 2,107,604 infants enrolled to develop the sex-specific birth weight percentiles. From 2007 to 2017, mean birth weight decreased with an increased incidence of SGA, which had significantly increased from 10.5% to 12.1% ($p<0.01$). Mean maternal age had increased from 29.5 to 32.0 years old. The proportion of native pregnancy had increased from 91.2% to 93.9%. Infants born as SGA were more likely to be as males, less gestational age, preterm infants, cesarean sections, and younger or Taiwanese mothers. Results were consistent after adjustments. Infants born with native mothers were significantly more likely to be SGA compared with those whose mothers came from central Asia, southeast Asia, or America.

Conclusion: The study updated the birth weight percentiles for gestational age in Taiwan. Incidence of SGA was increased. Future research aims to further investigate maternal and neonatal adverse outcomes with respect to infant birth weights.

Keywords: small for gestational age, maternal nationality, National Health Insurance Research Database

N.30

The Correlation between Exposure of Antibiotics in Early Childhood and Risk of Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder

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Aim/Objective: The purpose of this study is to evaluate the correlation between exposure of antibiotics in early childhood and risk of autism spectrum disorder (ASD) and/or attention-deficit/hyperactivity disorder (ADHD).

Methods: We conducted a retrospective cohort study consisted of livebirths born between 2004 and 2016 from the National Health Insurance Research Database in Taiwan. Children were separated into singleton cohort and sibling cohort and further categorized by their status of antibiotic exposure in the first two years of lives. Propensity score matching were adopted in the singleton cohort. As for the sibling cohort, discordant-pair analysis was used. Potential confounders and risk factors from neonates and parents were included as covariates. ASD and/or ADHD were the composite outcome of our study. The follow-up time started from the second birthday to the event of interest, death or the end of the study. Cox proportional hazards model was used to estimate the event risks.

Results: 2,617,069 livebirths from 2004 to 2016 were identified. The final sample contained 1,873,785 children. 318,777 pairs of singleton children were matched by propensity score, and baseline characteristics were well balanced. Antibiotic exposure slightly increased the risk of ASD and/or ADHD in the singleton cohort [adjusted hazard ratio (aHR) 1.054, 95% confidence interval (CI) 1.035-1.073, p-value < 0.001]. For the sibling cohort, 168,780 exposure-discordant pairs were identified. The risk of ASD and/or ADHD decreased slightly (aHR 0.918, 95% CI 0.896-0.941, p-value < 0.001).

Conclusion: Exposure of antibiotics in early childhood might slightly increase the risk of ASD and/or ADHD in singleton families but not in exposure-discordant pairs sibling settings. Further research in regard to siblingship is needed to ascertain these findings in the future.

Keywords: antibiotics, gut microbiota, autism spectrum disorder, attention-deficit/hyperactivity disorder