ePoster abstracts

100 Use of medical services among individuals at risk of developing diabetes identified by the Japanese specific health checkup program

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Aims: Following a new health checkup program in 2008 in Japan to reduce the risk of metabolic syndrome, there is a need for effective health guidance for high-risk individuals to receive appropriate medical services (re-examination or pharmacotherapy initiation). This study focused on individuals with fasting plasma glucose (FPG) ≥100 mg/dL at health checkups and who qualified as candidates to visit the physician for re-examinations, to identify appropriate medical services according to the FPG level and health-related lifestyle.

Methods: From health checkups and claims databases, individuals aged 40-74 years, with FPG of 100-159 mg/dL, and follow-up physician visits with diagnostic codes for diabetes, were selected as the study population. Medical services selected within 6 months of the first physician's visit were classified as no follow-up, observation, or pharmacotherapy according to the FPG levels. Likelihood of initiating pharmacotherapy within 6 months was estimated based on the FPG level using logistic regression analysis with/without adjusting for self-reported lifestyle.

Results: We identified 7,793 individuals whose FPG levels were categorized as high-normal (n= 2,389), borderline (n=3,324), or diabetic (n=2,080). There were positive trends for pharmacotherapy initiation by FPG levels, and dipeptidyl peptidase-4 inhibitor was the popular choice. Logistic regression analysis results revealed hemoglobin A1c as a unique independent predictor of the need for pharmacotherapy among individuals at risk of developing diabetes.

Conclusion: Laboratory test results combined with lifestyle behaviors at health checkups constitutes useful information for predicting future medical service usage and enables the health professionals to provide effective health guidance.

101 Analysis of factors related to not accessed to Peginterferon alfa-2a and ribavirin in patients with chronic hepatitis C virus

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Objective: To explore factors related to not accessed to Peginterferon alfa-2a and ribavirin in patients with chronic hepatitis C virus through high-cost medicines E2 program, the National List of Essential Medicines Thailand.

Methods: Data were collected retrospectively by electronic record from outpatient and inpatient with chronic hepatitis C virus infection under Universal Coverage (UC) Scheme in Maharaj Nakorn Chiang Mai Hospital from 1st January 2013 to 31th December 2016.

Results: A total of 203 patients were included in the study, 26.1 percent received treatment and 73.9 percent did not received treatment. Not received treatment group had more HCV-related decompensated cirrhosis and HCV-related HCC than receiving treatment group. Most patients in not receiving treatment group were patients with incurable cancer or had disease-free survival less than 6 months and patients who intolerance to interferon or ribavirin, followed by patient with decompensated cirrhosis. Moreover, the result revealed the important characteristic related to not accessed to medication such as patients greater than 65 years of age, chronic alcohol consumption within 6 months before diagnosis, HIV-coinfection, and lost to follow up.

In conclusion, the most factors related to not accessed to medicines were hepatocellular carcinoma and condition of interferon intolerance that mostly caused by delayed diagnosis. Therefore, early diagnosis remains key for effective treatment of chronic hepatitis C virus infection.

Keywords: access to peginterferon, HCV, high-cost medications

102 Effectiveness of polypharmacy reduction policy in Japan: Nationwide retrospective observational study

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Objective: Polypharmacy is an important global health issue. In Japan, an amended policy has been implemented in April 2016 by including incentives for hospitals to reduce polypharmacy. However, there is no evidence on the nationwide effectiveness of polypharmacy reduction policy. Therefore, this study aimed to evaluate the effectiveness of the polypharmacy reduction policy in Japan using National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) as the primary data source.

Methods: This nationwide retrospective observational study was conducted using outpatient prescription reimbursement claims data available in NDB Open Data over 3 years (April 2015 to March 2018). The primary outcome was the polypharmacy reduction ratio in each prefecture calculated by the proportion of polypharmacy. Factors associated with policy effectiveness were identified by multiple linear regression analysis using independent variables. Independent variables were proportion of elderly and male residents, a number of pharmacies, clinics, and clinics per 100,000 residents.

Results: After implementing the new policy, a 7.3% polypharmacy reduction ratio was observed, particularly in the elderly (8.2%). Multiple linear regression analysis revealed that the proportion of elderly residents (aged ≥65 years), number of hospitals per 100,000 residents, and number of clinics per 100,000 residents were statistically significantly associated with this reduction.

Conclusion: The polypharmacy reduction policy showed clinically significant association with polypharmacy reduction in Japan. The proportion of elderly residents and availability of hospitals and clinics might be important factors that enhance the effectiveness of the polypharmacy reduction policy.

Keywords: nationwide, polypharmacy, policy, Japan

103 Affordability of cardiovascular medicines in Armenia

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Objective: The objective of this work was to study the situation with prices and affordability of cardiovascular medicines (CVMs) in Armenia.

Methods: Data on prices for 12 selected CVMs were collected from 60 pharmacy outlets from different regions of Armenia. Affordability of medicines was calculated using methodology developed by World Health Organization/Health Action International.

Results: Selected CVMs were available at least at 60 % of all the community pharmacies studied. Originator brands (OB) were found for 6 medicines, generics - for 11 CVMs. OBs for 4 of 5 medicines were much higher priced than lowest-priced generics (LPGs), however for 2 of 5 studied medicines prices of highest priced generics (HPGs) were higher than those for OBs. Using matched medicine pairs (OBs:LPGs ratio), OBs were from 1.9 to 9.7 times the price of LPGs. 5 of 12 medicines were affordable, 2 (Perindopril, Nifedipine) – unaffordable (1.8-3.6 days' and 1.3-3.4 days' salary is needed to purchase one course of treatment for worker with the minimal salary approved by the Government, correspondingly), generic products of Simvastatin and Verapamil were affordable only if prescribed at low doses and unaffordable at higher doses; only generic products of Captopril, Enalapril and Amlodipine were affordable (the cost for a course of treatment does not exceed an one-day salary of worker with the minimal wage).

Conclusion: There is a large difference in prices of OBs and LPGs of selected cardiovascular medicines available at pharmacy outlets in Armenia. Unaffordability of some medicines compromise access to treatment for outpatients with cardiovascular diseases. It is important to introduce policy strategies aimed to improve access to essential medicines.

Keywords: cardiovascular medicines, access, policy

104 Evaluation of the national system of pharmacovigilance in Armenia

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Aim/Objective: The aim of this work was to assess Pharmacovigilance (PV) system in Armenia and evaluate whether it meets recommendations of the World Health Organization (WHO).

Methods: Four components (legislation and regulation, structure, data management and communication) were analyzed. Data were collected from official regulation documents and other publication, web-sites of official organizations: Ministry of Health, Scientific Centre of Drug and Medical Technologies Expertise (SCDMTE).

Results: The results of assessment show certain achievements. In the Law “On Medicines”, approved in 2016, provisions on ADRs Monitoring were expanded (when comparing with the previous Law “On Medicines” approved in 1998); in particular, the current system involves reporting cases of falsified medicines, lack of efficiency and medication errors. However, the term Pharmacovigilance is not used in the Law; the terms and definitions of ADR, adverse event are not available. New Regulation document and Form for reporting ADR were approved in 2017. For implementing functions of a national PV center the Pharmacovigilance Department has been established at SCDMTE; its duties include detection, assessment, understanding of Adverse Drug Reactions (ADRs) reports, providing expertise and training, etc. SCDMTE is a member of the WHO International Program of ADR Monitoring since 2001.

Conclusion: PV system in Armenia mostly meets minimum requirements that should be present in any national PV system: national PV centre, national spontaneous reporting system, national database, and clear communication strategy are in place. There is need in further strengthening PV system through certain changes in legislation, regulation, improving knowledge and motivation of physicians and pharmacists. Inclusion PV topic in an appropriate curricula taught at the Medical University would be helpful. A special lecture on PV has been prepared and included in the Program of Course on Continuing education for pharmacists at the Yerevan State Medicines University.

Keywords: pharmacovigilance, regulation, national system

105 Comparison of Assessment Results for Periodic Safety Update Report among the European Union, Korea, the United States, and Japan

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Objective: To improve the post-market safety management system, comparison and analysis should be conducted for the Periodic Safety Update Report (PSUR). The aim of this study was to analyze the status of drug safety labeling in Korea, the United States (US) and Japan with the evaluation results of the PSUR of the European Union (EU) by comparing measures such as label changes in each country.

Methods: The number of drugs subject to PSUR review and the status of action for labeling were analyzed by action after PSUR review presented on the European Medicines Agency (EMA) website for the past three years. For the same products that their PSURs have been reviewed by the EMA, the label changes in Korea, the US, and Japan were checked, and the degree of consistency with the actions of the four regulatory authorities was analyzed.

Results: Of the 607 PSUR reviews published by EMA, 59 cases (9.7%) were subject to label change. The review cases were in the order of nervous system group 16.3%, cardiovascular system group 15.5%, and respiratory system group 9.5%, and the therapeutic groups with the most label changes were group including antiparasitic products, insecticides and repellents 25.0%, musculo-skeletal system group 17.9%, respiratory system group was 14.3%. Of the 59 EMA label changes, 13 cases (22.0%) were changed in Korea, 13 cases (22.0%) in the US, and 20 cases (33.9%) in Japan.

Conclusion: These findings suggest that label changes in Korea, the US and Japan may be not very consistent with the EU. Further studies are needed on the details of the label change and the reasons for this discrepancy.

106 The impact of clinical pharmacist interventions on intravenous administration of antimicrobials by nurses

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Objective: To analyze the impact of clinical pharmacist intervention on the administration of selected antimicrobials by nurses.

Methods: A one-group pre-test post-test interventional study was conducted for a 6-month period among nursing professionals in a tertiary care hospital using a validated KAP questionnaire. The study assessed the knowledge, practice, and attitude level of the respective nurses regarding intravenous administration of antimicrobials. An in-person monitoring system was formulated to evaluate the rationality in the practice of iv admixture and to identify the administration errors. Customized corrective education was provided by the clinical pharmacists based on the pre-test performance and in-person monitoring. A post-test was conducted to evaluate the effectiveness of these interventions. Paired t-test analysis is conducted and a $p<0.05$ is considered statistically significant.

Result: The study enrolled 106 nurses and 88 of them had completed the evaluation. Among these 88 nurses, the majority (54.7%) were diploma holders and the mean age was found to be 38±12.3. On analyzing the years of experience in professional nursing, it was found that the majority had 1-5 years experience (61.3%) followed by 5-10 years (23.6%). On comparing the pre-test with the post-test, knowledge (6.7 vs 10.5, $p<0.0001$), attitude (6.7 vs 8.9, $p<0.001$), and practice (7.1 vs 8.3, $p<0.001$) of the nurses regarding the administration of selected antimicrobials has unveiled a statistically significant improvement in the post-test evaluation. No significant association is found between the educational level or years of experience with the knowledge, attitude, and practice of the nurses.

Conclusion: Clinical pharmacist-initiated continuing education programs related to therapeutic and administrative aspects of antimicrobials can significantly contribute towards knowledge and practice enhancement, irrespective of educational background or years of experience.

107 Trend analysis of prescription patterns of psychotropic drugs for elderly patients in Japan: A nationwide population-based study

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Background: Globally, polypharmacy is one of the most challenging public health issues. In Japan, a polypharmacy reduction policy was introduced from 2012 to 2018, which reduces the reimbursement of medical fees when three or more types of psychotropic drugs are prescribed. We aimed to examine the impact of the polypharmacy reduction policy on the total amount of dosages of psychotropic drug prescriptions in elderly patients, and elucidate the relationship between policy interventions and multidrug prescriptions.

Methods: We used data from the National Database of Health Insurance Claims, the Specific Health Checkups of Japan (NDB) open database. The NDB collects data from more than approximately 126 million patients and 1.9 billion health insurance claims annually, covering over 95% of current health insurance claims information in Japan. We selected outpatients aged ≧65 years who started at least one of the available oral benzodiazepines (BZs), anxiolytics, hypnotics, antidepressants, and antipsychotics for elderly patients between April 2015 to March 2019. All statistical tests were two-sided, and a linear regression model was applied to determine whether the prescribed dosage amount (Unit: mg) of drugs changed after the policy intervention.

Results: Among in-hospital prescriptions, the prescribed amount for BZs, anxiolytics, hypnotics, and antipsychotics significantly decreased over the analyzed periods, while antidepressants significantly increased (p-value < 0.001). In addition, among out-of-hospital prescriptions, the prescribed amount for anxiolytics and antipsychotics significantly decreased over the analyzed periods, while antidepressants significantly increased (p-value < 0.001).

Conclusions: The present study indicated that the polypharmacy reduction policy intervention could be effective for reducing psychotropic drug prescription in elderly patients, while further research is needed to verify the factors for the increase in prescriptions of antidepressants. Hence, an effective policy for polypharmacy reduction should be established based on the clinical guideline while also keeping the quality of medical care.

Keywords: Polypharmacy, Psychotropic drug

108 Can external control studies supplement single-arm trial data as part of regulatory, reimbursement and HTA submissions in Asian countries?

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Aim/Objective: Real-world external control studies (ECS) can provide synthetic comparator data to supplement single-arm studies in disease areas with small patient populations and/or when it is ethically unacceptable to have a control group. However, there are no established guidelines on how these data are submitted to or evaluated by HTA/reimbursement agencies. This study investigates the use and acceptance of ECS to inform HTA and reimbursement decisions in Asia, where no established guidelines on this type of RWE exist.

Methods: A targeted literature review of published RWE studies provided the foundation for focused interviews with HTA and RWE experts in Japan, South Korea, China, and Taiwan.

Results: The literature research found no examples of ECS supplementing single-arm trial data in Asia. Most interviewees had limited experience with ECS as these are not commonly seen for HTA/reimbursement assessments. In Japan, China & Taiwan, ECS are generally considered on a case-by-case basis, while in South Korea, ECS are usually not accepted as part of the HTA evaluation. Taiwanese HTA authorities seemed most likely to consider ECS if it matched the trial population. Further, acceptance of ECS by regulators and HTA bodies around the world can influence acceptance in some Asian countries. Recent guidance on RWE from regulators in China & Taiwan has not influenced consistent acceptance of such data among regulators and HTA bodies. Early engagement with regulators or HTA/reimbursement decision-makers is key to optimize the assessment of ECS for the decision-making process.

Conclusions: Consideration of ECS as part of regulatory or HTA/reimbursement decision-making is still limited, and randomized controlled studies remain the gold standard in most countries. Concerns remain regarding data quality and generalizability of external data to a single-arm trial and local populations; however, there is increased willingness to consider external control data for regulatory and HTA/reimbursement assessments.

Keywords: RWE; HTA

109 Comparison between comparison group of CASPIAN trial and its reproduction by Medicare 5% sample data

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Aim/Objective: Producing comparison group for randomized controlled trial (RCT) using real-word data (RWD) is desirable considering the patients' burden and cost. A CASPIAN trial is an RCT that assesses the efficacy of durvalumab compared with comparison groups, including a combination with etoposide and either cisplatin or carboplatin (etoposide–platinum: EP) in treatment-naive patients with extensive-stage small cell lung cancer. We examined the possibility to produce the EP arm in the CASPIAN trial using RWD.

Method: Medicare beneficiaries having at least one claim with ICD10 diagnosis code of C34.9 (Malignant neoplasm of unspecified part of bronchus or lung) from Medicare 5% sample data (US, 2016-2019) were selected. To identify new patients, we excluded the patients with <1 year from the beginning of the observation period to the earliest diagnosis of C34.9 (first diagnosis). We included only the patients with initiated EP, regarded as the patients under this analysis. Their dates of the initial treatments were regarded as the index dates. The overall survival (OS) curve was depicted by Kaplan-Meyer method and compared by the EP arm of the CASPIAN trial.

Result: Among 2.8 million beneficiaries of Medicare 5%, 51,602 beneficiaries had at least one claim with C34.9 at any position and at any time, of which, 27,899 patients had the first diagnosis dates, and 1,067 patients were identified for the analysis. The median (95% CI) of the OS curve was 10.4 (9.7-11.0) months which is close to that in CASPIAN trial (10.3 (9.3-11.2) months). The p-value of the log rank test was 0.108, suggesting that the curves are not statistically significantly different.

Conclusion: Our result suggests the possibility to produce control group in RCT using RWD.

Keywords; RWD, historical comparison, external control, drug development

110 Impact of COVID-19 pandemic on medicine supply chain: Experiences of community pharmacists

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Background: Coronavirus diseases out broke towards the end of December 2019 in China, soon it started spreading rapidly to various countries leading to an outburst of pandemic. Various strategies were adapted across the world to control the spread of the infection.

Objective: This study aimed to explore the perspectives of the pharmacists on the medicine supply chain during COVID-19 pandemic in India.

Methods: This study is a prospective, qualitative research involving telephonic, semi-structured in-depth interviews. An interview guide for pharmacists was prepared and validated using "Interview Protocol Refinement" method. Purposive sampling method was used to recruit the pharmacists, a telephonic oral consent was obtained and an interview was scheduled as per their convenience. The interview session was audio recorded and the recordings were transcribed verbatim. Further, transcripts were validated and analysed using NVivo software.

Results: A total of 5 participants were interviewed during our study. Thematic analysis of the transcripts resulted in seven main themes containing sub-themes The study revealed that pharmacists were involved in creating awareness regarding COVID-19 and educating the customers on precautionary measures to prevent transmission. Remote mode of communication like telephone and mobile phones were used for counselling the patients. The study also exposed that there was deficiency in medicine supply during the COVID-19 pandemic and the pharmacists faced several challenges in procuring and storing the medication. There was also the scarcity of manpower leading to extra workload and working overtime.

Conclusion: Our study observed that there were many challenges and barriers to medicine supply during the COVID-19 pandemic, though pharmacists were taking maximum efforts to re-establish the supply channel. Uninterrupted supply of essential medicine is the backbone of the health care system. Hence an effective plan is vital to combat such future emergencies. Appropriate strategies are to be developed to enhance the medicine supply system.

111 Clomiphene Citrate and associated risk of blindness

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Introduction: Clomiphene citrate is an orally administered nonsteroidal agent, which has both estrogenic and anti-estrogenic properties used for induction of ovulation. Blindness is a lack of vision. It may also refer to a loss of vision that cannot be corrected with glasses or contact lenses.

Aim/Objective: The aim of this review is to evaluate the risk of blindness associated with the use of clomiphene citrate and to suggest regulatory recommendations if required.

Methods: Signal Detection team at the National Pharmacovigilance Center (NPC) of Saudi Food and Drug Authority (SFDA) performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database (VigiBase), to retrieve related information for assessing the disproportionality and causality between clomiphene citrate and the risk of Blindness. We used the WHO criteria as standard for assessing the causality of the reported cases.

Results: The disproportionality of the observed and the expected reporting rate for drug/adverse drug reaction pair is estimated using information component (IC), a tool developed by WHO-UMC to measure the reporting ratio. Positive IC reflects higher statistical association while negative values indicates less statistical association, considering the null value equal to zero. The results of (IC= 1.4) revealed a positive statistical association, which means “Blindness” with the use of “Clomiphene citrate” have been observed more than expected when compared to other medications available in WHO database. Additionally, we assessed the causality for the documented 10 case-reports, which shows about half of them supportive for association.

Conclusion: The weighted cumulative evidences identified from the data mining and the reported cases, are sufficient to support a causal association between clomiphene citrate and the risk of blindness. Health care professionals must be aware of this potential risk and shall monitor eye health periodically in treated patients.

Keywords: Pharmacovigilance, clomiphene, Blindness, Drug Safety

112 Adverse drug reactions to first-line anti-tuberculosis drugs and their impact on quality of life in tuberculosis patients

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Backgrounds: Although effective anti-tuberculosis(TB) drugs are readily available, the treatment of TB is not always successful because adverse drug reactions (ADRs) to anti-TB drugs often lead to treatment interruption and further decrease of quality of life (QoL) of the TB patients. The aim of the study was to investigate incidence of ADRs to the first-line anti-TB drugs and to assess QOL of the TB patients prospectively.

Methods: We enrolled TB patients (age > 18 years) treated with first-line anti-TB medications from five hospitals of Hallym University Medical Centers in Korea for two years (2018.01-2019.12). Questionnaire survey for ADRs and blood tests were performed four times serially during TB treatment. QoL assessment was conducted using World Health Organization Quality of Life-Bref (WHOQOL-Bref) at 4th week (± 2 weeks) of TB treatment. Statistical analyses were performed using R program.

Results: A total of 432 TB patients were enrolled. 266 patients (61.6%) were male. Mean age was 52.9±18.4 years and 123 (28.5%) were ≥ 65 yrs. 41 patients (9.7%) were changed treatment regimen due to ADRs to TB drugs. More than 40 percent of the patients complained of anorexia (41.6%), itching (41.6%), and fatigue (52.7%). Liver enzyme were increased in 30% of the patients, however, 17 (4%) were meet the definition of drug-induced hepatotoxicity. Elderly patients had more ADRs of anorexia, dyspepsia, rash, dizziness, ALT increase, anemia, BUN increase, Cr decrease, and uric acid increase ($p<0.05$, respectively). Patients with any ADRs and elderly patients had significantly lower QoL ($p< 0.05$, respectively). Risk factors for hepatotoxicity were longer treatment regimen (OR: 4.76, 95%CI: 1.27-17.31, $p=0.02$).

Conclusion: ADRs to first-line anti-TB drugs were common, and 9.5% were changed regimen due to ADRs. ADRs had significant impact on QoL of the TB patients. Elderly patients had more ADRs and lower QoL during TB treatment.

113 Exploring measurement issues with the proportion of days covered method used to calculate adherence to cardiovascular medicines: A scoping review

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Aim/Objective: Medication adherence is essential for preventing cardiovascular events and is commonly monitored in administrative data using the proportion of days covered (PDC) method. However, variations in the PDC method exist, making comparisons between studies difficult. We aimed to systematically review the scope of existing methods for calculating the PDC for cardiovascular medicines to provide guidance for future use of this metric.

Methods: We initiated a scoping review based on pre-specified methods outlined in a registered protocol. Ovid Medline, Embase, Scopus, and CINAHL Plus databases were searched from 1 July 2012 through 14 December 2020. Relevant articles contained the terms “proportion of days covered” and “cardiovascular medicine” in the title or abstract, or synonyms and related subject headings. Two reviewers independently screened articles for eligibility using Covidence. Standardised data were extracted from each included article on the PDC approach, including any assumptions used to handle missing prescribed daily doses, medication pre-supply, stockpiling, switching, hospitalisations and death.

Results: Of the 513 potential articles identified, 331 were reviewed in full, and 75 were included (85% cohort studies; sample size range: 46-1,679,957). Of the 75 included articles, 35% focussed on lipid-lowering, 29% antihypertensive, and 16% antithrombotic medications. The PDC was most commonly measured for 1 year (57%), usually from the first prescription/dispensing date (65%). Authors variably reported approaches to account for pre-supply (63%), stockpiling (65%), switching (67%), hospitalisations (49%) and death (68%). Authors reported the prescribed daily dose was either available from the data (36%) or was imputed (39%). Only 4 articles followed the EMERGE reporting guideline and referred to the “implementation” phase of medication adherence.

Conclusion: There is widespread variation in the methods and assumptions used to estimate the PDC for cardiovascular medicines. Standardised methods and transparent reporting of the PDC are needed to reliably compare estimates of medication adherence between studies.

114 Mortality associated with carbapenem for patients with Carbapenemase-Producing Enterobacteriaceae colonization: A population-based cohort study

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Background: Carbapenmase-producing enterobacteriaceae (CPE) is one of the most critical bacteria defined by the World Health Organization that new antibiotics are urgently needed. There are limited therapy options including some drugs in aminoglycoside, colistin, carbapenem, etc. However, there is lack of enough evidence about treatment outcomes of carbapenem use among CPE colonized cases.

Methods: A cohort design was implemented with the use of Clinical Data Analysis and Reporting System (CDARS) in Hong Kong from 2009-2019. The patients with CPE positive were included and the index date was the prescription start date of the antibiotic exposure. The exposure of antibiotics was identified within 14 days after the next day of CPE testing assuming that the exposure was related to the laboratory test results. The CPE patients treated with carbapenem were compared with those non-carbapenem antibiotic exposure randomly selected. We excluded those who were exposed to aminoglycosides, polymyxins, tetracyclines and quinolones among the control group to minimize inclusion of severe cases. The outcome of interest was period from date of antibiotic use until death, within 1 year after index date, or study end, whenever comes first. Covariates were used for calculating propensity score, which include age at admission, sex, index year, Charlson Comorbidity Index, hypertension, immunosuppression status, invasive procedures, and acid suppressant drugs (H2-receptor antagonists and Proton pump inhibitors). Cox-regression with inverse propensity score weighting was conducted by R (version 3.6.0).

Results: 340 patients treated with carbapenem were found with 1971 non-carbapenem exposure group. 1-year mortality was higher in carbapenem groups (55.9% vs 23.3%, p <0.001). After inverse probability weighting, the hazard ratio for death was 2.68 (95% confidence interval: 2.23-3.22, p<0.001) for patients who using carbapenem therapy.

Conclusions: The mortality within one year is higher for carbapenem users. Study comparing mortality between different combination therapies with or without carbapenem is warranted.

115 A Disproportionality Analysis of Spontaneous Adverse Event Reports for Diabetes Insipidus Attributed to Sevoflurane to FDA Adverse Events Reporting System

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Aim: To detect Sevoflurane induced Diabetes Inspidus by disproportionality analysis in FDA database of Adverse Event Reporting System (FAERS) using Data Mining Algorithms (DMAs)

Methods: An analysis was performed using publicly available FAERS data. Signal strength was calculated by Reporting odds ratios (RORs) and Proportional reporting ratios (PRRs) with 95% confidence intervals (CIs). A value of ROR lower limit >1 and PRR >2, minimum 3 cases, and chi-square <4 indicates an association between the drug and the adverse events.

Results: FAERS database had a total of 1498 reports for Diabetes Insipidus. Amongst which, 36(2.41%) reports were associated with sevoflurane. sevoflurane-associated diabetes insipidus was found to have a signal strength of ROR: 63.162(42.071-94.826) and PRR: 62.763(41.912-93.986). sevoflurane without concomitant drugs associated with diabetes insipidus was found to have a signal strength of ROR: 71.242(48.533-104.577) and PRR: 70.735(48.318-103.533). The minimum and maximum age reported were found to be 15years and 71years respectively with a signal strength of ROR:7.673; PRR:7.656 for pediatrics, ROR:96.178; PRR:94.716 for adults. Diabetes insipidus was mostly reported in females(50%) compared to males (33.33%) with the signal strength of ROR: 57.191; PRR: 57.471 and ROR: 72.056.078; PRR: 72.756 respectively.

Conclusion: The present showed an association between Sevoflurane and Diabetes insipidus, while this adverse event is not listed in the pre-clinical trial or post-marketing data. Although a causal relation cannot be definitively proved, the number of cases reported suggests that there might be an association. Increased awareness of this risk among both prescribers and patients may help mitigate the number and severity of these adverse events.

116 Unravelling signals pertinent to citalopram induced hepatic steatosis-a disproportionality analysis in FAERS database validated through cutting-edge bio-informatics and insilico techniques

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Aim/Objectives: To detect the association between hepatic steatosis and Citalopram through disproportionality analysis in FAERS database. To extract crucial differentially expressed genes (DEGs) pertinent to hepatic steatosis from gene expression omnibus (GEO) dataset by employing bio-informatic techniques. To carry out molecular docking studies to capture the interactions between aforementioned hepatic steatosis specific DEGs and Citalopram.

Methods: Publicly available FAERS data was used in this study. Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR) were used as a measure of disproportionality. A value of ROR-1.96SE >1 (SE-standard error) and PRR≥2, with an associated $\chi 2$ value of 4 or more was considered as threshold for signal. Open vigil 2.1 was used for data extraction and curation. The Differentially expressed genes (DEGs) associated with HS were identified from GSE151158 and analyzed by using GEO2R. Binding affinity of citalopram against hub genes were estimated by using Autodock Vina.

Results: FAERS database had a total of 11859 reports for hepatic steatosis out of which 111 (0.94%) reports were associated with citalopram. The ROR and PRR value for the Citalopram induced HS were 3.33 (95%CI 2.87-3.87) and 3.32 (95%CI 2.86-3.85) respectively. After removing reports which includes drugs causing hepatic steatosis, ROR and PRR were 3.30 (95% CI 2.843-3.851) and 3.25 (95% CI 2.78-3.78) respectively. APOA1, an over expressed hub gene with high node degree was docked against citalopram. The results revealed a significant interaction of drug-target complex.

Conclusion: The results showed an association between HS and citalopram use. Although a causal relation cannot be proved, the number of cases reported and strong affinity of DEG with citalopram suggests that there might be an association. The findings of this study should be investigated using superior study designs prior to clinical application.

117 Adverse drug event surveillance system for common people: Effective utilization of a Whatsapp based drug information platform

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Aims: To characterize the Adverse Drug Events (ADEs) reported through the WhatsApp Drug Information Platform (WDIP) and to evaluate the causality of those events.

Methods: The adverse drug event data received through the WDIP from 25/09/2020 to 25/05/2021 were collected and the Naranjo algorithm scale was used for causality assessment. Confirmed ADRs were classified according to the Wills & Brown method and the severity of the reactions was assessed using the Hartwigs severity scale.

Results: Out of the total of 14 ADEs reported via WDIP, 12 reports were confirmed as ADRs with the occurrence being prominent in females (7). All the reactions were classified as probable. The age of the study participants had a statistically significant association with the occurrence of the events ($p<0.001$). The majority of the reactions were classified as type H (10, 83.3%) which indicates that they were not predictable and not potentially preventable. Hartwigs Severity Scale revealed that all the reactions reported were mild. 8 events were advised for drug discontinuation and outpatient clinic review.

Conclusion: Social media communications including WhatsApp messaging could be used as a potential pharmacovigilance tool for collecting and evaluating ADRs.

Keywords: ADR, ADE

118 Indirect cost and utility associated with persistence to treatment in patients with acute coronary syndrome after percutaneous coronary intervention

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Objective: To investigate the association between persistence to treatment with indirect cost and utility in patients with acute coronary syndrome (ACS) after percutaneous coronary intervention (PCI).

Methods: A retrospective cohort study with 2 years follow-up was conducted with 367 patients recruited. Among the recruited patient, 68 were eligible for interview to estimate indirect cost and to measure health utilities with the EQ-5D-5L questionnaire. Indirect cost during the follow up period were reported descriptively. Association between persistence to treatment with indirect cost and utility was analyzed with Mann Whitney test.

Results: The study found that 7 (10%) patients persistently taking cardiovascular drugs and 61 (90%) patient were non-persistent. Indirect costs incurred by persistent patients were smaller than non-persistent patients (IDR 1,503,523 versus IDR 1,887,272; p = 0.13). Average utility value in the patients from this study was 0.85. Utility value in the persistent group was lower than the non-persistent group, although it was not significantly different (0.67 versus 0.87; p = 0.06). Patient characteristics that significantly affect the average utility in this study were age and employment status. Repeat revascularization, stroke incidence, myocardial infarction, and comorbidities doesn't significantly affect patient's utility.

Conclusion: There were no significant differences in indirect cost and utility in persistent and non-persistent patient with ACS after PCI.

119 Comparative risk of arterial thromboembolic events between aflibercept and ranibizumab in patients with maculopathy

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Purpose: To compare the risk of arterial thromboembolic events (ATE) between aflibercept or ranibizumab for maculopathy.

Methods: We conducted a retrospective population-based cohort study analyzing the Taiwan's National Health Insurance Database during 2009-2017 to identify patients with maculopathy receiving intravitreal aflibercept or ranibizumab. The primary outcome was any hospitalization or emergency room visit due to ATE, including ischemic heart disease (IHD), ischemic stroke (IS) and transient ischemic attack (TIA). The secondary outcome was mortality within 30-days after occurrence of the ATE. We employed propensity score methods to generate more homogeneous groups for comparisons.

Results: Compared to the ranibizumab group, the aflibercept group was associated with a lower risk of ATE (HR: 0.85; 95% CI: 0.80-0.91); with HR of 0.86 for IHD (0.80-0.93), 0.87 for IS (0.76-1.00) and 0.57 for TIA (0.46-0.71). The risk of 30-day mortality after ATE (HR: 1.39; 95% CI: 0.80-2.43) and the risk of all-cause mortality (1.02; 0.89-1.17) of the aflibercept group was similar to the ranibizumab group

Conclusion: The use of aflibercept in patients with maculopathy was associated with lower risk of ATE compared to the use of ranibizumab. The findings provide evidence to aid treatment selection while taking patients' baseline ATE risk into consideration.

120 COVID-19 and post COVID-19 symptoms as adverse events of Amphotericin B: A chronicle with FDA adverse event reporting system (FAERS)

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Aim: To correlate the symptoms of COVID 19 and post COVID 19 symptoms as adverse events of Amphotericin B using FDA adverse event reporting system (FAERS).

Methods: Amphotericin B was utilized for the treatment of post COVID-19 complication mucormycosis. But amphotericin B is reported to cause mucormycosis and analogous symptoms of COVID-19 as adverse events. To correlate, the data of amphotericin B was extracted from FAERS data and utilized to determine the incidence rate of adverse effects. The number of reports received each year, age category, gender, adverse reactions, and type of reporters was retrieved from the FAERS. The serious complications of COVID-19 and post COVID-19 was correlated with the reported adverse effects of amphotericin and assessed by Reporting Odds Ratio (ROR). The ROR-1.96SE >1, (SE-Standard Error) was considered as the criteria to confirm it as positive signal strength. The outcomes of adverse events are analyzed with OpenVigil, a pharmacovigilance data analysis tool for data mining and analysis.

Results: The adverse events of amphotericin are reported from 1969 to 2021. Higher reporting rate was observed in the year 2019 as 1177(10.74%) followed by 1133(10.34%) adverse events in 2020. The number of cases reported was greater 5397(49.25%) in the age group of 18-64 years. Almost 9293(84.81%) adverse events were reported by healthcare professionals. Pneumonia 291(2.66%), dyspnoea 327(2.98%), dysgeusia 5(0.05%), mucormycosis 131(1.20%), cardiac arrest 178(1.62%) was reported. The ROR of mucormycosis is 195.312(158.896-240.073), gastrointestinal mucormycosis is 1874.626(419.472-8377.725) and rhinocerebral mucormycosis is 843.834(306.596-2322.457). The serious outcome like death as adverse event of interest is found to be 279.

Conclusion: The health professionals should be kept aware of the COVID symptoms, post COVID symptoms and the adverse effects of amphotericin B, as it is widely utilized for the treatment of the post COVID symptom mucormycosis.

Key words: COVID-19, Post COVID-19, Amphotericin B, Mucormycosis

121 Drug induced mucormycosis reports: A pharmacovigilance study employing FDA Adverse Event Reporting System (FAERS)

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Aim: Drug induced mucormycosis is a renowned adverse drug reactions of various category of medications. The study explores the various category of medications associated with mucormycosis and followed by death employing FDA Adverse Event Reporting System (FAERS). The adverse events reported in FAERS was analyzed with the preferred therapeutic term Mucorrmycosis.

Methods: A total of 2199 mucormycosis associated adverse events reported in FDA from 1999 to May 2021 was retrieved from the database. The adverse events were categorized based on the class of medications. Later the drugs were analyzed for its death outcomes. A total of 2199 mucormycosis associated reports documented from 1999 to 2021 were retrieved.

