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Insights of Healthcare Work-Force On Establishing Medication Error Reporting System In A Tertiary Care Teaching Hospital: A Survey Questionnaire

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Objective: To determine the perceptions of Healthcare professionals towards establishing medication error reporting programme.

Methods: A questionnaire was designed, validated and circulated among the health care professionals of a tertiary care teaching hospital by clinical pharmacists to understand their perception on Medication Error Reporting System.

Results: A total of 622 HCPs were approached with this questionnaire. Of which 535 HCPs, i.e., 376 (70.2%) Nursing staff, 32 (5.9%) Interns, 78 (14.5%) Post-graduation students in various disciplines of Hospital, 49 (9.1%) Doctors had responded to the survey with an overall response rate of 86%. General awareness of existence of Medication Error/ Error Reporting Centre was observed in doctors (51.5%) and nurses (61.9%) among whom doctors (18.2%) and nurses (44.4%) only were aware of existence of Medication Error/ Error Reporting Centre in India. During their practice, doctors (72.3%) and nurses (5.5%) have reported at least one medication error and doctors (81.7%) and nurses (83.5%) welcomed Medication Error Reporting and Monitoring system at their practice site. Further, the importance of clinical Pharmacist for independent assessment of medication error was appreciated by doctors (22.8%) and nurses (64%). Medication Error Reporting and Monitoring Centres' role for Health Care Professionals in medication safety was accepted by doctors (18.5%) and nurses (57.3%). Preference towards electronic reporting of medication error was shown by of doctors (26.5%) and nurses (16.2%). The willingness to report the medication errors to the Medication Error Reporting and Monitoring system if made available at their practice site is observed in doctors (62.2%) and nurses (81.6%).

Conclusions: The senior workforce entourages mandatory reporting with identity disclosure, while the newer staff wishes to remain anonymous in reporting medication errors. Balancing the perceptions of all stakeholders on reporting medication errors and thereof to enhance the acceptance of medication error reporting system will be the key in success of this programme.

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Current status of Re-Examination of New Drugs on Regulatory Safety Actions in Korea

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Objective: To identify the status in the re-examination system conducted over the past 10 years in South Korea as well as to assess the importance of the safety information provided by to the re-examination results according to the safety action after the re-examination.

Methods: We investigated the announcements of drug labelling changes, safety letters and alerts, and the administrative measure information announced by the Ministry of Food and Drug Safety from August 2009 to 30 April 2019 and then identified the safety actions based on the safety information obtained from the re-examination results.

Results: No action was taken for the safety letters and alerts of the drug nor the recall or disposal of the drug as a direct result of re-examination, other than receiving administrative action for licensed cancellation, recall, or disposal of the drug from January 2009 to April 2019. However, the changes for the license of the pharmaceutical ingredients based on the re-examination results accounted for 306(43%) all the cases from August 2009 to April 2019, which was the highest in 2012 and 2013. There were 239(83%) drug ingredients of six years, 40(14%) for four years, and 8 for other periods except where the examination period is not specified, as well as 162(53%) for 600 to 3000 subjects, and 102(33%) for more than 3000 subjects. The number of 185(60%) components were conducted in accordance with the Regulations for Re-examination, whereas the rest 121(39.6%) cases were passed through the regulations in consideration of the national prevalence rate, insurance benefits and market. Among the reported adverse events of the medication the unexpected adverse events that could have causation were 231(75%) and the significant adverse events that could have causation were 95(31%).

Conclusion: As a result of re-examination of medicines, reviews are usually added to the drug license list, and in practice, significant warning of adverse events are rarely added.

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Trends and pattern of antibiotic prescriptions for adult outpatients with acute upper respiratory tract infections in Japan, 2008-2018

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Aim: This observational study aimed to characterize the pattern and trends in consumption of major oral antibiotics prescribed for adult outpatients who were diagnosed with acute upper respiratory tract infections (AURTIs) in Japan from 2008 to 2018.

Methods: We identified patients aged over 20 years old with a diagnosis of AURTIs who were prescribed with oral antibiotics between 1st April 2008 and 31st September 2018, using a medical claims database. The diagnosis of AURTIs is based on ICD-10-CM codes, from J00 to J06, and antibiotic prescription of J01 was classified according to the Anatomical Therapeutic Chemical codes of the World Health Organization (ATC code). Patients who had a diagnosis that indicates bacterial infections within the same month were excluded. We assessed the pattern and trends by calculating the proportion of each class of antibiotics and the number of claims per 1000 patients during a year.

Results: About 7.54 million antibiotic prescriptions among 1,937,379 adult outpatients with AURTIs were analyzed. Acute nasopharyngitis was the most common indication with 4,159,596 (55.17%) prescriptions, followed by acute pharyngitis (23.89%), acute tonsillitis (8.68%), acute sinusitis (8.56%), acute laryngitis and tracheitis (3.66%) and acute obstructive laryngitis and epiglottitis (0.04%). Cephalosporins (35.20%), macrolides (32.18%), fluoroquinolones (24.58%), penicillins (5.88%), tetracyclines (0.81%) were the most commonly prescribed antibiotic classes. The percentage of antibiotic prescription kept falling down from 49.89% in 2008 to 39.03% in 2018. The number of antibiotic claims increased slightly from 3458.7 to 4044.1 per 1000 patients per year between 2008.4 and 2012.3 and fluctuated after then. The majority (93.94%) of antibiotics were still broad-spectrum while the usage of penicillins had an increase mostly after 2016.

Conclusion: Although the percentage of antibiotic prescription decreased, the prescription pattern still needs to be improved. A further approach is urgently required to be carried out to reduce antibiotic consumption, especially for the board-spectrum.

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Prevalence of potential drug-drug interactions in patients undergoing chemoradiotherapy and the impact of an expert team intervention

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Aim: To determine the prevalence of potential drug-drug interactions (DDIs) in patients receiving chemoradiotherapy and assess the usefulness of expert team recommendations in minimizing DDIs.

Methods: Patients undergoing chemoradiotherapy and treated with two or more drugs, at least one of them being an anticancer drug, were included in the study. The study was initiated following approval from the institutional ethics committee. One prescription per patient was screened for potential DDIs using the Lexicomp® software. The DDIs were classified as X, avoid combination; D, consider therapy modification; C, monitor therapy. The oncologist was informed regarding the DDIs detected; number of changes done in the prescription based on this information was recorded. The information was also shared with an expert team of two pharmacologists, and their recommendation was shared with the oncologist. The number of decisions of the expert team accepted by the oncologist was recorded.

Results: A total of 220 prescriptions were screened for the presence of DDIs; 106 prescriptions (48.18%) containing 620 drugs and 211 DDIs were identified. Of the 211 DDIs identified, 6.64% (14/211), 18.48% (39/211), and 74.88% (158/211) DDIs belonged to category X, D, and C, respectively. Of the 53 category X and D DDIs, 27 (50.94%) were accepted by the oncologist; 13 additional DDIs were flagged by the expert team, and 11 (84.62%) of these were accepted by the oncologist. The number of drugs prescribed showed a moderate positive correlation with number of DDIs ($\tau = 0.530$, $p < 0.001$) and was predictive of the number of DDIs even after controlling for other variables.

Conclusion: The prevalence of DDIs in our study sample is in agreement with those reported by earlier studies. A large number of the detected DDIs do not require any change in prescription. Expert team intervention contributes significantly to avoiding clinically relevant DDIs.

Keywords: Drug interactions, Prescription, Chemoradiotherapy

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Impact of drug safety communication on the use of hydroxyethyl starch in Taiwan: an interrupted time series study

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Aim/Objective: Hydroxyethyl starch (HES) has been widely used for volume resuscitation. However, accumulating evidence have suggested increased risks of acute kidney injury and mortality associated with HES, which push the US Food and Drug Administration (FDA) to add a boxed warning in June 2013 to restrict its use in critically ill patients. In response, the Taiwan FDA has issued a drug safety communication (DSC) in July 2013. The aim of this study was to investigate the impact of this DSC on HES use in Taiwan.

Methods: An interrupted time series study was conducted using Taiwan's National Health Insurance Research Database. Quarterly data of HES prescriptions from 2005 to 2016 were assessed, and the study period was divided into pre-DSC period (2005-2012), transition period (2013), and post-DSC period (2014-2016). Segmented regression models adjusted for autocorrelation were used to estimate the level change and the trend change of HES prescriptions. The estimated prescriptions were compared with the predicted prescriptions based on pre-DSC projections to calculate the relative reduction. Stratified analyses by prescriber characteristics (such as accreditation levels of hospitals or physician specialties) were also performed.

Results: The DSC was associated with a significant reduction in HES prescriptions (level change: -16594; trend change: -1208), and the relative reduction was -67.6% (95% confidence interval: -72.6%, -62.5%). Among different accreditation levels of hospitals, the relative reductions were more pronounced among medical centres (-72.4%) and regional hospitals (-64.7%) compared to district hospitals (-43.9%). Among different physician specialties, the greatest relative reduction was seen in emergency medicine specialists (-90.3%), while the least was seen in orthopaedists (-54.8%).

Conclusion: After the DSC issued, HES prescriptions in Taiwan were reduced by more than two-thirds; however, more attention should be paid to the variations in the effects of DSC by accreditation levels of hospitals or physician specialties.

Keywords: Drug Safety Communications, Hydroxyethyl Starch, Interrupted Time Series Study

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Association between pharmaceutical industry payments and prescribing a fixed-dose combination memantine extended released and donepezil: a cross-sectional study

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Objective: Once-daily extended-released memantine/donepezil (hereafter memantine/donepezil) may improve medication adherence but has a 60-fold higher cost compared to using generic memantine and donepezil separately. Pharmaceutical industry payments may influence prescribing high-cost products. We examined the association between pharmaceutical industry payments to physicians and prescribing memantine/donepezil in Medicare in the United States (US).

Methods: In this cross-sectional study using 2015-2016 Centres for Medicare and Medicaid Services (CMS) Open Payments and Medicare Part D prescription databases, we identified unique physicians who prescribed at least 1 prescription for memantine/donepezil in 2015 or 2016. The outcome was the number of prescriptions for memantine/donepezil written per physician per year. We characterized the key independent variable regarding physician receipt of industry payments in two ways: (1) number of payments, and (2) amount of payment (every $1000 unit) for memantine/donepezil received per physician per year. Multivariable linear regression was used to adjust for potential confounders including physician specialty, physician gender, total number of Alzheimer's disease prescriptions (i.e., donepezil, rivastigmine, galantamine and memantine, except for memantine/donepezil) written per physician per year, region in the US, rural/urban, and type of payment.

Results: Among the 4,895 eligible physicians, the average number of memantine/donepezil prescriptions per physician per year was 31.3 prescriptions (median=19.5, interquartile range (IQR)=13.0-32.0). On average, each physician received 2.1 payments (median=1.0, IQR=0-2.5) for memantine/donepezil, totalling $92 per year (median=$10.5, IQR=$0-33.2). In multivariable analyses, every 1 additional payment physicians received for memantine/donepezil was associated with nearly 1 additional memantine/donepezil prescription prescribed (β=0.82, standard error (SE)=0.21; P<0.001). In addition, every $1000 increase in receipt of payment for memantine/donepezil was associated with nearly 3 additional prescriptions for the product (β=2.68, SE=0.001; P=0.02).

Conclusion: Receipt of industry payments for memantine/donepezil, regardless of number or amount of payments, was independently associated with increased likelihood of physician prescribing memantine/donepezil in Medicare.

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Validity assessment of self-reported medication use in a pharmacoepidemiology research (by comparing to medical and pharmacy insurance claims)

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Aim/Objective: A self-reported questionnaire on medication use is widely used in epidemiology research, but its validity has not been assessed enough. The aim of this study was to evaluate the validity of the questionnaire by comparing self-reported medication usage to medical and pharmacy insurance claims (MPIC).

Methods: Participants were 1783 beneficiaries of the National Health Insurance (NHI) who joined the follow-up survey of the Tsuruoka Metabolomics Cohort Study in 2015 and those who answered completely to the self-reported medication-use questionnaire. Information on the lifestyle and medications (hypertension, diabetes and dyslipidemia) was collected through a standardized, self-administered questionnaire by the face-to-face interview. Data on MPIC are used as a reference. Sensitivity and specificity of the self-reported medication-use questionnaire was calculated by matching against MPIC data using 3- and 5-month fixed windows. Potential predictors of discordant self-report were assessed by 5-month fixed windows, including age, gender, education, marital status, employment, if they got dispensed medicines during the same month as the study, and the frequency of getting dispensed medicines.

Results: Sensitivity and specificity of questionnaire data which predicted insurance claims covering 5 months were, respectively, 96% (95% CI:0.95-0.98) and 82% (0.80-0.85) for hypertension, 96% (0.93-0.99) and 96% (0.96-0.97) for diabetes, 88% (0.85-0.90) and 91% (0.89-0.93) for dyslipidemia. Although both 3- and 5-month fixed windows showed high validity, the 5-month fixed window was slightly higher. As a potential predictor of discordant self-report, gender was found to be associated especially in dyslipidemia, whereas other predictors were not associated. Sensitivity and specificity were 74% (0.68-0.79) and 95% (0.93-0.97) for men, 94% (0.92-0.96) and 89% (0.86-0.92) for women.

Conclusion: High validity was found between the self-reported medication use and MPIC for hypertension, diabetes, and dyslipidemia medication use. Men tended to under-report the use of dyslipidemia medication.

Keywords: Pharmacoepidemiology, self-report, medicines, cohort-study, agreement

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Impact of Pharmacist Care in Medication Handling Practices of Paediatric Dosage Forms among Caregivers

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Aim: Accurate use of medicines in paediatric population serves as a specific challenge to caregivers. Our study aims to identify and correct any discrepancies in medication administration due to wrong practices and analyse the impact of pharmacist intervention w.r.t medication utilisation practices.

Methods: A case-control study was conducted in the department of paediatrics at a tertiary care hospital. Subjects were randomly allotted to an interventional group and control group. A validated questionnaire to assess the Knowledge, Attitude and Practice (KAP) were administered to both groups and baseline scores were obtained. Information leaflets and patient counselling were provided to the interventional group and KAP questionnaire was re-administered after 30 days of intervention.

Results: A total of 149 caregivers were enrolled in the study. Mixing drugs with milk and stopping medicines once the child feels better were the most common and potentially wrong practices recorded and corrected. 34.9% (interventional group) and 39.9% (control group) reported the use of non-standardized liquid dosing instruments, which decreased to 19.9% post intervention. Significant increase was observed in the knowledge (30.8%), attitude (20.3%) and practice (31.6%) after the intervention was made ($t=29.93$, $p<0.01$). Correct medication measurement practice (36% to 65.1%), checking active ingredients that are written on the label (8% to 38.7%) and following medication storage instructions (17% to 63.1%) were domains which showed significant improvement. There was a significant increase in knowledge ($p<0.01$), attitude ($p<0.01$) and practice ($p<0.01$) scores amongst the interventional group when compared to the control group.

Conclusion: Our findings emphasize the need to provide caregivers with essential knowledge about disease conditions and their drug therapy as suggested by healthcare providers. This empowers them to remain dedicated to being proactive with respect to medication handling practices.

Keywords: Pediatrics, medication handling practice

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Validating the diagnosis of acute stroke in Japanese DPC data from Shiga Stroke and Heart Attack Registry

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Background: The DPC data can be useful in acute stroke research in Japan. However, few works have focused on validation of acute stroke diagnosis of DPC data. The aim of this study was to validate the accuracy of DPC data in identifying acute stroke.