Results: The number of disseminated mucormycosis was 223(9.93%), pulmonary mucormycosis 205(9.13%), gastrointestinal mucormycosis 32(1.42%), cutaneous mucormycosis 17(0.75%), and rhinocerebral mucormycosis 130(5.79%). Maximum number of reports 1140(50.80%) were observed from patient in the age group of 18-64 years. Preponderance was higher among males 1228(55.78%). Health care professionals have reported 2016(89.83%) adverse events. Among antineoplastics, vatalanib showed higher PRR 1980.818 and ROR 2640.75(274.48, 2506.28). Arbekacin was found to have higher PRR 345.071 and ROR 360.711(113.254, 1148.84) compared with other antibiotics. Antilymphocyte immunoglobulin (Horse) showed greater PRR 147.781 and ROR 150.56(55.89, 405.56) equated with other immunosuppressants. The PRR of danaparoid was 58.259 and ROR was 58.683 (8.2, 419.984) among other anticoagulants. Antitubercular medication ethambutol showed a PRR 7.881 and ROR 7.88(3.53,14.16). Death outcome was high among antineoplastics (571). Higher rate of death outcome was observed for the immunosuppressant tacrolimus (153).

Conclusion: The rate of prevalence of mucormycosis was found to be higher among antineoplastics followed by antibiotics, immunosuppressants, anticoagulants and antitubercular medications. The death outcome was found to be high among antineoplastics.

Keywords: mucormycosis, FAERS, rhinocerebral mucormycosis, disseminated mucormycosis

122 Investigation of adverse events reported for sennosides through FDA Adverse Event Reporting System (FAERS)

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Aim: The study was to explore the signal strength of adverse events linked with utilization of sennosides reported in FDA Adverse Event Reporting System (FAERS).

Methods: The FAERS data was utilized to extract the adverse events of senna documented from first quarter of 2014 to first quarter of 2021. OpenVigil is a pharmacovigilance analytical tool was used to access FAERS data and for computation of outcomes of the adverse event. The suitable drug name utilized for data extraction was found to be sennosides. The data mining was done to categorize the events based on organ system classification. The Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR) are the data mining algorithm used for the analysis. A value of PRR≥2, and ROR-1.96SE>1, was considered as positive signal strength. The outcome of the adverse events, like congenital anomaly, death, disability, either initial or prolonged hospitalization and life-threatening events were analysed.

Results: The data obtained was for 3940 unique reports. Out of 3940 reports, the potential adverse events were educed to be 994, of which 905 were identified to be relevant. Our analysis exhibited multiple events associated with senna. In the overall events reported for senna, higher PRR and ROR value was observed for radiculitis cervical (214.08) and 214.24(83.45; 550.01) followed by magnesium metabolism disorder (171.27) and 171.34(51.58; 569.15). Outcome analysis revealed higher rate of occurrence of congenital anomalies associated with cardiovascular system like truncus arteriosus (3), cardiomegaly (3), pericardial effusion (3), and 1 hypotension. Higher rate of death (118) was observed among patients experienced cardiovascular complications.

Conclusion: These data extracted are based on clinical remarks and recommend the importance of pharmacovigilance of herbal medications. Health care professionals should be open-minded to monitor, identify and report the adverse events linked with herbal medications.

Key words: FAERS, Senna, Adverse events, Pharmacovigilance

123 Validating an approach to reduce immeasurable time bias in cohort studies: A real-world example and Monte Carlo simulation study

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Objective: The validity of approach proposed to reduce the immeasurable time bias remains unclear in varying degrees of immeasurable time. Thus, this study aimed to assess the validity and performance of approaches proposed to reduce this bias in cohort studies in a Monte Carlo simulation and real-world example.

Methods: In the Monte Carlo simulation, we generated immeasurable time depending on factors related to hospitalization; duration, frequency, and timing. In total, 9 scenarios were created: 3 duration scenarios based on a poisson distribution (0.5, 1.0, 2.0) across 3 frequency scenarios based on an exponential distribution (0.5, 1.0, 2.0), where the empirical cohort distribution of hospitalization was used to simulate the 'timing'. For both simulation and empirical studies, we used Korea's healthcare database and a case example of β-blockers and mortality among patients with heart failure. Exposure was defined as time-varying. We estimated the gold standard hazard ratio (HR) with 95% confidence intervals (CI) using in- and outpatient drug data, and that of the pseudo-outpatient setting using outpatient data only. We assessed the validity of the approach of adjusting for time-varying hospitalization in the 9 different scenarios, using relative bias and mean squared error (MSE) compared to the empirical gold standard estimate across 500 bootstrap resamples. For sensitivity analysis, we applied different statistical distributions to generate the simulated datasets; gamma distribution for hospitalization frequency, and negative-binomial distribution for hospitalization duration.

Results: With the real-world gold standard (HR 0.73, 95% CI 0.67-0.80) as the reference estimate, adjusting for time-varying hospitalization (0.71, 0.63-0.80) effectively reduced the immeasurable time bias and had the following performance metrics across the 9 scenarios: relative bias (range -7.08% to 0.61%) and MSE (0.0005 to 0.0031).

Conclusion: Adjusting for time-varying hospitalization consistently reduced the immeasurable time bias in both real-world and simulated data.

124 Cefaclor-induced hypersensitivity: Differences in the incidence of anaphylaxis relative to other 2nd and 3rd cephalosporins

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Aim/Objective: Cefaclor, a second-generation oral cephalosporin, is the most frequently prescribed cephalosporin in Korea. Studies, however, have yet to analyze the incidence of cefaclor-associated adverse drug reactions (ADRs), including hypersensitivity (HS), according to total national usage rates. This study aimed to investigate the incidence rates and clinical features of cefaclor ADRs reported to the Korean Adverse Event Reporting System (KAERS) and Health Insurance Review and Assessment Service (HIRA) database for the most recent 5 years.

Methods: Reviewing the HIRA database, which contains information on all insurance claims, including prescribed medications and patient demographics, we identified the total number of individuals who had been prescribed cefaclor and other cephalosporins including 2nd generation without cefaclor and 3rd generation antibiotics from January 2014 to December 2018. Additionally, we retrospectively analyzed all ADRs reported to the KAERS for these drugs over the same study period.

Results: Incidence rates for ADRs, HS, and anaphylaxis to cefaclor were 1.92/10,000 persons, 1.17/10,000 persons, and 0.38/10,000 persons, respectively, lower than those to other 2nd and 3rd cephalosporins. Among all ADRs, HS (60.9% vs. 43.6% vs. 44.8%, P <0.001) and anaphylaxis (19.8% vs. 4.6% vs. 4.7%, P <0.001) were more common for cefaclor than for other 2nd and 3rd cephalosporins. Females, individuals under 65 years of age, concomitant use of drugs, and serious ADRs were more strongly associated with HS to cefaclor than with HS to other 2nd and 3rd cephalosporins.

Conclusion: In a nationwide database for the Korean population, the incidence of cefaclor-induced ADRs, particularly HS and anaphylaxis, was high. Female sex, age younger than 65 years, and concomitant use of drugs may be associated with HS to cefaclor.

125 Recurrent pregnancy loss and incidence of thrombotic diseases: A retrospective cohort study using large claim database

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Aim: To investigate the relationship between the maternal miscarriage diagnosis during pregnancy and the long-term incidence and treatment of venous or arterial thrombosis.

Methods: Women who has a pregnancy record at the JMDC claims database, which is a claim database and is not developing thrombosis at the time of final pregnancy confirmation were eligible for study subjects (193, 137 subjects, as of December 2017). The end point was defined as the time from the date of final confirmation of pregnancy to the day of onset of venous thrombosis or arterial thrombosis (myocardial infarction and cerebral infarction). As a main analysis, Cox regression analysis was performed with exposure variables as absence of habitual miscarriage, adjustment variables as age, diabetes, hypertension, hyperlipidemia, atrial fibrillation, and thyroid abnormality. As secondary analysis, we also evaluated some thrombotic predisposition, such as diagnosis of APS and protein deficiency syndrome, the presence or absence of heparin treatment during pregnancy.

Results: The number of women who received a diagnosis of recurrent pregnancy loss was about 318 thousand persons. In women with recurrent pregnancy loss, the hazard ratio of onset of venous thrombosis is 3.30 times [95% confidence interval (95% CI) = 1.29-5.11], the hazard ratio of arterial thrombosis onset is 3.12 times [95% confidence interval 95% CI) = 2.10 - 5.02]. Even in the secondary analysis, all positive relationships were shown between the secondary exposure (APS, protein deficiency syndrome and pregnancy heparin or aspirin therapy treatment) and venous thrombosis · arterial thrombosis onset.

Conclusion: A positive relationship was shown in Japanese women between recurrent pregnancy loss and thrombosis onset at long-term postnatal period from a retrospective cohort study based on the large claim database.

126 Antipsychotics and other risk factors of mortality in patients with delirium

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Background: The use of antipsychotics in patients with delirium and the associated risk factors of mortality remains debated.

Objective: To evaluate antipsychotics and other predictors associated with the risk of mortality in patients with delirium.

Methods: We conducted a nested case-control study using the National Health Insurance Database (NHID). We included hospitalized patients newly diagnosed with delirium between 2011 and 2018. We excluded patients underlying schizophrenia, depression, or bipolar disorder to rule out the condition which was not delirium. Cases were defined as patients who died within 180 days after discharge; otherwise, control groups were 1:5 matched by age and sex. We performed multivariable conditional logistic regression models to generate odds ratios (OR) with 95% CI to assess the association between antipsychotic use, comorbidities, medications, and the risk of mortality.

Results: We identified 69,520 patients with delirium. The mean age of patients was 79.2 (SD 13.1) years old. Majority of them were male (55.2%). We found 13,219 cases of mortality and 56,301 matched controls. Compared with non-users, we found only haloperidol use (OR 1.14, 95% CI 1.03-1.26) was associated with increased risk of mortality. Other factors associated with mortality included cardiovascular disease, chronic obstructive pulmonary disease, encephalopathy, infection, opioids.

Conclusions: The findings suggested an elevated risk of patients receiving haloperidol compared to non-users. Some other mortality risk predictors in patients with delirium warrant clinical attention.

Keywords: Antipsychotics, Delirium, Nested Case-Control Study

127 Effectiveness of sodium-glucose cotransporter-2 inhibitors in frail people with diabetes

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Aim/Objective: The effectiveness of sodium-glucose cotransporter-2 inhibitors (SGLT-2Is) in reducing Heart Failure (HF) hospitalizations, and to a lesser extent Major Adverse Cardiovascular Events (MACE), has been clearly demonstrated in general T2D populations. The aim of this study was to determine if beneficial effects of SGLT-2Is on MACE, HF and mortality are also evident in people who are frail.

Methods: We conducted a cohort study of Victorian hospitalized patients aged ≥30 years with T2D initially discharged between July 2013 and June 2017, who received SGLT-2Is or dipeptidyl peptidase-4 inhibitors (DPP-4Is), within 60-days of this discharge. The 365-day follow-up commenced 60 days after the initial discharge and MACE, HF hospitalization and mortality were recorded during this period. Cox Proportional Hazards Regression with competing risks, where relevant, and stabilised inverse probability weights was used to generate hazard ratios (HRs) with 95% Confidence Intervals (CIs). Analyses were stratified into frailty quartiles according to Hospital Frailty Risk Scores (HFRSs), with quartiles 1 and 2 pooled together.

Results: Of the 26,913 patients, (42% female and 5.2% ≥80 years) in the cohort, 3,132 (11.6%) were dispensed SGLT-2Is and 23,781 DPP-4Is. MACE was less likely among SGLT-2I recipients in the third (HR 0.55; 95%CI 0.34—0.87) and fourth (HR 0.45; 95%CI 0.29—0.70) frailty quartiles. HF hospitalization (HR 0.72; 95%CI 0.41—1.29) and mortality (HR 0.97; 95%CI 0.62—1.53) risks for those in the third frailty quartile, did not differ between SGLT-2I and DPP-4I recipients.

Conclusion: There is preliminary evidence to suggest SGLT-2Is may be preferred to DPP-4Is in the prevention of MACE in frail people living with T2D.

128 Comparison of methods to estimate diabetes-related cost using claims data in China

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Objectives: The disease burden is commonly evaluated using claims data, and disease-related cost is especially considered as a key indicator for both public health management and severity of diseases. We aim to compare four methods of estimating disease-related cost to quantify the extent of underestimation/overestimation when using real-world databases in China.

Methods: This study identified a diabetes cohort using one city of CHIRA claims database in 2017. Patients aged 18 and older with two diagnoses for diabetes in 2017 were included. In methods 1 and 2, diabetes-related costs were defined as all visits with diabetes diagnosis, reflecting the scenarios that claims level costs may not be available or highly unstructured in the database. In methods 3, diabetes-related costs were defined as difference in total cost between disease cohorts and matched controls. Disease cohorts were matched to controls using age, gender, and insurance type. In addition, method 2 identified diabetes from any diagnoses whereas method 1 only identified from primary diagnosis, reflecting the number of diagnoses available in the database. Method 4 served as our benchmark method by manually review all free text of claims by two clinician reviewers.

Results: A total of 25,067 diabetes patients were included with average age of 61.2 and 49.9% of male. Average total direct medical cost was $4,002.33 per diabetes patient per year. Diabetes-related cost as a percent of total cost for method 1-4 were: 13.2%; 21.7%; 39.4%; 15.8%. Diabetes-related costs were 1.5 times and 2.5 times higher in method 2 and method 3, compared with manually reviewed results. Manually reviewed results was closest to method 1.

Conclusion: We found that cost identified by primary diagnosis of visits is the most accurate methods to evaluate diabetes-related cost. Further comparison of methods in different disease area may help for comprehensive selection of methods.

129 Patient-reported Outcome Measures (PROMs) Utilization in clinical trials and real-world studies of psoriasis in China: A literature review

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Aim: The utilization of PROMs can assist physicians in evaluating the disease burden and its impact on patient's quality of life in the studies of psoriasis. However, so far there has been little discussion on the difference of PROMs utilization between Clinical trials and real-world studies (RWS). This study aimed to compare the utilization of PROMs between clinical trials and RWS on psoriasis in China.

Methods: A literature review was undertaken to identify used PROMs in clinical trials and RWS of psoriasis conducted in China from 2015 to 2020 in PubMed, global clinical trial registry database (ClinicalTrial.gov) and two domestic registry databases in China (including the Center for Drug Evaluation [CDE] and the Chinese Clinical Trial Registry [ChiCTR]).

Results: Overall, 52 publications and 446 trials were identified. Of the 53 relevant (with effectiveness/efficacy outcomes), 32.1% were real-world studies. Among which 6 studies (35.3%) collected PROs and 5 studies reported dermatology life quality index (DLQI) to assess quality of life. Over half of the relevant phase I-III clinical trials collected DLQI to investigate quality of life. One phase III studies included both DLQI and 36-Item Short Form Survey (SF36). PROMs for disease symptoms such as patient global assessment, itch visual analogue scale (VAS) and itch-related sleep loss Numeric Rating Scale (NRS) were also collected multiple clinical trials.

Conclusion: Collecting PROMs in conjunction with investigator's assessment will increase the value for drug effectiveness/efficacy assessment. However, in practice there is relatively limited implementations of PROMs, especially in RWS in China. As a dermatology specific PRO for QoL, DLQI has been most widely implemented in both RWS and RCT, comparing to other general QoL. The utilization of PROMs is not often recognized in psoriasis studies in China. This indicates a challenge for more comprehensive disease assessment.

Keywords: PROMs, Psoriasis, Real-world Study

130 The design considerations for disease registry studies in China

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Background: The trend of registration research is emerging in China. A registry study can be used to further understand the real-world disease natural history, as well as the long-term effectiveness and safety of treated and untreated patient, especially for rare diseases. Considering that registration research usually costly along with long-term observation time, a registry study design with careful balance between completeness and feasibility is extremely important.

Objectives: To summarize the different approach for disease registry study design in China and special considerations for methodology adaptation.

Methods: We searched two domestic registry databases in China, including the Center for Drug Evaluation (CDE) and the Chinese Clinical Trial Registry (ChiCTR) for ongoing and/or finalized registry studies. We aim to summarize the major considerations for a registry study from following perspectives: case report form (CRF) design; data collection/patient visit schedule and window period; study outcome/progress evaluate indicators for natural history and effectiveness outcomes etc.

Results: Overall, 64 registry studies in China were identified during January 1st 2015 to December 31st 2020. Coronary artery disease and stroke are two disease areas with the greatest number of registries. Among the total, 39% (25/64) of studies were disease registry which enroll eligible patients of specific indications. The rest of registries focus on either a specific medication or a procedure. The average study duration for a disease registry was 3.9 years (from firs-patient-in to estimation study end date) which is almost one-year longer than the average duration for all registries. Average number of enrolled/plan-to-recruit patients in both disease and treatment registries are similar.

Conclusion: The study and CRF design, visit schedule, and analysis plan need adaptive considerations when conduct a registry study in China, and will be the key factors for a high-quality registry study.

131 Trajectories of severity pattern among patients with systemic lupus erythematosus in Korea

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Objectives: To define the trajectories of longitudinal course of severity patterns in patients who were newly diagnosed with systemic lupus erythematosus (SLE) using group-based trajectory modeling (GBTM) and to recognize characteristics according to trajectory groups.

Methods: We performed a cohort study using the National Health Insurance Service-National Sample Cohort database of Korea from 2002 to 2015. Individuals with SLE were defined as patients who received at least one diagnostic for SLE (International Classification of Diseases, 10th revision code M32 with rare disease registration code V136). To assign SLE severity every month, we examined the algorithm for determining disease severity combining elements of disease activity with elements of cumulative damage and/or usage of SLE medications. GBTM was applied to assess severity patterns during a 3-year follow-up in new SLE patients. The optimal GBTM was determined on the basis of the balance between each model's Bayesian information criterion and the percentage of patients in the smallest group in each model. In addition, chi-square tests and analysis of variance were used to compare characteristics between groups.

Result: A total of 147 SLE were included in the analysis. Four severity groups by GBTM were suggested by the optimal model, and patients were categorized as demonstrating mild-then-moderate, consistently mild, moderate-then-mild, consistently moderate during follow-up. The optimal model clearly categorized SLE severity for one month after first diagnosis. All characteristics included age, sex, geographic region, insurance type, and income level at index date were not significantly different groups ($P>0.05$).

Conclusion: We identified four trajectories of severity pattern in patients first diagnosed with SLE through GBTM. In the present study, severe condition was not classified, which may represent exacerbation, due to the small sample size. Further research with a larger sample size is needed to clearly elucidate the factors that influence severity groups.

Keywords: Lupus Erythematosus, Systemic;

132 Assessing the performance of Physician's Prescribing Preference as an instrumental variable in Comparative Effectiveness Research with moderate sample sizes

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Objective: Instrumental variable (IV) analyses are used to account for unmeasured confounding in Comparative Effectiveness Research (CER) in pharmacoepidemiology. To date, simulation studies assessing the performance of IV have been based on large samples. However, in practice, sample sizes may be moderate or smaller, for example in investigations of new drugs or of rare conditions. The main objective of this study is to assess the applicability of Physician's Prescribing Preference (PPP) as an IV in studies of different size and for different levels of unmeasured confounding.

Methods: We designed a simulation study for the setting of drug comparison studies with a moderate (around 2500) and small (around 600) sample size. The outcome and treatment variables were binary and there were three variables to represent confounding (a binary and a continuous variable representing measured confounding, and a further continuous variable representing unmeasured confounding). We compare the performance of IV and non-IV approaches using two-stage least squares (2SLS) and ordinary least squares (OLS) methods, respectively. Further, we test the performance of different forms of proxies for PPP as an IV.

Results: The PPP IV approach results in a percent bias of approximately 20%, while the percent bias of OLS is close to 60%. The sample size is not associated with the level of bias for the PPP IV approach. However, smaller sample sizes led to lower statistical power for the PPP IV. Using proxies for PPP based on longer prescription histories result in stronger IVs, partly offsetting the effect of smaller sample sizes.

Conclusion: Irrespective of sample size, the PPP IV approach leads to less biased estimates of treatment effectiveness than conventional multivariable regression. Particularly for smaller sample sizes, we recommend constructing PPP from long prescribing histories to improve statistical power.

Keywords: simulation study, comparative effectiveness research, instrumental variables, Physician's prescribing preference

133 Safety signal of dulaglutide and the risk of arthralgia: Evidence from pharmacovigilance data

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Introduction: Dulaglutide is glucagon-like peptide-1 (GLP-1) receptor agonist indicated to treat type 2 diabetes mellitus (T2DM). Arthralgia is joints pain that may range in intensity from mild to severe.

Aim/Objective: The aim of this review is to evaluate the risk of arthralgia associated with the use of dulaglutide.

Methodology: The Pharmacovigilance Center of Saudi Food and Drug Authority performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database, to retrieve related information for assessing the causality between dulaglutide and the risk of arthralgia. We used the WHO criteria as standard for assessing the causality of the case-reports.

Results: The number of retrieved cases for the combined drug/adverse drug reaction are 190 case. The reviewers have selected and assessed the causality for the well-documented case-reports with completeness scores of 0.6 and above (26 cases); the value 1.0 indicated the highest score for best-written cases. Among the reviewed cases, about half of them provides supportive association (2 probable, and 8 possible cases). In literature, we found one randomized controlled trial (RCT) studied the efficacy and safety of dulaglutide versus sitagliptin in T2DM patients. As compared to sitagliptin and placebo, dulaglutide showed higher rate of arthralgia after 26 and 52 weeks of treatment. Another RCT studied the efficacy and safety of dulaglutide added onto pioglitazone and metformin versus exenatide in T2DM. The results showed an increased number of Arthralgia in patients treated with GLP-1 agonist (dulaglutide and exenatide) as compared to placebo.

Conclusion: The weighted cumulative evidences identified from the reported cases and literature are sufficient to support a causal association between dulaglutide and the risk of arthralgia. Health regulators and health care professionals must be aware of this potential risk and it is advisable to monitor any signs or symptoms in treated patients.

134 Non-vitamin K-dependent oral anticoagulants versus warfarin for atrial fibrillation in morbid obese patients

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Background: Non-vitamin K-dependent oral anticoagulants (NOACs) in extremely obese patients are still controversial. We aimed to compare NOACs versus warfarin to manage atrial fibrillation (AF) in patients with a body mass index (BMI) of 40 Kg/m2 or more.

Methods: We enrolled 755 patients who required anticoagulation for AF from 2015 to 2016. We grouped the patients into four groups. Group 1 (n= 297) included patients with BMI< 40 Kg/m2 treated with NOACs, Group 2 (n= 358) included patients on warfarin with BMI < 40 Kg/m2, Group 3 (n= 57) had patients on NOACs with BMI≥ 40 Kg/m2 and Group 4 (n= 43) included patients on warfarin and BMI≥ 40 Kg/m2. Study outcomes were survival and the composite endpoint of bleeding and stroke.

Results: Stroke/bleeding was not affected by the study groups (HR: 1.09 (95% CI: 0.79- 1.51); P= 0.62) and older age was the predictor of stroke/bleeding (HR: 1.03 (95% CI: 1.01- 1.06); P= 0.02). Predictors of mortality were heart failure (HR: 2.23 (95% CI: 1.25- 3.97); P= 0.007), creatinine clearance (HR: 0.98 (95% CI: 0.97- 0.98): P< 0.001), Group 2 (HR: 3.51 (95% CI: 1.6- 7.7): P= 0.002) and Group 4 (HR: 6.7 (95% CI: 2.51- 17.92); P< 0.001). (Figure 1)

Conclusion: NOACs could have a similar risk profile compared to warfarin in obese patients but may have a beneficial effect on survival. Larger randomized trials are recommended.

Keywords: Non-vitamink, Anticoagulation, AF, Obese

135 Pfizer-Biontech vaccine associated with myocardial infarction as adverse events- signal review

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Introduction: Pfizer-Biontech vaccine indicated for prevent coronavirus disease caused by severe acute respiratory syndrome coronavirus. It's purified single stranded messenger-RNA produced using cell-free in vitro transcription from corresponding DNA templates, encoding viral spike protein of SARS-CoV-2.
Myocardial-infarction also called heart-attack take place in sudden blockage or very low blood flow to heart's coronary arteries. Most common cause of blockage coronary artery is blood clot narrowed by atherosclerosis helps its formation. Saudi-Food-and-Drug-Authority (SFDA) initiated signal review based on detected signal from Saudi-National Pharmacovigilance-Centre-database. Purpose of this review to evaluate the risk of Myocardial-infarction associated with Pfizer-Biontech-vaccine use to suggest regulatory recommendations.

Methods: Signal-Detection-team performed signal review using NPC-database, WHO-VigiBase, literature screening to retrieve related information to assess causality between Myocardial-infarction and Pfizer-Biontech vaccine. search conducted March-29,2021.

Results:
Local-Cases
-Saudi-NPC-database been searched for ICSR has reported for Myocardial-infarction and Pfizer-Biontech vaccine, resulted in four local-cases. two were possible according to WHO-UMC causlity assessment.
Global-Cases
-WHO-database (VigiBase) searched for ICSRs reported with “Myocardial-infarction” and “Pfizer-Biontech vaccine” yielded to 183 ICSRs. Initial review revealed that 134 cases weren't documented sufficiently for proper medical assessment. However (49) been furthered evaluated resulted in 38 cases with possible association, 11 cases with unlikely association according to WHO-UMC-causality assessment.

Literature
-scientific literature search conducted for Pfizer-Biontech and Myocardial-infarction, no relevant articles retrieved by this search and there was no evidence of causality.

Datamining
-Disproportionality between observed and expected reporting rate of drug-adverse drug reaction combination calculated using Information-Component (IC). The combination of Pfizer-Biontech vaccine and Myocardial-infarction has observed less than expected (IC -2.4).

Conclusion: Weighted cumulative evidences identified from local and global cases sufficient to validate and suggest causal association between Pfizer-Biontech vaccine and Myocardial-infarction. Therefore, health-care-professionals should be aware of this potential risk and may consider monitoring any signs or symptoms of Myocardial-infarction in patients treated with Pfizer-Biontech.

136 Experience of COVID-19 Vaccine use and evaluate side effect in Maioli County

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According to World Health Organization, COVID-19 is the worldwide issue. There were over hundred million cases and million people died by this disease. Until now, we have our weapon to protect us, COVID-19 vaccines. As of 18 February 2021, at least seven different vaccines across three platforms have been rolled out in countries. Vaccination is important, but side effect was reported. Not only the efficacy, safety is also important. We evaluated the side effect in patient who received vaccine in Maioli county, Taiwan.

137 Risk of Vascular Adverse Events associated with Multiple Myeloma Treatments in Taiwan: A nested case control study

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Aim/Objectives: The aim of this population-based nested case-control study was to examine the association between different combinations of multiple myeloma (MM) medications and the risk of vascular adverse events (VAEs) using the Taiwan Cancer Registry (TCR) and National Health Insurance Research Database (NHIRD).

Methods: We identified a study cohort consisting of adult patients newly diagnosed with MM between 2008 to 2016 from the TCR. Among them, we indentified patients who developed VAE after the diagnosis of MM (cases) and their matched controls (matched by age, sex and duration of MM diagnosis at a ratio of 1:5). The exposure of MM treatment regimens were grouped into six mutually exclusive categories including steroid monotherapy, thalidomide/bortezomib/steroid combination, thalidomide monotherapy, thalidomide/chemotherapy/steroid combination, thalidomide/steroid combination and others. Multivariable conditional logistic regression was used to examine the association between different MM treatment regimens and the risk of VAE.

Results: Within the MM cohort, we identified 379 VAE cases and 1,895 matched controls. The mean age at diagnosis was 70.7 years old and 64.4% was male. Among the 6 regimens exaimed, only thalidomide/steroid combination was associated with increased risk of VAEs (odds ratio (OR), 2.59; 95% confidence interval (CI), 1.11-6.08). Other risk factors, including older age, male, prior history of diabetes mellitus without chronic complications, prior history of VAEs, prior history of major surgery and use of antiplatelet, were associated with increased risk of VAEs.

Conclusions: We found that only the use of thalidomide/steroid combination was associated with increased risk of VAEs. Other risk factors including older age, male, history of diabetes mellitus, VAE, surgery, and use of antiplatelet.

138 Signal detection of co-administration of MMR vaccine with other vaccines

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Aim/Objective: Measles, mumps, and rubella (MMR) vaccine may be given at the same time as other vaccines. However, the safety of concomitant vaccination is controversial, especially depending on whether live or inactivated vaccines are simultaneously administered. This study was to perform to detect adverse events (AEs) signals of the MMR and live vaccine co-administration group and MMR and inactivated vaccine co-administration group compared to the MMR only group.

Methods: We used the Korea Adverse Event Reporting System (KAERS) database between January 2015 and December 2019. The co-administration defined as when two or more vaccines are reported on the same report. We analyzed the frequency and basic characteristics of reports for each group. We compared the AEs between MMR only group and the co-administration groups by calculating reporting odds ratios (RORs) and 95% confidence intervals (CIs).

Results: Among a total of 23,328 reports, there were 70 in the MMR only group, 149 in the MMR and live vaccine group, and 100 in the MMR and inactivated vaccine group. 'Injection site inflammation' was detected as a signal when MMR vaccine was co-administered with either live or inactivated vaccines. 'Somnolence' (ROR 16.79; 95% CI 2.28-123.68) and 'vomiting' (ROR 6.14; 95% CI 1.44-26.24) have been reported more in MMR and live vaccines co-administration than MMR only group.

Conclusion: The MMR and live vaccines co-administration group showed a few more signal than the MMR and inactivated vaccines simultaneously vaccinated group. However, because these AEs were mild and co-administration of MMR and other vaccines may be considered acceptable. Further studies are needed to evaluate the causal relationship of these signals.

Keywords: MMR vaccine, KAERS, Simultaneous vaccination

139 Current state of adverse event reports concerned with age-contraindicated drugs on Korea Pharmaceutical Association Database

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Background: Inappropriate use of age-contraindicated drugs can cause serious adverse events (AEs) but information about their AE reports is limited.

Objective: The aim of this study is to investigate current state of AE reports concerned with use of contraindicated drugs for specific ages submitted to pharmacies in 2018.

Methods: We conducted a safety surveillance study using spontaneous reports of the Korea Pharmaceutical Association in 2018. Study drugs involved 177 age-contraindicated drugs according to the notification of Ministry of Food and Drug Safety. We calculated the proportion of AE reports induced by study drugs among all AE reports, and described their characteristics. Furthermore, we identified drug-AE pairs evaluated as certain, probable, and/or possible in causality assessment and compared them with the labeling information of Lexicomp.

Results: Of 23,941 AE reports, 98 (0.4%) were reported with use of study drugs; there were no AE reports for study drugs in over 18 years. Among AE reports for study drugs, aged 6-12 years had the most reports (50.0%) and the proportion of AE reports was higher in male (58.7%) than in female (38.8%). When analyzing drug-AE pairs, dihydrocodeine and its AEs were most frequently reported (73.5%). We also identified 19 drug-AE pairs not included in labeling information of Lexicomp, but they were not significant results.

Conclusion: The proportion of AE reports for age-contraindicated drugs was not substantial; however, the adverse events related to dihydrocodeine were still reported. There is a need to monitor the age-contraindicated drugs where adverse events are frequently reported.

Keywords: age-contraindicated drugs, dihydrocodeine, monitoring

140 Signal detection of drospirenone-containing oral contraceptives using the Korea Adverse Event Reporting System Database, 2008–2017

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Safety concerns persist regarding the association of thrombosis and the use of drospirenone-containing oral contraceptives (DCOCs). Signal detection is a data mining technique to explore hidden associations between drugs and reported adverse events (AEs). We aimed to describe the reporting pattern of AEs caused by DCOCs and detect the signals for DCOCs, compared with second/third generation oral contraceptives. Hence, we compared the labels of DCOCs between Korea, US and UK.

The characteristics, death cases, and the annual pattern of AE reports were compared between DCOCs and second/third generation oral contraceptives using the Korea Institute of Drug Safety & Risk Management-Korea Adverse Event Reporting System database. The proportional reporting ratio, adjusted reporting odds ratio from a multivariate model, and the information component were used as data mining algorithm.

Of the 242 DCOC-related AEs, 54 signals were detected and 10 were identified as new signals that were not included in Korea, US and UK label. The newly detected signals include chest pain and frequent urination. Serious AEs were more likely to be reported with DCOCs (7.85%) than with second/third generation oral contraceptives (2.92%). Five deaths from DCOCs were all caused by vascular AEs, such as pulmonary embolism or thrombosis.

We found higher reports of the deaths and vascular AEs associated with DCOCs than with second/third generation oral contraceptives, which warrants careful monitoring to ensure the safe use of DCOCs. Additionally, we identified 10 new signals related to DCOCs that were not included in the current label.

141 Early safety monitoring of COVID-19 vaccines in elderly over 75

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Objectives: The purpose of this study was to compare adverse events after the first and second dose of the BNT162b2 mRNA COVID-19 vaccine in elderly people aged over 75.

Methods: We conducted active surveillance via telephone to those who complained of adverse reactions in the observation time (15-30 minutes) and to other randomly selected people. A subset of selected people was followed up by telephone surveys in 7 to 10 days after each vaccination.

Results: We conducted 439 telephone surveys after vaccination of the first dose and 345 people (78.6%) responded. Among the respondents, 320 people (92.8%) also responded after vaccination of the second dose. Fifteen people experienced adverse reactions in 15 or 30 minutes of observation time. Common symptoms were dizziness, headache, nausea, and chest discomfort. The frequency of each adverse reaction was analyzed by classifying respondents into three age groups (75-79, 80-84, and 85 and above). In the older groups, frequency of local and systemic adverse events decreased. After vaccination of both the first and the second dose, people in the older age group experienced less pain at the vaccination site. People in the older age group experienced less myalgia and nausea after vaccination of the second dose. There was no significant difference in the rate of other adverse reactions after vaccination of the first and the second dose. Females tend to have chills, fatigue, myalgia, and overall systemic reactions more than males. A significantly lower percentage of people experienced injection-site pain after vaccination of the second dose than the first dose. However, the frequency of feeling feverish and muscle pain was significantly higher after vaccination of the second dose than the first dose.

Conclusion: This study is the first to investigate adverse events of the COVID-19 vaccine in elderly people aged over 75 in South Korea.

143 Trends and factors in relation to metformin related adverse drug reactions in older adults in Jiangsu Province of China

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Aims: To examine the trend of metformin-related Adverse Drug Reactions (ADRs) among older adults aged 45 years and over and to identify potential factors associated with the incidence of metformin-related ADRs.

Methods: Data were extracted from the spontaneous reporting system (SRS) of ADR surveillance in Jiangsu Province of China. We estimated the age-adjusted incidence rate of metformin-related ADRs among older adults between 1st July 2010 and 30th June 2020, and used the percent change annualised estimator to evaluate trends over time. Negative binomial model was employed to quantify association with the ADR occurrence in terms of incidence rate ratio (IRR) and 95% confidence interval (CI).

Results: A total of 3940 confirmed ADR cases related to the use of metformin in older adults were reported. Tertiary hospitals accounted for the largest proportion of metformin-related ADR reports. The age-adjusted rate of metformin-related ADRs increased significantly by 15.95% (95%CI: 5.6-27.3%) per annum from 2011 to 2020. Compared with those aged 45-64 years, the older olds aged 85 years and over had a higher risk of ADR occurrence (IRR:5.51, 95%CI:4.09-7.44). Compared with males, females experienced an elevated risk (IRR:1.12, 95%CI:1.02-1.23). Metformin-related ADRs were the least likely occurred in winter (IRR:0.75, 95% CI: 0.65-0.86).

Conclusion: Despite being the first-line pharmacotherapy, metformin demonstrated a source of ADRs in patients with type 2 diabetes. Intervention strategies are necessary to improve metformin safety in older adults.

144 Development of risk prediction model for hypocalcemia in bone metastasis patients treated with denosumab plus natural vitamin D/Ca supplement

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Objective: Treatment of bone metastasis patients with denosumab often induces hypocalcemia. A natural vitamin D/Ca preparation (DENOTAS®) can prevent hypocalcemia in some, but not all, patients. The purpose of this study was to develop a risk prediction model for hypocalcemia in patients receiving denosumab plus DENOTAS®.

Methods: Using the hospital claims database, we conducted a retrospective study of 1,869 patients with bone metastasis who received denosumab supplemented with DENOTAS® from June 2013 to May 2020. Univariable analysis was conducted to compare patients who developed Grade 2 or higher hypocalcemia within 28 days after the first dose of denosumab with those who did not. Using selected variables for which the p value was less than 0.1 or which are judged clinically important, we conducted multivariable logistic regression analysis to develop the risk prediction model for hypocalcemia. Multiple imputation was adopted to replace missing values, and fractional polynomials were used for continuous variables. The model performance was evaluated in terms of receiver operating characteristic - area under the curve (ROC-AUC) and sensitivity.

Results: Hypocalcemia was observed in 132 patients. In univariable analysis, lower corrected serum Ca (9.21 vs. 9.58 mg/dL, $p<0.001$), higher alkaline phosphatase (1,656 vs. 423 U/L, $p<0.001$) and more gastric cancer (36 vs. 14%, $p<0.001$) were observed in the case group. Multivariable logistic regression analysis yielded a prediction model incorporating, corrected serum Ca, albumin, alkaline phosphatase, prostate cancer, breast cancer and gastric cancer, etc. The ROC-AUC of this model was 0.85, and its sensitivity was 0.74.

Conclusion: Baseline Ca, alkaline phosphatase, breast cancer and gastric cancer were highly associated with the development of hypocalcemia. Multivariable logistic regression analysis yielded a high-performance predictive model that could be useful for risk management in clinical practice.

Keywords: denosumab, natural vitamin D/Ca, hypocalcemia, risk prediction model

145 Cancer risk associated with use of valsartan in Korea: A nationwide cohort study

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Objectives: To evaluate an association between the use of valsartan and the risk of cancer.

Methods: We conducted a retrospective cohort study using the National Health Insurance database from January 1, 2002, to December 31, 2015. Patients aged ≥ 30 years who used valsartan or other angiotensin II receptor blockers (ARBs) were included. The eligible patients were required to have no history of the use of any ARBs, diagnosis of cancer, and organ transplantation for 4 years before the first use of drugs of interest. The primary and secondary outcomes were the occurrence of all cancer and site-specific solid cancers, respectively. After applying propensity score (PS) matching, a Cox regression was used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). We also examined whether the risk of cancer differed by the duration of exposure and cumulative dose of valsartan.

Results: A total of 1,550,734 individuals were identified as new users of valsartan or other ARBs. Of the 153,047 valsartan users, 16,047 were diagnosed with cancer. In the PS matched cohort, the mean follow-up duration was 7.04 years and the overall incidence rate of cancer was 14.9 per 1000 person-years. No increased risk of overall cancer was observed in valsartan users compared to other ARBs users (aHR= 1.00, 95% CI; 0.98, 1.02). However, for the specific-solid cancers, valsartan was associated with a higher risk of liver cancer (aHR=1.09, 95% CI; 1.01, 1.16) and kidney cancer (aHR=1.11, 95% CI; 1.02, 1.22). The risk did not increase with the increasing duration of exposure and cumulative dose of valsartan.

Conclusions: Our results revealed no association between valsartan use and the risk of overall cancer. However, a higher risk of some solid cancers observed in this study suggests the need for further studies.

Keywords: angiotensin II receptor blocker, cancer, N-Nitrosodimethylamine, valsartan

146 Relationship between the early initiation of insulin treatment and incidence of diabetic complications in type 2 diabetes in Korea

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Objective: To evaluate the relationship between the early insulin initiation within 1 year after diagnosis of type 2 diabetes and the risk of diabetic complications.

Methods: We conducted a cohort study using the Korean National Health Insurance Service-medical health check-up database. The study subjects were newly diagnosed with type 2 diabetes between January 1, 2009, and December 31, 2013. We conducted a propensity-score matching and computed hazard ratios (HRs) and 95% confidence intervals (CIs) using a Cox proportional hazards regression to compare the risk of diabetic complication and all-cause mortality between patients who received two or more oral antidiabetic drugs (OADs) and those who received insulin as the first prescription within one year after the first diagnosis of type 2 diabetes,

Results: Among 711,254 patients who were newly diagnosed with type 2 diabetes, 52,188 and 1,804 received ≥2 OAD and insulin, respectively, as the first prescription. After propensity score matching (1:1), 534 patients remained in each group. Compared to the OAD group, the risk of overall microvascular complications was significantly higher in the insulin group (aHR=1.48; 95% CI, 1.28-1.71). No increased risks of overall macrovascular complications (aHR=0.90; 95% CI, 0.62-1.30) and all-cause mortality were observed (aHR=1.06; 95% CI, 0.67-1.68).

Conclusion: In our study using a large-scale database, insulin treatment at the early stage of type 2 diabetes did not increase the risk of increased the risk of macrovascular complications and all-cause mortality compared to the use of ≥2 OAD; however, there was an association between insulin treatment and a higher risk of microvascular complications. Although insulin is an essential treatment as the most potent hypoglycemic agent, careful consideration should be given to the potential risk of diabetic complications associated with insulin.

Keywords: type 2 diabetes, insulin, oral antidiabetic drug, diabetic complications

147 Knowledge of community pharmacists in the Kathmandu Valley, Nepal about the risks associated with medication use during pregnancy

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Background: Community pharmacists are among the most accessible health care providers. This study evaluates their knowledge about the risks associated with medication use during pregnancy.

Methods: A cross sectional study was carried out in March 2021 among community pharmacies in the Kathmandu Valley, Nepal. The total number of community pharmacies in three districts of the Kathmandu Valley were 3276 and the sample size calculated from Raosoft software was 344. Convenience sampling was used for data collection using a structured and validated questionnaire. The data were analyzed using descriptive and inferential statistics.

Results: Majority of participants were males 264(76.7%); 94.2% were between the age of 21 to 30 years and 53.1% had work experience of less than one year. Over half had completed diploma in pharmacy. Less than ten medicines were dispensed to pregnant women daily in 61.6% of the pharmacies. Only 28.8% of the community pharmacists always inquired about pregnancy status from women in the reproductive age group.

The mean knowledge score was significantly different among individuals with different work experience and qualifications ($p<0.001$). There was also difference in mean scores according to average number of medicines dispensed daily ($p=0.006$). The knowledge score also differed according to average number of medicines dispensed to pregnant woman and inquiry by the pharmacist about pregnancy status ($p<0.001$).

Conclusion: The mean knowledge scores need improvement. Education programs to increase the knowledge of community pharmacies about the use of medicines during pregnancy must be conducted.

Keywords: Community pharmacy, medication, pregnancy, Kathmandu valley

148 Establishment of Severance contrast media safety & management office

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Objective: Establishment of Severance contrast media safety & management office to manage immediate adverse drug reactions (ADRs) by contrast media used in computed tomography (CT).

Methods: The contrast media safety & management office was established near the CT examination room in Severance Hospital in November 2018, and a nurse was assigned to be in charge of the office. Patients with history of immediate ADR to CT contrast media were registered with this office and provided management support; those with a history of moderate to severe reactions underwent a skin test using the contrast media. The results of the skin test were used for selecting alternative contrast media. In addition, a window warning about the immediate ADR to contrast media was programed to appear on the electric medical program so that adverse reactions could be known in advance and prevented.

Results: The frequency of immediate ADR to contrast media significantly decreased in 2019 compared to that in 2018 (0.60% vs. 0.41%, $p<0.001$). The percentages of moderate to severe adverse reactions (23.0% vs. 18.9%) and breakthrough reactions (8.2% vs. 7.3%) were decreased compared to the respective percentages in 2018.

Conclusion: Severance contrast media safety & management office has been helping to reduce immediate ADRs through systemically managing patients who had previously experienced ADRs to contrast media.

149 The status of collection and provision in post-marketing drug adverse event reports in the Republic of Korea

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Objective: The Korea Institute of Drug Safety & Risk Management (KIDS) has collected, analyzed, evaluated the individual case safety reports (ICSRs) through the Korea Adverse Event Reporting System (KAERS) and provided customized data from the KIDS-KAERS database (KIDS-KD). In this study, we review the reporting status as well as provision trends of the KIDS-KD.

Methods: The ICSRs in the KIDS-KD were analyzed by type of sender and type of report. Additionally, the trends of KIDS-KD provision and the characteristics of the requester were identified.

Results: From 1989 to 2020, the number of ICSRs reached 2,121,284 in Korea. Approximately 3,700 cases were reported in the first 17 years. However, with the operation of regional pharmacovigilance centers (RPVCs) since 2006, the number of ICSRs increased rapidly, and 259,089 cases were reported in 2020. Among the ICSRs received in 2020, 23,966(9.3%) were serious ICSRs. In regard to sender type, 184,861(71.4%) ICSRs were submitted by RPVCs and 61,770(23.8%) by marketing authorization holders (MAHs). For report collection routes, there were 215,446(83.2%) spontaneous ICSRs and 22,354(8.6%) reexamination ICSRs from Report from study. Of 656 cases of KIDS-KD provided from October 2014 to 2020, 264 cases were requested by researchers, and 392 cases by MAHs. The number of requests by MAHs increased sharply, doubling to 204 in 2020 compared to 100 in 2019, due to the revision on the regulation on the renewal of marketing approval for drug products.

Conclusion: We have confirmed that national-level actions, like RPVCs operations and regulations on pharmacovigilance, had substantial influence on the KIDS-KD. Further research is necessary on the impact of the transition to International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E2B(R3) on its reports.

Keywords: Pharmacovigilance, Korea Institute of Drug Safety & Risk Management, KAERS, KIDS-KD.

150 An active surveillance study to trace the risk factors associated with adverse drug reactions in COVID-19 treatment

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Objectives: To characterize the adverse drug reactions (ADRs) and the risk factors in COVID -19 treatment in a secondary care hospital in South India.

Method: A prospective observational study was carried out on 327 patients admitted between April 1 and May 15, 2021, using an active in-person surveillance system. The demographic characters of all the patients including the time of admission, comorbid diseases, length of stay, history of drug allergies, and the number of medications used during hospitalization were collected. After identification of an adverse drug event, the causality, suspicious drugs, and prognosis of ADRs were also recorded. Descriptive statistics and multivariate logistic regressions were carried out to analyze the risk factors of ADRs.

Result: Out of the 327 patients, 194 (59.3%) were men and the mean age was 45.7± 16.6 years. 122 ADRs were reported among 87 patients with an incidence rate of 26.6%. Most of the reactions were associated with dexamethasone (31.9%), remdesivir (18%), and favipiravir (14.7%) with dexamethasone-induced hyperglycemia being most prominent. The majority of the suspected ADR cases were categorized as probable (61.8%) according to the WHO-UMC causality assessment. When compared with the No ADRs group, the length of stay ($p=0.004$), history of drug allergies ($p<0.001$), number of drugs used in treatment ($p<0.001$) were significantly higher in the ADRs group. Multivariable analysis revealed that length of stay (OR: 2.03; 95% CI 1.02–3.98; P = 0.04), comorbidities (OR: 2.08; 95% CI 1.05–4.18; P = 0.04), number of drugs used for treatment (OR: 3.17; 95% CI 1.60–6.27; P = 0.001) and were independent risk factor for ADRs in the patients.

Conclusion: Active surveillance measures are important in case of all drugs used for COVID treatment to keep the living guidelines the most live one.

Keywords: ADR, COVID-19

151 Osimertinib-assoiciated pulmonary embolism: Results from serious adverse event review system in the Republic of Korea

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Objectives: To effectively manage monthly serious adverse events (SAEs) and generate safety information.

Methods: Among the individual case safety reports (ICSRs) reported to Korea Adverse Event Reporting System (KAERS) in December 2018, SAEs were extracted. Every single ICSR reviews are carried out for cases reported as 'resulting in death' or 'causing congenital anomaly'. Then, assessment is done for whether the relationship between ADRs and 'death' or 'congenital anomaly' could not be ruled out. Data mining methods is applied for quantitative analysis. If the data mining results show significant statistical significance, case-reviews are performed for further evaluation. Designated Medical Event (DME) is adopted for another way of quantitative analysis in order to minimize the possibility of missing the information about severe but rarely occur AEs. After evaluation, drug-adverse event combinations, of which relationship cannot be excluded through the qualitative and quantitative analysis, are managed as accumulation. After further investigation and the review of recent a year, we can propose drug labeling changes to Ministry of Food and Drug Safety (MFDS) in Korea, if necessary.

Results: A total of 1,897 SAE cases (2,444 combinations) were found in KAERS. During the evaluation process of SAE reports, 28 combinations were identified for which a causal association between the drug and event could not be excluded. After excluding 27 combinations, which were included in the domestic drug labels, the one remaining combination, osimertinib-pulmonary embolism, was decided to perform further evaluation. Pulmonary embolism, which included on the DME list, was labelled for osimertinib in the United States and Japanese product labels. Additionally, a few published studies on pulmonary embolism associated with epidermal growth factor receptor tyrosine kinase inhibitor as well as osimertinib were identified.

Conclusion: We proposed to MFDS about the new safety information. MFDS, then made drug label changes after reviews by Central Pharmaceutical Affairs.

152 Adverse Events Following Immunization (AEFI) of COVID-19 Vaccine in a Province of Thailand

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Aim: To report AEFIs of COVID-19 vaccination in a province of Thailand.

Methods: The cross-sectional descriptive study was conducted by collecting data from Ministry of Public Health Immunization Dashboard of Thailand between April 7- May 17, 2021. The AEFIs were reported by healthcare professionals and on-line self-reporting system. 15,439 vaccination records were collected, 9,219 and 6,220 records for 1st and 2nd dose vaccination, respectively.

Results: Most vaccinated subjects were 6,143 females (66.6%). The subjects almost worked as healthcare workers (81.99%) and had average age 40.00±10.49 years old (min-max=17-69). Out of 15,439 records, 2,297 events were found as AEFIs (14.88%). The most common AEFIs were myalgia (6.43%, 2.04%) headache (5.36%, 1.66%) injection site reaction (4.44%, 2.27%) and fatigue (3.77%, 1.01%) on 1st and 2nd dose vaccination, respectively. Other AEFIs were found less common (0.09-1.63%) such as nausea, vomiting, fever, diarrhea, weakness, rash, numbness, dizziness, drowsiness, high blood pressure and transient ischemic attack (TIA).

Conclusion: This study has shown that AEFIs are common with other vaccination and are relatively rare. Therefore, the government should give more information to the people for more cooperative in vaccination.

Keywords: SARS-CoV2, Adverse drug events (ADEs), Side effects, Corona virus vaccine.

153 Risk factors of adverse reactions following preventive treatment for latent tuberculosis infection in household contacts of active tuberculosis

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Background: Treatment of latent tuberculosis infection (LTBI) is necessary to prevent it from progressing to active TB. However, adverse drug reactions (ADRs) are known as the main cause of poor adherence to treatment, so it is important to identify associated factors of ADRs.

Objective: This study aimed to explore factors related to ADRs by comparing the group with and without ADRs among the patients with LTBI treatment.

Methods: We used the Korea Disease Control and Prevention Agency (KDCA)'s household contact investigations database from 2015 to 2018 and in connection with the TB registry database in KCDC and the data of the National Health Insurance Service (NHIS). We defined study subjects as an individual who was positive for tuberculin skin test or interferon-γ releasing assay and performed treatment among the household contacts. The treatment regimens include 6 to 9 months isoniazid (6-9H), three months isoniazid/rifampin (3HR), and four months rifampin (4R). We set ADRs as hepatotoxicity, skin reactions, platelet disorders, gastrointestinal disorders, pain, and others. Other covariates were steroid use and age, which were divided into six groups. We calculated odds ratios (OR) and 95% confidence intervals (CI) to analyze factors associated with ADRs using logistic regression analysis.

Results: Among 120,676 household contacts, 73,264 performed LTBI screening and 21,171 (28.9%) were positive for LTBI. Of the LTBI patients, 11,913 (56.3%) initiated treatment and 9,584 (80.5%) completed treatment without ADRs and 633 (5.3%) had ADRs. The ADRs after treatment were significantly associated with female (adjusted OR 1.27; 95% CI 1.07-1.51), ≥76 years (aOR 9.09; 95% CI 5.12-16.15), steroid use (aOR 1.31; 95% CI 1.11-1.54), 3HR regimen (aOR 0.76; 95% CI 0.61-0.94), and 4R regimen (aOR 0.57; 95% CI 0.41-0.79).

Conclusion: When treating LTBI, more detailed management of ADRs is needed considering the risk such as sex, age, steroid use, and treatment regimens.

154 Signal Detection of Adverse Events of piperacillin/tazobactam using the Korea Adverse Event Reporting System (KAERS) Database

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Aim/Objective: Piperacillin/tazobactam is used frequently as a first-line drug for bacterial infections like Pseudomonas aeruginosa. In a recent study, one of the drugs most commonly associated with hospital acquired ADRs in a Korean tertiary hospital was piperacillin/tazobactam. The objective of this study was to detect signals by analyzing AEs using Korea Adverse Event Reporting System (KAERS) database.

Methods: We conducted disproportionality analysis to detect the potential signals about piperacillin/tazobactam using the KAERS database from 2015 to 2019. We calculated reporting odds ratio (ROR), proportional reporting ratio (PRR), and information component (IC) of AEs based on WHO-ART preferred terms (PTs). Criteria for detecting signals were defined as ROR ≥ 2 or PRR ≥ 2, chi-squared ≥ 4, and reported AEs ≥ 3. Also, a signal for IC was considered when the lower limit of 95% confidence intervals (CIs) was at least 0. When all three indices (PRR, ROR, IC) satisfied the criteria, we defined them as a detected signal. Also, we compared the detected signals and drug labels in Korea and Micromedex.

Results: The KAERS database contained a total of 2,372,236 drug-AEs pairs from January 2015 to December 2019. During that period, 12,977 pairs were attributed to piperacillin/tazobactam. The frequent AEs after taken piperacillin/tazobactam were rash (14.22%), pruritus (11.34%), and diarrhoea (9.91%) and 33 AEs were detected as signals. Among the signals, azotaemia, hyperpyrexia, and le syndrome were not labeled in both Korea and Micromedex.

Conclusions: We identified 3 new signals of piperacillin/tazobactam that were not listed on the labels. Therefore, further research on clinical significance, causal association, and preventability of the signals will be needed.

155 Skin test based strategy for selecting alternative iodinated contrast media in patients with hypersensitivity reaction: A prospective confirmative study

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Objective: Due to increased use of computed tomography (CT) scans, iodinated contrast media (ICM) became a common cause of drug hypersensitivity. Although skin test has been suggested as a useful tool for diagnosing IgE-mediated reaction and selecting safe alternatives, its role has never been evaluated prospectively so far.

Methods: We conducted a multicenter study from July 2018 to December 2020. The patients who had experienced immediate hypersensitivity to ICM were recruited and underwent intradermal test (IDT) with a causative ICM. The safe alternative agent was recommended based on the results of IDT as follows; 1) When culprit ICM showed positive result, further skin tests with other six ICM were conducted and IDT-negative agents were recommended for the next CT scan. 2) When culprit ICM was negative on IDT, any different ICM was recommended without additional skin tests. The recurrence and severity of hypersensitivity was assessed in the following CT exam. Premedication (corticosteroids or antihistamines) was administered according to the severity of index event.

Results: A total of 213 patients were recruited. Our IDT-based strategy reduced recurrence of hypersensitivity reactions in the following CT scans by 86.4% (vs. 60.7% when our strategy was not applied). The severity of hypersensitivity (15 severe, 4 moderate, and 10 mild initial cases) also diminished substantially even in 29 subjects with recurred hypersensitivity reactions (5 severe, 5 moderate, and 19 mild reactions).

Conclusion: We have shown that IDT-based strategy significantly reduced recurrence of hypersensitivity reactions to ICM. Our results provided evidence to encourage IDT to diagnose ICM allergy and find safe alternatives.

Key words: Iodinated Contrast Media, hypersensitivity, intradermal test, skin test

156 Korean Medicinal Narcotics exclusive monitoring system using Real World Data reported on NIMS

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Aim: Introduction of NIMS (Narcotics Information Management System)

Background: The importance of safety guidance for narcotics has been emphasized, because of global social issue regarding narcotics misuse & abuse. MFDS and KIDS are operating Narcotics Information Management System also known as NIMS. It is the world's first narcotics management system that utilizes online monitoring of medicinal narcotics by Real World Data.

Methods: NIMS is a sustainable monitoring system which collect handling data of medicinal narcotics from start to end-users. NIMS started operating in earnest 2018, and by June 2021, over 400 million cases of medicinal narcotics big data were collected. Through this system, an average of 500,000 cases per day from 60,000 handlers are being accumulated.

Results: The major advantage of NIMS data is that it is primary data on all the medicinal narcotics use linked to EMR, EHR and direct reporting to NIMS. To analyze and evaluate the risk management of medicinal narcotics, MFDS and KIDS organized a NIMS dataset by medicinal narcotics handler, prescribing pattern, and efficacy group of medical drugs etc. MFDS and KIDS analyze the collected NIMS RWD and provide 'Helper for safe use' and 'Utilization review letter' to perform pro-active monitoring. As a result of analyzing the prescription of physicians who received 'Utilization review letter*' before and 3 months after receipt, the average prescription amount per patient decreased by about 9.2%.

Conclusion: The active monitoring and analyzing through NIMS RWD in Korea is now expected to lay the foundation for safe guidance of medicinal narcotics to reduce the risk of misuse and abuse.

*Analyze NIMS data for 3 types of medicinal narcotics (Zolpidem, Propofol, Appetite suppressant) and send letter to physicians who have prescribed narcotics much more or inappropriate than others in 2019.

Key word: Narcotics, RWD, Active monitoring system, NIMS

157 Signal detection of rotavirus vaccine adverse events using the Korea Adverse Event Reporting System Database

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Objective: Rotavirus vaccine can prevent rotavirus disease. To date two rotavirus vaccines are licensed in Korea, RotaTeq® and Rotarix® were introduced in June 2007 and March 2008, respectively. This study purposed to detect the signals of the rotavirus vaccine using the Korea Adverse Events Reporting System (KAERS) database.

Methods: We detected potential signals of rotavirus vaccine at 28 days to less than 24 months of age through data mining using the KAERS database from June 2007 to December 2019. We used two disproportionality analyses (proportional reporting ratio (PRR) and information component (IC)) and the tree-based scan statistic (TBSS) for signal detection. The disproportionality analyses used the reported WHO-ART preferred terms to calculate PRR and IC. TBSS calculated the log-likelihood ratio based on all the reported hierarchical level terms. We defined a signal when all disproportional analysis indices or TBSS were satisfied. The detected signals were compared to the drug labeling from South Korea and the United States.

Results: Among the 38,211 reports related to vaccines between 2007 and 2019, 4,401 reported on all kinds of vaccines at 28 days to less than 24 months of age. 1,305 reports were related to rotavirus vaccine. We found 21 signals, including vomiting and urinary tract infection, upper respiratory tract infection, gastroesophageal reflux, and medication error-related problems met the disproportionality analysis and TBSS. Most of which were included in labels in South Korea and the United States, except for 'medication error related problems'.

Conclusion: Most of the detected AEs could found on the label. Medication error-related problems are occurred by 'incorrect dose administered' and 'incorrect dose prescribed'. However, medication error after rotavirus vaccination were determined as a signal, further researches are needed on the high incidence of medication errors associated with rotavirus vaccination.

Keywords: KAERS; Rotavirus vaccine

158 Cefepime-induced neurotoxicity: A retrospective cohort study in a tertiary healthcare facility

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Objective: The study aimed to determine the incidence and risk factors for cefepime-induced neurotoxicity compared to other antibiotics.

Methods: A retrospective cohort study was conducted with 738 patients over eight months in a tertiary healthcare facility. Patients with cefepime were selected as study cohort (SC; n= 496), and other antibiotics were reference cohort (RC; n=242).

Results: The results showed 53 (10.7%) patients developed neurotoxicity in the SC, whereas 12 (5%) patients in the RC. A significant association was found between neurotoxicity and cefepime use (X2 =6.641; p=0.01). SC has 2.29 times increased risk of neurotoxicity compared to RC (OR: 2.29; 95%CI: 1.2-4.38). Risk estimation showed renal failure patients have a 5.5 times higher risk for cefepime-induced neurotoxicity compared to non-renal failure patients (OR: 5.5; 95% CI: 2.98 - 10.17). Cefepime-induced neurotoxicity symptoms were disorientation (38.5%), loss of consciousness (23.1%), drowsiness (18.5%), etc. The calculated number needed to harm (NNH) for cefepime was 17.2.

Conclusions: The study found a higher incidence of cefepime-induced neurotoxicity than other antibiotics-induced neurotoxicity and a harmful association between cefepime use and the development of cefepime-induced neurotoxicity. Besides, renal failure is a risk factor for cefepime-induced neurotoxicity. Therefore, the study warrants the use of cefepime, where no other alternatives are available.

Keywords: Adverse effects; Cefepime; Drug safety; Neurotoxicity

159 Drug-related problems of patients in primary health care institutions: A systematic review

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Objective: Drug-related problems (DRPs) are not only detrimental to patients' physical health and quality of life, but also lead to a serious waste of health care resources. The condition of DRPs might be more severe for patients in primary health care institutions. This systematic review aimed to comprehensively review the characteristics of DRPs for patients in primary health care institutions.

Methods: We searched three English databases (EMbase, The Cochrane library, PubMed) and four Chinese databases (CNKI, CBM, VIP, Wanfang). Two of researchers independently conducted literature screening, quality evaluation and data extraction. Qualitative and quantitative methods were combined to analyse the data.

Results: From 3368 articles screened, 27 met the inclusion criteria and were included in this review. The median (inter-quartile range, IQR) of the incidences of DRPs was 70.04% (59%), and the median (IQR) of the average numbers of DRPs per patient was 3.4(2.8). The most common type of DRPs was "treatment safety". The causes of DRPs were mainly in the prescribing section including "drug selection" and "dose selection", while patients' poor adherence in the use section was also an important cause of DRPs. Risk factors such as the number of medicines, age and disease condition were positively associated with the occurrence of DRPs. In addition, the medians (IQR) of the rate of accepted interventions, implemented interventions and solved DRPs were 78.8% (22.3%), 64.15% (16.85%) and 76.99% (26.09%), respectively.

Conclusion: This systematic review showed the condition of DRPs in primary health care institutions was serious. In pharmaceutical practice, the patients with risk factors of DRPs should be monitored more closely. Pharmacists could play important roles in the identification and intervention of DRPs, and more effective intervention strategies need to be established in the future.

Keywords: Drug-Related Problems, Primary Heath Care, Systematic Review, Pharmaceutical Service

160 Comparison of enhanced safety monitoring for COVID-19 vaccine between United States, United Kingdom, Canada, Australia and Korea

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Background: Enhanced monitoring for rapid detection of previously unknown adverse events (AEs) and the discovery of safety profile of COVID-19 vaccines is important.

Objectives: To compare the enhanced safety monitoring system and information sharing system of the COVID-19 vaccine by country.

Methods: We investigated COVID-19 post-vaccination safety monitoring systems in the United States, United Kingdom, Canada, Australia and Korea. We investigated two aspects to explore the enhanced safety monitoring system and the information sharing system. In terms of enhanced monitoring systems, tools and contents of survey for AE reporting were reviewed. In terms of information sharing system, the sharing cycle, the media in which the sharing takes place, and the contents in which it is shared were reviewed.

Results: It was common to receive reports of adverse event through SMS-based surveys; V-safe from CDC in the US, Yellow card app from MHRA in the UK, and FluWatch in Canada were monitoring as a separate application. The details of the survey included personal information, information on vaccines received, and information on adverse reactions. For sharing Information of COVID-19 vaccine safety monitoring States, all five countries were daily updating the dashboard by official agencies operated by the country. Also, the five countries were publishing weekly reports, and they were commonly reported in the categories cases, deaths, and vaccination, and some countries were additionally updating hospitalization rates.

Conclusion: The AE monitoring activities for COVID-19 recommended by the WHO for all countries were well followed. Our research could contribute to strengthening the COVID-19 vaccine monitoring system for each country.

Keyword: COVID-19 Vaccines

161 An analysis of prescription patterns and occurrence of cardiac disorders in Hydroxychloroquine users in Korea

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Objective: The aim of this study is to identify characteristics and occurrence of cardiac disorders in hydroxychloroquine users in Korea.

Methods: We conducted descriptive analysis using the National Health Insurance Service (NHIS) Database and the MOA CDM (Medical record Observation and Assessment for drug safety-Common Data Model) from 2013 to 2018 in Korea. The study population includes the patients who used hydroxychloroquine at least one time during 2013-2018. We identified prescription patterns of hydroxychloroquine in study population and their characteristics including demographics, comorbidities, and concomitant drugs. We analyzed occurrence of cardiac disorders before and after hydroxychloroquine use. And then we examined frequency and percentage for categorical variables and used the chi square test. We calculated mean and standard deviation for continuous variables.

Results: A total of 286,074 hydroxychloroquine users (276,945 in NHIS database and 9,129 in MOA-CDM) were identified during 2013-2018. A majority of the hydroxychloroquine users were female, 40~69 years old. The prevalence of cardiac disorders varied from 4% in CDM to 12% in NHIS database. The most common types of cardiac disorders were angina, arrhythmia, and heart failure. Major comorbidities were rheumatoid arthritis, gastritis and hyperlipidemia. Major concomitant drugs were antiinflammatory analgesic drugs, anti-rheumatoid drugs and gastrointestinal agents. In addition, we found that 0.3% (NHIS database) ~ 0.4% (CDM) of hydroxychloroquine users got prescription for amiodarone in conjunction with hydroxychloroquine.

Conclusion: In this study, we analyzed prescription patterns, major characteristics and occurrence of cardiac disorders in hydroxychloroquine users in Korea. Although it is known that the risk of QT prolongation and arrhythmia can be significantly increased by interaction between amiodarone and hydroxychloroquine, we found that some patients got amiodarone while using hydroxychloroquine. Based on these results, we will review to develop Drug Utilization Review information on the concomitant use of amiodarone and hydroxychloroquine.

162 Detecting adverse drug events with the use of Protamine as a trigger tool

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Objectives: To identify adverse drug events (ADEs) from anti-coagulants with the use of protamine as a trigger tool and to evaluate the cause of preventable adverse drug events.

Methods: This is a retrospective descriptive study involving medical record review of hospitalized patients at a university hospital from January 2015 to December 2018. Patients that received protamine were enrolled in the study. ADEs were evaluated by 3 pharmacists and a cardiologist, assessing causality and preventability using Naranjo's algorithm and the Schumock and Thornton scale. Finally, the preventability of ADEs were classified using the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) harm scale.

Results: There were ten- ADEs (28.57%) out of 35 medical records reviewed in which protamine was prescribed. Among the ten ADEs, six were found to be preventable ADEs (60%) and the symptoms included two major bleedings, two minor bleedings and two prolongations of Activated Partial Thromboplastin Time (aPTT). All of the preventable ADEs were categorized as level E based on the NCC MERP scale. Enoxaparin was the most common drug causing preventable ADEs (50%). An inappropriate dose was the most common cause of preventable ADEs (83.33%).

Conclusion: The use of protamine as a trigger tool leads to increased identification of ADEs. In this study 60% of ADEs were preventable and the major causes of preventable ADEs were inappropriate dose of anti-coagulants.

Key words: adverse drug event, trigger tool, protamine

163 Efficacy and safety of inhaled corticosteroid containing combinations in patients with chronic obstructive pulmonary disease: A systematic review and meta-analysis

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Objective: To assess the efficacy and safety of Inhaled Corticosteroid (ICS) containing combinations in patients with moderate to very severe Chronic Obstructive Pulmonary Disease (COPD).

Methodology: A thorough literature search was performed in PubMed, Cochrane CENTRAL, and Google Scholar from the inception to 31st January 2021. A combination of keywords, MeSH terms, and entry terms on COPD and ICS combinations was used in combination with Boolean operators. All randomized controlled trials (RCTs) investigating the efficacy ((in terms of FEV1, exacerbations and QoL) and safety (in terms of adverse events and tolerability outcome) of ICS combinations on COPD 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 2814 non-duplicate RCTs identified through database searching, a total of 30 high quality studies (Jadad score ≥3), with 36,894 patients were included in this study. ICS combinations showed a significantly better Quality of Life in SGRQ-C score (MD: -1.46; P:0.001) and CAT score (MD: -1.08; P=<0.00001) compared to the control group. There was no significant difference between groups in terms of FEV1 (MD: 32.00ml; P:0.14), exacerbations (OR:0.85; P:0.15) and TDI score (MD: -0.03; P=0.67). Cardio Vascular side effects (OR:0.88; P=0.05) and treatment discontinuation due to lack of efficacy (OR: 0.64; P= 0.0001) was appeared significantly lesser in ICS combinations compared to the control group.

Conclusion: This systematic review and meta-analysis identified a significant association between ICS containing combinations and efficacy outcomes like QoL and CAT score. Less population size and a smaller number of outcomes may be the reason for non-significant results, hence there is a need for large and long-term studies to address these issues further.

164 Detecting drug-drug interaction signal of concomitant use of warfarin and statin using Korea Adverse Event Reporting System Database

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Aim/Objective: Warfarin and statin are commonly co-administered to cardiovascular disease patients. However, there is a potential risk of drug-drug interaction (DDI). The objective of this study was to detect signals of adverse events (AEs) for DDI after concomitant use of warfarin and statin using Korea adverse events reporting system (KAERS) database.

Methods: KAERS database from January 2015 to December 2019 was used. Ω shrinkage measure model and Chi-square statistics model were used to calculate the criteria for detecting AEs signal resulting from concomitant use of warfarin and statin. Three indices were used to define signals: Ω025 (frequentist) > 0, Ω025 (Bayesian) > 0, and $\chi > 2$. Detected signals were compared with AEs listed on the drug label in Korea, Micromedex, and SIDER for warfarin and statin, respectively.

Results: Among a total of 2,372,236 drug-AEs pairs, 5,508 pairs were associated with warfarin only, 30,805 pairs were associated with statin only, and 856 pairs were associated with concomitant use of warfarin and statin. Twenty-eight AEs on reports of concomitant use were detected as signals. Of these signals, 15 satisfied only one index, 6 satisfied two indices, and 7 satisfied all indices. Of 28 detected signals, 11 signals, including breath odour not otherwise specified (NOS), depersonalization, gastrointestinal neoplasm NOS, hyperhaemoglobinaemia, medical device complication, menopausal symptoms, oedema cerebral, osteitis, prostatic hyperplasia, pulmonary congestion, and skin hypertrophy, were not listed on drug label. One of these signals, haemorrhage rectum, might be associated with increased international normalized ratio. It is a known interaction after concomitant use of warfarin and statin.

Conclusions: We identified signals for concomitant use of warfarin and statin. Careful monitoring and further pharmacoepidemiological studies of DDI associated with new signals using other databases are needed.

Keywords: Drug-drug interaction; Warfarin; Statin; KAERS Database

165 Cisplatin-induced nephrotoxicity in childhood cancer: Comparison between two countries

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Objective: To evaluate the incidence of kidney injury according to commonly used and alternative definitions in two different cohorts of children who received cisplatin.