Methods: The study subject was all patients with stroke-related diagnosis codes at Shiga University Medical Science Hospital between 2011 and 2015. First, the hospital discharge data of patients with stroke-related diagnosis codes were obtained from Shiga Stroke and Heart Attack Registry (SSHR). Second, DPC information was also collected from the same hospital independently. Three stroke types were tested to identify discharges with acute stroke for 2 database [ischemic stroke (IS), intracranial hemorrhage (ICH), or subarachnoid hemorrhage (SAH)]. Diagnosis of SSHR was based on the information of electric records and re-diagnosed by 2 or 3 medical doctors at SSHR datacenter. We used diagnosis of SSHR as gold standards. We also set 3 algorithm to diagnose the acute stroke of DPC data.

Results: The sensitivity for ICH and SAH were both >95% for all 3 algorithm. Regarding IS, only algorithm 1 yielded better agreement (sensitivity=88.2%), other two algorithm showed worse agreement (sensitivity=70-75%).

Conclusion: Discharge with ICH and SAH were identified with high reliability in administrative DPC data. A substantial level of agreement was also obtained for IS, despite variation between the algorithms which set diagnosis.

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Regimen and adverse drug reactions of anti-tuberculosis treatment and its associated direct medical costs – a patient cohort-based analysis.

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Aim/Objective: The global End-TB strategy requires no affected families facing catastrophic costs due to TB. Although 1st-line anti-TB drugs is free of charge in China, additional drugs for adverse drug reactions (ADRs) and other examinations could bring in out-of-pocket payments. This study aimed to understand the occurrence of ADRs under different treatment regimen, and its related direct medical costs in Chinese TB patients.

Methods: The study participants were pulmonary TB patients diagnosed between June 2017 and May 2018 in the outpatient department of two TB designated hospitals in East and West China. Multidrug-resistant TB cases were excluded. The participating patients were followed-up until the end of treatment. Patients treated only by 1st-line anti-TB drugs were regarded as group A, and patients had the upgraded rifapentine, pasiniazid, or 2nd-line levofloxacin, and/or Chinese traditional anti-TB pills were regarded as group B. Information on prescriptions, examinations, ADRs and hospital bills of each patient were extracted from the hospital information system and medical charts.

Results: In total, 112 TB patients were recruited: 53 in group A and 59 in group B. The prevalence of ADRs such as abnormal liver function, renal function, gastrointestinal reactions, etc. was 71.7% in group A, while it was 89.8% in group B (P=0.001). The ADRs happened more frequently in group B (P<0.001). The total medical cost, the cost of registrations, examinations, drugs including anti-TB drugs, drugs for comorbidity or reliving symptoms in group B were significantly higher than those in group A (P<0.05). However, the medical cost related to ADRs was similar between the two groups (P=0.151).

Conclusion: Patients under standardized 1st-line anti-TB treatment had lower prevalence of ADRs and lower direct medical costs. Evaluating ADRs in patients treated with different anti-TB regimens may help reduce the direct medical costs of patients and formulate supportive financing strategies.

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Validation of renal failure diagnosis using laboratory data in the MDV database

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Aim/Objective:
We reported at the 2018 JSPE conference that positive predictive values (PPVs) for renal failure were low (≤50%). In this study, we re-designed and assessed the outcome definitions for acute kidney injury (AKI) and chronic kidney disease (CKD) by establishing gold standards based on the AKI and CKD practice guidelines.

Methods:
Data in the Medical Data Vision (MDV) database, from April 2008 to January 2018, were used. Of the 870,000 patients who used oral diabetic drugs, we included the 98,904 patients with laboratory data. The outcome was defined as a combination of the following: diagnosis (excluding suspected diagnosis) coded by the International Classification of Diseases, 10th Revision (ICD-10), medical tests, and drugs. We used creatinine values as the gold standard for AKI, and eGFR values for CKD. The validity of the outcome definitions were evaluated by PPV.

Results:
The outcome definitions for AKI diagnosis (ICD-10, N179) resulted in a PPV of 81.4% against the gold standard defined as “an increase in serum creatinine 0.3 mg/dl or a 1.5 fold increase from baseline”. Combined with the condition “diagnosis of CKD (ICD-10, N189) and eGFR value was available”, this resulted in a PPV of 93.8% against the gold standard defined as “reduced eGFR <60 mL/min/1.73m2 for at least 90 days” (PPV was 61.7% when the outcome was defined as only “diagnosis”). Adding “drugs” and/or “medical tests” to the outcome definitions increased the PPV.

Conclusions:
For AKI, the outcome definition with only “diagnosis” showed high PPVs. For CKD, the presence of “eGFR value” in addition to “diagnosis” showed high PPVs. These suggest that these outcome definitions can be useful for MDV database studies.

Keywords: database, validation study, acute kidney injury, chronic kidney disease

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Effect of Antipsychotics Use on Ischemic Stroke in Patients with Atrial Fibrillation and Dementia

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Aim: Investigate the effect of haloperidol, risperidone and quetiapine use on the risk of ischemic stroke in patients with AF and dementia. Evaluate the dose-response relationship of antipsychotics use in the same cohort.

Methods: This is a nationwide population-based retrospective cohort study with data from the National Health Insurance Research Database (NHIRD). The cohort consisted of patients with atrial fibrillation (AF) and dementia who initiated antipsychotic treatment between January 1, 2006, and December 31, 2010. Cox proportional hazards model were performed to evaluate the association between treatment groups and time to ischemic stroke. To ensure the appropriateness of study definitions and the robustness of results, several sensitivity analyses were conducted.

Results: We indicated that patients treated with quetiapine (HR=0.776, 95% CI, 0.631-0.955) were significantly associated with a lower risk of stroke while risperidone (HR=0.832, 95% CI, 0.653-1.060) showed no significant difference in risk of ischemic stroke compared to patients treated with haloperidol. The results of the dose-response analysis show us that patients receiving high dose risperidone (> 50mg/day chlorpromazine equivalent dose) use was significantly associated with increased risk of ischemic stroke (HR=1.601, 95% CI, 1.070-2.396) compared to the low-dose group (< 50mg/day chlorpromazine equivalent dose). Patients treated with a high dose of haloperidol or quetiapine showed the insignificant risk of stroke compared to low dose groups.

Conclusion: This study indicated that the use of quetiapine was significantly associated with a lower risk of stroke in patients with AF and dementia than other antipsychotics. When the use of antipsychotics is inevitable, the findings of this study suggest prescribing quetiapine in the lowest possible dose in this population who possess a pre-existing high risk of stroke.

Keywords: atrial fibrillation, dementia, antipsychotics, stroke

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The Effectiveness of Early Use of Long-Acting Injectable Antipsychotics in patients with Schizophrenia

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Objective: To assess whether patients adding or switching to LAIAs during early treatment of schizophrenia have decreased risks of hospitalization and improved antipsychotics adherence compared with those remaining OAPs.

Methods: Using the Taiwan National Health Insurance database, we conducted a population-based cohort study from January 1, 2002, to December 31, 2005. The based cohort consisted of a new user of OAPs. Within this cohort, LAIAs group were identified as patients who added or switched to LAIAs during hospitalization, had used LAIAs within 90 days after discharge, and received further prescription of LAIAs at least 6 times within 1-year postdischarge (n=312). The LAIAs group was matched 1:1 to patients who remained on OAPs (n=312). Study outcomes were measured by rehospitalization and antipsychotic adherence. The antipsychotic adherence assessed by the modified medication possession ratio (MPR). All patients were followed up from the index date to the date of re-hospitalization. A Cox proportional hazard model was to estimate the risk of re-hospitalization between LAIAs group and OAPs group.

Results: Among the 624 patients with schizophrenia were included. A total of 312 patients added or switched to LAIAs within the first 3 years of OAPs initiation. Patients who added or switched to LAIAs had lower risks of hospitalization compared with patients treated with OAPs alone (Hazard ratios = 0.56, 95% CI: 0.45-0.69). The mean of MPR in patients who added or switched to LAIAs was significantly higher than those who received OAPs alone ($p < 0.01$).