Methods: This retrospective cohort study included children at three pediatric academic health centers in Vancouver, Canada (one centre) and Mexico City, Mexico (two centres), who were treated with cisplatin-based chemotherapy for a variety of solid tumours. Serum creatinine-based definitions (Kidney Disease: Improving Global Outcomes [KDIGO] and Pediatric Risk, Injury, Failure, Loss, End Stage Renal Disease [pRIFLE]), electrolyte abnormalities consisted of hypokalemia, hypophosphatemia and hypomagnesemia (based on National Cancer Institute Common Terminology Criteria for Adverse Events v5), and an alternative definition (Alt-AKI) were used to describe nephrotoxicity. Incidence with the different definitions, definitional overlap and inter-definition reliability were further analyzed.

Results: A total of 173 children (100 from Vancouver and 73 from Mexico) were included. Depending on the definition used, cisplatin-induced nephrotoxicity occurred in 38%–92% of the children. Nephrotoxicity and all electrolyte abnormalities were significantly more common in the Vancouver cohort than in the Mexico City cohort except when using the KDIGO definition. The most common form of electrolyte abnormalities was hypomagnesemia (88.9%, in Vancouver cohort) and hypophosphatemia (24.2%, in Mexico City cohort). The KDIGO definition provided the highest overlap of cases in Vancouver (100%), Mexico (98.6%) and the combined cohort (99.4%). A moderate overall agreement was found among Alt-AKI, KDIGO and pRIFLE definitions (κ = 0.18, 95% CI 0.1-0.27) in which KDIGO and pRIFLE showed moderate agreement (κ = 0.48, 95% CI 0.36-0.60).

Conclusions: Compared to pRIFLE and KDIGO criteria, Alt-AKI criteria detected more patients with cisplatin-induced nephrotoxicity. pRIFLE is more sensitive to detect not only the actual kidney injury but also the patients at risk of cisplatin-induced nephrotoxicity, while KDIGO seems to be more useful to detect clinically significant kidney injury.

166 Ustekinumab use associated with Vasculitis as Adverse Events - Signal Review

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Background: Ustekinumab is human IgG1κ binds with high affinity and specificity to p40 protein subunit of human-cytokines interleukin (IL)-12 and IL-23. treat psoriasis and improving quality-of-life moderate to severe plaque psoriasis patients. Vasculitis is inflammation of blood-vessels, present when body's immune system attacks its own blood-vessel. caused by infection, medicines, other disease. Saudi-Food-and-Drug-Authority has initiated signal review based on detected signal from World-Health-Organization. This review will aim to evaluate risk of Vasculitis associated with Ustekinumab.

Methods: Signal-Detection-team performed signal review using NPC database, and World-Health-Organization, along with literature screening to retrieve related information would be beneficial to assess the causality between Vasculitis and Ustekinumab. Searched on 11/22/2020.

Results:
Local-Cases: No local-cases reporting Vasculitis with Ustekinumab.

Global-Cases: WHO-database-(VigiBase) searched for individual-case-safety-reports-(ICSRs) reporting Vasculitis and Ustekinumab yielded to 35-ICSRs. initial review revealed 26 cases were not sufficiently-documented for proper assessment. the rest 9 cases evaluated resulted in five-cases with positive-dechallenge, thee negative rechallenge, after applying WHO causality assessment two cases with possible association, three cases unlikely association, and four unassessable cases due to lack-of-information.

Literature: Two case report found supporting association: 55 year-old-woman with history of psoriasis presented with painful, purpuric, and ulcerative eruption on legs four-weeks after starting Ustekinumab. The patient diagnosed with drug-induced vasculitis. And, 28-year-old female with history of Crohn's disease and diverting ostomy, Ustekinumab 90 mg begun. Three years later, patient presented with painful and palpable purpura in abdomen and legs, Ustekinumab stopped, started prednisone then symptoms resolved. After period, dose of ustekinumab administered, reappearance of the same cutaneous lesions.

Datamining: combination Ustekinumab and Vasculitis observed more than expected (IC0.3) when compared with other medications in VigiBase.

Conclusions: weighted evidence in this review sufficient to support causal-association between Vasculitis and Ustekinumab. Therefore, HCPs should be aware of possible-risk and monitor Vasculitis signs in patients treated with Ustekinumab.

167 Identification of therapeutic potential of Ginsenosides against the Autism spectrum disorder by bioinformatics interlaced with in-silico techniques

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Objective: Autism spectrum disorder (ASD) is a multi-factorial neurodevelopmental disorder allied with a set of heterogeneous symptoms such as deficit in social interaction with repetitive and stereotyped behavior. The molecular mechanism underpinning ASD is still obscure, owing to its genetic and epigenetic heterogeneity. The current treatment modalities focused on symptomatic treatment offer modest benefits. This situation demands the discovery of novel lead molecules to confront ASD with an appreciable safety profile. Ginsenosides from Korean Red Ginseng is well renowned for its therapeutic potential in rescuing abnormalities against neurodevelopment disorders barring autism, in both animal and human studies. This study aims to identify key genes associated with ASD and their possible interaction with Ginsenosides in order to decipher their therapeutic potential.

Method: GEO dataset GSE18123 encompassing the microarray data of blood samples of autistic children was analyzed through GEO2R for retrieving significant Differential Expressed Genes (DEGs). Protein-protein interactions were constructed between DEGs and literature derived genes (LDGs) using the Search Tool for Retrieval of Interacting Genes database and visualised using Cytoscape. KEGG pathway enrichment analysis of DEGs was performed using ClueGo. The DEGs exhibiting substantial interactions with the LDGs were identified as potential targets and screened against Ginsenosides using AutoDock-Vina.

Result: KEGG pathway analysis revealed that the significant DEGs were mainly enriched in amino acid metabolisms, VEGF signaling pathways and carcinogenesis pathways. HLA-DQB1, which is substantially overexpressed in autism was identified as a potential druggable target. Among the 10 Ginsenosides, Rb1 (-9.5) and Rb2 (-9.3) exhibited appreciable affinity towards the target in parallel to the conventional autistic drug Risperidone (-9.2).

Conclusion: This study reveals key genetic underpinnings of ASD and suggests the pertinence of Ginsenosides in the management of Autism. These in silico research findings should be validated further via in vitro and in vivo studies.

Keywords: Autism, Ginsenosides

168 The association between HLA Class II Alleles and ICM Anaphylaxis

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Aim/Objective: The use of contrast media has increased with the advancement of diagnostic imaging technology, and iodinated contrast media (ICM) has become one of the major culprit agents of drug-induced anaphylaxis. For effective prevention, identifying the risk factors associated with ICM anaphylaxis is essential. The aim of this study is to evaluate the genetic susceptibility of ICM anaphylaxis.

Methods: Patients who experienced ICM anaphylaxis were recruited. After obtaining consent to participate, HLA-DRB1, DQB1, DPB1 were genotyped and compared with those of the Korean general population.

Results: A total of 116 patients with a history of ICM anaphylaxis were recruited from 7 hospitals. The phenotype frequencies of DRB1*15:02 (28.4% vs. 6.6%, odds ratio (OR) 5.63, PC < 0.001), DQB1*06:01 (44.0% vs. 18.4%, OR 3.49, PC < 0.001), and DPB1*09:01 (22.4% vs. 4.3%, OR 6.36, PC < 0.001) were significantly higher in patients with ICM anaphylaxis than those of the Korean general population. These associations were stronger in patients with anaphylaxis to iohexol (DRB1*15:02, OR 11.01, PC < 0.001; DQB1*06:01, OR 5.04, PC < 0.001; DPB1*09:01, OR 11.52, PC < 0.001) and in patients who were repeatedly exposed to the culprit ICM prior to the development of anaphylaxis (DRB1*15:02, OR 5.59, p < 0.001; DQB1*06:01, OR 4.07, p = 0.001; DPB1*09:01, OR 3.70, p = 0.008). In patients with the HLA-DRB1*15:02 allele, the OR increased up to 17.35 in the subgroup with four times or more exposure to the culprit ICM before the occurrence of anaphylaxis compared to those who had anaphylaxis at the first exposure (p < 0.001). Such findings indicate that repeated exposure to the culprit ICM may result in a higher risk of ICM anaphylaxis.

Conclusion: This study suggests that genetic susceptibility may contribute to the development of ICM anaphylaxis in patients with repeated exposure to the culprit ICM.

169 Beta-agonists maintenance therapy to prevent perinatal mortality in preterm labor: A network meta-analysis

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Objective: Beta-agonists have been used for decades as a treatment for preterm labor. However, the use of beta-agonists for maintenance therapy to improve infant outcomes remains controversial. Therefore, this network meta-analysis aims to determine the best beta-agonist maintenance therapy to prevent perinatal mortality in patients at risk of preterm labor.

Methods: A literature search from Pubmed, Embase and Medline databases on randomized controlled trial of the use of beta-agonists in preterm labor was done. Data including study characteristics, patient characteristics and primary outcome were extracted. A network meta-analysis was done using bayesian random effects in WinBUGS14. A sensitivity analysis was carried out by removing study with high risk of bias.

Results: A total of 1,673 women and 1,674 infants in nine randomized controlled trials were included. Five treatments were ritodrine, salbutamol, fenoterol, terbutaline and placebo. Compared with placebo, none of the beta-agonists other than fenoterol (odds ratio (OR) 0.07, 95% confidence interval (CI) 0.01 to 0.32) showed a significant result on preventing perinatal mortality. Fenoterol ranked the highest with a Surface Under the Cumulative Ranking curve (SUCRA) score of 0.988. The SUCRA scores for salbutamol, ritodrine, terbutaline and placebo were 0.5827, 0.5229, 0.2568 and 0.1497, respectively.

Conclusion: Network meta-analysis showed that fenoterol had the highest probability of being the best maintenance therapy among beta-agonists to prevent perinatal mortality in preterm labor.

Keywords: Beta-agonist, maintenance therapy, perinatal mortality, network meta-analysis

170 Physician's attitude towards clinical pharmacists advice on the rational prescribing of antibiotics

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Aim: To evaluate the clinical pharmacist interventions on antibiotic therapy and the response of physicians toward these interventions

Methods: The surveillance study was conducted under the initiative of the clinical pharmacy department in a secondary care hospital in South India from December 2020 to May 2021 to evaluate the appropriateness and rationality of the antibiotic prescription at the Internal Medicine Department. Demographic details of the patients including the age, sex, and medication error (in drug selection, dose, frequency, route of administration) were documented. and category of intervention was prospectively recorded. The category, as well as the implementation status of the interventions, were compared with various associated factors using the chi-square test and p-value < 0.05% considered statistically significant.

Results: Of a total of 413 interventions, the overall acceptance rate was 56.1% (232). Frequently observed irrationality in antibiotics prescribing was with improper dosage adjustment in comorbid conditions. The interventions for antibiotic therapy optimization include IV to oral conversion and spectra-based drug selection. The acceptance of clinical pharmacist opinion was positively correlated with the good interpersonal relationship of the physician ($p=0.007$) as well as the evidence from standard references ($p<0.001$). The intervention acceptance rate was more among the patients with insurance claims, but this has no statistical significance.

Conclusion: The study highlights the importance of evidence-based therapy and multidisciplinary healthcare team workups.

Keywords: Clinical Pharmacist, PharmD

171 A big data analysis of perioperative transfusions and risk factor in autologous breast reconstruction

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Objective: To identify the status and risk factors for transfusion in patient with immediate autologous breast reconstruction (ABR) using a large national claims database.

Methods: Women aged 18 to 59 years who were firstly diagnosed with breast cancer and underwent total mastectomy alone or immediate ABR between April 1, 2015 and December 31, 2017 were extracted from Health Insurance Review and Assessment Service (HIRA) in Korea. The status of transfusion was compared between total mastectomy-only group and immediate ABR group. For patients with immediate ABR, a multiple logistic regression model was used to estimate the odds ratios (OR) of transfusion for each type of surgical method and to identify the risk factors for transfusion.

Results: Of the 30,384 patients, 28,221 patients underwent total mastectomy-only and 2,163 patients immediate ABR. The overall transfusion rate of the total mastectomy-only group and the immediate ABR group was 1.2% and 16.1%, respectively. Of immediate ABR patients, 36.5% of patients received deep inferior epigastric artery perforator (DIEP), 21.3% free transverse rectus abdominis myocutaneous (fTRAM), 19.3% latissimus dorsi (LD) flap, and 16.8% pedicled TRAM (pTRAM). The transfusion rates were highest in pTRAM (24.2%). The transfusion risk of pTRAM (OR: 3.06; 95% CI: 2.03-4.63; p<0.001) and fTRAM patients (OR: 2.50; 95% CI: 1.68-3.71; p<0.001) were significantly higher than LD flaps. The risk factors of transfusion for immediate ABR patients were the medical institutions located in the provinces (OR: 1.47; 95% CI: 1.13-1.90; p=0.004) and coronary artery disease as comorbidity (OR: 2.11; 95% CI: 1.06-4.21; p=0.03).

Conclusion: Transfusion rates were significantly higher in ABR patients who underwent TRAM or had coronary artery disease. Further studies are needed to evaluate health outcomes after transfusion. Development of transfusion guidelines considering surgical methods and underlying risk factors in breast reconstruction patients is required.

Key words: autologous breast reconstruction; transfusion

173 The influence of diabetic history in the prognosis of hospitalized COVID-19 Patients - A prospective observational study.

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Objective: To evaluate the association between a known history of diabetes mellitus (DM) and its clinical outcomes in hospitalized COVID-19 diabetic patients.

Methods: This prospective cohort study categorized COVID-19 positive patients admitted to a secondary care hospital in South India into DM patients and Non-DM patients. Data regarding the past medical and medication history was collected on the day of admission and the patients were regularly followed up till discharge or death. The outcome measures including duration of hospital stay, mortality, need for ICU care/mechanical ventilation were compared between the two groups. Data is extracted and statistically analyzed using Pearson correlation.

Results: A total of 118 patients were observed, 53 patients were diabetic and 65 were non-diabetic. Out of the 53 hyperglycemic patients, 39 patients were on metformin therapy while 15 patients were on insulin before admission due to COVID-19. A higher mortality rate was observed in the DM group when compared with the Non-DM group [26.4% (14) vs 9.23% (6)]. An increased random blood glucose level at the time of admission had a positive correlation with mortality ($p = 0.003$). While insulin administration prior to admission had negative correlation with mortality [R value is -0.282 ($p = 0.02$)], increased insulin requirement during hospitalization is associated with poor outcomes [R value is 0.327 ($p = 0.002$)].

Conclusion: People with diabetes when infected with COVID-19 are at a greater risk of morbidity and mortality. The study highlights the need for rational management of hyperglycemia in COVID patients with a history of diabetes mellitus.

Keywords: Diabetes Mellitus, COVID-19

174 Real-world Evidence of prognosis in the special population of HCV-coinfected with HBV patients receiving direct-acting antiviral agents

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Aim/Objective: Hepatitis C virus (HCV) co-infected with hepatitis-B virus (HBV) patients are special high-risk population infection for the late virologic relapse, HBV reactivation, or HCC recurrence after receiving oral direct-antiviral agents (DAAs). The HBV reactivation rate may up to 50% in active HBV infection patients. Taiwan consensus statement on the management of hepatitis C (2020) suggested that nucleoside/nucleotide analog prophylaxis and regularly monitor for HBV reactivation in HBsAg(+) patients (level of evidence: B1). However, no available recommendation was made for HBsAg(-) patients due to no evidence. The aim of this study was to provide real-world evidence of the prognosis in HCV co-infection with active or resolved HBV patients.

Methods: We retrospectively and consecutively enrolled naïve chronic hepatitis C adult patients receiving DAAs from April 2015 to May 2020 in KSVGH. Patients with complete treatment were evaluated for the sustained virologic response (SVR). Besides, we collected data about the prognosis outcomes of HBV reactivation, HBV reactivation-related hepatitis flare, hepatocellular carcinoma (HCC), and death.

Results: We enrolled 536 HCV co-infected with HBV patients receiving complete DAAs treatments, among them, 40 (7.5%) or 496 (92.5%) patients were active or resolved HBV infection, respectively. The overall SVR12 was achieved in 521 (97.2%) patients (100% vs 97.0% in active vs resolved HBV patients). The HBV reactivation was observed in 3 (0.6%) patients (2.5% vs 0.4% in active vs resolved HBV patients). None of them received nucleoside/nucleotide analog prophylaxis at the beginning of DAAs treatment. None of these 3 patients developed HCV reactivation. HBV reactivation-related hepatitis flare and new-onset HCC was observed in the active HBV infection patient.

Conclusion: HBV reactivation was lower in our population of naïve DAAs treatment patients. Nevertheless, the high burden of HBV reactivation-related HCC deserved regular prophylaxis and monitoring for the high-risk population.

175 Risk of fracture with GLP-1 RAs, DPP-4i, or SGLT-2i for type 2 diabetes mellitus: A systematic review and network meta-analysis

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Objective: To investigate the association between the use of glucagonlike peptide-1 receptor agonists (GLP-1 RAs), dipeptidyl peptidase-4 inhibitors (DPP-4i), or sodium-glucose cotransporter-2 inhibitors (SGLT-2i) and the risk of fracture among patients with type 2 diabetes mellitus (T2DM).

Methods: Medline, Embase, Cochrane Library and Clinical Trials were searched from inception through September 2019 for randomized controlled trials (RCTs) assessed the fracture risk of GLP-1 RAs, DPP-4i, SGLT-2i versus placebo or other anti-diabetic drugs in T2DM. ORs with 95%CIs were estimated through network meta-analysis, followed by subgroup analysis.

Results: A total of 117 RCTs (n = 165 081) involving risk of fracture were identified(a median follow-up of 26 weeks). GLP-1 RAs, DPP-4i or SGLT-2i were compared with placebo or other antidiabetic agents [metformin (Met), insulin, sulfonylurea (SU), thiazolidinedione (TZD), alpha-glucosidase inhibitor (AGI)]. GLP-1 RAs did not increase fracture risk compared with insulin (OR=1.05, 95% CI:0.54-2.04), Met (OR=1.72, 95% CI:0.55-5.38), SU (OR=0.94, 95% CI:0.55-1.62), TZD (OR=1.00, 95% CI:0.32-3.10), AGI (OR=5.99, 95% CI:0.28-130.37) and placebo (OR=1.27, 95% CI:0.88-1.83), respectively. DPP-4i did not increase fracture risk compared with insulin (OR=0.86, 95% CI:0.39-1.90), Met (OR=1.41, 95% CI:0.48-4.19), SU (OR=0.77, 95% CI:0.50-1.20), TZD (OR=0.82, 95% CI:0.27-2.44), AGI (OR=4.92, 95% CI:0.23-103.83) and placebo (OR=1.04, 95% CI:0.84-1.29), respectively. SGLT-2i did not increase fracture risk compared with insulin (OR=0.88, 95% CI:0.39-1.97), Met (OR=1.44, 95% CI:0.48-4.30), SU (OR=0.79, 95% CI:0.48-1.31), TZD (OR=0.83, 95% CI:0.27-2.57), AGI (OR=5.01, 95% CI:0.23-107.48) and placebo (OR=1.06, 95% CI:0.81-1.39), respectively.

Conclusion: The results suggest that the use of GLP-1 RAs, DPP-4i, or SGLT-2i is unlikely to increase the risk of fracture among T2DM patients.

Keywords: GLP-1 receptor agonists; DPP-4 inhibitors; SGLT-2 inhibitors; fracture; type 2 diabetes mellitus, network meta-analysis

176 Association between Vitamin E intake and risk of prostate cancer: A meta-analysis involving 6,00,954 subjects

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Background: The epidemiologic evidence on vitamins E use and prostate cancer is controversial. Therefore, a meta-analysis was carried out to investigate the role of vitamins E in the etiology of prostate cancer.

Methods: PubMed, Cochrane Library, and Google Scholar databases were searched up to December 02, 2019, stratified according to statistical method of outcome odd ratios (ORs). The quality assessment of included studies was evaluated by using the Newcastle-Ottawa Scale for observational studies and Risk of bias tool for randomized controlled trials (RCTs). Random effects model was employed to study the association between Vitamin E use and the risk of Prostate cancer. Between-study heterogeneity was quantified by using Cochran's Q-statistic and I2 statistics. Sensitivity analysis was done by ommiting the studies one by one, and publication bias was analyzed by using funnel plots.

Results: Twenty-six studies with 600,954 subjects were identified for inclusion in the meta-analysis, which was based on the comparison of RCTs, cohort studies, and case-control studies. The pooled OR of prostate cancer for the vitamin E intake was 0.96 (95%CI: 0.88-1.05; p = 0.40) with evidence of a moderate heterogeneity (I2 = 68.3%, p = 0.04). Stratifying the overall study according to study design yielded pooled ORs of 1.11 (95%CI: 0.96-1.29, p = 0.16) among cohort studies, 0.76 (95%CI: 0.58-1.00, p = 0.05) among case-control studies, and 0.96 (95%CI: 0.85-1.08, p = 0.49) among RCTs.

Conclusion: Our findings document the absence of an association between recent dietary vitamin E intake, or supplementation, and prostate cancer incidence overall or prostate cancer grade at diagnosis. Based on this, and other available evidence, vitamin E intake does not seem to hold promises with regard to prostate cancer prevention.

Keywords: vitamin E, prostate cancer, population-based, etiology, prevention, meta-analysis

177 Efficacy and safety of corticosteroids in acute respiratory distress syndrome: A systematic review of meta-analyses

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Aim: Evidence-based recommendation on efficacy and safety of corticosteroids in acute respiratory distress syndrome (ARDS) remains a therapeutic challenge and inconsistent. We aimed to assess the published meta-analyses and provide further insight into the existing uncertainty.

Methodology: We searched PubMed/MEDLINE, SCOPUS, Cochrane, and Google Scholar from inception to February 2021. Patient-related outcomes such as prevention of ARDS, mortality, ventilator days, ICU stay, and occurrence of adverse effects were considered. The review also assessed meta-analysis design-related outcomes which include the quality of meta-analysis, factors contributing to the risk of bias, extent, and sources of heterogeneity, publication bias, and robustness of findings. AMSTAR-2 checklist was used to assess the quality of published meta-analyses.

Results: Eighteen meta-analyses comprising a total of 38 primary studies and 3760 patients were considered. Fourteen studies were in ARDS, 3 in community-acquired pneumonia, and one in critical care. The overall quality of meta-analyses was observed to be critically low to high. A non-significant risk of publication bias and non-significant level of heterogeneity observed in the reviewed meta-analysis.
Corticosteroid was significantly effective in preventing ARDS among CAP patients, but not in critically ill patients. The effect of corticosteroids on mortality was observed to be inconsistent, whereas significant improvement was observed with ICU stay or ventilator outcomes with the steroid group compared to the control group. We observed a significant reduction of mortality in RCTs (RR: 0.78; 95%CI: 0.61 to 0.99) and duration of mechanical ventilation (MD: -4.75; 95%CI:-7.63 to -1.88); a significant increase in ventilator-free days (MD: 6.03; 95%CI: 3.59 to 8.47) and ICU-free days (MD: 8.04; 95%CI: 2.70 to 13.38) in patients treated with corticosteroids compared to the control group.

Conclusion: The evidence base on mortality reduction following corticosteroid therapy in ARDS is still inconclusive, though it was effective in ICU and ventilator outcomes with minimal safety concerns.

178 Global prevalence of hyperuricemia among chronic kidney disease patients - a systematic review and meta-analysis

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Aim: Despite the growing evidence suggesting a potential pathogenic role of serum uric acid in the progression of chronic kidney disease, information pertaining whether, how and when to optimize the serum uric acid levels among chronic kidney disease patients remains indeterminate and undetermined. This systematic review aims to synthesize quantitatively the prevalence of hyperuricemia among chronic kidney disease patients globally.

Methods: A systematic review and meta-analysis was conducted by using a literature search of online databases including MEDLINE/PubMed, ScienceDirect, Google scholar, and Cochrane library. The effect size with corresponding 95% confidence interval was calculated to evaluate the pooled prevalence of hyperuricemia among chronic kidney patients. Subgroup analysis was also performed for gender and geography by using comprehensive meta-analysis version 2.0.

Results: Twenty-four studies containing 220815 participants were eligible for quantitative synthesis. The overall pooled prevalence of hyperuricemia in chronic kidney disease patients was found to be 37.6% (31.7-43.8) globally. Taiwan comprises 3 studies and has the highest pooled prevalence 43.8% (29.7-58.9) of hyperuricemia among chronic kidney disease patients followed by China (28.4%) and Japan (27.9%) comprising seven each. The prevalence in India was found to be (38.4%). The prevalence in case of male patients 25.7% (11.3-48.5) was significantly higher than female patients 7.6% (2.6-20.6) with 95% confidence interval.

Conclusions: Given the high prevalence of hyperuricemia among chronic kidney disease patients globally, this information may support to raise the awareness and enhance the implementation of effective clinical service programs that address hyperuricemia in kidney disease at all levels of decision-making.

Keywords: Hyperuricemia, Chronic kidney disease, Prevalence, Geography, Uric acid

179 Efficacy of antifungal therapy in the management of fungal co-infections in COVID-19 patients: A systematic review and meta-analysis

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Objective: To summarize the evidence of efficacy of antifungal therapy (AFT) in the management of fungal co-infections in COVID-19 patients.

Methods: This comprehensive study was conducted following the PRISMA 2020 statement: an updated guideline for reporting systematic reviews. A literature search was conducted using predefined search terms in eight online search engines to review all the human studies published in English that included patients with a confirmed diagnosis of COVID-19 with fungal co-infections across all the age groups in whom at least one antifungal drug was used. Case reports, case series, prospective studies, retrospective studies, and clinical trials were included. All the necessary and relevant data were extracted from the included records and were documented in a specifically designed data extraction tool. The methodological quality & synthesis guide (for case reports and case series) and Newcastle-Ottawa Quality Assessment Form for Cohort Studies (prospective and retrospective studies) were used for evaluating the risk of bias.

Results: A total of 520 patients' data from sixty published records that satisfied the study criteria were included for analysis. A majority [333/520, 64%] of these patients were presented with COVID-19 Associated Pulmonary Aspergillosis (CAPA), followed by candida infection [129/520, 24.8%]. AFT was prescribed for 389 patients. A majority of these patients received a single antifungal agent, followed by dual AFT. The meta-analysis revealed that there is no significant association between the use of either mono- or combination AFT and death [RR: 1.08 (0.48-2.43), p=0.85], similarly, there is no significant association between duration of AFT (either ≤ 28 days or ≥ 29 days) and death [RR: 1.46 (0.74-2.89). p=0.28] in COVID-19 patients with fungal co-infections.

Conclusion: Neither mono- nor combination AFT is superior and overall death rates are not related to the duration of AFT in COVID-19 patients.

Keywords: Fungal co-infections, COVID-19, Antifungal therapy, and Efficacy.

180 Adverse drug reactions of GLP-1 agonists: A Systematic review of descriptive studies

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Background: Glucagon-like peptide-1 agonists (GLP-1 agonist) is a newer class of antidiabetic drug and commonly used 2 nd line therapy as recommended by clinical practice guidelines. However, data regarding the safety issues of these classes of drugs is very limited.

Objective: To review and evaluate all the descriptive studies on the adverse drug reactions (ADR) of GLP-1 agonists to summarize types of ADRs, preventability, predictability, severity, and outcome.

Methodology: A comprehensive search strategy was performed in Scopus and PubMed to find the descriptive studies on the ADRs associated with GLP-1 agonists in patients with type 2 diabetes. We also searched additional sources and bibliography of included studies. Study screening, data abstraction, and quality assessment were performed by two authors independently and disagreements were settled through consensus or through discussion with a third reviewer.

Results: The study comprised 105 cases with 88 case reports (83.8%) and 17 cases from 10 case series (16.2%) published with GLP-1agonists associated with ADR. The major ADRs reported was gastrointestinal disorder 35(33.3%) followed by renal adverse effects 22(21.0%). Out of 105 cases, 102(97.1%) cases were improved after withdrawing the drug.

Conclusion: Among the Glucagon-like peptide-1 agonists' liraglutide and exenatide were found to cause the maximum number of adverse drug reactions. The severity of ADRs was under the moderate category. Our study findings can provide insight regarding safety issues GLP-1 agonist in diabetes patients.

181 Quality assessment of randomized controlled trials and observational studies published on COVID-19 in 2020

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Objective: To assess the quality of randomized controlled trials (RCTs) and observational studies (cohort and case-control studies) published on COVID-19, and to investigate the reasons behind compromising the quality, if found.

Methods: A comprehensive literature search was performed in PubMed, Google Scholar, and Cochrane CENTRAL to identify the RCTs, cohort and case-control studies published on COVID-19 between 1st January to 31st December 2020. Studies conducted either for the prevention, diagnosis, management, and treatment of COVID-19 were included for the quality assessment. met with study criteria were included in the study. Assessment of quality of RCTs was performed by using the modified Jadad scale and that of cohort and case-control studies were done using the NewCastle-Ottawa scale.

Results: A total of 21,259 records of RCTs were identified through the database searching, out of which 61 RCTs were included in the study. Among the 61 RCTs, 33 (50.0%) were of moderate quality, and 8 (12.1%) were of low-quality studies. Among 8129 identified records of cohort studies, 48 studies were included in the study, out of which 24 (50.0%) consists of high risk of bias, and 2 (4.16%) were very high risk of bias studies. Out of 7278 identified records of case-control studies, 13 studies were included in the study, among which nine (69.23%) were of high risk of bias studies.

Conclusion: Findings from this quality assessment study indicate that the accelerated publication of COVID-19 research along with the fast-track review process has resulted in lowering study quality scores, irrespective of study design. With the emergence of stronger evidence, COVID-19 clinical studies with lower methodological quality should be revisited.

182 Comparative efficacy and safety of treatment regimens for advanced, recurrent or metastatic endometrial cancer: A systematic review

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Objective: With the growing incidence of Endometrial cancer (EC), it is important to understand the disease effects, patient's needs, therapies available to improve the survival rates and quality of life of the patients. This study aimed to systematically review the efficacy and safety of available treatment options in patients with advanced, recurrent, or metastatic endometrial cancer.

Methods: A comprehensive search strategy was developed to identify relevant articles in PubMed, Embase, and Cochrane from inception to 28 January 2021. We examined overall survival (OS), progression-free survival (PFS), gastrointestinal and hematological adverse events across English language Randomized Control Trials (RCTs) that evaluated treatments for advanced, recurrent, and metastatic endometrial cancer. The study quality was assessed using the Cochrane Risk of Bias tool.

Results: In total, 5029 studies were screened, 210 studies underwent full-text screening, and 16 were included in the final review. The median age of studied patients ranged between 54 - 66 years while the median follow-up time varied from 6 months to 7 years. Paclitaxel and Carboplatin were the most commonly used doublet chemotherapy regimens across the RCTs, this regimen was as effective as triplet treatment regimens. Bevacizumab given with chemotherapy combination has shown marginally better survival rates (OS, PFS) than chemotherapy alone; however, these differences were not statistically significant. Nausea, vomitings, and diarrhea were the commonly observed gastrointestinal adverse effects while anemia, leukopenia, and neutropenia were the most common hematological adverse events, occurring at rates of 11 – 15% (grade 3 and above). As hypothesized, rates of gastrointestinal and hematological adverse events varied by treatment type.

Conclusions: Double or triple-drug combinations, particularly of chemotherapies, are the most commonly studied regimens in advanced EC cases. The combination of targeted and chemotherapy may have promising results, but more head-to-head trials are required to clarify their comparative benefits.

183 Evaluation of practice on antimicrobial medicines dispensing from community pharmacies

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Objective: The objective of this work was to study the situation on dispensing antimicrobials from pharmacy outlets in Armenia.

Methods: The study has been implemented at 30 community pharmacies from different regions of Yerevan, the capital of Armenia. All the medicines dispensed to 900 patients/caregivers (30 visitors in each pharmacy outlet) were analysed. The following indicators were calculated: the percentage of antimicrobials prescribed by physicians, the percentage of visitors, who got antimicrobials without providing a prescription and so on.

Results: 1513 medicines have been dispensed to selected 900 patients/caregivers. Antimicrobial medicines (n=171) have consisted 11.3% of all the dispensed medicines. Only 25 (14.6%) antimicrobials were dispensed to visitors who had prescriptions. Only 19 (12.6%) of 151 medicines provided without prescription were OTC-medicines, other 132 (87.4%) were prescription only medicines. According to information received from visitors, 58.5% of all dispensed antimicrobials were selected by physicians, 10.5% of antimicrobials were advised by pharmacists and almost one third was selected by patients, family members, etc. More than 90% of the total number of visitors, to whom antimicrobials were dispensed, got them without providing a prescription. 13 patients received 2 and more antimicrobials.

Conclusions: The great majority of prescription only antimicrobials are dispensed from community pharmacies without prescription, despite the local regulation requires dispensing of systemic antibiotics with prescription. Many of antimicrobials are not prescribed by physicians and are for self-medication. That means many of prescription only antimicrobials are used in Armenia inappropriately. There is need in a political will that could help to prevent dispensing antimicrobials without prescription. Recommendations for decision-makers on additional strategies aimed to improve the situation have been formulated.

Keywords: antimicrobial medicines, community pharmacies

184 Clinical outcomes of gestational age based parenteral nutrition initiation in very low birth weight preterm neonates – a pharmacist's purview

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Objective: To evaluate the clinical outcomes of gestational age-based initiation of parenteral nutrition (PN) in very low birth weight preterm neonates in neonatal ICU.

Methods: A prospective study was conducted in neonates <32 weeks of gestation or weighing <1500 g at birth. Data on gender, gestational age (weeks), birth weight (g), anthropometry (height, length, head circumference [cm]), PN start time, total days of PN, composition on initiation and maximum, day of initiating enteral feed were obtained. PN was initiated within 24 hours of birth (early PN) for neonates with gestational age < 28 weeks and after 24 hours (late PN) for 28-34 weeks. Clinical outcomes were assessed through improvement in extrauterine growth (anthropometry), regain weight (g) from birth to discharge and time to regain weight. Differences in continuous data were analyzed using Unpaired sample t-test and categorical data using Chi-square test, considering $P< 0.05$ as significant.

Results: Of 74 neonates (41 males; 33 females), early PN was given for 36 and late PN for 38 neonates. No significant difference in mean birth weight, mean duration of PN between both groups. A significant improvement in anthropometry, mean regain weight from birth to day of discharge was observed in both, but weight gain was greater in early PN and mean time to regain weight was 14 ± 4.0 and 21 ± 3.0 days respectively ($P<0.05$). Average initiation carbohydrates, proteins and lipids in early PN Vs late PN were (7.5; 1.5; 1.75 Vs 6.5; 1.0; 1.5 g/kg/day respectively) and average maximum were (12.0; 2.5; 3.05 Vs 12.0; 2.0; 2.5 g/kg/day respectively). Enteral feed was started on day 1 and day 2 respectively.

Conclusion: Early PN had better growth and weight gain, demonstrating the importance of evaluating early PN protocol implementation for preterm neonates, and clinical pharmacists could contribute through timely standard PN preparation.

185 A point prevalence survey of antimicrobial utilisation patterns and quality indices amongst hospitals in South Africa; findings and implications

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Objectives: Antimicrobial use is growing, driven mainly by rising demands in developing countries. Knowing how antimicrobials are prescribed is important. Consequently, we undertook a point prevalence survey (PPS) quantifying antimicrobial consumption among 18 public sector hospitals across South Africa.

Method: A purpose-built web-based application was used to collect PPS data.

Results: Out of 4407 patients surveyed, 33.6% were treated with an antimicrobial. At ATC level 3, penicillins were the antimicrobial class mostly used (J01C: 34.8%; n = 766), followed by the other beta lactams (J01D: 20.8%; n = 458) and agents against amoebiasis and other protozoal diseases (P01A: 9.4%; n = 206) (. Amoxicillin combined with an enzyme inhibitor accounted for 21.4% total DDDs. In the medical and surgical wards, Access antimicrobials (54.1%) were mostly used, while in the ICU, Watch antimicrobials (51.5%) were mostly used. More than half (64.3%; n = 1418) of all antimicrobials were administered intravenously, with the IV route most prevalent in ICU and on the surgical wards. For surgical prophylaxis, cefazolin (J01DB04) was the most commonly used antimicrobial (45.5% of cases), majority (73.2%; n = 108) of cases, prophylaxis was prescribed for more than 1 day. Compliance with the South African Standard Treatment Guidelines and Essential Medicines List was 90.2%; however, concerns with extended use of antimicrobials for surgical prophylaxis (73.2% of patients).

Conclusion: The web-based PPS tool was easy to use and successful in capturing PPS data since the results were comparable to other PPS studies across Africa. High use of amoxicillin combined with an enzyme inhibitor, possibly because it was among the broad-spectrum antimicrobials in the Access group. The findings will assist with future targets to improve antimicrobial prescribing among public sector hospitals in South Africa.

186 Assessing the circumstances of poisoning and antidote therapy in a tertiary care teaching hospital

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Objectives: This study was conducted to assess the incidence, pattern and appropriateness of antidote use in poisoned patients in a tertiary care hospital

Methods: A prospective observational study was conducted from November 2020-April 2021 in the emergency department (ED) of the hospital. Patients who fulfilled the study criteria were followed on a regular basis and data such as demographics, nature of poisoning case and treatment provided was documented. The collected data was reviewed to analyze the appropriateness of the antidotes prescribed according to the institutional poison protocols, Micromedex and relevant guidelines

Results: Out of the 117 patients, 71 (60.68%) patients were admitted with cases of suicidal poisoning, and were found to have a 24 fold higher chance of suffering from severe poisoning than other types of poisoning (OR=25.79, 95% CI= 1.18 – 56.45, P=0.039). Pesticides were the most implicated agents in poisoning (44, 37.6%). Antidotes were used in 82 of the poisoning cases. Atropine was the most widely used antidote in 30 (36.85%) patients followed by anti-snake venom (ASV) in 15 (18.29%) cases and magnesium sulphate in 12 (14.63%) cases. Intravenous (IV) was the most common route of antidote administration (51.21%). In 70 (85.36%) patients, antidote was given according to the hospital poison protocol and was justified. After therapy, 93 (79.48%) patients were discharged post recovery.

Conclusion: With the large number of poisoning cases received daily in emergency departments, prompt and effective use and administration of antidotes can prevent significant morbidity and mortality in patients. Therefore, it is crucial that all health care professionals (HCPs) are educated and updated on proper administration and criteria for use of antidotes. It is also important that awareness programs for HCPs are conducted regularly to update the current directory of information regarding antidote utilization.

Keywords: Antidote, Antidote Utilization, Poisoning, Atropine

187 Adherence and associated factors of treatment regimen in drug-susceptible tuberculosis patients

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Background: Adherence to tuberculosis (TB) drugs is one of the key aspects of global TB control, yet there is a lack of epidemiological evidence on the factors influencing adherence to TB drugs. Thus, this study aimed to explore the adherence and factors associated with adherence among TB patients in South Korea.

Methods: We conducted a cohort study using a sampled national healthcare database from 2017 to 2018. Our study population included incident TB patients initiating quadruple or triple regimen who were available for follow-up for 180-days. Adherence was evaluated using the proportion of days covered (PDC): 1) adherent group: patients with PDC ≥80%; 2) non-adherent group: patients with PDC <80%. Kaplan-Meier analysis was conducted to calculate the median time-to-discontinuation in the study population. We calculated the adjusted odds ratios (aOR) with 95% confidence intervals (CI) to assess factors associated with adherence to TB drugs using logistic regression.

Results: Of 987 patients, 558 (56.5%) were adherent and 429 (43.5%) were nonadherent, with the overall mean PDC of 68.87% (standard deviation, 33.37%). The median time-to-discontinuation was 113 days (interquartile range 96–136) in the study population. Patients initiating quadruple regimen were more likely to adhere in comparison to the triple regimen (aOR 4.14; 95% CI 2.78–6.17), while those aged ≥65 years (aOR 0.53; 95% CI 0.35–0.81), with a history of dementia (aOR 0.53; 95% CI 0.34–0.85), and with
history of diabetes mellitus (aOR 0.70; 95% CI 0.52–0.96) were less likely to adhere to the drug.

Conclusion: Approximately 45% of TB patients were non-adherent to the drug, which is a major concern for the treatment outcome. We call for intensified attention from the authorities and healthcare providers to reinforce patients' adherence to the prescribed TB drugs.

Keywords: adherence, drug-susceptible tuberculosis, nationwide study, discontinuation, claims database

188 Sub-optimal use of evidence-based medical therapy in chronic limb-threatening ischemia patients undergoing lower-limb revascularization in Singapore

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Aim/Objective: International Guidelines strongly recommend that all patients with chronic limb-threatening ischemia (CLTI) receive statins and antiplatelets, and control their hypertension and diabetes. However, adherence is highly variable. The aim of this study was to determine the pattern of evidence-based medical therapy (EBMT) use in CLTI patients.

Methods: This was a retrospective cohort study of all patients undergoing lower-limb revascularization from May 2018 to December 2019. De-identified data comprising demographics, visit details, comorbidities and dispensed drugs were extracted from electronic medical records. For each of the 4 classes of EBMT (statins, antiplatelets, antihypertensives and antidiabetics), 5 measures of EBMT use were calculated: i) use at admission, ii) use at discharge, iii) proportion of days covered (PDC) in 1-year period post-discharge, iv) time to non-persistence and v) time to starting EBMT. Time-to-event outcomes were analysed using competing risks analysis with death as the competing event.

Results: 756 patients were included. The proportions of patients taking statins, antiplatelets, antihypertensives and antidiabetics at admission were 66.3%, 51.5%, 61.0% and 44.5%, respectively. The corresponding proportions at discharge were 85.7%, 91.1%, 88.2% and 71.3%, respectively. The corresponding median 1-year post-discharge PDC were 41.0%, 68.1%, 89.3% and 51.6%, respectively. Among those who were on EBMT at discharge, the 1-year cumulative incidence of non-persistence of all 4 classes of EBMT ranged from 61.8% to 70.7%. Among those who were not on EBMT at discharge, the 1-year cumulative incidence of starting EBMT ranged from 11.1% to 38.5%.

Conclusion: A significant proportion of CLTI patients are not receiving the necessary EBMT during presentation and follow-up. Treatment appears to be instituted for most patients during admission but about two-thirds stop taking their medications within 1-year post-discharge. Further research is needed to understand the factors affecting treatment decisions and patients' medication adherence.

Keywords: medication adherence, peripheral arterial disease, CLTI, drug utilization

189 Treatment escalation among steroid dependent patients in inflammatory bowel disease: Before and after approved policy on biologicals

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Background: Since biologics approved for inflammatory bowel disease (IBD), use of immunomodulators (IMM) was changed. However, limited information associated escalation to IMM after the impact of policy. The aim of this study was to assess the magnitude of treatment escalation in IBD patients with steroid-dependent between pre- and post-biological era.

Method: A retrospective cohort study using National Health Insurance Database (2003-2018), patients with IBD, had 1 hospitalization or 5 diagnoses for ulcerative colitis (UC) or Crohn's disease (CD) and at least 4 claims for IBD medications within 1-year following 1st diagnosis, met the criteria of steroid-dependency, defined as more than 3 months steroid use and an any dose is over 10 mg of prednisolone equivalent from the 3rd month. Patient with 1st IBD-related prescription after 2011/7/1 (reimbursement of adalimumab for CD) was assigned to post-biological group (POB), and vice versa to pre-biological group (PRB). The proportion of treatment escalation of IMM in the first 1 month, 1-3 months and 3-6 months after index date (1st date of steroid prescribed) was determined.

Result: A total 1076 patient were included, PRB/POB (CD :180/188, UC:373/335). After excluded prevalent patients, experienced IMM half-year prior index date, treatment escalation of IMM within first 1 month, 1-3 months and 3-6 months was 2.7%, 2.0%, 1.4% in PRB and 6.3%, 10.5%, 7.4% in POB, respectively. Overall, within first 6 months in PRB and POB, the proportion of treatment escalation was 6.1% and 24.2%. We also found the similar trend of treatment escalation in UC patients within first 1month, 1-3 months and 3-6 months was 1.2%, 0.9%, 2.4% in PRB and 5.8%, 4.6%, 2.9% in POB, respectively.

Conclusion: After the policy of biologics, explicit early awareness of IMM treatment escalation was found in IBD patients with steroid-dependent, especially in CD patients.

190 Nationwide patterns of prescribing contraindicated drug-drug interaction pairs in Korea

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Objective: We aimed to identify the outpatient prescribing pattern of contraindicated drug-drug interaction (DDI) pairs in Korea.

Methods: Using 2018 Health Insurance Review and Assessment Service-National Patient Sample data (HIRA-NPS), we extracted prescriptions containing contraindicated DDI pairs according to Korea's Drug Utilization Review (DUR) criteria. We grouped DDI pairs by the third level name of the WHO ATC code. The proportion for the pair was derived from the ratio of the number of prescriptions containing both and the number of prescriptions containing either one. For each DDI pair, we applied the risk rating from Lexicomp® Drug Interactions.

Results: From the 28,313,162 prescriptions of HIRA-NPS 2018, 18,018 had DDI pairs. Patients were aged 65 or older in 1,817 (10.0%). The majority were issued by clinics, with 6,751 (37.5%) among healthcare providers. The most prescribed DDI pair was "NSAIDs+NSAIDs" (15,402 prescriptions, 0.097%). The risk rating from Lexicomp was X (Avoid combination) since it increases the risk for gastrointestinal toxicity. "Propulsives+Propulsives" (831, 0.10%) was second, designated as a contraindication in the DUR criteria due to QT interval prolongation concerns. Among the top DDI pairs, "Quinolones+Anxiolytics" (225, 0.0084%) was rated B (No action needed), where ECG monitoring may be considered in patients only at high risk for QT interval prolongation.

Conclusion: Although the proportions were all low, there were several contraindicated DDI pairs with high-risk ratings. Further studies that analyze the clinical necessity and risk of those pairs are needed.

Keywords: Drug Utilization Reviews, Drug Interactions, Drug Prescriptions, Republic of Korea

191 Pregnancy outcomes of women on antiretroviral therapy in Jos University Teaching Hospital: A retrospective study

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Background and Objectives: Antiretroviral therapy (ART) transformed infection with human immune deficiency virus from a death sentence to a chronic syndrome. Thus, infected individuals could lead a life as near normal as possible, including getting pregnant and bearing children. Notwithstanding, concerns remain about effects of ART in pregnancy. Previous studies on the ART and pregnancy outcomes yielded contradictory findings. Therefore, objectives of this study were to determine proportion of adverse pregnancy outcomes in a cohort of pregnant women who accessed ART from Jos University Teaching Hospital between 2004 and 2017; and to identify predictors of these outcomes.

Methods: This retrospective study of 5080 participants used a pro-forma to abstract data, which were managed using IBM's statistical package for the social sciences SPSS® version 22.Chi-squared test for independence was used to calculate proportions of pregnancy outcomes. One way analysis of variance tested the effect of antiretroviral drug regimens on mean birth weight and gestational age at delivery. Multivariate logistic regression was used to determine predictors of adverse pregnancy outcomes. All levels of significance were set at $p < 0.05$. Ethical and administrative clearances were obtained from relevant authorities.

Results: Adverse pregnancy outcomes were: stillbirth 0.2%, preterm delivery 6.6% and low birth weight 23%. There was statistically significant association between ART in pregnancy and low birth weight. ($\chi 2$ [(5, n= 3439) = 11.99, p= 0.04]). Highest mean birth weights were recorded in women on drug combinations with protease inhibitors or nevirapine, in contrast to those on stavudine and truvada based regimens. Maternal age, ART initiation before pregnancy, duration of foetal exposure to ART and maternal viral load were significant predictors of adverse pregnancy outcomes.

Conclusion: Findings support benefits of early ART initiation in pregnancy, with no strong evidence of a link between individual ART regimens and the observed outcomes.

192 Influencing factors for medication in patients with mental disorders in middle-aged-older Chinese: Results from Charls

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Backgrounds: Mental disorders are common in China, especially among middle-aged-older people, who are unable to adapt to the changes in social roles, social relationships and physical functions brought by retirement and other factors. As a result, they may suffer from anxiety, depression and even suicide. Effective medication can reduce the functional disability and complications in patients. Thus, accelerate the rehabilitation process and save social resources.

Objective: To explore the medication rate and its influencing factors in the middle-aged-older population with mental disorders in China.

Methods: Data were collected from China Health and Retirement Longitudinal Study (CHARLS) over the period from 2011 to 2015. We analyzed the prevalence of mental disorders and drug treatment and compared demographic, health status and functioning data between non- medication and medication groups. Influencing factors were estimated by using Logistic regression.

Results: In 2015, a total of 19,246 participants aged 45 years and older were included in this study. The prevalence of mental disorders slightly increased from 0.75% in 2011 to 0.82% in 2015. As for medication, although the percentage of patients who didn't take any treatments dropped from 56.73% in 2011 to 54.48% in 2015, taking sleeping pills was the first preferred treatment (about over 20%). Compared with medication group, non- medication group showed higher proportion of female and patients with better physical ability (P<0.05). Logistic regression analysis showed that the major risk factors was patients with better physical ability (OR=1.71,95%CI:1.20-2.43).

Conclusion: As the prevalence of mental disorders increased, the proportion of taking medication in elderly patients was relatively low in China. Unlike other diseases, mental disorder is often ignored by middle-aged-older people, especially in those with good health, intervention and education should be strengthened for those patients.

193 Effect of drug subsidy policy on empagliflozin utilisation in Singapore: An interrupted time series analysis

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Aim: On 1 October 2018, empagliflozin was included on the Medication Assistance Fund (MAF) as a second-line therapy for managing type 2 diabetes mellitus (T2DM). The MAF provides financial assistance to eligible patients at public healthcare institutions (PHIs). This study assesses the effect of MAF listing on empagliflozin utilisation.

Methods: We conducted an interrupted time series analysis using dispensing data from January 2017 to December 2020. Segmented regression models were constructed to assess the degree of level change (LC) and trend change (TC) in utilisation volume by defined daily doses (DDDs), before and after subsidy implementation. Autocorrelation was tested and corrected by including an autoregressive or moving average term in our models. We performed subgroup analyses by care setting (hospitals and polyclinics) and patients' subsidy status (subsidised and private) to explore possible differential effects, and sensitivity analyses using volume per T2DM patient as the outcome measure.

Results: The overall utilisation trend (in thousand DDDs per month) increased from 2.5 to 19.5 post-subsidy, with a significant TC of 17.1 (95% CI 15.7,18.4). The TC in subsidised patients was significant [16.3 (95% CI 15.1,17.6)], but not in private patients [0.5 (95% CI -0.04,1.0)]. Significant TC was observed in both polyclinics [14.8 (95% CI 10.9,18.7)] and hospitals [2.3 (95% CI 0.7, 4.0)]. The proportion of empagliflozin utilisation in subsidised patients increased from 70% in September 2018 (pre-subsidy) to 90% in December 2020, while the proportion of empagliflozin utilisation in polyclinics increased from 0.2% to 63%, respectively. No significant LC was observed in all the models. Similar results were found using volume per T2DM patient in the sensitivity analyses.

Conclusion: The drug subsidy policy had a significant positive impact on the utilisation trend of empagliflozin, particularly, in subsidised patients and in the polyclinics.

Key words: Empagliflozin; drug subsidy; interrupted time series; Singapore

194 Evaluation of antimicrobial use and its impact in a private and public hospital: A prospective comparative from in India.

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Objectives: To evaluate the inappropriateness of antimicrobials prescription and comparing the clinical and economic outcomes in a private hospital and a public hospital in the Indian state of Kerala.

Methods: This prospective observational study evaluated and compared the use of antimicrobial agents (AMAs) given for the treatment of infections in patients with the signs of infection or diagnosed with an infection in Private and Public hospitals, which were the sites of study.

Result: Among the total 216 patients included, 143 and 73 were enrolled from the government and private hospital respectively with age category 31 -60 and female gender being predominant. Urinary tract infections and dengue are the frequently observed infection in Government and Private hospitals respectively. Even though the MA use pattern revealed that the government hospital is found superior in terms of the average number of antimicrobials prescribed per hospitalization (2.06 versus 1.72) and average duration of antimicrobial therapy (5.24 vs 4.86), the private hospital is found dominant in terms of average cost of (86.47 vs 31.04). Cephalosporins, broad-spectrum antibiotics, and the injectable dosage form are commonly used in the government as well as the private sector. On evaluating the adherence of prescribed antimicrobial therapy towards standard treatment guidelines of the corresponding infectious diseases, the majority of Lower Respiratory Tract Infections and Urinary Tract Infection cases were fully adherent. Education ($p<0.001$) and economic status ($p=0.044$) of the patient had a statistically significant association with the selection of antimicrobial protocol.

Conclusion: Irrational AMA usage can lead to resistance and further complications. Antibiotic usage must be limited to the necessary conditions according to the standard guidelines and prescribing indicators.

Keywords: Antibiotics, Antibiotic Resistance

195 Outcomes and adverse events of methylphenidate treatment in pediatric patients: A cross-sectional study

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Objective: To determine the prescribing pattern, clinical outcome, and adverse drug events (ADEs) of treatment with methylphenidate in pediatric patients.

Method: A retrospective, cross-sectional study was conducted in pediatric patients age 6-18 years, started treatment with methylphenidate and received care at a child and adolescent psychiatric hospital during October 2016 to September 2018. Patient demographics, diagnosis, type of medication, age at first prescription, dose adjustment, clinical responses and ADEs were extracted from medical charts and electronic hospital database.

Results: From 156 patients, 85.2% was male, and the average age when methylphenidate was initiated was 8.1±1.6 year. Methylphenidate was mainly prescribed for ADHD (93.6%) and initiated as monotherapy at the dose of 2.5-5.0 mg/day (60.0%), while maintenance dose was 5.0-10.0 mg/day in 42.5% of the patients. In one year of the treatment, 45.8% of the patients continued the same dose, while 43.1% dose increased and 11.1% dose decreased. Symptom improvement was reported in 88.4% of the patient after one-year treatment without dose adjustment. ADEs occurred in 12.2% of the patients, including loss of appetite (5.8%), headache (2.6%), nausea/vomiting and drug allergy (1.3% each). Management of ADEs included decreased dose (42.1%), mediation discontinuation and prescribing of other medications (26.3% each).

Conclusion: Methylphenidate was frequently prescribed for the treatment of ADHD in pediatric patients, initiated at low dose, and produced good outcomes with some common ADEs observed in one year.

Key words: methylphenidate, ADHD, adverse drug event

196 Drug Use Evaluation on Favipiravir for COVID-19 Patients, Hua Hin Hospital

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Aims: To evaluate an appropriate prescription of Favipiravir in term of indication, dose, effectiveness and safety according to a criteria created by Hua Hin Hospital.

Method: This retrospective study collected data from the electronic database of patients who received favipiravir at Hua Hin Hospital from 1 to 29 May 2021.

Results: A total of 157 patients who received favipiravir with an average age of 34.31 ± 15.64 years and 98 patients were females (62.42%). In term of indications, 153 patients (97.45%) had an appropriate prescription according to the criteria. Among cases with appropriate prescribing, the most common indication was proven invasive SARCoV2 by nasopharyngeal swab of respiratory sample with the Chest CT scans. Regarding to dose, 154 patients (98.09%) were given the correct dosage regimen according to the criteria. In term of efficacy, good responses and had a 5day dosing duration were found in 122 patients (77.71%), treatment failure and duration of dosing was more than 5 days in 35 (22.29%). The average dosing duration was 6 ± 1.95 days. About safety caution, no prescribing was found in patients with caution. Adverse drug reaction were found in 6 patients, where the most found adverse drug reaction was abdominal discomfort (4 patients or 2.55%).

Conclusion: Most patients (96%) received appropriate prescription of Favipiravir in term of indication and dose according to the criteria. As a result, the effectiveness of favipiravir was about 77% and safety was about 90% of the patients.

197 Impact of guideline on prescribing practice in antipsychotics in patients with dementia

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Aim/Objective: The study aims to assess if there is a change in prevalence of antipsychotics prescriptions in patients with dementia following the American Psychiatric Association guideline on antipsychotics use in dementia patients.

Methods: This is a retrospective population-based study using data from Clinical Data Analysis and Reporting System. We identified patients of all ages who were diagnosed with any types of dementia from 2001 to 2019. All their regular outpatient and discharge prescription for antipsychotics from 2005 to 2019 were studied. Trends of prevalence and duration of use were analyzed. A segmented linear regression was conducted with pre-specified breakpoint at the date of publication of the guideline in 1st May 2016. A sensitivity analysis was conducted using the R-package "segmented" wherein the breakpoint was automatically estimated by the model instead of pre-specified.

Results: A total of 148,834 patients with dementia and 45,657 outpatient and discharge prescriptions for regular antipsychotics were identified. A significant but small level increase was found in the prevalence of antipsychotics prescriptions around publication of APA guideline in May 2016 using segmented regression analysis. The estimate of level change was 4.85 x10-3 (95% CI: 1.19x10-3 – 8.52 x10-3, p = 0.0103). No significant slope change was found. Sensitivity analysis using R package "segmented", reported one breakpoint in November 2014 with decreasing slope before and a smaller decreasing trend after the breakpoint, indicating that no significant change in prevalence were found around publication of APA guideline in May 2016. An increasing trend of antipsychotics being prescribed for longer than 4 months, which was the maximum duration recommended, was observed.

Conclusion: Publication of the guideline did not have much impact on the prescribing practices of antipsychotics in patients with dementia.

Keywords: antipsychotics, prescribing trend, dementia

198 Drug utilization review on antimicrobial agents in ENT Department

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Introduction: Drug utilization studies are used as potential tool in the evaluation of the healthcare system. The disease of ear, nose, and throat are very common problems in the general population and cause impairment in routine life.

Aim: To review the drug utilization pattern of antimicrobials in an Ear nose and throat department and assess the rationality of antimicrobials used in the ENT department.

Method: A Prospective study was carried out in the ENT outpatient department of Adichunchanagiri Hospital & Research Center for 3 months. All the patients who had been prescribing with antimicrobials in the ENT department were included. The rationality of antimicrobials was assessed by using Kunins modified criteria.

Results: A total of 225 prescriptions were studied. 51.5% were female and 48.4% were male. The most common disease reported was Acute tonsillitis (23.9%) followed by Acute otitis media (15.3%). The most common antibiotics prescribed were Cefopodoxime/Clavulanic acid (36.57%) followed by Amoxicillin/clavulanic acid (19.45%). 94.4% of antimicrobial agents were prescribed by brand names. As per Kunin's modified -criteria, 87.5% of antimicrobials were prescribed appropriately and 12.4% of antimicrobials were prescribed inappropriately.

Conclusion: The females are more susceptible than males to ENT infections. cefpodoxime/clavulanic acid was the most common antimicrobial prescribed and acute tonsillitis was the most common disease identified. The study concludes that there is a scope of improvement in the case of medicines prescribed by generic name.

Keywords: Drug Utilization, ENT, Antimicrobials, Rationality, Kunin's modified criteria

199 Evaluation of empirical antibiotics for community acquired pneumonia in a hospital in Indonesia

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Objective. The study aims to describe the suitability of empiric antibiotics against the antibiogram profile and treatment outcomes in inpatients with CAP in a Hospital.

Methods. This study was conducted under the descriptive-analytic observational study design with a retrospective cohort design where the data source came from secondary data, namely the medical records of community pneumonia patients in 2019 and hospital antibiogram data. The data were collected by using the total sampling method.

Results. There were 79 community pneumonia patients. There was no significant relationship between the suitability of empirical antibiotics to the leukocytes (p = 0.550; RR = 0.725; 95% CI = 0.252-2.086), temperature (p = 0.545; RR = 0.576; 95% CI = 0.049-6.747) and length of stay (p = 0.631; RR = 0.767; CI95 = 0.258-2.275).

Conclusion. There was no significant relationship between the appropriateness of empirical using of antibiotics and antibiogram profile (p>0.05).

200 Pharmacoepidemiology of antibacterials use by Russian hospitals during the period 2009-2019

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Objective: The Russian hospital antimicrobial procurement accounted for substantial public costs. Around 30% of budget funds are spent for ATC group J Antiinfectives for systemic use by Russian hospitals annually. The evaluation of hospital antibiotic consumption trends and patterns is key to correct antimicrobial procurement.

Materials: The retrospective pharmacoepidemiological study of the hospital procurement dynamics of ATC group J01 Antibacterials for systemic use in Russia was carried out. The study based on hospital procurement data posted in public resources of electronic trading platforms and the IQVIA Holdings Inc. database. Detailed analysis was performed for recently approved in Russia antibacterials active against the ESKAPE pathogens: piperacillin/tazobactam, daptomycin, tigecycline, ceftaroline fosamil, telavancin, dalbavancin, ceftazidime/avibactam, cefotaxime/sulbactam, ceftolozane/tazobactam, cefepime/sulbactam.

Results: The Russian hospital procurement of J01 in value terms remained steady at of 14-16 billion Russian rubles (RUB) per year, despite the negative dynamics in natural volume of consumption. A stable growth had been recorded for selected antibacterials in 2009-2019, the annual growth rate was 122%. By 2019, purchases of selected antibacterials have expanded to 1.5 billion RUB thus amounted 9% of public funds spent on the J01. Dynamics of the selected antibacterials procurement in Moscow varied significantly. The largest amount of budgetary funds spent on tigecycline as 36% of total. Enormous amounts of cefotaxime/sulbactam purchased by Moscow hospitals in 2019 at more than 210.000 packages, while dalbavancin was purchased only as 30 packages per 2018. Volumes of piperacillin/tazobactam remained flat as 46.000 packages average per year.

Conclusion: The study showed the increase of public expenditures on antibiotics against the ESKAPE in recent years in Russia. Original imported antibacterials purchased in small volumes while Russian generics and original ones well over. The trend noticed towards Russian antibacterials in the 2018-2019. The overall consumption of J01 antibacterials reduced in natural terms while selected antibiotics expanded.

201 Evaluation of epidemiology in poisoned patients and cost analysis of antidotes at a tertiary care hospital

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Aim/Objective: To evaluate regional epidemiological data on poisoning from the poisoned patients and assess the economic outcome of the antidote prescribed.

Methods: The study design employed was a prospective observational study conducted in a teaching tertiary hospital for a period of 6 months. Data was obtained from the patient's case sheets with their consent and was duly filled into data collection forms. The collected epidemiological data were reviewed and analyzed using the chi-square test and the economic outcome of the antidotes prescribed was analyzed using cost-minimization analysis.

Results: Out of 117 cases, 21.36% (n=25) of the victims were residents of rural areas followed by 78.63% (n=92) from the urban areas out of which the gender from urban and rural were males (11.11% and 48.71%) and females (10.25% and 29.91%). The subgroup analysis of urban areas using the Chi-square test was performed, a statistically significant p-value (P=0.002) was obtained. The male population located in urban areas was found to be at a higher risk of poisoning. The majority of the poisoned patients came from the urban areas with Pesticide poisoning (34) followed by Drug overdose (30) and rodenticide(12). The economic outcome was assessed for 10 antidotes used in various poisoning by comparing the cost between different brands.

Conclusion: The findings of our study concluded that irrespective of gender urban residents were more prone to poisoning. Rational antidote administration will reduce morbidity and mortality. During critical management, unintended errors can be minimized with continuous monitoring. It is also important that cheaper alternatives are available in order to offer high-quality treatment to reduce the financial burden on the patient.

Keywords: Poisoning, Epidemiology, Cost, Antidote

202 Utilization pattern of anti-thrombotic agents in Peripheral Artery Disease patients with Chronic Kidney Disease: A nationwide retrospective cohort Study

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Objective: To evaluate prescribing pattern of Peripheral Artery Disease (PAD) patients with Chronic Kidney Disease (CKD) in Taiwan and the bleeding risk among different antithrombotic regimens.

Methods: We conducted a retrospective cohort study using the Taiwan's National Health Insurance Database (NHID) from 2011-2018 and selected adult (≧20 years old) patients who enrolled into pre-end stage renal disease program (Pre-ESRD program) with newly PAD diagnosis in the program and had any antithrombotic agents within 3 months after newly PAD diagnosis. The date patient used antithrombotic drug was defined as index date. We grouped them based on which antithrombotic agents they used on index date and follow-up them 1 year to observe whether a major bleeding event occurred . We use intention-to treat (ITT) analysis and cox proportional hazard model to assess major bleeding risk.

Results: We identified 2,573 patients. The prescribing pattern of them consists of mono-antiplatelet (70%) followed by antiplatelet combination (24%) mono-anticoagulants (4%) and lastly antiplatelet plus anticoagulant (2%). Patients with atrial fibrillation (AF)、venous thromboembolism (VTE) prefer to use mono-anticoagulant than mono-antiplatelet. The result of secondary bleeding outcome showed that both mono-anticoagulant and antiplatelet combination treatment have a significantly higher major bleeding risk than mono-antiplatelet therapy (HR： 1.385 (1.044-1.837) and 1.227 (1.076-1.398) respectively.)

Conclusion: The findings indicated that prescribing pattern among PAD patients with CKD in Taiwan are mainly composed of mono-antiplatelet treatment. Also, mono-anticoagulant or antiplatelet combination users were associated with significantly higher major bleeding risk than mono-antiplatelet group.

Key word: Peripheral artery disease, Chronic kidney disease, Prescribing pattern, nationwide cohort study

203 Long-term utilization of extended-release methylphenidate among patients with attention-deficit hyperactivity disorder in Asia and North America

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Aim: Attention-deficit hyperactivity disorder (ADHD) is a psychiatric condition typically marked by childhood onset with (or without) a persistent course to adolescence or adulthood. This study aimed to provide knowledge on real-world long-term utilization of extended-release methylphenidate (ER-MPH) among people with ADHD in different countries.

Methods: This was a retrospective cohort study using Japan Medical Data Center (JMDC) database from 2008-2019 and the IBM Commercial Claims and Encounters (CCAE) database from 2000-2019. ADHD patients who initiated ER-MPH during childhood (6-12 years) or adolescence (13-17 years) were first identified, and only those who were enrolled in databases for two or three successive life stages (i.e., childhood-adolescence or early adulthood, and adolescence-early adulthood) after ER-MPH initiation were included in this study. Proportions of long-term ER-MPH users were calculated, and ER-MPH consumption was described. Long-term use was defined as using ER-MPH for two or more life stages continuously or intermittently.

Results: In the JMDC and CCAE, 4,934 and 160,142 eligible patients were included, with mean ages at cohort entry of 11.8 (SD: 2.7) years and 11.7 (SD: 2.9) years respectively. Long-term ER-MPH users accounted for 55.3% (N=2,632) in JMDC and 38.6% (N=61,826) in CCAE. Among the long-term users in JMDC, the majority (73.3%, N=1,930) used ER-MPH from childhood to adolescence, with a mean prescription number of 36 (SD: 28) covering a mean overall duration of 48 (SD: 24) months. Similar to JMDC, 74.9% (N=46,288) of long-term ER-MPH users in CCAE used it from childhood to adolescence, and the mean prescription number was 22 (SD: 18) covering a mean duration of 41 (SD: 24) months.

Conclusions: Among ADHD patients with ER-MPH treatment, a substantial proportion of patients used it for long term and similar results were observed in Asia and North America.

Keywords: extended-release methylphenidate, long-term utilization, ADHD, Asia and North America

204 Evolving trends in consumption of direct oral anticoagulants in 65 countries from 2008 to 2019: Analysis of pharmaceutical sales data

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Aim/Objective: This study aimed to describe global patterns and trends in consumption and cost of each DOAC with comparisons across geographical regions. Understanding DOAC consumption at an international level help identify regional differences and provide evidence for formulating national policies.

Methods: We conducted a cross-sectional study using pharmaceutical sales data from IQVIA to estimate consumption of each DOAC in 65 countries from Q4 2007 to Q2 2019. We assessed consumption trends, proportion of use, time to adoption and manufacturer price of each DOAC by country and geographical region.

Results: The average consumption of dabigatran, rivaroxaban, apixaban and edoxaban in the countries studied were 0.31, 1.05, 1.08 and 0.78 defined-daily-doses/1000-inhabitants/day for respectively in Q2 2019, compared to 0.23, 0.54, 0.21 and 0.03 in Q2 2015, with highest consumption in Western and Northern Europe, and lowest in Southern and South-Eastern Asia. In most countries, rivaroxaban accounted for greatest proportion and more than 30% of DOAC consumption, whereas dabigatran accounted for less than 30%. Edoxaban accounted for less than 20% in Northern America and Europe but contributed a significant portion in Japan (28.58%) and South Korea (31.37%). The costs of all DOACs were approximately 6 times higher in US than other countries where costs were generally lower than 3 USD/day-of-therapy. No significant correlation was observed between cost and consumption of individual DOACs considering all countries as a whole.

Conclusion: Regional differences exist in consumption patterns and trends of each DOAC. Consumption of rivaroxaban and apixaban gradually overtook dabigatran in most countries. Use of edoxaban remains limited except in certain East Asian countries. Adoption of apixaban and edoxaban is relatively delayed compared to dabigatran and rivaroxaban. There is no significant correlation between consumption and manufacturer price of DOACs in general.

Keywords: Direct oral anticoagulants; global consumption patterns; time to adoption; price

205 Prescribing antibiotics in children by primary care physicians

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Objective: This study evaluated attitudes of primary care pediatricians and family physicians concerning prescribing antibiotics in children.

Methods: Survey was conducted in all 11 regions of Armenia. A questionnaire was developed, pretested and distributed to pediatricians and family physicians in primary health care settings.

Results: 80.6% of 293 responded pediatricians and family physicians reported that they are “completely” and “mainly” agree that when prescribing antimicrobial medicines for children local doctors select medicines from the Armenian List of Essential Medicines (AEML), 69.2% consider that doctors select from the World Health Organization Model List of Essential Medicines for children and 72.0% believe that medicines are selected from national clinical guidelines (NCGs) approved by the Ministry of Health, Armenia. 64.8% of physicians reported that they mainly prefer monotherapy. 24.0% of participants prescribe antibiotics after microbiological test. When asked about selecting the medicine for the first-line empiric treatment of pneumonia in children, 45.2% of participants indicated amoxicillin, 27.0% - amoxicillin/clavulanic acid, 19.6% - ceftriaxone. In total, 12 different medicines were pointed, although approved NCGs recommend only amoxicillin. When asked about the second-line empiric treatment for pneumonia in children, 40.0% of participants pointed azithromycin, 27.0% - ceftriaxone, 11.0% - amoxicillin/clavulanic acid. In total, 20 medicines were indicated by participants as a second-line treatment in children with pneumonia; only 8 of 20 of mentioned medicines were in line with NCG.

Conclusions: The majority of primary care physicians believe that doctors prescribe in children antimicrobials which are selected from appropriate approved documents - AEML and NCGs. However, only less than a half of pediatricians and family physicians prescribe a medicine recommended by the approved NCG, as the first-line empiric treatment for pneumonia. Educational strategies could be useful for improving physicians’ knowledge and adherence to treatment guidelines.

Keywords: prescription patterns, antimicrobial medicines, children

206 Oxytetracycline residues in chicken table eggs sold in Gombe, Nigeria are within acceptable levels but may have cumulative effect

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Aim/Objective: The study detected and quantified OTC residues in chicken table eggs from selected poultry farms in Gombe, Nigeria using High Performance Liquid Chromatography (HPLC) technique.