Conclusion: Administration of LAIAs during early treatment profoundly decreased risks of rehospitalization and improved antipsychotics adherence.

Keywords: antipsychotics/long-acting injectable/schizophrenia/early stage

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The Effectiveness of febuxostat in Moderate to Advanced Chronic Kidney Disease patients with Hyperuricemia or gout： A population-based study

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Objective: This study was aimed to evaluate the characteristics, utilization and severe cutaneous adverse reactions (SCAR) rate of febuxostat in patients with moderate to advanced CKD, including end stage of renal disease (ESRD).

Methods: We retrieved CKD patients treated by febuxostat with stage 3b, 4 and 5 whose disease status were confirmed through Pre-ESRD patient care and health education programs and registry for catastrophic illness from the National Health Insurance Research Database (NHIRD) during 2012 to 2015.

Results: A total of 12,570 patients in the pre-ESRD group and 1207 patients in the ESRD group were enrolled. The baseline characteristics in pre-ESRD group were mean age 68.1 years, men 68.6%, HTN 83.4% and DM 51.7%. The ESRD group were: mean age 61.2 years, men 63.6%, HTN 85.9% and DM 52.8%. The differences for baseline characteristics of patients between both groups were age, gender, HTN, CV disease, hyperlipidemia and initial dosage. The mean initial dosage of febuxostat was 48.6mg per day in the pre-ESRD group and 46.9mg per day in the ESRD group. The SCAR incidence rate was 1.8 per 100,000 person-year. And the incidence rate of patients had received colchicine for acute gout prophylaxis and treatment during 180 days follow-up were 2.8 versus 2.6 per 1000 person-year. The overall mortality rate was 82.3 per 1000 person-year, and in the pre-ESRD group was significantly lower than ESRD group (80.2 versus 104.0 per 1000 person-year, $p<0.05$).

Conclusion: Our study showed that febuxostat was prescribed in pre-ESRD patients were older than ESRD patients. The mean initial dose for patients with moderate to advanced CKD stage was 48mg daily. The overall incidence of the SCAR was no difference but have a trend for receiving colchicine therapy in ESRD more than pre-ESRD patients, especially at initial 3 months.

Keywords: febuxostat, CKD, ESRD

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Longitudinal Impact of Frailty and Polypharmacy on Risk of Mortality in the Elderly: A Retrospective Cohort Study

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Aim/Objective: The individual association between frailty or polypharmacy on risk of mortality has been examined. However, limited evidence has taken into account the potential combined effect of frailty and polypharmacy on risk of mortality in the elderly. This study aimed to examine the association between different status of frailty and polypharmacy and risk of mortality.

Methods: We identified 100,000 people aged from 65 to 100 years old from the National Health Insurance reimbursement database (NHIRD). Frailty was categorized into fit, mild frailty, moderate frailty and severe according to the multimorbidity frailty index. The chronic use of 5 to 9 medications was considered as polypharmacy, and 10 medications or more as excessive polypharmacy. Subjects were further classified into 12 groups taking into account both their status of frailty and polypharmacy. Generalized estimating equation model was used to examine the association between these groups and risk of mortality.

Results: Mean age of our subjects were 74.12 years, with 51.59% of women. Most of the subjects were categorize as fit / non-polypharmacy (61.01%), followed by fit / polypharmacy (16.16%).
Compared to fit / non-polypharmacy group, severe frailty / non-polypharmacy group had the highest risk of mortality (adjusted odds ratio (aOR)=9.39 [95% confidence interval (CI): 8.81-10.00]). Noteworthy, the risk of mortality varied among different polypharmacy status within each frailty groups. In fit and mild frailty groups, the risk of mortality increased as subjects used more medications. For example, within the fit frailty group, the aORs of mortality were 1.59 and 2.65 for the polypharmacy and excessive polypharmacy groups. This phenomenon is the opposite within moderate and severe frailty groups.

Conclusion: By demonstrating that frailty and polypharmacy would both modify the risk of mortality in the elderly, this study indicates that these factors should be monitored to optimize the quality of care of older people.

Keywords: Elderly, Frailty, Polypharmacy, Mortality

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Real-world effectiveness of switching from statin monotherapy to ezetimibe/simvastatin combination therapy

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Objectives: To investigate the short-term effectiveness of switching from statin monotherapy to ezetimibe/simvastatin 10/20 mg in lowering low-density lipoprotein cholesterol (LDL-C) level.

Methods: We performed a retrospective cohort study. We identified new users of ezetimibe/simvastatin from electronic medical records of a medical center in southern Taiwan from 2013 to 2018. Patients who had not been on statin monotherapy for at least 3 months before ezetimibe/simvastatin use or those who had been concurrent statin users were further excluded. The changes in lipid profile including LDL-C, high-density lipoprotein cholesterol (HDL-C) and total cholesterol level after 3 months were estimated. We employed descriptive statistics and paired t-test to evaluate the mean change in LDL-C, HDL-C and total cholesterol level.

Results: We identified 1304 eligible patients who switched from statin monotherapy to use of ezetimibe/simvastatin. This population was aged 62±12 (mean±SD) years and 57.7% were male. There were 64.8% patients with history of hypertension, 44.6% with type 2 diabetes mellitus and 27.6% with coronary heart disease. Before ezetimibe/simvastatin use, 17.9% of these patients had been on high-intensity statin while 82.1% on low- to moderate-intensity statin. After switching to ezetimibe/simvastatin, the mean change in LDL-C and total cholesterol level decreased significantly from 134.4±37.2 mg/dL and 212.9±43 mg/dL to 103.2±40 mg/dL and 179.4±47 mg/dL (n=865, $p < 0.0001$ and n=694, $p<0.0001$) respectively. This resulted in 23.2% decrease in LDL-C and 15.7% decrease in total cholesterol level. Change in HDL-C was not significant (from 46.6±12.4 mg/dL to 46.1±12.7 mg/dL, p=0.29). Subgroup analysis showed different intensity of original statin monotherapy did not affect LDL-C lowering effectiveness when shifting to ezetimibe/simvastatin use (mean difference of high-intensity vs. low- to moderate-intensity original statin users were -27.1±45.1 mg/dL and -31.9±39.9 mg/dL, p=0.20).

Conclusions: Combination therapy of ezetimibe/simvastatin 10/20 mg was effective in reducing LDL-C and total cholesterol level in patients who failed statin monotherapy.

Keywords: ezetimibe/simvastatin, LDL-C, statins

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Effectiveness of statins for primary prevention of cardiovascular disease in an elderly Asian population

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Aim/Objective: To evaluate the effectiveness of statins for primary prevention of atherosclerotic cardiovascular disease (ASCVD) in elderly Asians.

Methods: A retrospective cohort study was conducted using 2008-2017 linkage of the electronic health records in a medical center and the National Health Insurance Research Database. Patients aged over 65, without an ASCVD history and having a diagnosis of hypertension, diabetes or dyslipidemia were included. Statins new users were identified and 1:4 matched to non-users on age (±2 years), gender, index date (±30 days), presence of diabetes, low-density-lipoprotein cholesterol (LDL-C) level and propensity score. Effectiveness of statins on preventing major adverse cardiac events (MACE; includes myocardial infarction, ischemic stroke, and cardiovascular death) was analyzed by Cox proportional hazards model. The effect of statins was also assessed in subgroups of age (65-74, ≥75), diabetes status, and LDL-C levels (<50, ≥50 percentile).