Methods: Five poultry farms were randomly selected in Gombe, Nigeria. Validated questionnaire was used to obtain information on farm practices at the farms. Thereafter, 165 eggs were randomly collected over three-week period (11 eggs/farm/week) from the farms. Each egg was broken, the content was weighed and homogenized. From 5g of each sample, OTC was extracted as previously described by United States Department of Agriculture, Food Safety and Inspection Services. HPLC system was calibrated using 0.008, 0.016 and 0.032 µg/ml of standard OTC, a linear curve was prepared and detection limit was established at 0.005 µg/ml. OTC was detected at wavelength of 350 nm and retention time of 8±0.5 minutes. OTC residues in the homogenized eggs were determined by separately running 100 µl of extracted OTC samples in the calibrated HPLC system. Each sample was ran in triplicates. Maximum residue limit (MRL) of 400 µg/kg was adopted as prescribed by Codex Alimentarius Commission.

Results: The prevalence of detectable OTC residue in the egg sample was 92.7 % (153/165) and was similar across the five farms sampled ($p>0.05$). The overall mean concentration of OTC in the 153 eggs with detectable level was 51.1±36.5 (22.9-193.1) µg/kg and this was highest among eggs collected from farm B with mean value of 164.4±17.0 µg/kg ($p<0.05$). All the 153 eggs with OTC residue had values lower than MRL.

Conclusion: The prevalence of OTC residue in eggs from poultry farms in Gombe metropolis was high but the residue levels were within the acceptable limits. The eggs appear safe for human consumption, however, cautions must be taken to avoid cumulative effects of the residues.

Keywords: Oxytetracycline; Drug residue, Safety, Eggs

207 Effect of information provision using video media on patients' knowledge about antibiotics and anti-inflammatory drugs

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Aim/Objective: The purpose of this study was to compare the level of knowledge, understanding, and behavior about antibiotics and anti-inflammatory drugs before and after viewing the video media.

Methods: A quasi-experimental study. Which is a one-group research model, pre-post measurement results. Collect information from 79 people who come to serve in the outpatient dispensary area, Samitivej Srinakarin Hospital from 1 September 2019 to 31 December 2019. This study using self-answer questionnaires before and after watching video material.

Results: After watching video material, the average knowledge score of participants increased from 2.53 ± 1.3 to 4.86 ± 0.9 (full score of 6). Most patients mistakenly understood that antibiotics were able to eliminate all types of pathogens, both bacteria, and viruses (70.9%). While the mean behavior about antibiotics and anti-inflammatory drugs score increased from 1.47 ± 1.2 to 3.32 ± 0.7 points (a full score of 4). Most patients are of the opinion that when having a cold, fever, sneezing, cough, sore throat, clear mucus, they will immediately take antibiotics. To expect the symptoms to speed up (69.6%). Found that after watching video media, participants had higher knowledge scores and drug-use behavior scores before viewing the video material, statistically significant ($p < 0.001$).

Conclusion: This study shows that the use of video media on antibiotics and anti-inflammatory drugs in hospitals may cause patients to have knowledge, understanding, and attitude about antibiotics and anti-inflammatory drugs use behavior more accurately.

Keywords: knowledge, antibiotics, anti-inflammatory drugs

208 Drug-related problems in prescribing for outpatients in Vietnam

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Objectives: Drug-related problems (DRPs) are one of the leading causes of treatment failure, hospital admissions, and deaths. We aimed to determine the prevalence and determinants of DRPs in outpatient prescriptions in Vietnam.

Methods: A retrospective cross-sectional study was conducted on outpatients at a provincial hospital in Vietnam. DRPs were classified according to the Pharmaceutical Care Network Europe classification (PCNE) of 2020 and were determined using Vietnam Ministry of Health guidelines, Vietnamese National Drug Formulary 2018, and the website drugs.com. Multivariable regression was used to identify the determinants of DRPs.

Results: The study included 500 patients (mean age 57.6 ± 15.2; 58.0% female). The proportion of prescriptions with at least one DRP was 53.0%. DRPs were classified including wrong time of taking medications (44.2%), inappropriate indication (24.2%), wrong time of dosing relative to meals (13.6%), major drug-drug interactions (7.4%), inappropriate frequency of use (5.7%), and inappropriate dosage (4.9%). Patients who were prescribed ≥5 drugs (OR=6.375; 95%CI=3.959-10.264; p<0.001), or who who had >2 diseases (OR=1.523; 95%CI=1.051- 2.206; p=0.026), or who were at the age 60 or older (OR=1.455; 95%CI=1.021- 2.074; p=0.038) were more likely to have DRPs.

Conclusion: The proportion of outpatient prescriptions with at least one DRP was quite high, especially in patients with >60 years old, >2 diseases, and ≥5 drugs. Further studies should evaluate the clinical relevance and appropriate interventions.

Key words: Drug-related problems; prescribing; outpatients; Vietnam.

209 Antibiotic prescribing and cost after implementation of rationale drug use policy in health care settings in Thailand.

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Objective: To evaluate the effects of Rationale Drug Use (RDU) policy on antibiotic prescribing and costs in health care settings.

Methods: A cross-sectional study was conducted to measure antibiotic prescribing in defined daily dose (DDD) unit and cost of antibiotics. RDU policy was implemented in public hospitals in 2017. Both oral and injectable antibiotic prescribing and antibiotic cost were collected from electronic medical records from outpatient department at a secondary care hospital and 20 primary care hospitals (PCU) in Phimai district, Nakhonratchasima province, Thailand during fiscal year 2016 to 2019. Oral antibiotic prescribing was measured in DDDs per 1,000 out-patient visits per day for outpatients, while injectable antibiotic prescribing in inpatient department was measured in DDDs per 100 patient-bed day.

Results: In hospital, oral antibiotic prescribing in out-patients were decreased from 20.04 ± 3.22 in 2016 to 15.88 ± 1.84 DDDs/1,000 visits/day in 2019 (P=0.002). Likewise, the DDD of injectable antibiotics in in-patients were decreased from 108.27 ± 6.32 to 99.95 ± 6.21 DDDs/100 patient-bed day (P<0.001). In PCU, the oral antibiotics prescribing in out-patients were decreased from 50.06 ± 5.56 to 31.76 ± 2.72 DDDs/1,000 visit/day (P<0.001). Total cost saving of antibiotics was 1,321,064 Baht in 3 years.

Conclusion: There was a decreasing trend of antibiotic prescribing and cost of antibiotics in public hospitals after RDU policy implementation.

Keywords: Rationale Drug Use, Antibiotic, Defined Daily Dose

210 Criteria used by professionals for selecting resources of medicines information

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Aim: The aim of this study was to identify criteria which pharmacy professionals in Armenia use for selecting the sources of medicines information, as well as the main resources used by them.

Methods: Face-to-face interviews were conducted with 348 pharmacy professionals from all the regions of Armenia. The results were analysed using SPSS statistical software, version 22.0.

Results: The most of professionals consider the following criteria for selecting sources of medicines information as important and very important: accessibility (98.8%), recency (97.4%), comprehensibility (96.9%), reliability (94.3%), completeness (88.2%) and labour intensity (85.7%). All respondents use one or more sources of information. The great majority (88.2%) of respondents reported that they always and often look for medicines information in Patient Package Inserts. 66.7% of professionals seek information in the Reference book “Medicines” by M. D. Mashkovski; 44.8% - in the Reference book “Vidal”. 27.6% of responders seek information in the Armenian National Formulary (ANF). The number of professionals who always and often use ANF among those who completed continuing education courses is significantly higher than among those who have not completed ($p<0.001$). 59.5% of participants look for information on the Internet. Only 37.1% of participants noted that they would like to have an access to references with up-to-date information.

Conclusion: Although the great majority of professionals consider the main criteria, necessary for correctly selecting sources of information, as important, some of them still do not acknowledge enough value of using reliable, up-to-dated and comprehensive information. Professionals use different sources of medicines information, both printed and electronic. There is an urgent need in publishing a Reference book in Armenian that would include objective and up-to-date information on all the authorized medicines in Armenia.

Keywords: medicines information, resources, community pharmacists

211 The prevalence of inappropriate sale of drugs in grocery stores

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Objectives: To evaluation the situation of inappropriate distribution of drugs in grocery store.

Methods: This study is cross-sectional analysis research. The data were collected from a total of 27 stores in districts. Data were collected by pharmacists and consumer Protection Network, responsible for consumer protection in these districts, who had received training of procedure and instrument to collect the data.

Results: Of the grocery stores, 85.18 % distributed inappropriate drug. The percentages of grocery store selling “non-household and non-antibiotics drug”, traditional drug with non-household drug antimicrobial agent and Ya-Chud (several drug in same package intended to use for treating a particular condition) were 51.85%, 59.25% 22.22% and 3.70%, respectively. This study found 2 drugs without drug registration number. The most non-household and non-antibiotics drug were the drug with combined Paracetamol, Chlorpheniramine maleate and Phenylephrine, followed by paracetamol (package 100 tablets) and Dimenhydrinate (package 10 tablets). The most common antibiotic was Tetracycline, followed by Penicillin and sulfamethoxazole/trimethoprim. The most common sources of drug in grocery stores were modern drugstores, followed by wholesale stores and caravan of hawker. The drug storage in the stores ,60.86 % was inappropriate. The 77.77% of entrepreneurs have been trained about law prohibiting the sale of drugs in grocery stores 5 years ago, but found that 81.81% still sell inappropriate drugs.

Conclusion: A large number of inappropriate drugs in grocery stores in this study. This may lead to inappropriate use and drug resistance in the future. Therefore, all sectors should be involved and participated to resolve this problem.

Keywords: Grocery store, Inappropriate drugs Consumer Protection Network.

212 Reference books as sources of information on use of medicines in children

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Objective. Availability of high-quality information about medicines prescribed for children is an important precondition of their appropriate use. The objective of this work was assessing availability of information on use of medicines in children in reference books in the Republic of Armenia (RA).

Methods. Two reference books (National Formulary of RA (NF) and Vidal) were studied in order to identify availability of articles on 377 randomly selected medicines. Content of the articles was analyzed for assessing availability of information on use of a medicine in children. Reference books were selected based on the results of our previous study on identifying the main sources of information for family physicians and pediatricians working at primary health care facilities.

Results. In Vidal articles for 197 (52.3%) of 377 medicines studied were available, in NF- for 103 (27.3%). The percentage of selected medicines, articles about which are available and include any information on use in children, of the number of medicines articles about which are available, in Vidal was 61.4% (121of 197); in NF - 75.7% (78 of 103). In 10.2% of articles from Vidal and in 23.3% of articles from NF in which at least some information on use in children has been available, age of children was not specified. Information on the use of medicines in neonates and children up to one year was very limited. In Vidal the percentage of selected medicines, articles about which include any information on use in children, of the total number of medicines studied was 32.1% (121of 377); in NF - 20.7% (78 of 377).

Conclusion. There is a limited access to reliable information about medicines use in children in reference books used by family physicians and pediatricians in Armenia. Lack of information is a challenge for appropriate medicines prescribing.

213 Real-world evidence of herpes zoster's disease burden and characteristics: A retrospective study in Fuzhou, China

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Objective: Herpes zoster (HZ) leads to large disease burden in China, especially with the aging population. This retrospective real-world data analysis aims to evaluate epidemiological characteristics, treatments, and costs associated with HZ patients, in all ages and age 50 and above (50y+) in Fuzhou, China.

Methods: The regional healthcare data from 37 hospitals in Fuzhou were assessed during the period of 01/01/2015 to 12/31/2020, which covered 9.4 million residents. HZ cases and its related complications were identified using ICD-10 codes and the diagnosis names of corresponding diseases in Chinese.

Results: A total of 66,038 HZ cases were identified from 9,452,843 people, of which, 38,059 (57.63%) cases occurred in patients aged 50y+, including 1,148 recurrent HZ cases. Slightly more than half of the patients are female (33,607/66,038, 50.90%). The overall estimated incidence rate of HZ was 1.17 per 1000 person-years (PY), while the rate was 2.82 per 1000 PY in patients aged 50y+. The incidence of Postherpetic Neuralgia (PHN) in general population aged 50y+ was approximately three folders higher than in the overall (0.41 vs 0.14 per 1000 PY). HZ patients were commonly treated with western medicine, especially antiviral therapy (63.90%), while PHN patients were more frequently treated with neuropathy (57.13%) and analgesics (28.91%). The average HZ treatment cost of inpatient and outpatient were approximately ¥4038.72 and ¥44.23 per visit, respectively. However, the associated PHN treatment costs increased to ¥4043.16 and ¥102.17, respectively.

Conclusion: The real-world evidence shows that the incidence of HZ/PHN and recurrence of HZ increased by age. The antiviral therapy and neuropathy were most frequently used treatment among HZ and PHN patients, respectively. HZ patients with HZ-related complications (e.g., PHN) resulted in higher direct medical costs. Our study findings were consistent with similar studies in other regions of China.

Key words: Herpes zoster, postherpetic neuralgia, epidemiology, disease burden

214 Trends of polypharmacy in patients living with dementia from 2005 to 2019

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Title: Trends of polypharmacy in patients living with dementia from 2005 to 2019

Aim/Objective: The study aims to estimate the prevalence of polypharmacy and potentially inappropriate medications (PIMs) prescribed to patients with dementia.

Methods: This is a retrospective population-based study of patients with dementia in Hong Kong from 2005 to 2019 with data from Clinical Data Analysis and Reporting System.
We identified patients of all ages who were diagnosed with any types of dementia from 2001 to 2019. All their outpatient and discharge prescription from 2005 to 2019 that were intended for regular and systemic use were included in the analysis.
We defined polypharmacy and excessive polypharmacy as using 5 and 10 or more medications concurrently respectively. All medications whose prescribed duration span across or fell within the same calendar month were considered to be used concurrently. Annual prevalence and prevalence stratified according to different age groups was calculated.
We identified PIMs specified in Beer's criteria and Screening Tool of Older Persons' Prescriptions v2 criteria that were inappropriate for older persons with dementia. Annual prevalence of PIM and prevalence stratified by duration of prescriptions was calculated.

Results: A total of 148,834 patients with dementia and 20,711,114 outpatient and discharge prescriptions for regular systemic use were identified. Prevalence of polypharmacy increased from 2005 to 2019 across all age groups which has quadrupled in excessive polypharmacy in those aged 95 or older. The prevalence of patients with PIMs remained stable at 55% across the years, with an average of one PIM prescription per patient. Prescriptions of duration of ≤30 days was found to decrease across the years.

Conclusion: Monitoring of medication safety in patients with dementia is warranted with prevalences of polypharmacy and excessive polypharmacy increasing steadily and the prevalence of PIMs remained high.

Keywords: polypharmacy, PIMs, dementia

215 Using real world data to investigate the relationship between Chinese herbal medicine decoction pieces and acute kidney injury

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Objective: We aimed to investigate the relationship between Chinese herbal medicine decoction pieces (CHMDP) and acute kidney injury (AKI) by using real world practice data.

Methods: We performed a retrospective cohort study by using electronic medical records of a medical center in southern Taiwan. New users of CHMDP from 2017 to 2019 were identified and laboratory data of serum creatinine (SCr) were collected. We then compared the 3 months incidence rates of AKI before and after usage of CHMDP. AKI was defined as increasing in SCr to ≥1.5 times baseline within the prior 7 days or increasing in SCr by ≥0.3 mg/dl within 48 hours using Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guideline for acute kidney injury. We employed descriptive statistics to examine the patients' characteristics. Occurrence of AKI events were described by the Kaplan-Meier estimate curve, and the risk of AKI events before and after 3 months were compared by the Cox proportional hazard model and presented as hazard ratio with 95% confidence interval.

Results: There were 44 eligible patients in this study. This population was aged 57.8±16.6 (mean±SD) years and 59.1% were male. The incidence of AKI was 40.9/1000 person-months and 39.0/1000 person-months after and before usage of CHMDP. There was no significant difference in the Kaplan-Meier estimator curve (p=0.9545). The hazard ratio after usage of CHMDP was 1.037 (HR=1.037, 95%Cl 0.300-3.581, p=0.9545).

Conclusion: The results of the study showed that the use of CHMDP did not increase the short-term risk of acute kidney injury. However, this study was limited by the small sample size and the short-term safety evaluation. Large-scale studies are required to further evaluate the relationship between Chinese herbal medicine decoction pieces and acute kidney injury.

Keywords: Chinese herbal medicine decoction pieces, acute kidney injury, real world data

216 Incidence of nonalcoholic fatty liver diseases and their associated risk factors among type-2 diabetic population in Telangana, India

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Background and aim: The purpose of this study was to establish the incidence and factors linked with non alcoholic fatty liver disease (NAFLD) among type-2 diabetes mellitus (T2DM) patients in Warangal, Telangana state of India.

Methodology: It was an observation from cohort cross sectional study, a target sample of 100 T2DM patients were recruited from a single study site of Warangal. A detailed medical history and laboratory examinations and Ultrasound imaging was performed to evaluate the NAFLD.

Results: The overall incidence of NAFLD was 80%. The risk of NAFLD was significantly high in patients with uncontrolled blood glucose levels, abnormal waist circumference, increased aspartate aminotransferase (AST) and elevated triglyceride levels ($P<0.05$). In our study subjects, consumption of alcohol is the predominant risk factor (OR: 6.652; 95% CI: 1.86-23.74 and P=0.00*) significantly casing NAFLD among the study subjects.

Conclusion: Grade-1 and 2 fatty liver are typically associated with elevated AST levels and high incidence was observed in men.

Key words: Non-alcoholic fatty liver disease; type-2 diabetes mellitus; South India

217 Prevalence and characteristics of unsafe health products in community in Chiang Mai, Thailand

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Objective: This study aimed to examine the prevalence and geographic distributions of unsafe health products and factors related to the contamination of health products.

Methods: A cross-sectional study was conducted to collect unsafe health products, i.e., illegal-labeled medicines and cosmetic products with prohibited ingredients in households in Suthep subdistrict, Chiang Mai province, Thailand, according to announcement of Ministry of Public Health. Screening test kits for steroids in medicines, mercury compounds, retinoic acid, and hydroquinone in cosmetics were used to identify unsafe health products. Data on product label, registration number, product characteristics, color, and sources of products were collected and recorded in the standard form of the Department of Medical Sciences. Descriptive statistics were used to analyze the prevalence and geographic distribution of unsafe health products.

Results: The results showed that from 93 medicines surveyed in 120 households, 59.2% was unsafe medicines found in 51 households. Top three most common product problems included no registration number (39.8%), counterfeit registration number (10.8%), steroid contamination in traditional medicines (6.4%), while 65.2% was unsafe cosmetics from 92 products found in 56 households. This study found that 41.7% of the tested products was adulterated with prohibited substances such as mercury compounds, retinoic acid, and hydroquinone, while 26.1% had no registration number. Product characteristics and source of products were associated with adulteration of synthetic corticosteroids. (p=0.031 and 0.019, respectively).

Conclusion: The problems on unsafe health products were still prevalent in Suthep subdistrict. Appropriate interventions for consumer protection are needed.

Keywords: unsafe health products, steroids, unsafe cosmetics, public health pharmacy

218 Use of beta blockers and death from breast cancer in New Zealand breast cancer patients

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Background: Beta blockers (BB) have been associated with improved, worsened, or unchanged breast cancer outcomes in previous studies. This study examines the association between the use of BBs and death from breast cancer in a large, representative sample of New Zealand (NZ) women with breast cancer.

Methods: Women diagnosed with a first primary breast cancer between 2007 and 2016 were identified from four population-based regional NZ breast cancer registries and linked to national pharmaceutical data, hospital discharges, and death records. The median follow up time was 4.51 years. Cox proportional hazard models were used to assess the hazard of breast cancer specific death (BCD) associated with post-diagnostic BB use.

Results: Of the 14,976 women included in analysis, 21% used a BB after diagnosis. BB use was associated with an increased risk of BCD in unadjusted analysis (hazard ratio (HR): 1.49; 95% CI: 1.31-1.70), but after controlling for demographic variables, clinical variables, comorbidities, and other medication use, only a small and non-significant association remained (HR: 1.08; 95% CI: 0.93-1.26). The increased risk was seen only in those with at least one cardiac condition, and this was reduced by lagging the exposure by 2 years, suggesting that BBs first dispensed close to the end of life may be causing some of the excess risk. After adjustment, an increased risk confined to short term use (0-3 months) was seen (HR: 1.37; 95% CI: 1.11-1.70), but the risk of BCD was lower in those using BBs for more than 1 year, and this risk steadily decreased and became statistically significant at 3+ years of use (HR: 0.53; 95% CI: 0.33-0.85).

Conclusions: Any increased risk associated with BB use is likely to be due to a combination of short term use and confounding by indication. Long-term BB use may confer some protection for BCD.

219 Prescriptions errors and role of pharmacists in ensuring patient safety

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Objective: The objective of this work was to study prescriptions errors and involvement of community pharmacy professionals in ensuring patient safety in Armenia.

Methods: Community pharmacists and technicians from all the regions of Armenia were asked to complete previously designed questionnaire. 353 professionals completed self-administered questionnaire. Data were analysed with SPSS statistical software, version 22.0.

Results: 87.8% of respondents have reported that they observe prescribing errors when evaluating prescriptions at community pharmacy. 69.4% of pharmacy professionals have indicated that the main error is a wrong dose; 32.3% of study participants have pointed medicines interactions; and 32.0% - contraindications. Number of respondents from Yerevan, who have indicated wrong dose, is higher than number of those who are from other regions ($p < .001$). Only 5.1% of participants have reported that they register errors at pharmacy. 83.0% of pharmacy professionals have indicated that they always or often evaluate therapeutic aspects of prescriptions; 12.0% of professionals do it sometimes; and 3.0% of respondents - rarely or never. 42.2% of respondents have noted that, when patient is pressing, they never dispense a medicine without being sure that it is safe for a patient; 27.5% of professionals do it very rarely. 76.8% of responders are sure that their services ensure safe use of medicines by patients. 26.1% of pharmacy staff reported having Standard Operating Procedures (SOPs) at their pharmacy; 80.3% of professionals are interesting in introducing this strategy.

Conclusion: Various prescription errors are observed by community pharmacists; however pharmacy professionals mainly not register them (there is no such a requirement). In some cases prescriptions are not evaluated at community pharmacies. Approval of new standards for pharmacy practice seems to be very beneficial for improving patient safety. Recommendations are drafted for submitting to the Ministry of Health.

Keywords: patient safety, prescription errors, pharmacists

220 Effects of pharmacist-based education on drug allergies in hospitalized patients

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Objective: To evaluate the effectiveness of a pharmacist-based education on drug allergy in hospitalized patients with drug allergy.

Methods: A quasi-experimental study with a control group study was conducted at a university hospital. In-patients, age 18 years or older experienced drug allergies during hospitalization were included in this study. Patients were divided into education group and usual care group. Every patient who had drug allergies during hospitalization received drug allergy assessment and drug allergy card. Hospital pharmacist provided 15-minute education on drug allergies using one-on-one education with flipchart for patients in the test group. The usual care group received a brochure with information about drug allergies. Patient knowledge on drug allergy was assessed by another pharmacist 1 day after receiving education using 5-question interview on drug name, drug class, symptom of drug allergy, actions when experienced drug allergy, and prevention of allergic reactions.

Results: A total of 100 patients, 50 in each group, were included in the study, 52.0% were male. Most patients (84.0%) were allergic to one drug. The most common drug that the patients were allergic to was ceftriaxone (15.2%). The most common allergic reaction (65.3%) was maculopapular rash. Baseline characteristics, occupation and number of drugs that cause allergies, were similar in both groups. Knowledge of drug allergy in education group was significantly higher than those of the control group (median 4 (IQR 3-5) and (2, IQR 1-3), ($P < 0.001$), respectively.

Conclusions: Hospitalized patients with drug allergies had higher knowledge compare with the usual care group after receiving pharmacist-based education on drug allergy.

Keywords: drug allergy, patient knowledge

221 Drug-related problems in inpatients in orthopedic wards at a regional hospital

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Aim/Objective: To identify drug-related problems (DRPs) and physicians' response to proposed intervention to DRPs reports.

Methods: A cross-sectional descriptive study was conducted in patients in orthopedic wards received medication reconciliation services by pharmacists during January 2018 to June 2019. Researcher collected the data from 706 patients. Once DRPs were detected, pharmacists reported proposed interventions to prescribers. DRPs were categorized according to Cipolle's classification.

Results: This study included 706 patients, with an age average of 63.2 (±14.6) years and 371 patients (52.5%) were female. The most common chronic disease categories were cardiovascular diseases (398, 56.4%), diabetes mellitus (154, 21.8%), chronic kidney disease (64, 9.1%) and respiratory tract diseases (21, 3.0%). Pharmacists detected 321 DRPs. The most frequent DRPs detected were needs of additional drug therapy (76.3%), unnecessary drug therapy (5.9%), dosage too high (5.9%) and dosage too low (5.0%). Prescribers' acceptance rate of proposed interventions for DRPs was 58.6% (188 from 321). All of identified 19 adverse drug reactions and 7 dosage too high were accepted (100% of both), whereas 116 from 245 (47.4%) of additional drug therapy were accepted.

Conclusion: Medication reconciliation process by pharmacists at orthopedic wards could identify DRPs leading to the measure for patient safety during admission and discharge.

Keywords: medication reconciliation; drug related problems; patient safety; hospital pharmacy

222 Methadone education initiative for ethnic minorities in northern Thailand

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Mae Hong Son lies in upper northern Thailand. It is the most mountainous province and the westernmost province. More than half of its population are ethnic hill tribes. Tai and Karen are the largest groups with their own language and culture. Opioids dependence is an ongoing health problem. Methadone maintenance therapy has been used to treat opioids dependence. Counselling is needed to provide patients with methadone information. However, those ethnic minorities and health care providers struggle with language barriers leading to communication discrepancy. It might increase the risk of medication error and methadone misuse. The methadone education initiative for ethnic minorities was developed. It includes a pictogram booklet, plus verbal explanation of trained translators providing information about methadone, its effects, side effects, drug interactions, and self-care.

Objective: To compare knowledge about methadone of ethnic minorities receiving methadone therapy, before and after the educational intervention.

Methods: Tai and Karen patients with opioids dependence receiving methadone therapy at Thanyarak Mae Hong-Son Hospital were recruited. Patients' knowledge on methadone was assessed before and after receiving the educational intervention. The intervention comprised a pictogram booklet with verbal explanation in their own language from trained translators. Information on indications, administration, side effects, drug interactions, and self-care of methadone was given. Data were analyzed by paired T-test statistics.

Results: The mean knowledge of patients receiving the educational intervention increased from 2.14 to 3.57. The knowledge about indication, administration, side effects and the differences between methadone and opium was significantly increased ($p=0.02$, 0.01 and <0.01). However, the knowledge about methadone misuse was not significantly different ($p = 0.62$).

Conclusion: Methadone educational initiatives as pictograms with verbal explanation designed for the ethnic minority patients could improve their knowledge in many aspects. It helps health care providers overcome language barriers during counselling.

Keyword: Methadone, Opioids dependence, Ethnic minority

223 Impact of clinical pharmacist collaborative care in identifying and resolving drug related problems in systemic autoimmune disorders patients

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Objectives: Drug related problems (DRPs) are among the most common problems in current medical practice and may promote negative health outcomes. Systemic autoimmune disorders may possess a high risk of DRPs due to chronic complex treatment required in such patients. We aimed to assess the impact of a clinical pharmacist-led multi-disciplinary care team in the detecting and managing of DRPs in patients with systemic autoimmune disorders.

Methods: This prospective interventional study was conducted for eighteen months at the rheumatology department of a tertiary care teaching hospital. A dedicated clinical pharmacist collected and documented all the necessary and relevant data from the eligible participants. Collected data were assessed for the presence of DRPs and were categorized following Pharmaceutical Care Network Europe (PCNE) V8.02. The clinical pharmacist proposed the interventions to resolve the identified DRPs. The data were statistically analyzed using SPSS Version 26.

Results: A total of 1297 DRPs were detected in 765 patients with an average of 1.69 DRP per patient. Treatment safety [497 (38.3%)] and drug use process [321 (24.13%)] was the most commonly encountered problem and causes of DRPs respectively. Around 90% of the interventions proposed by the clinical pharmacist were accepted leading to a resolution of 1173 DRPs. The use of more than five drugs was identified as the major risk factor for DRPs occurrence.

Conclusion: This study found that two-thirds of the patients with systemic autoimmune disorders had at least one DRPs. The primary problems and causes of DRPs were related to treatment safety and drug use process respectively. Patients taking ≥5 drugs were at higher to develop DRPs. Hence, clinical pharmacist-led collaborative care in early detection of DRPs and risk factors can help to mitigate the majority of DRPs in systemic autoimmune disorders patients.

Keywords: systemic autoimmune disorder; drug related problems; clinical pharmacist, collaborative care

224 Assessment of clinical pharmacist initiated interventions in a Pediatric Intensive Care Unit

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Background: Pharmacists are considered as an integral part of the medical team for better drug selection and information's regarding the dose maintenance especially in concern with the pediatric critical care patients.

Objective: This study was conducted to assess the clinical pharmacist initiated interventions in a pediatric intensive care unit (PICU) and its impact in clinical outcome.

Methodology: This prospective interventional study was conducted in PICU for a period of nine months. All children admitted to PICU were enrolled for the study and children housed for less than 24 hours were excluded. Medical records of the enrolled children were reviewed on daily basis from the day of admission to identify any drug related problems (DRPs) and medication incidences (MI) and appropriate intervention was made to the health care team. Predictors of DRPs and MIs leading to interventions were identified using chi square test.

Results: A total 80 children were enrolled during the study period with an incidence of DRP of 48.5% and MI of 12.5%. Antibiotics were most commonly involved in the interventions with 44 interventions related to treatment safety and 38% of the DRPs were prevented. Drug duplication(40%) was the most commonly seen MI followed by wrong dose(30%) or incorrect dosage form(30%) and 40% of the events were Category C. Use of 10-15 medications or doses per day, 7-9 parenteral formulations per day, more than 2 antibiotics per day and hospitalization of more than 20 days with more than 8 days in PICU were the identified predictors leading to interventions. 84% of the intervention were accepted by the health care team and significant impact was observed following interventions in 80% of the cases.

Conclusion: Clinical Pharmacists can significantly improve the clinical outcome among children in critical care units being a part of the health care team.

225 Understanding by patients medicines information presented in patient package inserts

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Objective. The Patient Package Inserts (PPIs) is the main source of medicines information for patients. Results of recent studies show that there are various problems associated with using PPIs effectively. The objectives of this study was to study the situation with understanding a content of PPIs by patients in Armenia.

Methods. Face-to-face interviews were conducted with 1059 visitors of community pharmacies in all the regions of Armenia. The results were analysed with SPSS statistical software, version 22.0.

Results. Only 36.7% of 908 participants who read PPIs before taking medicine, understand content; 60.2% understand it partially and 3.1% do not understand at all. The extent of patients' understanding of information in PPIs depends on their educational level. 42.8% of respondents with university degree and 29.2% of those who completed a high school, college and basic school mentioned that they understand contents of PPIs entirely; 1.8% of respondents with higher education and 4.7% of participants graduated from a high school, college and basic school - do not understand the information in leaflets at all ($p<0.001$). The most common reasons of a lack of understanding mentioned by respondents who did not understand a content of PPIs or understand it partially, were technical language and overload of content with medical terms (67.3%), the language used other than Armenian (43.0%) and a small font size (32.2%).

Conclusions. Many patients do not understand the content of PPIs due to barriers which can be removed by introducing appropriate regulatory provisions for PPIs' content and readability.

Keywords: patient package inserts, leaflets

226 Real world effectiveness of methadone maintenance treatment on the reduction of suicidal attempts in patients with opioid use disorder

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Aim/Objective: To evaluate the association between MMT and the risk of suicide attempt.

Methods: We conducted a case-crossover study by analyzing the data from the Suicide Prevention System and Drug Abuse Case Management System. We included patients who were enrolled in methadone maintenance treatment (MMT) program for opioid use disorder (OUD) with a record of suicide attempt from 2013 and 2020 in Tainan metropolitan city. The first date of suicide attempt were considered as event date. The dates 3, 6, or 12 months (i.e., the wash-out period) prior to the date of suicide attempt were considered as reference dates, respectively. We performed conditional logistic regression to obtain the odds ratios (OR) and the confidence intervals (CI) of patients received MMT within s days before the event dates. A sensitivity analysis was redefined the exposure of MMT as at least 3 days within 7 days before event dates.

Results: We included a total of 882 cases with records of suicide attempts. The average age was 42.67 (SD 8.66) and 65.3% were male. Compared with the patients who did not receive MMT, patients with MMT had lower risk of suicide attempt (OR = 0.64; 95% CI = 0.44-0.94). The result remained consistent (OR = 0.69; 95% CI = 0.48-0.99) when the exposure of MMT at least 3 days within 7 days before event dates were considered as exposed group.

Conclusion: We found MMT was associated with a 36% reduced risk of suicide attempt in patients with OUD. The finding could be a fundamental ground for future investigation and policy decision making to enhance patients' motivation to receive or maintain the MMT.

Keywords: methadone maintenance treatment, suicidal attempts, opioid use disorder

227 Incidence and risk factors of steroid-related damage in Korean patients with Systemic lupus erythematosus, compared to general population, 2002-2018

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Objective: To quantify incidence of steroid-related damage by matching systemic lupus erythematosus (SLE) and Psoriasis (PS) with general population, respectively.

Methods: We conducted a cohort study using the National Health Insurance Service-National Sample Cohort database of Korea from 2002 to 2015. We assessed steroid-related damage in patients with SLE (at least one diagnosis of M32 with rare disease registration code V136 during 2004~2009 and without history of steroid-related damage) and PS (at least one diagnosis of L40 during 2004~2009 and without history of steroid-related damage). General population was defined as people with no rheumatic diseases. Steroid-related damage was defined as incident diagnosis of avascular necrosis (AVN) (at least one diagnosis of M870x, M871x, M872x, M873x, M878x, M879x, M905x during 2010~2015), osteoporotic fracture (OF) (at least one diagnosis of S720, S721, S722, S422, S52 during 2010~2015). Study population were followed up until incident diagnosis of steroid-related damage or up to December 2015. Each Incidence rate ratios (IRRs) were calculated based on the group comparing SLE with general population and the other group comparing PS with general population.

Results: A total of 433 SLE and 14,084 PS and 1,033,434 general population were included in this study. IRR was 2.67 [2.64-2.70] for the risk of steroid-related damage in SLE patients compared to general population. Comparing IRRs by sex, IRR in female patients with SLE was 2.49 [2.46-2.53]. Comparing IRRs by age, IRR in SLE patients was 3.30 [3.14-3.46] in their 10's, 10.92 [10.39-11.48] in their 20's, 6.40 [6.14-6.67] in their 30's. Also, IRR was 1.47 [1.45-1.48] for the risk of steroid-related damage in PS patients compared to general population.

Conclusion: SLE patients have a higher risk of steroid-related damage compared to PS patients. Female patients with SLE, especially 10~39 years, have an increased risk of steroid-related damage compared to general population.

228 Incidence and prevalence of moyamoya disease in urban China: A nationwide population-based study

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Background and Objective: Moyamoya disease (MMD) is an increasingly recognized cause of stroke, mainly described in East Asia. China is the largest nation in Asia, but few studies reported the epidemiology of MMD, especially at a national level. We aimed to estimate the incidence and prevalence of MMD in China.

Methods: We performed a population-based study using data from the national databases of Urban Basic Medical Insurance between 2013 and 2016, covering approximately 0.50 billion individuals. MMD cases were identified by diagnostic code (ICD-10 I67.5) or related diagnostic text. The incidence and prevalence were described by sex, age, and region. Associated costs for hospitalization and length of stay were also calculated.