Results: There were 4,447 statins new users and 17,130 non-users included after matching. The mean age was 73.8 years, and 65.8% were male. As a whole, 38.8% of the patients had diabetes, 68.3% had hypertension, and 71.1% had baseline LDL-C level over 130 mg/dL. With an as-treated analytic approach, 631 MACE occurred during a median follow-up of 2.7 years (incidence rate 9.3 per 1000 person-years), and statin use was not associated with a reduced risk of MACE (hazard ratio, 0.82; 95% CI, 0.64-1.05). However, when an intention-to-treat analytic approach was used, statin users appeared to have a significantly lower risk of MACE (hazard ratio, 0.84; 95% CI, 0.72-0.99) over a median follow-up of 4.8 years. No significant difference in the effect was found across subgroups.

Conclusion: Statin use could be beneficial for primary prevention of cardiovascular disease in the elderly over 65 years. Further cost-effectiveness analysis is required to weigh the treatment costs and benefits for clinical decision making.

Keywords: Statins, primary prevention, cardiovascular disease, elderly

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Treatment evolution and improved survival in multiple myeloma in Taiwan

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Aims/Objectives: The incidence of multiple myeloma (MM) is increasing worldwide, but the rate of increase is greatest in Asia. We described disease trends, treatment evolution and clinical outcomes in patients with newly diagnosed MM in Taiwan.

Methods: This retrospective cohort study used claims data from the Taiwan National Healthcare Insurance Research database, a population-based database containing information on all medical services for the whole population in Taiwan. All patients with newly diagnosed MM between 2007-2015 were enrolled. Patients with other pre-existing primary cancers other than MM were excluded. Eligible patients were followed-up until death or end of the observation period (31 December 2016), whichever occurred first.

Results: A total of 4,387 patients with newly diagnosed MM were included in the cohort analysis from 2007 to 2015. The mean age was 67.6 years (SD 12.1 years) and 55.7% were male. Crude annual incidences of newly diagnosed MM increased from 1.74 to 2.48 per 100,000 population. The age-adjusted annual incidence increased from 1.41 to 1.65 per 100,000 population.
With the introduction of novel agents in Taiwan during the study period, the percentage of patients treated with first-line therapy with novel agents increased from 0.4% to 89.4%, autologous stem cell transplantation doubled. As a result, all-cause case fatality decreased from 25.5% to 18.3% and median overall survival time increased from 2.1 years in 2007-2009 to 3.12 years in 2013-2015.

Conclusion: Comprehensive national data covering 9 years of follow-up confirm a substantial increase in the MM disease burden in Taiwan since 2007. The uptake of novel agents for first line treatment of MM in Taiwan has been high and the use of transplantation continues to increase. Over the study period, MM case fatality decreased and overall survival improved. Nevertheless, MM remains an incurable disease.

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Enoxaparin versus aspirin and aspirin combination in patients with spontaneous intracerebral hemorrhage

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Aim: To assess the long-term efficacy and safety of low dose aspirin in achieving thromboprophylaxis as compared with enoxaparin and aspirin combination in patients diagnosed with spontaneous intracerebral hemorrhage (SICH).

Methods: This prospective observational study evaluated 214 SICH patients admitted in a tertiary care teaching hospital. Patients of both gender aged 18 years and above and admitted during August 2017 - August 2018 with SICH were included. SICH due to an alternative cause such as trauma, tumor or an aneurysm, use of dual antiplatelet therapy, other indications for anticoagulation therapy or anticoagulant therapy prior to the index ICH (Intracerebral hemorrhage) were excluded. The primary efficacy endpoint was deep vein thrombosis (DVT) at 180 days follow-up analyzed via physical examination/ultrasonography. Singular aspirin regimen was tested for non-inferiority to combination therapy based on the DVT risk assessment score and muscle power grading scale. The principal safety endpoint was re-bleeding. Physicians' staged process for thromboprophylactic decision-making was assessed.

Results: Aspirin alone or in combination with enoxaparin showed 100% thrombo-protective effects with zero bleeding outcomes. In the intention-to-treat analysis, a trend (P <0.001) favoring singular aspirin use in both low (85.7%) and moderate (58.5%) probability of DVT-risk subsets was observed. Among 70 high-risk subsets, 47 (67.1%) were on dual therapy and 23 (32.9%) on monotherapy. A similar trend (P: 0.002) was observed with regard to muscle power grading where singular aspirin use was non-inferior to combination therapy with progressive paralysis. Out of 36 patients with complete paralysis, 16 (44.4%) were on monotherapy and 20 (55.6%) on dual therapy.

Conclusion: Low dose aspirin was non-inferior to standard enoxaparin and aspirin combination with respect to achieving thrombopropylaxis and prevention of bleeding complication. This study also shed light on thromboprophylactic decision-making patterns for DVT in SICH patients.

Key words: Spontaneous intracerebral hemorrhage, Deep vein thrombosis, Enoxaparin, Aspirin

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Duloxetine use and risk of coronary artery disease: systematic review and meta-analysis

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Aim/Objective: To identify association between duloxetine use and coronary artery disease through heart rate and blood pressure change.

Methods: We searched medical database to find relevant articles: PubMed, EMBASE, CENTRAL (Cochrane Central Register of Controlled Trials), clinicaltrials.gov, and psycINFO. Main keywords were duloxetine, safety, and randomized controlled clinical trials. The title, abstract, and full text were checked in order to obtain articles on duloxetine use with heart rate and blood pressure change. Meta-analysis was conducted with random effect model and quality of articles was evaluated Cochrane risk of bias 2.0. The manuscript has been written according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) harm guideline.

Results: Finally 110 articles were retrieved. According to the indication of duloxetine, 55 articles were selected as having indication of pain control, 31 articles with mood disorder, 9 articles with urinary incontinence, and 15 articles with other indications. Meta-analysis showed 60 to 120mg/day dose duloxetine increased 1.62 heart rates/min (95% confidence intervals [CIs]:1.53-1.71). When the 120mg/day dosing use, heart rates were increased to 2.68 rates/min (95% CIs:2.46-2.90). Sixty to 120mg/day dose duloxetine increased 1.53mmHg systolic blood pressure (95% CIs:1.00-2.05).

Conclusion: Duloxetine increased heart rate and systolic blood pressure. Well-designed pharmacoepidemiolgic studies to evaluate the causal relationship between duloxetine and coronary artery disease will be needed.

Keywords: duloxetine, coronary artery disease, systematic review, PRISMA-harm guideline

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Combination of glycopeptide and β-lactam and risk of acute kidney injury

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Aim: To compare the risk of acute kidney injury (AKI) among patients receiving the following glycopeptide and β-lactam combinations: 1) teicoplanin (TA) plus piperacillin/tazobactam (TZP) versus vancomycin (VAN) plus TZP (i.e., TA+TZP vs. VAN+TZP) and 2) VAN plus TZP versus VAN plus other β-lactams with similar antibacterial spectrum to TZP (i.e., VAN+TZP vs. VAN+β-lactam).

Methods: This was a retrospective cohort study using electronic health records from a medical center in Taiwan. Patients were included if a combination of glycopeptide and TZP or other selected β-lactam were used during hospitalization. Three study groups were identified: TA+TZP, VAN+TZP and VAN+β-lactam. In each group, two antibiotics of interest were required to overlap for at least three days. Patients with estimated glomerular filtration rate <15 mL/min/1.73m2, renal replacement therapy, or recent AKI history were excluded. We used propensity score matching to control for potential cofounders, and hazard ratio (HR) of AKI between study groups was calculated.

Results: The final sample contained 216 TA+TZP and VAN+TZP pairs (1:1 match). The median dose of TA and VAN was 10.8 and 27.5 mg/kg/day, respectively. The median trough level of VAN was 12.0 mg/L. AKI risk was similar in the TA+TZP group compared to that in the VAN+TZP group (13.0% vs. 12.5%; HR=1.17, 95% confidence interval [CI]=0.68-2.00, P=0.57). For the second comparison, there were 205 VAN+TZP and VAN+β-lactams pairs (1:4 match), and the median dose of VAN was both around 28.0 mg/kg/day. There was higher risk of AKI in the VAN+TZP group (13.2% vs. 9.6%; HR=1.72, 95% CI=1.10-2.68, P=0.02).