Results: A total of 1987 MMD patients (mean age 44.45 ± 14.30 years, female-to-male ratio 1.12) were identified, representing a national crude incidence of 0.59 (95% CI: 0.49 to 0.68) and a prevalence of 1.01 (95% CI: 0.81 to 1.21) per 100 000 person-years. Rates were higher in females than in males for the incidence (0.66 vs. 0.52) and prevalence (1.05 vs. 0.90). And the age-specific rates showed a bimodal distribution, with the highest peak in middle-aged group and the second peak in child group. Additionally, 64% of patients were hospitalized for MMD, with an average length of stay of 18.69 days and an average cost of $7945 per patient.

Conclusions: Our results confirm that MMD is relatively common in East Asians, but the rates in China were lower than those in other East Asian countries such as Japan and Korea. The unique epidemiologic features, including a relatively weak female predominance and a shift in the highest peak of incidence from children to adults, revealed new sight into MMD. Further research is expected to explore the potential pathogenesis of MMD.

Keywords: Moyamoya disease, Incidence, Prevalence, Medical insurance database

229 Pharmacovigilance studies of atenolol among hypertensive patients in Government secondary care hospital of Hyderabad, Pakistan

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Aim/Objectives: To know the safety of medicines is as important as to know the efficacy. The current study are designed to assess the adverse drug reactions among hypertensive patients in government secondary care hospital of Hyderabad, Sindh, Pakistan.

Methodology: The descriptive study was designed in cardiac out patients department of a well renowned hospital of Hyderabad, Pakistan. A total of 217 patients are enrolled who had confirmed diagnosis of hypertension and on atenolol medicine. The sampling was purposive. The adrs were categorized based on narenjo's scale.

Results: Out of 217 patients, male patients are more than 50% as compared to female. All patients are on atenolol 50mg. 14 different brands of atenolol were taken by the patients. ADRs were categorized on two different stages i.e. maximum and minimum. The maximum ADRs were hypotension and tiredness while minimum are dizziness and fatigue. All ADRs are significance and p value is less than 0.005. All ADRs are mild based on narenjo's scale.

Conclusion: ADRs assessment of atenolol reveals that hypotension are the common problem after taking the medicine so proper counselling will require how to manage by the patients. Moreover based on type of hypertension, atenolol should be prescribed.

230 Real-world effectiveness of lenvatinib and sequential treatment in the patients with hepatocellular carcinoma: An evidence from Taiwan

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Background: Lenvatinib was approved to be the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC) in late 2018. However, the evidence about second-line treatments after lenvatinib failure was still limited.

Objective: To investigate the prescription pattern and the effectiveness of sequential treatments after lenvatinib.

Method: This was a retrospectively cohort study by using the electronic medical records database from Chang Gung Medical Foundation in Taiwan. We included the advanced HCC patients with newly initiating lenvatinib between March 2018 and March 2019. We followed the patients from the first date of lenvatinib to the all-cause death, loss of follow-up and end of December 2020. The primary outcome was the pattern of sequential treatment after lenvatinib. The secondary outcome was overall survival (OS) between the patients with or without sequential treatments and different sequential treatments.

Result: We included a total of 79 lenvatinib users with mean age 66.9 (SD 10.1) and 75.9% of men in our study. There were 94.8% patients with Eastern Cooperative Oncology Group (ECOG) < 2, 86.1% patients belonged to Child-Pugh A. Overall, 79 patients were included of which 43 patients (54.4%) received previous systemic treatment before using lenvatinib. The most common sequential therapy was nivolumab (n = 24; 30.4%) followed by pembrolizumab (n = 6; 7.6%), whereas 36 patients were not treated with any sequential treatments (45.6%). The median OS was 14.1 months. The patients with sequential treatments had significantly longer median OS than without any sequential treatments (10.7 vs. not reach, $p < 0.05$). There was not significantly difference between immunotherapies and multi-target tyrosine kinase inhibitors as second-line treatments after lenvatinib (not reach vs. 14.1 months, $p = 0.54$).

Conclusion: Immunotherapies remain the most common second-line treatments. Future large-scale studies were suggested to compare the real-world effectiveness of different sequential treatments after lenvatinib.

231 LDL-C trajectories of statin initiators among patients with diabetes

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Aim/Objective: Diabetic patients with increased LDL-C level are recommended to initiate statin therapy due to increased risk of cardiovascular events. This study aims to describe the changes of LDL-C in these patients.

Methods: Patients with diabetes who initiated statins in 2014 were identified from a medical center in southern Taiwan. We further included those with at least one record of LDL-C exam after their initiation of statin therapy. Sex, age, cardiovascular comorbidities and baseline lipid profile data at statin initiation were collected. We applied group-based trajectory model to identify patterns in 2-year LDL-C changes of these patients after starting statin therapy. We further describe characteristics of these patients between different LDL-C trajectory groups.

Results: We identified a total of 1145 statin initiators of patients with diabetes. Their mean age were 60.6 years old and 57% were men. The 2-year dynamic change of LDL-C in these patients revealed 3 trajectories, with 64.1%, 34.4% and 1.5% patients grouped into the lowest (group 1), the middle (group 2) and the highest (group 3) LDL-C trajectory, respectively. The level of LDL-C was kept constantly at approximately 75 and 110 mg/dL for group 1 and group 2 respectively during the study period, while the level of LDL-C varied within a range of 140 to 240 mg/dL in group 3. When compared to group 1, the other two groups had significantly younger ages and higher baseline levels of LDL-C and total cholesterol and group 3 had higher baseline HbA1c level. Other comorbidities were not significantly different between groups.

Conclusion: Most diabetic patients who initiated statin therapy reduced their LDL-C level to 75 or 110 mg/dL and kept a constantly low LDL-C level during a 2-year follow-up. Baseline LDL-C and total cholesterol level were found to be associated with the LDL-C trajectories after statin therapy.

232 Delayed cutaneous adverse reactions to ChAdOx1 nCoV-19 vaccine

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Among the various types of the COVID-19 vaccines available at present, cases have been reported regarding delayed large local reaction to the mRNA vaccines including mRNA-1273 Moderna COVID-19 vaccine and BNT162b2 COVID-19 vaccine by Pfizer-BioNTech. However, there were no cases regarding adenovirus-vectored COVID-19 vaccines. We have recently observed delayed cutaneous reactions around the injection site of the ChAdOx1 nCoV-19 (AZD1222) vaccine, a replication-defective chimpanzee adenovirus-vectored vaccine.

Four female patients (age, 30 to 58 years old) showed delayed cutaneous reactions around the injection site of the ChAdOx1 nCoV-19 vaccine, which developed at least three days (range, Day 4 to 17) after the first dose of vaccination. They did not have a previous history of hypersensitivity reactions to drugs or any vaccine. Only one patient had allergic rhinitis but did not require regular medication. All patients had a large delayed skin reaction that started with erythematous swelling and three developed systemic symptoms including fever, chill, and myalgia from the day of vaccination and that resolved before the delayed skin reactions. Thus, none of the patients experienced concurrent systemic symptoms at the development of delayed local skin reactions. The delayed skin lesions resolved after short-term treatment, such as oral antihistamines or topical or oral corticosteroids, while the duration of skin reaction varied from 4 to 18 days. Skin biopsy from three patients showed superficial perivascular and perifollicular lymphocytic infiltration with sparse eosinophils. These findings suggest that the delayed local cutaneous reactions are mediated by hypersensitivity mechanisms.

Our report suggests that the delayed local cutaneous reactions to the COVID-19 vaccines are not vaccine-specific, since both mRNA vaccine and viral-vector vaccine showed such reactions. Before implementing a mass vaccination campaign with various COVID-19 vaccines, clinicians should be aware of the possible ‘COVID arm’ to avoid unnecessary tests or treatment.

233 Detecting early safety signals for infliximab using machine learning algorithms in the Korea adverse event reporting system

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Aim/Objective: Machine learning (ML) algorithms have been proposed as an alternative to the conventional data mining methods in generating safety signals. This study aimed to investigate the utility of the ML algorithms on timely detection of the known safety signals in a spontaneous reporting system.

Methods: We conducted a signal detection analysis of the adverse events (AEs) reported for infliximab in the Korea Adverse Event Reporting System (KAERS) database between 2009 and 2018. We constructed a novel input dataset required for training of the ML algorithms to calculate signaling probability. The input dataset included information on the known and unknown AEs of infliximab (labeled data) and quantifiable properties and characteristics of the AEs (feature data). We stratified the KAERS data by calendar year, and then created 10 cumulative yearly datasets by adding each subsequent year data to the 2009 data. Two supervised ML algorithms (gradient boosting machine [GBM], random forest [RF]) were used to detect five pre-specified AEs in each yearly dataset. An early signal was defined as an AE detected prior to it being updated in the labeling information of infliximab.

Results: Of the five pre-specified AEs analyzed, RF and GBM both generated 4 early signals for infliximab. All 4 signals were detected in the first year they were reported with infliximab in the KAERS. RF demonstrated best balance between sensitivity (74%) and specificity (89%), followed by GBM with 57% and 95%, respectively.

Conclusion: ML algorithms demonstrated optimal performance in generating early signals of infliximab, highlighting a potential for routine application of these methods in pharmacovigilance.

Keywords: Machine learning algorithms; signal detection; disproportionality analysis; infliximab

234 Effects of ambroxol on COVID-19 patients: A retrospective cohort study of 1922 patients

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Objective: Ambroxol is a widely used secretolytic and mucoactive agent primarily used to treat respiratory diseases associated with viscid mucus, which was seemed as a potential therapeutic option in COVID-19, but no data has been available. The present study was aimed to evaluate the effectiveness of ambroxol on COVID-19 patients.

Methods: A retrospective, single-center cohort study enrolled 1922 consecutive hospitalized COVID-19 patients who were followed up from February 8 to April 15, 2020. Patients were grouped to either ambroxol treatment group or control group. An analytical study of clinical outcomes including mortality, 14-day negative conversion of COVID-19 RNA and exacerbation rate of disease were conducted.

Results: Of the 1922 patients included (920 [47.87%] male, median age, 60 years (IQR 49,68), 26.38% received ambroxol. The overall in-hospital mortality was 2.34%.

In adjusted logistic models, there were no significant differences in mortality for patients receiving ambroxol compared with control group (adjusted OR, 2.99 [95% CI, 0.97,9.86]). The 14-day negative conversion of COVID-19 RNA was significantly higher in ambroxol group of non-hypertensive patients during the first three days (adjusted OR, 1.64 [95% CI, 1.12,2.42]) and non-severe patients (adjusted OR, 1.66 [95% CI, 1.14,2.46]). The exacerbation rate was lower in patients receiving ambroxol in propensity score matching model (adjusted OR, 0.36 [95% CI, 0.25,0.51]) and adjusted logistic model (adjusted OR, 0.43 [95% CI, 0.31,0.59]). We further found that the 14-day exacerbation rate was lower in patients receiving ambroxol during the first three days (adjusted OR, 0.52 [95% CI, 0.34,0.78]) which was also lower in non-hypertensive patients receiving ambroxol (adjusted OR, 0.54 [95% CI, 0.33,0.86]).

Conclusion: Treatment with ambroxol was not significantly associated with differences in in-hospital mortality. While the administration of ambroxol reduced exacerbation rate and increased negative conversion of COVID-19 RNA in patients with COVID-19.

Key Words: Ambroxol; COVID-19; Effectiveness

235 Real world effectiveness of immunotherapy in advanced non-small cell lung cancer patients with versus without documented psoriasis or rheumatoid arthritis

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To assess the real-world effectiveness of first-line immune checkpoint inhibitor (ICI) therapy in advanced non-small cell lung cancer patients with psoriasis or RA versus without using a de-identified database.

We conducted a cohort study of aNSCLC patients with versus without documented psoriasis or RA using ICD codes who initiated ICI-based systemic therapy in the first-line treatment setting from January 1, 2011 to April 01, 2020. This study used the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database. Patients with incomplete historical treatment data were excluded. The primary outcome was overall survival (OS), measured from start of first-line ICI or ICI in combination with chemotherapy (index date) to date of death or last confirmed activity. Propensity score-based inverse probability of treatment weighting (IPTW) was used to address confounding in Kaplan-Meier and Cox regression hazard ratio estimates.

Of 64,203 aNSCLC patients in Flatiron Health database, 9,576 received first-line ICI or ICI in combination with chemotherapy. Of these, 17 patients had ICD-recorded psoriasis and/or RA. Baseline characteristics were well balanced between groups after IPTW weighting (all $|$standardized differences$|<0.1$). Median follow up time from the index date was 176 days (psoriasis or RA) vs 213 days (no psoriasis or RA), respectively. Having psoriasis or RA was not associated with mortality either in the first six months (IPTW-adjusted hazard ratio [HR 0.94], 95% CI 0.35–2.54) or overall (IPTW-adjusted HR 1.34, 95% CI 0.80–2.23). Study limitations include limited power to detect clinically important differences, the potential for unmeasured confounding, and potentially limited generalizability.

Results of this preliminary analysis do not suggest that psoriasis and RA affect survival in aNSCLC patients treated with ICI, and should be confirmed in a larger data set. Future studies should consider comparing survival estimates to clinical trial estimates to reassure (or caution) clinicians using these therapies in such populations.

236 SGLT2 inhibitors and risk of pancreatitis: A disproportionality analysis and systematic review of case reports

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Objective: To identify the risk of pancreatitis for the Sodium-Glucose Cotransporter-2 (SGLT2) inhibitors.

Methods: A retrospective pharmacovigilance data analysis was performed in FDA Adverse Event Reporting System (FAERS), VigiBase, and Canadian database by considering the preferred term “Pancreatitis” reported for the SGLT2 inhibitors such as canagliflozin, dapagliflozin, empagliflozin from the date of approval to 31st March 2021. Disproportionality analysis was performed by calculating the Proportional Reporting Ratio (PRR) with an associated chi-square (X2) value, lower bound of the 95% two-sided confidence interval of Reporting Odds Ratio (LL ROR), and lower bound of the 95% two-sided confidence interval of the Information Component (IC025). In addition to this, a systematic review was performed through a comprehensive literature search of electronic databases like PubMed and Google Scholar for the case reports published on SGLT2 inhibitors induced pancreatitis.

Results: Disproportionality analysis in FAERS database identified the signals between the SGLT2 inhibitors and pancreatitis [Canagliflozin: NComb=381, PRR=7.5 (X2=2144.4), LL ROR=6.9, IC025=2.7; Dapagliflozin: NComb=91, PRR=6.4 (X2=413.5), LL ROR=5.3, IC025=2.3; Empagliflozin: NComb=255, PRR=7.4 (X2=1401.1), LL ROR=6.6, IC025=2.7]. The analysis of VigiBase and the Canadian database reiterated the findings of FAERS. A total of 11 case reports identified SGLT2 inhibitors induced pancreatitis. All the patients experienced abdominal pain or discomfort along with nausea and vomiting, and in some patients, it radiates to the spine and flank. The abdomen was soft and there was a significant tenderness to palpation over the epigastric region. The lipase enzyme was elevated above the normal range in all reports. The CT scan and MRI scan of the abdomen and pelvis also showed evidence of pancreatitis.

Conclusion: A new safety signal of pancreatitis for the SGLT2 inhibitors was identified through the disproportionality analysis of spontaneous reports and a systematic review of case reports, which needs further evaluation and action by the regulatory authorities.

237 Anticholinergic drugs use and risk of falls in the elderly: A retrospective cohort study

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Aim/Objective: To measure association between anticholinergic drugs and falls in the elderly.

Methods: This retrospective cohort study used data from electronic medical records from one general hospital and 22 affiliated health promoting hospitals from January 1, 2010 through December 31, 2019. New user design was used to identify patients aged over 65 years old who first received any anticholinergic drug at least over 30 days and followed up within 5 years for falls. Anticholinergic drugs were identified by local drug codes. Anticholinergic cognitive burden scale (ACB) was calculated and patients were classified into 2 groups (ACB≤1 vs. ACB≥2). Falls were identified by ICD10 (W00-W220, Y30-Y31) and text searching. Propensity scores (PS) from covariates were included in the Cox PH model with inverse probability of treatment weight (IPTW).

Results: Of 32,832 patients aged over 65 years old identified, 2,186 cases had prior falls before starting anticholinergic drugs, 3,265 cases had anticholinergic drug less than 30 days, 7,746 cases started drugs after inclusion period, 2,547 cases had prior exposed to anticholinergic drugs, 464 cases met other exclusion criteria. Of 16,624 patients included, 1,619 were anticholinergic users in ACB≥2 group. Falls were observed in 531 cases (11.02%) in ACB≥2 group whereas 1,654 cases (32.89%) in control group. Cox PH model revealed that anticholinergic users with ACB≥2 were at higher risk of fall than control groups (95% HR=1.27-1.87, p-value<0.001). Other significant risk factors included depression (95% HR=1.04-3.70, p-value=0.037), anxiety (95% HR=1.48-2.64, p-value<0.001), diabetes (95% HR=1.05-1.99, p-value=0.025), benign prostatic hyperplasia (95% HR=1.69-3.24, p-value<0.001), history of syncope (95% HR=1.30-4.34, p-value=0.004), vision problems (HR=1.32-2.20, p-value<0.001, and difficulty walking (HR=1.84-2.94, p-value<0.001).

Conclusion: The elderly who used anticholinergic drugs with ABC≥2 had elevated risk of falls. Recommendation to prevent falls must be provided and falls must be actively monitored.

Keywords: Anticholinergic Drugs, Anticholinergic Cognitive Burden, Falls, The Elderly

238 Prescription of atypical antipsychotics and the risk of hypothyroidism: A Population-Based, Case-case-time-control study

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Aim/Objective: To investigate the risk of development of hypothyroidism with atypical antipsychotics using a case-case-time-control design to determine the effects of drugs in an individual.

Methods: We applied a case–crossover design and case-case-time control design to estimate the risk of hypothyroidism associated with the use of each atypical antipsychotic using 2010-2017 national health insurance data. The hazard period was defined as 30-day before the event of hypothyroidism and was matched to 1 control period at 120-days of washout period which was set to minimize the carryover effects of exposure. The conditional logistic regression was performed to calculate the odds ratio for hypothyroidism in case-crossover and case-case-time control settings. Stratified analysis was performed by sex, age group, and presence of psychiatric comorbidities.

Results: From the 1 899 071 people who received prescriptions for at least one atypical antipsychotic between 2010 and 2017, a total of 18,312 patients met the study inclusion criteria. In case-crossover analysis, increased risk of hypothyroidism was showed with exposure to all atypical antipsychotics in the recent 30 days. The highest odds ratio was found among patients with quetiapine (2.55; 95% CI 2.39, 2.72), followed by olanzapine (2.25; 95% CI 1.94, 2.60), risperidone (1.94; 95% CI 1.77, 2.13), and aripiprazole (1.88; 95% CI 1.65, 2.14)). For case-case-time-control analyses, similar statistically increased OR was showed for quetiapine (1.23; 95% CI 1.11, 1.36), risperidone (1.24; 95% CI 1.07, 1.44), aripiprazole (1.35; 95% CI 1.10, 1.67) and olanzapine (1.33; 95% CI 1.06, 1.68) after adjusting exposure-time trends. When stratified according to sex, both groups showed similar ORs in case-crossover analysis and case-case-time control analysis in all atypical antipsychotics. Risks were not statistically differed among the age groups.

Conclusion: The use of antipsychotics was significantly related to an increased risk of hypothyroidism in this population-based case-case-time control study.

239 Steroid stewardship as a tool to tackle glucocorticoid induced hyperglycemia in COVID -19 patients

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Objective: To characterize the incidence of Glucocorticoid-Induced Hyperglycemia (GCIH) in COVID -19 patients and to evaluate the effectiveness of a Steroid Stewardship Program in countering this effect.

Methods: This prospective, interventional study included 100 COVID-19 confirmed patients admitted between March 12 – May 12, 2021, who are categorized into B & C as per the guidelines of the Directorate of health services, Kerala, India. A five-item Steroid Appropriate Index (SAI) was prepared based on the onset of symptoms, weight of the patient, CT Thorax severity score, the preferred route of administration, and the underlying diseases for choosing the appropriate doing of the preferred corticosteroid. The demographic profile of these patients was collected and they were followed up till discharge/death to track the incidence of worsening of hyperglycemia or new onset of diabetes. The effectiveness of SAI was analyzed by comparing the data of treatment and clinical outcome among 100 COVID-19 confirmed patients admitted before and after implementation of the scale.

Results: The majority of the patients were males (57) and the mean age was 45.7± 16.6 years. The incidence of new-onset of hyperglycemia i.e., GCIH was more among the retrospective cohort when compared with the SAI cohort (7% vs 26%, $p< 0.001$). The study also revealed that history of diabetes ($p<0.001$), age ($p = 0.002$), number of medicines used for treatment ($p<0.001$) are significantly associated with glucocorticoid-induced hyperglycemia.

Conclusion: The appropriate selection of corticosteroids based on real-world scenarios can decrease the incidence of adverse events associated. Implementation of steroid appropriate index and proper monitoring can be an aid for the same.

Keywords: COVID-19, Corticosteroids, Hyperglycemia

240 Outcomes of 821 desensitization cases performed in a single tertiary hospital

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Aim/Objective: Drug desensitization is required for patients who experience hypersensitivity reactions (HSR) to antineoplastic agents. However, some patients experience breakthrough reactions (BTRs) regardless of the desensitization process.

Methods: One-bag desensitization procedures conducted from July 2018 to June 2020 were analyzed and outcomes were compared among the major drug types (platins, taxanes, and monoclonal antibodies). The risk factors for BTRs were assessed by comparing the characteristics of patients who did and did not experience BTRs during desensitization.

Results: A total of 821 cases of one-bag desensitization were done in 180 patients with a 98.2% completion rate and 29.0% of BTR rate. The severity of most BTRs was lower than that of index HSRs. The overall BTR rate had no associations with gender, age, the severity of the index HSR and premedication. However, in patients with an index HSR severity of CTCAE grade 4, the BTR rate was significantly lower with corticosteroid premedication (odds ratio (OR) = 0.16, 95% confidence interval (CI) = 0.04-0.72, p = 0.007). The BTR rate was highest in patients who were desensitized to platins (35.5%) followed by those desensitized to monoclonal antibodies (20.2%) and taxanes (15.9%) (p = 0.001). Among patients who received platin desensitization, those with abdominal pain in the index HSRs showed a significantly higher rate of BTRs (OR = 4.37, 95% CI =1.34-14.2, p = 0.01).

Conclusion: Most patients with HSRs to antineoplastic agents can safely receive chemotherapy through desensitization despite BTRs. Corticosteroid premedication may be beneficial in lowering BTRs in patients with severe index HSRs.

Keywords: drug hypersensitivity, desensitization, breakthrough reaction, premedication

241 Prevalence of immediate ADR from repetitive administration of iodinated RCM: Effectiveness of premedication and alternative RCM

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Objectives: To verify the effect of premedication and changing RCM for preventing recurrence of ADR, and to find a relatively safe alternative RCM.

Methods: From 2015 to 2020, 7,052 computed tomography (CT) cases with contrast media from 3,658 patients that were registered in the electrical medical record system at the Severance Hospital were analyzed. The severity of the immediate ADR, culprit RCM, type of premedication, RCM used in subsequent examinations, and the ADR in subsequent examinations were reviewed and statistically verified.

Results: The recurrence rate of immediate ADR was most likely to occur in the following next CT scan with RCM ($p<0.001$). In subsequent CT scans, with the exception of the following next CT scan, the rate of recurrence of immediate ADR was relatively low, but still present. There were 3,559 case pairs in which immediate ADR appeared at the first CT scan and subsequent CT scan with RCM. Changing the RCM reduced the recurrence of immediate ADR and the severity of recurrence ($p<0.001$). Premedication with antihistamine reduced mild ADR ($p<0.001$). Premedication with antihistamine and steroid reduced moderate-severe ADR when changing RCM together ($p<0.001$). In patients with moderate-severe ADR, replacing iobitridol, iopamidol, and iopromide with iohexol reduced the recurrence of immediate ADR ($p=0.057$, $p=0.025$, and $p=0.011$, respectively), while changing iohexol for iobitridol reduced the recurrence of immediate ADR ($p<0.001$).

Conclusions: To reduce the recurrence of immediate ADR to RCM, it is important to change the RCM used. In moderate-severe cases, premedication with antihistamine and steroid should be performed together with changing the culprit RCM. The recurrence rate of immediate ADR is highest in the next following CT after ADR occurrence. However, since recurrence may occur in subsequent CT scans, continuous monitoring is required in patients with a history of immediate ADR to RCM.

242 How to reduce breakthrough response in contrast media re-exposure in patients with contrast media anaphylaxis?

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Goal/Aim: In high-risk patients with a history of ICM hypersensitivity, the use of iodinated contrast media (ICM) is sometimes unavoidable. Although changing the culprit ICM or pretreatment can be used as options to reduce the recurrence of ICM hypersensitivity, an optimized pretreatment protocol to effectively reduce breakthrough responses has not yet been established.

Methods: A retrospective cohort of ICM anaphylaxis from 18 tertiary care institutions was recruited and the outcomes of ICM re-exposure were monitored.

Results: A total of 263 patients with a history of ICM anaphylaxis were recruited, 131 (49.6%) patients reused ICM 547 times, and breakthrough response (BTR) occurred in 77 cases (14.1%); mild 28 cases (36.4%), moderate 20 cases (26.0%), and severe 29 cases (37.6%). The incidence of BTR was lowered by changing the culprit ICM and premedication. Premedication consisted mainly of antihistamines and corticosteroids. ICM changes significantly reduced the BTR rate compared to re-exposure to the culprit ICM use (32.2% versus 11.1%, odds ratio (OR) = 0.26 [95% confidence interval (CI) 0.14-0.50], $p < 0.001$) in premedicated cases while there was no difference in cases without premedication. In multivariate regression analysis, the BTR rate was statistically lowered by ICM change (OR = 0.32 [95% CI 0.17-0.57], $p < 0.001$) or corticosteroid premedication (OR = 0.43 [95% CI 0.22-0.83], $p = 0.012$). However, antihistamine premedication did not reduce BTR rate.

Conclusions: When ICM is reused in patients with ICM anaphylaxis, avoidance of the culprit ICM and corticosteroid premedication should be considered to reduce the incidence of BTR.

243 Identification of putative drugs for the treatment of myalgic encephalomyelitis/chronic fatigue syndrome using inverse FAERS

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Objective: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a severe, long-term illness that affects several body systems. The exact aetiology of this disease is unknown, but it can be triggered by factors such as viral infections and psychological stress. There is no approved treatment for this disease, but research is being conducted. This study aimed to identify the drugs which have the possibility for treating chronic fatigue syndrome by exploiting the FAERS database and utilizing the inverse signal method.

Method: Drugs associated with Chronic Fatigue Syndrome were extracted from the US FAERS pharmacovigilance data 2004Q1 to 2020Q2 using Open Vigil 2.1-MedDRA24 in this observational, retrospective, pharmacovigilance study. We scanned for inverse signals of existing drugs. The filtration was done for significant inverse associations (reporting odds ratio <1 and adjusted P < .05), and implausibility or clinical infeasibility was also checked. Further categorization was done by their WHO Anatomical Therapeutic Chemical classification code.

Result: Cleaning and mapping of drug names in FAERS by using Open Vigil corresponded to successfully imported reports yielding a total of 40 candidates being identified. Anatomical Therapeutic Chemical (ATC) clustering of the manually curated list of 40 candidate drugs discovered various classes of drugs as a putative treatment for myalgic encephalomyelitis/chronic fatigue syndrome. Some of the drugs with the highest inverse signals included: methotrexate, metoprolol, warfarin, aspirin, adalimumab, fluticasone, and duloxetine.

Conclusion: This study detected the inverse signals in pharmacovigilance data and provided hypotheses for Chronic Fatigue Syndrome drug repurposing. Thus, it reviewed the evaluation and highlighted the possibility of a new treatment for chronic fatigue syndrome. This provides an opportunity to investigate the drugs mentioned in the study and resolve the challenging issue of insufficient treatment options for Chronic Fatigue Syndrome through applied research.

Keywords: Chronic Fatigue Syndrome, Inverse FAERS, Treatment

244 Spontaneous reporting of adverse events following COVID-19 Vaccination: First 90 days experience from a hospital in South India.

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Background: COVID-19 Vaccination program introduced in India on January 16, 2021.the fact sheet was the only source for understanding the possible AEFIs for the health care professionals. Hence, the study was planned with the objective to assess the AEFIs reported following COVID-19 vaccination in a tertiary care teaching hospital.

Materials and Methods: Spontaneous reporting of AEFIs was the method used for the study for a period of three months. Eligible study population was enrolled and collected their details on vaccines and adverse events following Immunization (AEFI) in a suitably designed data collection form and followed them until their recovery. The causality assessment committee performed causality assessment of the AEFIs using World Health Organization's causality assessment algorithm.

Results: A total of 11654 doses of COVID-19 vaccine doses administered at the study site during the study period which consists of 9292 doses of COVISHIELD™ and 2364 doses of COVAXIN™. During the study period, 438 AEFIs were reported from 269 study population with an incidence rate of 2.30%. Majority of the study population with AEFIS belong to the age group of 18-45 Years. Out of the total AEFIs, 411 AEFIs were expected as per the fact sheets, which accounts for 402 with COVISHIELD™ and 9 AEFIs with COVAXIN™. Most of the AEFIs [47.03% (n=206) were observed at the system organ class of 'General disorders and administration site conditions'. After the causality assessment, 94.13% of events with COVISHIELDTM and all AEFIs with COVAXIN™ were categorized to have 'consistent causal association to immunization'. All of them recovered from their adverse events without any sequel.

Conclusion: Spontaneous reporting is one of the cheapest method which can be used for the reporting of AEFI at any set-up. This method helps the health care professionals to identify rare events and potential signals.

245 Relationship between Serum 25-Hydroxycholecalciferol status and patients with Polyarthralgia

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Aim/Objective: To study the impact of serum 25-Hydroxycholecalciferol (25-(OH)D) status and efficacy of Cholecalciferol supplementation on quality of life in patients with Polyarthralgia in southern India.
Methods: A panel study was conducted on 114 patients with polyarthralgia for the duration of six months. Patients were recruited from the outpatient Orthopaedics department of a tertiary care hospital. Patients with polyarthralgia with low serum 25-hydroxycholecalciferol (25-(OH)D) were included in the analysis. Patients with malabsorptive disorders, autoimmune disorders, congenital anomalies, inflammatory joint conditions, and pregnant or breastfeeding women were excluded from the study.

Results: In our study, female subjects were predominant (77.2%). Polyarthralgia due to low serum level of 25-(OH)D was seen highest of 47.36% in middle age subject population (41 to 60 years age group) followed by 44.73% in 21 to 40 years age group. The mean of serum 25-(OH)D was found to be 20.81 ng/dL. The highest percentage of low 25-(OH)D status was detected in unexplained polyarthralgia subject population (52.63%), who did not have any comorbid condition except a low serum level of 25-(OH)D level and demonstrated a significant relationship between low serum 25-(OH)D and decreased QoL in patients with polyarthralgia. The RAND-36 analysis showed that in patients with polyarthralgia whose serum level of 25-(OH)D was found below the optimal range, correction with Cholecalciferol supplementation improved their symptoms dramatically at the end of two months of supplementation.

Conclusion: Polyarthralgia due to low 25-(OH)D status affects all aspects of life and health including physical, psychological, and social well-being. It is a common and disabling condition, with a high impact on health in the community. we strongly recommend screening for vitamin D deficiency in those who are at risk, as features of low vitamin D are mostly reversible with proper supplementation.

Keywords: Polyarthralgia, 25-Hydroxycholecalciferol, Quality of life, Cholecalciferol supplementation

246 Association between Body Mass Index and short term-outcomes of stroke: Shiga Stroke and Heart Attack Registry

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Aim: We aimed to evaluate the relationship between body mass index (BMI) and death by the index stroke within first week or month.

Methods: Shiga Stroke and Heart Attack Registry is an ongoing population-based registry study of stroke covering around 1.4 million residents of Shiga Prefecture in Japan. We included patients whom stroke occurred in 2011-2016, and identified death by the index stroke for all patients. One week and one-month cumulative survival rates after onset were estimated using the Kaplan-Meier method. Cox proportional hazards models were used to evaluate the association. We adjusted age, sex, prior stroke, medical history, smoking status, drinking history, and stroke severity.

Results: Of the 21631, we included 11,233 patients after exclusion criteria. 672 (5.9%) and 265 (2.3%) patients died within one month and one week by index stroke, respectively. In terms of BMI (kg/m2), 15.3% of patients were underweight (BMI<18.5), 63.0% were normal weight (BMI=18.5-25.0), 17.9% were overweight (BMI=25-30), and 3.6% were obese (BMI>30). Compared to patients with normal weight, there were significant difference in the risk of death by stroke in the first month among the underweight patients (HR=1.2 CI: 1.0-1.5), and no difference among other BMI groups. Patients aged ≥65 years being underweight had 1.28 (CI: 1.1-1.6) times higher risk of death. For subgroup analysis by stroke subtypes, obese patients were 4.25 (CI: 1.3-14.3) times higher risk of death by cerebral infarction whilst being overweight was related to death by subarachnoid hemorrhage (HR: 1.81, CI: 1.0-3.4). There was no significant difference in one-week index stroke death among BMI groups.

Conclusions: Association between BMI and death by index stroke was significant in underweight patients, and higher BMIs do not carry significant survival advantage in older age, and certain stroke subtypes.

Keywords: stroke, short term outcome, index stroke death, body mass index, stroke registry

247 How to develop a real-world evidence strategy: searching for a framework and validating it in cases from US and China

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Aim/Objective: With real-world evidence (RWE) being embraced by regulators and healthcare communities around the world, it becomes critical for a healthcare organization to develop a "real-world evidence strategy". However, the term "strategy" is messy and ambiguous, so is "RWE strategy". The aim of this review is to search for a trusted framework, and retrospectively validate this framework in two contrasting RWE cases.

Methods: Google Scholar searched for articles with keywords "Real-world Evidence Strategy". US federal healthcare agencies' websites were also searched for strategic frameworks applied to healthcare in general. Frameworks were assessed against "What Is Strategy?", a classical piece from Harvard Business Review. The best framework retrieved was applied to two RWE cases. One is the COVID-19 Evidence Accelerator in the US, the other is the medical pilot area of Boao Lecheng in China, where RWE has been used as the sole evidence for regulatory approval.

Results: Google Scholar search returned 38 results, but none of which elaborates on their strategy. Among US agencies, the strategic framework from the Centers for Disease Control and Prevention (CDC) meets the principles the best. This frameworks consists of core capabilities that enable the agency's strategic priorities. Applying it to the Evidence Accelerator, we could observe three core capabilities: an agreed way to prioritize research questions; common data model; repeatable data analysis. These enable their strategy priority: near real-time performance of COVID-19 therapeutics, diagnostics, and vaccines. Applying the framework to Boao Lecheng, we could see it develop two core capabilities: a high-quality disease registry that fits for well-defined research questions; dedication from a multidisciplinary research team. These enable their strategy priority: accelerate approval of innovative medicine in China.

Conclusion: Focusing on core capabilities and their enablement of strategic priorities is a succinct and useful way to frame a healthcare organization's RWE strategy.

248 Drug-induced hepatotoxicity: An analysis of drug injury relief applications in Taiwan

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Aim/Objective: To identify the patterns of the applications of drug-induced hepatotoxicity, especially the commonly implicated drugs, of Taiwan Drug Injury Relief System.

Methods: We retrospectively analyzed the applications of Taiwan Drug Injury Relief System from 1999 to 2019. Implicated drugs and adverse drug reactions (ADRs) were classified according to their ATC and MedDRA codes respectively. The approved applications whose adverse drug reactions by SOC fall into the category of hepatobiliary disorders were further analyzed. As herbal products was not within the scope of Taiwan Drug Injury Relief System, its impact was not assessed in our study.

Results: From 1999 to 2019, a total of 175 approved applications associated with drug-induced hepatotoxicity were identified. The main ADRs were as follows： acute hepatitis (N=67, 38%), hepatic failure (N=28, 16%), drug-induced liver injury (N=22, 13%), fulminant hepatitis (N=19, 11%), acute hepatic failure (N=14, 8%), abnormal hepatic function (N=9, 5%) and cholestatic hepatitis (N=7, 4%). The top 5 classes of implicated drugs were anti-tuberculosis agents (n=203, 62.1%), antifungals for systemic use (n=16, 4.9%), lipid modifying agents (n=15, 4.6%), antiepileptics (n=12, 3.7%) and NSAIDs (n=11, 3.4%). Of these, the number of application related to isoniazid, rifampin, pyrazinamide, ethambutol or, terbinafine was relatively high compared to other implicated drugs. Approximately half of the applications approved for drug injury relief payments were death applications. (Table 1)

Conclusion: The most prevalent ADR associated with drug-induced hepatotoxicity in our study was acute hepatitis. Anti-tuberculosis agents were the main causes of drug-induced hepatotoxicity, which were consistent with the findings in other Asian studies. Given that drug-induced hepatotoxicity could lead to devastating patient outcomes (i.e., 48.6% were death applications), safety measures should be implemented to mitigate the risks of drug-induced hepatotoxicity when prescribing those commonly implicated drugs.

Keywords: drug-induced hepatotoxicity, drug injury relief, adverse drug reactions

249 A widespread failure to disclose: Audit of conflict of interest statements by Australian authors of recent clinical trial reports

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Aim/Objective: The International Committee of Medical Journal Editors guidelines set clear standards for disclosure: Authors should report all financial relationships with commercial entities relevant to the study received within 3 years of submission of an article. Since 2015, Medicines Australia, Australia's national pharmaceutical industry association, has required member companies to report all payments to individual clinicians. We aimed to compare self-disclosure by Australian clinical trial authors with data reported by pharmaceutical companies.

Methods: To identify recent RCTs with at least 1 Australian author, we searched Medline (January to August 2020) using the Cochrane sensitivity and precision search strategy for RCTs, limited by mention of Australia in the text. Two researchers independently compared author's disclosure in included trials with information on the Medicines Australia Database.

Results: We identified 583 unique records, 440 of which were excluded after screening titles and abstracts. Of the remaining 143 articles, 120 met the inclusion criteria. Of the 120 published RCTs of drug trials with at least one Australian author, 56 (47%) had ≥ 1 authors with undisclosed COI. Of the 323 unique Australian authors in these 120 studies (28 of whom authored ≥ 2 studies), 83 (26%) had undisclosed COI. The most common type of non-disclosure was incorrectly declaring "no conflicts of interests" (53%), followed by partial disclosures of conflicts of interests (43%). In total, there were 94 non-disclosures among the 83 authors with undisclosed conflicts.
The median level of undisclosed payments was AUD$8,800 (₩7,500,00) [range AUD$140 (₩120,000 to AUD$97,600 (₩83,800,000)].

Conclusion: In this sample of recent RCTs with Australian authors, inaccurate and incomplete COI declarations were common. Cross-referencing the Medicines Australia database to identify undisclosed conflicts of interest prior to publication would vastly improve the accuracy of public disclosure of conflicts of interest.

Keywords: Conflicts of Interest Disclosure

250 Practice of face masking among young adults in South India: An online cross-sectional survey

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Objective: COVID-19 pandemic urges the need for respiratory protective equipment like face masks as a public health measure to control the spread of infection. This study aimed to investigate the trends followed in the practice of mask-wearing by the South Indian population amid the second wave of COVID-19 outbreak in 2021.

Methods: An online cross-sectional survey was conducted among the young adult population in India in late April 2021. An eight-item questionnaire was designed to assess the social perceptions and attitudes regarding wearing a face mask as a part of universal safety precautions. The social perceptions towards wearing masks were categorized as excellent, good average and poor on a scale (Social Perception Scale -SPS) scored out of 8. The details collected using predesigned google forms are statistically analyzed using the Chi-square test.

Results: Among the 1283 participants who completed the questionnaire, 57% wore cloth masks followed by 26% wearing N95 masks and 12% wearing a surgical mask. Even though the age of the study population varied from 19 – 76 years and with a male preponderance of 56.3% (n = 723), students and recent graduates participated largely in the study (71.8%, n = 922). A mean SPS score of 5.67±1.07 (out of 8) indicates that the social perception of the study population is good. A statistically significant association is observed between the SPS score and the age ($p = 0.003$), type of mask used ($p < 0.001$), and economic background of the study population ($p < 0.001$). Breathing difficulty, communication problems, additional cost incurred and dermatologic issues were commonly reported barriers against mask-wearing.

Conclusion: Adjunctive public health measures such as mask-wearing are crucial in curbing the COVID-19 transmission. By shaping an appropriate public attitude, policymakers can ensure compliance towards mask-wearing.

Keywords: Face masks, COVID-19

251 Descriptive analysis of Adverse Drug Reaction in a single hospital: A comparison of health insurance and medical aid patients

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Aim/objective: Adverse drug reactions (ADRs) were known to be affected by personal and social differences. In South Korea, most ADRs have been collected as anonymized data. There are a few studies that analyzed them in combination with socioeconomic information. Therefore, we would like to analyze ADRs combined with socioeconomic information.

Methods: Data from a single hospital between 2017 and 2019 were retrospectively reviewed. For descriptive analysis, we stratified the data by health insurance type. Statistical differences between categorical variables were analyzed by the Chi-square test.

Results: During this period, 2,247 cases were reported in 1,369 people. There were 987 health insurance patients (72.1%) and 382 medical aid patients (27.9%). By sex, women (57.8%) were more likely to report ADRs in health insurance, and men (52.9%) were more in medical aid. When divided by age group, the highest proportion of health insurance patients was in their 70s (26.7%), and 60s (28.0%) accounted for the highest proportion of medical aid patients. In health insurance patients, those who live with a partner were reported more ADRs (74.1%), and in medical aid patients, those without a partner (60.2%) were reported more ADRs. When assessing the severity of ADRs, the ratio reported as severe was higher in medical aid (3.1%) than health insurance patients (1.9%).

Conclusion: It is significant that socioeconomic information such as health insurance type, occupation, marital status, and ADRs are linked and analyzed, and can be used as basic data to prevent and manage ADRs for the vulnerable group in the future.

Keywords: Drug-Related Side Effects and Adverse Reactions, Pharmacoepidemiology, Medicaid

252 Evaluating the knowledge and practice regarding foot care in diabetes mellitus patients visiting a tertiary care hospital of South India.

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Objectives: This study aimed to assess the knowledge and practice of foot care in diabetes mellitus patients visiting a diabetes clinic associated with a tertiary care hospital in Kerala.

Methods: A cross-sectional study was conducted among diabetic patients using a pretested questionnaire to assess the knowledge and practice of diabetic patients regarding foot care. The knowledge score was classified as excellent if score >80%, and good if scored between 51 – 80%, and poor if the score was <50%. The practice score was categorized as good (>50%) and poor (<50%). Demographic details including the level of education, marital status, place of living, occupation were also collected. Descriptive and inferential statistics are performed using SPSS version 20.

Results: Among the 364 patients who completed the questionnaire, the majority (n=112, 30.76%) of respondents were between 46-55 years and the male gender was dominating (n=204 ,56.0%). The majority of respondents were from urban locality 269 (73.9%) and most of them were married (88.7%). Even though the majority of the respondents 80 (22.0%) were educated, a good number of them were either unemployed or homemakers (n=218 ,59.8%). A large number of respondents 58.8% had adequate knowledge and 62.4% had a poor practice of DM foot care. Place of living (p=0.003), level of education (p<0.001), marital status (p=0.007), occupation (p < 0.001) had a statistically significant association with knowledge and practice score. The gender of the participants has no statistically significant association with foot care practices.

Conclusion: Customized patient education strategies are necessary to enhance the overall knowledge and practice to ensure the decreased incidence of diabetic foot complications.

Keywords: Diabetes Mellitus, Foot Care

253 Intra family encouragement in self-management of Type 2 Diabetes: A cross sectional evaluation in the Indian population.

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Objective: Type 2 diabetes mellitus (T2DM) affect the patient and the family, potentially causing either psychological distress or an increased sense of responsibility in these families. The study evaluates the influence of intra-family support in the self-management of type 2 diabetes in an Indian population.

Methods: This cross-sectional observational study included 167 patients with a history of diabetes mellitus for the past 3 years visiting a diabetes clinic in South India. The patient and their close family were interviewed during routine appointments for diabetes care to collect demographic information, family members' knowledge, and attitude towards diabetes self-care through supportive and non-supportive behaviors. The adherence towards diabetes treatment was evaluated using Morisky Medication Adherence Scale – 8 item questionnaire. The most recent A1C was extracted from the medical record. Descriptive statistics and Odds ratio is calculated to identify the relationship between variables of interest.

Results: Among the study participants, a majority (114; 68.2%) of the T2DM patients belong to an age category of more than 60 years with a female preponderance of 52.6% (88). Out of the 80.8% (135) patients who were accompanied by a close family member, 113 (83.7%) patients experience very good support from family in maintaining a diabetic diet. Blood glucose monitoring (91; 67.4%) purchasing diabetes medicines and (76; 56.2%) partnering in exercise (41; 30.3%) are the various supportive activities from family members. Medication adherence ($p = 0.007$) and glycemic control ($p < 0.001$) was strongly associated with support from close family.

Conclusion: Better self-management of diabetes occurs within a friendly family environment. Involvement of family in diabetes care and their supportive behavior can contribute to improved glycemic control. A participatory Diabetes Self-Management Educational model which includes family engagement is crucial in ensuring improved diabetes care in future perspective.

Keywords: Diabetes Mellitus, Family Care

254 Risk classification and mortality prediction in patients with community-onset bacteremia: Machine learning derived algorithm

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Objectives: We aimed to explore homogeneous groups of patients within community-onset bacteremia by using cluster analysis and select important risk factors for 30-day mortality in different clusters through classification and regression tree.

Methods: A retrospective, single medical center, EMR database cohort study. Pathogens, comorbidity, McCabe score, Pitt bacteremia score, lab data, infection sources, and time-to-appropriate antibiotics were collected in our cluster analysis. Partition Around Medoids with Gower distance was used to clustering mixed types of our data. Classification and regression trees were used in each cluster to discover the important risk factors for 30-day mortality. We will separate 70% for the training data set and 30% for the testing data set to assess the accuracy of our predictive models.

Results: There were 1498 patients in cluster one. The main sources of infection were urinary tract, biliary tract, and liver abscess with gram-negative pathogens. The bacteremia severity was lower in cluster one. There were 710 patients in cluster two. The main sources of infection were skin and soft tissue infection, infective endocarditis, and pneumonia with gram-positive pathogens. The 30-day mortality was higher in cluster two (17.32% vs. 12.22%). The time-to-appropriate antibiotics were 20 hours longer in cluster two. In cluster one, there were five decision nodes for mortality 1. Pitt bacteremia score≧6 2. Fatal comorbidity 3. Urinary tract infection 4. Septic shock 5. Glucose<104 mg/dL. In cluster two, the decision nodes were 1. Pitt bacteremia score≧6 2. Septic shock 3. Malignancy.

Conclusions: Cluster two was characterized by the gram-positive pathogen. It had longer time-to-appropriate antibiotics and higher 30-day mortality. Cluster one had more risk factors to concern when it comes to predicting 30-day mortality.

Keywords: Cluster Analysis, Classification and Regression Tree, Community-Onset Bacteremia

255 Provision of answers to the poison information queries from public and healthcare practitioners (HCPS) at a tertiary care hospital

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Aim/Objective: To provide the answers for the poison information queries from public and healthcare practitioners in a tertiary care hospital.

Methods: The study designed employed was a prospective observational study conducted in a teaching tertiary hospital. Data was obtained from the patient's case sheets with their consent and was duly filled into data collection forms. Poison information queries were answered to the HCPs with the aim of better patient care and updating the knowledge whereas poison information queries were answered to the general public with the aim of rectifying their doubts, avoiding the unnecessary visits to hospital and educating them.

Results: Out of the 402 queries received, the majority were from health care professionals of tertiary care hospital, Mysuru (n= 385) followed by the general public (n = 17). The queries asked by general public were mainly to know the first aid tips for snake bite and accidental poisoning, to clarify their doubts regarding certain poisoning and to know working of Poison Information Centre (PIC). Assessment of the professional status of the enquirers showed that 56.88%(n= 219) of the queries were obtained from the clinicians,41.03% (n = 158) of the queries were from the post graduates (PGs) students of the department of general medicine, emergency medicine, pediatrics and so on and 02.07%(n=8) of the queries from the nursing staff and 75.84%(n= 292) . Other queries included regarding range of toxicity (n= 13), toxicodynamics (00.77%; 03) and toxicokinetics (00.51%; 02).

Conclusion: The findings of our study concluded that by providing the necessary information to the enquirer, proper management strategies were initiated by the clinician as early as possible whereby a significant reduction in mortality and morbidity among the poisoning cases were achieved.

Keywords: Poison Information Centre, Health Care Professional, Queries, Poisoning.

256 Effects of Pharmaceutical Care in CKD stage 3-4 patients and patients at risks of CKD at a secondary care hospital

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Chronic kidney disease (CKD) is one of the major health problems in Thailand. Diabetes and high blood pressure are the most common causes of CKD. The presence of CKD is associated with increase in risk of end-stage renal disease (ESRD).

The study was aimed to determine the effects of pharmaceutical care program on health outcomes in patients with stage 3 – 4 CKD and patients diagnosed with type 2 diabetes and hypertensive at risks of CKD. This was a pre-post experimental study with no concurrent control group. Patients visited outpatient clinic during July 2018 – June 2019 at secondary care hospital were invited to participate in this study. The pharmaceutical care program, including prescription review, medication dose adjustment, adherence evaluation and education on disease, nutrition and self-care was provided at 4 follow-up visits. Laboratory monitoring and drug – related problem (DRPs) also performed at each visit. Clinical outcome data, including kidney function, blood pressure (BP), fasting blood sugar (FBS), glycosylated hemoglobin (HbA1C), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) at 12 months. Baseline data were collected at 6 months before and 12 months after the intervention.

This study included 120 patients, average age of 71.0±10.7, and 51.7% were females. Most patients (73.3%) were at stage 3 – 4 CKD. The average estimated glomerular filtration rate (eGFR) was improved from baseline 51.85±14.71 to 54.84±16.53 ml/min/1.73m2 at 12 months (p=0.009). Significant reduction of serum creatinine was found from 1.33±0.41 at baseline to 1.27±0.39 mg/dL at 12 months (p=0.001). Other outcomes were not significantly change after receiving pharmaceutical care program (p>0.05). The pharmaceutical care program seemed to slow the deterioration rate of kidney function in patient with stage 3 – 4 CKD and patients at risks of CKD.

257 Effects of pharmaceutical care in patients with chronic kidney disease at a secondary care hospital

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Chronic kidney disease (CKD) is one of the major health problems in Thailand. Diabetes and high blood pressure are the most common causes of CKD.

The presence of CKD is associated with increase in risk of end-stage renal disease (ESRD). The study was aimed to determine the effects of pharmaceutical care program on health outcomes in patients with chronic kidney disease and having diabetes mellitus or hypertension or both as co-morbidities. This was a pre-post experimental study with no concurrent control group. Patients visited CKD clinic in outpatient apartment during July 2018 – June 2019 at secondary care hospital were invited to participate in this study. The pharmaceutical care program, including prescription review, medication dose adjustment, adherence evaluation and education on disease, nutrition and self-care was provided at 4 follow-up visits. Laboratory monitoring and drug – related problem (DRPs) also performed at each visit. Clinical outcome data, including kidney function, blood pressure (BP), fasting blood sugar (FBS), glycosylated hemoglobin (HbA1C), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) at 12 months. Baseline data were collected at 6 months before and 12 months after the intervention.

This study included 120 patients, average age of 71.0±10.7, and 51.7% were females. Most patients (69.2%) were at stage 3 CKD. The average estimated glomerular filtration rate (eGFR) was improved from baseline 51.85±14.71 to 54.84±16.53 ml/min/1.73m2 at 12 months (p=0.009). Significant reduction of serum creatinine was found from 1.33±0.41 at baseline to 1.27±0.39 mg/dL at 12 months (p=0.001). Other outcomes were not significantly change after receiving pharmaceutical care program (p>0.05). The pharmaceutical care program seemed to slow the deterioration rate of kidney function in patient with CKD and patients with type 2 diabetes and hypertensive at risks of CKD.

258 Attitudes and opinions of 5th-year pharmacy students toward online OPSE in the COVID-19 era: A preliminary survey

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Objective: This study aimed to explore attitudes and opinions of 5th-year pharmacy students toward online Objective Structured Practical Examination (OPSE) in the COVID-19 era.

Methods: A preliminary survey with a convergent parallel mixed method was conducted using online self-administered questionnaires to gain information from 5th-year pharmacy students who first time took the online OSPE. The questionnaire consisted of 3 main parts including demographic data, attitudes, and opinions toward online OPSE. The results were analyzed using descriptive statistics.

Results: The response rate was 82.54% (52/63). The majority were female (78.8%), with an average age of 23.50 ± 0.87 years and grade point average of 3.16 ± 0.38. For attitude toward online OPSE, most pharmacy students were overall satisfied with online OSPE at level of quite satisfied to very satisfied (46.15% VS 25.00%). However, they believed that online OSPE could not be a substitute for traditional OSPE (42.31% VS 13.46%) and should only be used in uncommon situation (73.08% VS 1.92%) because online OSPE was more stressful than traditional OSPE (48.08% VS 21.15%). Moreover, online OSPE was easier to cheat (46.15% VS 11.54%) and had more inequality in rating score than traditional OSPE (48.08% VS 15.38%).

Conclusions: Online OSPE is a powerful tool to evaluate clinical pharmacy practice during COVID-19 pandemic. However, online OSPE could not be a substitute for traditional OSPE and should be only used if necessary.

Keywords: Online Objective Structured Practical Examination, Pharmacy education

259 Validation of Interview Guide: By adapting interview protocol refinement method

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Background: Interviews have the potential to unveil the experiences of the participants through series of questions that focus on understanding the views, opinions, and experiences of the individuals. In the medical field, there is less acceptance for qualitative research due to poor execution of studies and data analysis which is mainly due to the issues in reliability, validity, sampling, and generalizability. As the interview guide serves as an important aid in capturing the experiences of the participants the instruments used for the interview process must be reliable in order to produce robust data.

Aim: The main objective of this study was to validate the interview guide which was prepared to study the pharmacist's perspectives on the medicine supply chain during the COVID-19 period.

Methodology: Interview Protocol Refinement (IPR) was employed to validate the interview guide. It has four phases 1) Confirming the alignment of interview questions and the research questions 2) Building an inquiry-based conversation 3) Collecting feedback on interview guide 4) Piloting the interview guide.

Results: We confirmed the alignment of the interview questions and research questions using a matrix map. In the second phase, prompt development was done for enhancing the conversation flow, the interview guide was then subjected to 3 rd phase. Expert feedback was obtained and the questions were modified and extra questions were added. Then again phase 1 to phase 3 was conducted again. The final interview guide was subjected to phase 4 which is pilot testing. Feedbacks were obtained from actual respondents for enhancing the interview guide.

Conclusion: The framework helped in revising the questionnaire and also the pilot testing facilitated in warranting that the enhanced questionnaire was understood by the participants and the questions were competent in acquiring the intended answers based on the proposed research objective.

260 Artificial Intelligence in Acute Respiratory Distress Syndrome: A systematic review

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Objective: Acute respiratory distress syndrome (ARDS) is a life-threatening pulmonary disease across the globe with a high clinical and cost burden. Artificial intelligence (AI) is an emerging area and observed to be used in various aspects of ARDS. We aimed to summarize the currently available literature on various applications of AI in the ARDS through a systematic review.

Methodology: PubMed was searched from inception to February 2021 to collate all the studies. Additionally, the bibliographic search of included studies and a random search in Google, Google Scholar, and Research Gate to identify any relevant articles. The English language studies which employed the data from the ARDS patients to develop and/or assess the role of AI in the various aspects of ARDS were considered for this review. Two independent reviewers performed the study selection and data extraction and any disagreements were settled through discussion or consulting a third reviewer.

Results: A total of 19 studies published between the years 2002 to 2020 were included in this review. The AI was used for various purposes such as diagnosis (n=10; 53%), risk stratification (n=1; 5%), prediction of severity (n=3; 17%), management (n=2; 10%), prediction of mortality (n=2; 10%), and decision making (n=1; 5%) among the included studies. The area under the curve among the developed models in the included studies ranged between 0.8 to 1, which is considered to be very good to excellent

Conclusion: AI is revolutionizing the healthcare field and is having a wide range of applications in ARDS, thereby minimizing the cost and enhancing the outcomes.

261 Assessment of public knowledge and attitude towards chronic kidney disease by using a validated questionnaire: A cross-sectional study

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Aim: Public awareness is considered as an important determinant of the uptake of screening programs. However, there is scarcity of the data with respect to public knowledge. This study aims to assess the knowledge and attitude towards chronic kidney disease (CKD) among general public in northern part of India.

Methods: This study was conducted through various social media platforms as well as offline by using a validated self-administered questionnaire. The data was summarized as frequencies and percentages for categorical variables. The multiple linear regression analyses regression analysis was also employed to identify predictors of the public knowledge. A p value of <0.05 was taken as statistically significant.

Results: A total of 507 participants completed the online/offline questionnaire based cross-sectional study. A majority of participants were male (67.7%), lived in the rural areas (53.5), had either a bachelor's or master's degree (77.4), and did not had a family history of kidney stones (91.9). Only 6.5% of participants knew that high blood pressure is a risk factor for CKD while only 10.84% knew that excess stress is not a risk factor. The kidney's function of keeping the bones healthy had lower knowledge score, other kidney functions had comparatively better knowledge scores. The multivariate analysis found higher knowledge scores associated with a higher level of education.

Conclusions: Indian adults demonstrated a good knowledge and positive attitude regarding chronic kidney disease. However, knowledge was lower among older adults and less educated groups. More collaborative efforts are needed to improve the public awareness regarding the essentials of chronic kidney disease.

Keywords: Chronic kidney disease, public knowledge, attitude, India

262 Evaluation on hand hygiene knowledge and behavior among general population - A cross sectional study

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Background: Communicable infections are rising in number thus resulting as a burden among both healthcare workers and general public. Hand hygiene (HH) is one of the actions to prevent such contamination. The aim of the study was to determine HH knowledge and behavior of the general population to understand the knowledge gap.

Methods: An investigation by using a cross-sectional study design was conducted within general population in southern part of India from November 2020 to February 2021 via online platform like what's app, LinkedIn and through emails. Hand washing and drying questionnaire was used to assess the knowledge and behavior in general population. Chi-square Anova statistical data analysis was performed with the help of SPSS software.

Results: A total of 379 study population were responded to the survey questionnaire. Overall, female gender had significantly better knowledge towards hand hygiene when compared to males (5.71±1.55 vs 5.18±1.32; $p<0.05$). 95.25% of the respondents answered that hand hygiene practice became more frequent during infectious outbreaks. Though most of our study population indicated that they perform hand cleaning under various explicit circumstances such as while cooking, prior to eating, after pee or defecation, and once they cough/sneeze, they indicated that they use water and soap for cleaning their hands than preferring ABHR, water alone. Concerning hand drying more males dry their hand utilizing personal towel than females (97.5% vs 94.22%) $p<0.05$.

Conclusion: The study results shows that female study population generally have an improved knowledge level and better HH conduct when compared to male study population. The fallacy of study population associated with HH were perceived among general public. The findings of this study can give information which can be helpful to enhance well-being advancement and make missions to achieve diligent improvement in HH practices.

Keywords: Hand hygiene, Knowledge level, pandemic

263 Comparison of drug safety reporting features among East and Southeast Asian countries

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Objective: Recently, global drug development among Asian countries, especially East and Southeast Asian countries, has been promoted, but population differences in adverse drug reactions (ADRs) which might emerge after marketing in Asians has not been well-investigated. This study aimed to overview the features of individual case safety reports (ICSRs) and compare ADR profiles of antidiabetic agents among East and Southeast Asian countries, and the U.S.A.

Methods: The World Health Organization global database of ICSRs, VigiBase, as of 4th October 2020 was used to compare the ICSR features among East Asia (Japan, Korea and China; total 3,544,903 ICSRs), Southeast Asia (Philippines, Thailand and Malaysia; total 568,833 ICSRs), and U.S.A. (11,616,090 ICSRs); i.e., rate of serious cases (death, life-threatening, caused/prolonged hospitalization), age, sex, reporters, suspected drug classes, and ADRs based on Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC). ADR profiles (percent SOCs) for each antidiabetic agent (insulin, insulin glargine, sitagliptin and metformin; total 157,677 ICSRs) and those reporting odds ratios (RORs) against insulin for major SOCs were compared among countries.

Results: Rate of serious cases, reporters and major suspected drugs varied among countries and between East and Southeast Asia. Major ADRs were “Nervous system disorders” in Japan, and “General disorders/administration site conditions” and/or “Skin/subcutaneous tissue disorders” in other countries. In both East and Southeast Asian countries, significantly higher RORs (lower limit of 95% confidence interval > 1) were detected in “Metabolism and nutrition disorders” for insulin glargine (vs. insulin), being different from U.S.A, and “Gastrointestinal disorders” for sitagliptin and metformin (vs. insulin) similarly to U.S.A.

Conclusion: This study suggests that the characteristic ADRs for each antidiabetic agent would be common among East and Southeast Asians, while the different ICSR features were observed. Further research would be needed to confirm population differences in ADRs among Asian countries.

264 Health literacy and awareness for COVID-19 prevention in Asia: A systematic literature review

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Background: COVID-19 is a viral infection caused by SARS-CoV-2 and classified as a pandemic; however, due to the non-availability of its cure, prevention is considered a best possible strategy to stop this pandemic. In this pandemic, the public has received an overabundance of information, which is sometimes considered inaccurate, making prevention challenging, especially in developing and underdeveloped countries. This study aims to provide a systematic literature review on the health literacy awareness among Asian countries about SARS-CoV-2 and its impact on COVID-19 prevention.

Methods: We performed an extensive literature search on health literacy among the Asian population related to COVID-19. Relevant articles from PubMed and EMBASE databases were extracted and evaluated by applying appropriate key search terms to obtain the information published from January 2020 to April 2021. We included data based on observational and questionnaire-based studies and gathered information on participant's characteristics, health literacy and awareness, fear of COVID-19, and health-related behaviours.

Results: The most eligible studies were identified from the available literature (N=154) searched through using appropriate key terms. The literature analysis showed that digital platforms such as social media and electronic media are the primary sources that spread awareness of COVID-19 pandemic-related information, prevention strategies, and severity.

Conclusion: Globally, digital media and platforms are a major source for disseminating and promoting health literacy about COVID-19 in the Asian population.

265 Bariatric surgery for glycemic control in patients with type 2 diabetes mellitus: A systematic review and meta-analysis

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Aims: This random-effects meta-analysis aims to assess and quantify the effect of bariatric surgery on glycemic control for patients with Type 2 diabetes mellitus in the overweight and obese range.

Materials and methods: A systematic literature search was performed for prospective studies. Data on body mass index, glycated hemoglobin, and fasting blood glucose level were pooled from each study for the random-effects meta-analysis.

Results: A total of 1126 patients in 30 studies comprising 36 treatment arms were identified. The intervention groups were classified into three major types of bariatric procedures, namely, Roux-en-Y gastric bypass, adjustable gastric banding, and sleeve gastrectomy. All three groups exhibited significant effects in reducing body mass index, glycated hemoglobin, and fasting blood glucose levels. In the short term, SG was associated with the greatest reduction in HbA1c and BMI (2.37%, 95% confidence intervals (CI) 1.67–3.08; 11.16 kg/m2, 95% CI 7.69–14.63, respectively), while RYGB resulted in the highest reduction in FBG (4.04 mmol/L, 95% CI 3.10–4.98).

Conclusion: Regardless of its type, bariatric surgery is effective for patients with type 2 diabetes mellitus in the overweight and obese range in terms of weight reduction and glycemic control. Post-SG offers comparable efficacy to that of RYGB in achieving both HbA1c and FBG reductions in the medium to long term.

266 Glycemic control of insulin therapy in diabetic patients at a tertiary care hospital

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Introduction: Different insulin therapy for the treatment of diabetes mellitus (DM) might produce glycaemic control and side effects. The objectives of this study were to assess the effects of different insulin injection on glycaemic control and side effects in diabetic patients initiated with insulin injection.

Methods: A cross-sectional analytical study was conducted. Diabetic patients at outpatient department started insulin therapy during January, 2011 to December, 2015 and continued the same insulin therapy for at least 6 months were randomly selected. Demographic data, HbA1C at baseline and 6 months, and side effects from insulin were collected from medical records.

Results: Ninety-seven diabetic patients were included in this study, 45 patients treated with premixed insulin, 31 with NPH insulin, and 21 with LAA insulin. Significant HbA1c reduction was found after 6 months in patients treated with NPH insulin and premixed insulin (p =0.040 and 0.020, respectively). HbA1c reductions from baseline were not different among 3 types of insulin therapy at 6 months (p = 0.842). The rate of attaining treatment goal of HbA1c < 7% was highest (28.89%) in patients treated with premixed insulin. The highest rates of mild hypoglycemic events and weight gain were reported in NPH insulin compared with other insulin therapies (19.4% and 63.0%, respectively), but they were not significantly different across the 3 types of insulin therapy.

Conclusion: HbA1c reduction at 6 months was found in diabetic patients initiated with NPH insulin and premixed insulin. HbA1c reduction and side effects were not different among NPH, premixed, and LAA insulin therapy.

Keywords: Diabetic patients, Patterns, Insulin, Glycaemic control

267 Prevalence and factors associated with periodontal disease and dental caries among patients with diabetes mellitus

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Aims: Patients with diabetes mellitus type 2 (DMT2) may have oral health problems including periodontal disease (gingivitis and periodontitis) and dental caries. This cross-sectional study aimed to determine the prevalence and factors associated with periodontal disease and dental caries.

Methods: The participants were patients with DMT2 treated and examined for oral health from 1 July 2018 to 31 October 2019 at a community hospital in northern Thailand. Data were collected from medical records of patients covering three parts: general information, illness information, and periodontal disease and dental caries information. Logistic regression, reporting as Odds Ratio with 95% confidence interval (OR with 95% CI), was used to determine factors associated with the dental outcomes.

Results: Of 100 patients, there were 43 males and 57 females, with a mean age of 58.36 (±9.26) years. The prevalence of periodontal disease was 56.0% (gingivitis 39.0%, periodontitis 17.0%) and dental caries was 34.0%. Factors associated with periodontal disease were the use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARB) antihypertensive drug, OR (95% CI): 0.30 (0.09-0.98), p = 0.048. Regarding gingivitis, fasting blood sugar (FBS) greater than 170 mg/dl was associated with gingivitis, OR (95% CI): 2.55 (1.03-6.29), p = 0.042. Regarding periodontitis, factors associated with periodontitis were being hypertension, OR (95% CI): 0.17 (0.05-0.60), p = 0.006, and the use of ACEI/ARB antihypertensive drugs, OR (95% CI): 0.22 (0.07-0.69), p = 0.010. However, we found no factors associated with dental caries.

Conclusion: We found that most of the patients with DMT2 had any oral health concerns with the most problem of periodontal disease following by dental carries. Factors associated with these oral problems were hypertension, using ACEI/ARB antihypertensive drugs, and a high level of FB. These factors should be carefully considered and managed by the patients and dentists when treating patients with DMT2.

268 Recent trends in the incidence and prevalence of inflammatory bowel disease (IBD) in Japan and the US

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Aim/Objective: To estimate the incidence and prevalence of inflammatory bowel disease (IBD) and its subtypes [i.e., Crohn's disease (CD) and ulcerative colitis (UC)]; to describe the trends of IBD in Japan and the US.

Methods: A retrospective cohort study using two claims databases, Japan Medical Data Center JMDC and IBM Commercial Claims and Encounters CCAE (US), was conducted with study period covering 10 years (2010-2019). All patients with continuous health plan enrollment for ≥12 months were eligible. Incidence rate (per 1000 person-years) and period prevalence (%) of IBD and its subtypes were estimated by age-group and calendar-year. IBD cases were identified adopting a validated algorithm based on diagnosis and treatment codes: ≥2 healthcare encounters on different days with IBD diagnosis records; or 1 IBD diagnosis and ≥1 pharmacy claim(s) for IBD-specific medications (i.e., 5-ASA, biologics). IBD subtypes were determined by frequency and recency of CD versus UC diagnosis codes.

Results: The average annual age-standardized period incidence rate (per 1000 person-years) of IBD was 0.65 (range: 0.50-0.81) in JMDC and 0.58 (0.52-0.65) in CCAE. The trend of the rates during the study period was increasing in JMDC (p=0.015), whereas no change (p=0.674) in CCAE. The rate was 0.10 (range: 0.08-0.11) for CD and 0.55 (0.43-0.70) for UC in JMDC, and 0.24 (0.21-0.28) and 0.34 (0.30-0.37), respectively, in CCAE. The average annual age-standardized period prevalence (%) was 0.21 (range: 0.16-0.26) for IBD, 0.04 (0.03-0.05) for CD and 0.17 (0.13-0.21) for UC in JMDC, and 0.79 (0.63-0.89), 0.39 (0.32-0.43) and 0.40 (0.31-0.45), respectively, in CCAE.

Conclusions: Among populations receiving employment-based insurance, the trend of incidence of IBD in Japan showed an increase from 2010 to 2019, whereas incidence was stable in the US. The trends of CD and UC also appeared different across the two countries.

269 Public perception towards expanding role of pharmacist in Sabah and Selangor, Malaysia

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Ongoing transformations in the range of roles played by pharmacists have a global reach. Traditionally, their role was limited to the distribution and dispensing of medications prescribed by doctors. Nowadays, the pharmacist also involved in health services and patient-oriented. Public perception is influenced by numerous determinants, both health-related and social, and these perceptions through pharmacists' role are expressed on patients' attitudes, trust, and expectations as health and illness consultants or qualified retailers of medicines. The objective of the conducted research was to describe how the public perceives pharmacists are working at pharmacies, what expectations they have surrounding their skills and the extent of their professional role. This study had applied a questionnaire based on a cross-sectional design to 281 adult respondents from February to March 2019. A questionnaire divided into demographic questions, public perception about the expanding role of pharmacists, and factors influencing the perception. The majority of respondents (>70%) agreed that the pharmacist's prominent roles are to let patients know how to use their medication and give any information regarding drug use. More than half of the total respondents (69%) also appreciated the roles of pharmacists. They expected that pharmacists would play a role in patient healthcare like members of therapeutic teams. Sociodemographic variables have no significant effect on the public perception of pharmacists. The most influential factor on public perception is pharmacist's expertise (75.15%), followed by environment and the facility of pharmacy (74,3%), and friendliness (72.25%).

In conclusion, the community had a positive perception of pharmacists' expanding roles, and they expect the pharmacy to play more roles in healthcare in the future.

Keyword: role of pharmacist, public perception