Conclusion: Our study does not support replacing VAN+TZP with TA+TZP clinically when AKI is of concern. The result of higher AKI risk among patients using VAN+TZP suggests VAN and other β-lactam might be the better choice in clinical practice.

Keywords: Teicoplanin, vancomycin, piperacillin/tazobactam, acute kidney injury

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Associations among antipsychotics, metabolism-related diseases, and cataracts in patients with schizophrenia: a retrospective cohort study

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Background: Antipsychotics are associated with cataract formation in patients with schizophrenia. However, metabolic-related diseases (MS) are highly prevalent in schizophrenia patients. While metabolic-related diseases increase the risk of cataracts, the relationship between antipsychotics and cataracts among schizophrenia patients with MS has not been elucidated.

Objective: To examine the long-term risks of cataracts associated with among individual antipsychotics, and to elucidate associations among antipsychotics, metabolism-related diseases, and the risk of cataracts.

Methods: Using National Health Insurance (NHI) data in Taiwan, we conducted a population-based cohort study enrolled 13,622 newly diagnosed schizophrenia patients from 2005 to 2009 and followed them until the end of 2013. Prescriptions of antipsychotics were available from prescriptions claims data. Cataracts and metabolism-related diseases were ascertained from NHI data. A Cox proportional hazard model that estimated metabolism-related diseases as time-dependent covariates and a propensity score-matching method were adapted to estimate the hazards ratios (HRs) for cataracts among individual antipsychotics.

Results: During the 8-year follow-up, patients receiving olanzapine, quetiapine, or risperidone had significantly higher risks of cataracts compared to those who received non-phenothiazines. Patients who developed diabetes mellitus (DM) or hyperlipidemia (HLP) after antipsychotic treatments had approximately 2.5-fold the risk of developing cataracts than those who did develop those diseases.

Conclusions: Olanzapine, quetiapine, and risperidone, are more likely to induce cataracts in patients with schizophrenia than non-phenothiazines. Furthermore, DM and HLP which developed during follow-up were independently associated with an increased risk of cataracts.

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Existence of Notoriety Bias in FDA Adverse Event Reporting System (FAERS) Database and Its Impact on Signal Strength

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Aim: Notoriety bias is defined as "a selection bias in which a case has a greater chance of being reported if the subject is exposed to the studied factor known to cause, thought to cause, or likely to cause the event of interest". This study aimed to determine the existence of notoriety bias in the FDA Adverse Event Reporting System (FAERS) database and estimate its impact on signal strength.

Methods: Publicly available FAERS data was used for analysis. 31 drugs which had label change/safety alert issued by the FDA were considered. These drugs were reviewed four quadrants before and after the safety alert for the number of reports, Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR). Wilcoxon signed rank test was used to compare the number of reports and signal strength before and after the alert.

Results: There was increased reporting for 11 drugs after the safety alert/label change by FDA. The reporting of 20 drugs decreased or remained unchanged after the safety alert/label change by FDA. Wilcoxon signed rank test showed that there is no statistically significant difference with respect to the number of reports before and after the safety alert (p: 0.330, Z: -0.974). 14 (45.16%) drugs had an increase in ROR, while 17 (54.83%) drugs had a decrease in ROR after safety alert issued by FDA (p: 0.953, Z: -0.059). 14 (45.16%) drugs had an increase in PRR, while 17 (54.83%) drugs had a decrease in PRR after safety alert (p: 0.914, Z: -0.108).

Conclusion: Although few FDA safety alert/ warnings had a strong and immediate impact, many had no impact on reporting of AE and signal strength. This study found that over-reporting due to notoriety bias does not exist in the FAERS database and the overall disproportionality in signal estimates is not altered by safety alert.

Keywords: FDA AERS, Pharmacovigilance, Notoriety effect, safety alert

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Aromatase Inhibitors Associated with Osteonecrosis of Jaw: A Disproportionality Analysis in the USFDA Adverse Event Reporting System (FAERS)

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Background: Osteonecrosis of jaw is a chronic, severe bone disease that affects the maxilla and mandible. Aromatase inhibitors are a class of drugs used in postmenopausal women for the treatment of hormone receptor-positive breast cancer. This study aims to find the association of Aromatase Inhibitors by disproportionality analysis in FDA Adverse Event Reporting System (FAERS).

Methods: Publicly available FAERS data was used in the study. Disproportionality analysis with Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR) with 95% confidence intervals (95% CI) were calculated. A value of ROR-1.96SE>1, PRR≥2, count of co-occurrences is 3 or more, with an associated $\chi 2$ value of 4 or more were considered as a positive signal.

Results: FAERS database had a total of 15,178 reports for Osteonecrosis of jaw. Amongst which 1,061 (6.99%) reports were associated with aromatase inhibitors. The number of reports for Exemestane, Letrozole and Anastrozole were 362 (34.11%), 448 (42.22%) and 251 (23.65%) respectively. The aromatase inhibitor which had the highest risk was Exemestane with PRR 18.59 (95% CI 14.92-22.15) and ROR 18.73 (95% CI 15.14-22.60). Letrozole had a PRR of 13.37 (95% CI 8.47-25.92) and ROR 13.28 (95% CI 8.34-26.89) and Anastrozole had a PRR of 8.04 (95% CI 6.65-13.19) and ROR 8.01 (95% CI 6.64-13.37). The Likelihood ratio and Reporting rate were 536.13 and 8.02 respectively for Letrozole, 214.12 and 5.29 for Anastrozole, 523.79 and 10.54 for Exemestane.

Conclusion: The present showed an association between aromatase inhibitors and osteonecrosis of jaw, 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.

Keywords: Osteonecrosis of Jaw, Exemestane, Letrozole, Anastrozole

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Population differences in incidence of allopurinol-related severe cutaneous adverse reactions in East Asians

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Objective: Allopurinol-related severe cutaneous adverse reactions (SCARs) are known to be associated with HLA-B*58:01, of which allele frequency (AF) is largely different among East Asians. However, evidence of population differences in SCAR development, and relevance of genetic factors and non-genetic factors in real world are still limited. This study was aimed to evaluate population differences in incidence of SCARs (including SJS, TEN and DIHS/DRESS) and possible relevance of genetic factors and/or non-genetic factors among East Asians using claims databases in East Asia.

Methods: Retrospective cohort studies were conducted using claims databases in Taiwan (the Health and Welfare Database), Korea (the Health Insurance Review and Assessment Service), and Japan (the Japan Medical Data Center claims database). Phenytoin or carbamazepine were used as a control drug, because population differences in the AFs of functional genetic factors for each SCAR development are little or much smaller than allopurinol among East Asians. Crude incidence rate ratios (IRRs) of SCARs were used for evaluation of population differences to cancel out the potential regional differences in diagnostic criteria and compared with authentic values of AFs. Stratification analysis by patient backgrounds were also conducted.

Results: The crude IRRs (95%CIs) of allopurinol compared to phenytoin were 0.63 (0.56-0.72), 0.34 (0.29-0.40), and 0.037 (0.016-0.083), and those to carbamazepine were 1.22 (1.01-1.47), 0.82 (0.59-0.61), and 0.16 (0.087-0.29) in Taiwan, Korea, and Japan, respectively. These trends were in accordance with the order of the AFs of HLA-B*58:01, 0.101, 0.061, and 0.004, respectively. In addition, relation of sex, age and renal function to incidences of allopurinol-related SCAR was commonly observed among regions.

Conclusion: This study showed the population differences in SCAR development among East Asians, which was associated with genetic factors in addition to other risk factors. This finding would suggest the importance of genetic factors for planning risk management strategy.

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Anomaly detection as a signal of adverse drug event from claims database: a case example of SGLT2 inhibitors

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Aim/Objective: Anomaly detection is the process of identifying unexpected events deviating from the “norm” in a dataset. Several machine learning (ML) approaches, namely unsupervised ones, have recently been implemented in anomaly detection. The motivation of this presentation was to explore, from the medical claims database, whether unsupervised ML has a potential role in detecting drug-related adverse events (AEs).

Methods: This study is a case example of time-series data of potential AEs associated with sodium-glucose co-transporter 2 (SGLT2) inhibitors, analyzed with a help of an open-source R package. From the employee-based insurance database in Japan, we extracted potential AEs of SGLT2 inhibitors; these AEs were decided based on a prespecified list from clinical trials of SGLT2 inhibitors, such as amputation, urinary tract infection, or ketoacidosis. The numbers of AEs were summarized on a monthly basis. Observed data were decomposed (i.e., split into components of seasonality, trend, reminder, and noise), and then were recomposed by removing the noise factor. We used the ‘anomalize’ R package, which was inspired by the ‘AnomalyDetection’ R package (Twitter. Inc.), which employed an extremely Studentized deviate test to detect outliners.

Results: A total of ~6 million potential AEs were identified from 2005 to 2018. After decomposition, we found three clusters of anomaly points, two of which were detected before 2014, when SGLT2 inhibitors were introduced in Japan. After recomposition, only two clusters before 2014 remained.

Conclusion: Although our example illustrates that the unsupervised ML technique could detect anomalies in claims records, specific anomaly patterns relevant to potential AEs of SGLT2 inhibitors were not observed in our case. Discussion and implications for future research will be extensively presented at the meeting.

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Association between Diabetes Treatment and Urinary Tract Infections: An Analysis Using Data from the JMDC Claims Database

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Objective: The sodium-glucose contransporter-2 (SGLT2) inhibitors are glucose-lowering drugs which inhibit glucose reabsorption from the early proximal tubule whereas there is also potential risk for urinary tract infections (UTIs). We analyzed the occurrence of UTIs among diabetic patients with single agent of SGLT2 inhibitor (SGLT2-i) and with combination therapy (SGLT2-i+), which is also commonly administered, by using data from the Japan Medical Data Center (JMDC) Claims Database.

Methods: Using claims data from April 2015 to March 2017 of those who were prescribed either SGLT2-i or SGLT2-i+, a Cox proportional hazards model analysis was performed (covariables: age, gender, and diabetes severity) and the incidence rate was calculated. Dipeptidyl peptidase-4 inhibitors (DPP4), biguanide (BG), sulfonylurea (SU) were analyzed as concomitant drugs.

Results: We were identified 2,265 SGLT2-i and 2,883 SGLT2-i+ users. There were 247 UTI events during 1371.7 person-years follow-up in the SGLT2-i users (incidence rate per 100 person-years 18.01 95%CI 15.83-20.4) and 326 UTI events during 2,379 person-years follow-up in the SGLT2-i+ users (13.7 95%CI 12.26-15.27). The adjusted hazard ratio for SGLT2-i+ versus SGLT2-i was 0.75 (95% CI 0.64-0.89). There was no dosage difference between SGLT2-i and SGLT2-i+ treatments.

Conclusion: The dosing period of SGLT2-i was shorter than SGLT2-i+. SGLT2-i had an increased risk and hazard ratio of UTI relative to SGLT2-i+. This may suggest that SGLT2-i is more likely to cause UTIs because SGLT2 inhibitors increase urinary glucose based on mechanism action whereas other antidiabetics included in SGLT2-i+ help control blood glucose. For future analyses, it may also be useful to use adverse events spontaneous reporting database to examine this topic.

Keywords: SGLT2, Combination/Single Use, RWD, Urinary Tract Infections

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Proton-Pump Inhibitor Use and the Risk of Progression to End-stage Renal Disease among Chronic Kidney Disease Patients in Taiwan

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Aim/Objective: Recent studies suggest proton pump inhibitors (PPI) associated with the risk of chronic renal failure. The evidence about CKD patients with PPI treatment and the risk to ESRD remain unclear. This cohort study evaluated the association between PPI use and the risk of ESRD among CKD patients in Taiwan.

Methods: We conducted a retrospective cohort study using subset of National Health Insurance (NHI) database, consisted of claims data of 2 million people randomly selected from the all 23 million insured individuals. We adopted new-user design, and H2 blockers (H2B) as active comparator. All participants were adults (≥ 20 years old) with newly diagnosis of CKD from 2012 through 2015, and followed up until ESRD, end of 1-year follow up, or disenrollment from NHI. We estimated the relative risk of ESRD among PPI users, as compared with H2B users, with HR from Cox proportional hazard models.

Results: We identified PPI users (n = 1,183) and H2B users (n = 3,214) from 2012 through 2015. Compared with H2B users, PPI users were older and mostly were men. PPI users had a similar prevalence of comorbidities and medication history with H2B users, but PPI users had significantly higher rate of gastrointestinal bleeding, esophageal cancer, acute kidney injury, and cerebrovascular disease. The result of primary outcome has showed PPI users has an increased risk of ESRD than H2B users (2.11% vs. 0.78%; adjusted HR 2.96, 95% CI 1.69-5.20); under as-treated design, result was consistent (0.85% vs.0.34%; adjusted HR 2.49, 95% CI 1.03-6.02). The subgroup analysis of CKD patients with early stage (CKD stage 1-3a) also showed that the PPI users has significantly higher risk of ESRD than H2B users (adjusted HR 2.86, 95% CI 1.47-5.57).

Conclusion: Our study showed that the use of PPI associates with increased risk of progression from CKD to ESRD in Taiwan.

Keywords: PPI, CKD population, ESRD, H2 blockers

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Undela sheet: one platform for all quantitative signal detection analyses in Pharmacovigilance

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Objective: To create an excel sheet with integrated formulas for identifying signals in Pharmacovigilance by using different quantitative methods.

Methods: From the literature, identified the formulas to calculate disproportionality measures like Proportional Reporting Ratio (PRR), Reporting Odds Ratio (ROR) and Information Component (IC), which are commonly used in Pharmacovigilance for signal detection. All the formulas were incorporated in an excel sheet such a way that it gives the results of all disproportionality measures in one click after entering four values on drug-reaction pair. A signal is detected by using PRR, if the count of co-occurrences is ≥3 and the PRR ≥2 with an associated Chi-square value ≥4. In the case of ROR, signal occurs if the lower bound of the 95% two-sided confidence interval exceeds 1. Using IC, a signal is detected when the lower bound of the 95% two-sided confidence interval of the IC (IC025) exceeds 0.

Results: An excel sheet was created with all integrated formulas to calculate disproportionality measures like PRR, ROR, and IC in one click, and it is named as 'Undela Sheet'. Just by entering four values from an adverse drug reactions database like numbers of reaction of interest and all other reactions for drug of interest and all other drugs in a database and click on 'get results', excel sheet generates components of PPR like PRR value, lower limit and upper limit of PRR and chi-square value; components of ROR like ROR value, lower limit and upper limit of ROR; and components of IC like IC value and lower limit and upper limit of IC (IC025 and IC975).

Conclusion: Undela Sheet is the first of its kind in the area of signal detection in Pharmacovigilance. Undela Sheet can be the platform for all quantitative signal detection analysis for regulatory authorities, industries and academic institutions involved in Pharmacovigilance activities.

Keywords: Pharmacovigilance, Signal detection, Undela sheet

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Cefoperazone-sulbactam and risk of coagulation disorders or bleeding: a retrospective cohort study

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Aim/Objective: Spontaneous reports of drug adverse events raised concerns about the safety of cefoperazone-sulbactam. Limited evidence from case reports and small uncontrolled studies suggested that cefoperazone-sulbactam might cause coagulation disorders or bleeding.

Methods: We conducted a retrospective cohort study that compared patients receiving cefoperazone-sulbactam versus those with cefoperazone-tazobactam or ceftazidime, using data from electronic medical records at West China Hospital from 1 January 2011 and 30 June 2014. Patient demographic characteristics, doctor's advice, laboratory tests, surgical and diagnostic information were collected. Propensity score matching model was used to explore whether treatment with cefoperazone-sulbactam was associated with increased risk of prothrombin time (PT) prolongation, coagulation disorders, bleeding or decrease in platelet (PLT). Sensitivity analyses using traditional logistic regression and propensity score weighting model in full cohort were performed to examine the robustness of effect estimates.

Results: Our cohort included 23,242 patients. Among patients treated with cefoperazone-sulbactam, the risk of PT prolongation, coagulation disorders, decrease in PLT, and any bleeding was 5.3%, 9.2%, 15.7% and 4.2%. The propensity-score matching analyses suggested that, compared to ceftazidime, cefoperazone-sulbactam increased the risk of PT prolongation (aOR 2.26, 95% CI 1.61 to 3.18), coagulation disorders (aOR 1.81, 95% CI 1.43 to 2.30) and decrease in PLT (aOR 1.46, 95% CI 1.25 to 1.72), but not the risk of bleeding (aOR 1.05, 95% CI 0.79 to 1.40). When compared to cefoperazone-tazobactam, patients treated with cefoperazone-sulbactam had higher risk of PT prolongation (aOR 1.53, 95% CI 1.11 to 2.10), coagulation disorders (aOR 1.53, 95% CI 1.21 to 1.95), but not decrease in PLT (aOR 0.93, 95%CI 0.81 to 1.07) and bleeding (aOR 1.11, 95%CI 0.87 to 1.42).

Conclusions: Patients receiving cefoperazone-sulbactam may have higher risk of PT prolongation and coagulation disorders compared to those using cefoperazone-tazobactam and ceftazidime. Their effect on bleeding, if any, was very small

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Safety analysis of pneumococcal vaccine in Korea using the KAERS database from 2005 to 2017

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Objective: To describe the safety profile of the pneumococcal vaccines, which were recently included in the national immunization program for infants, children, adolescents (pneumococcal conjugate vaccine (PCV)), or high-risk population (pneumococcal polysaccharide vaccine (PPSV)) in Korea.

Methods: Among the Individual Case Safety Reports (ICSRs) reported to Korea Adverse Event Reporting System (KAERS) between 2005 and 2017, ICSRs containing vaccines as suspected drugs were extracted. Vaccines of interest were PPSV (WHO-ATC, J07AL01) and PCV (J07AL02). We assessed demographic characteristics of reported cases and characteristics of ICSRs. Timeliness of reporting serious adverse event (SAE) within 15 days from the recognition were examined according to original reporters. To derive safety signals, we conducted disproportionality analysis by calculating the proportional reporting ratio, reporting odds ratio, information component and Chi-square of pneumococcal vaccine and all other vaccines. Then, we checked whether the safety signals were listed in the drug label.

Results: Among total of 29,128 vaccine ICSRs in KAERS database, number of ICSRs for PPSV and PCV were 1,048 and 2,118, respectively. Reports for cases aged 19 years or older were 37.8% in PCV, and 51% in PPSV. Reports of female were 52.6% in PCV and 56.9% in PPSV. Among SAE reports, 62.3% were reported within 15 days. Among original reporters, healthcare professionals (62.7%) were more likely to report SAEs within 15 days, then consumers (52.9%) ($p<0.01$). Among reporters, proportion of reporting SAEs within 15 days was higher in regional pharmacovigilance centres (81.1%) than manufacturers (56.5%). The disproportionality analysis yielded 72 statistical signals which includes several unlabelled adverse events including pneumonia, ineffectiveness, or septic shock.

Conclusion: Differential timeliness or AEFI reporting according to the original reporters and the reporters were observed. The safety signals of pneumonia or septic shock may be due to comorbid conditions of vaccine recipients' high-risk of infection, which warrants further study.

Keywords: Vaccine, Pneumococcal Vaccine, Adverse Event Following Immunization, Pharmacovigilance

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Predictors and Preventability of Adverse Events Following Anaesthesia: An Active Surveillance in a Tertiary Care Hospital

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Objectives: To assess the pattern, causality, predictability, preventability and predictors of adverse drug events (ADEs) following anaesthesia in a tertiary care hospital.

Methods: Clinical Pharmacist initiated active surveillance focusing on adverse events following anaesthesia amongst the patients who underwent surgery was carried out for nine months in a tertiary care teaching hospital. Causality, Preventability were assessed using Naranjo's and modified Shumock and Thornton's scales respectively. Odds Ratio (OR) was measured to evaluate the association between the reaction and predictor. The 95% confidence interval was used to estimate the precision of the OR.

Results: During the study period, a total of 302 patients were enrolled into the study with a mean duration of surgery 82.07 ± 63.28 minutes. Majority patients [154 (50.10%)] received spinal anaesthesia followed by general [132 (43.71%)]. A mean of 18.55 ± 5.00 drugs were used. A total of 77 ADRs were reported amongst 65 patients. The most frequently affected organ system was cardiovascular [33 (43.0%)] followed by gastrointestinal [21 (27.3%)] and skin and appendages disorder [17 (22.0%)]. The most frequently observed ADRs were bradycardia [17 (22%)] and hypotension [16 (20.8%)]. Majority [60 (78%)] of the adverse reactions were 'predictable' but 'not preventable' [77 (100%)] in nature. Causality assessment revealed 57% of these reports were probable. Bupivacaine and Propofol were majorly implicated. Elderly age [OR: 1.11 (0.28 – 4.46)], receiving 16 drugs or more [OR: 3.73 (0.95 – 14.61)] and longer duration of surgery [OR: 1.83 (0.74 – 4.52)] were the predictors.

Conclusion: Despite best preventive measures taken in peri, intra & post- operative periods, the anaesthetic agents have caused ADRs that were possible and non-preventable. Stringent monitoring and care is a must emphasising on sensitizing the HCPs to be proactive in identifying and reporting of ADRs associated with anaesthesia. Clinical pharmacists, in close liaison with the anaesthesiologists can facilitate early detection and handling the adverse events.

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Use of Stroke Registry and Data Linkage for Comparative Effectiveness Research: Overview and Methodology

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Introduction: Data on stroke patients in Malaysia are routinely collected via stroke registry, including patient demographics, risk factors, clinical presentation, and stroke details. Leveraging existing stroke registry data and integrating it with other sources of patient information to develop a population-based stroke cohort will create a robust dataset for longitudinal outcomes research. Herein we describe methods used to design and conduct a comparative effectiveness research of various antiplatelet therapy regimens for secondary prevention in ischaemic stroke and transient ischaemic attack (TIA) patients in Malaysia.

Method: This study sources data from the National Stroke Registry (NSR) and the UKM Medical Centre Stroke Registry. Both are prospective registries established to collect data on stroke patients admitted to hospitals in Malaysia. Stroke patients were identified among patients enrolled in the registries and a common identifier is used to match data with other sources.

Results: A total of 5887 stroke patients diagnosed with first ischaemic stroke or TIA between 2014 and 2017 were identified for record linkage. Data on stroke patients was further expanded to include detailed information on the course of treatment and stroke outcomes through medical chart reviews and linkage to other data sources such as pharmacy databases and the National Death Register. This involves selection of additional data variables, development of data collection tools, training, medical records abstraction, data matching, and quality assurance. Challenges encountered include data access, different record keeping systems across hospitals, missing records, and logistic issues.

Conclusion: Stroke registry provides a population base for stroke research and linkage to other database further enhance utility of registry to investigate a broader range of research questions. The ability to link registry with data from multiple other sources has provided unique opportunities to provide measure of stroke care and outcome.

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Prevalence, pain intensity and disability of Low Back Pain among Indian population. A cross-sectional study

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Aim/Objective: Low back pain (LBP) is a major public health problem that burdens an individual's families and societies in India. The annual economic cost of LBP is as high as $135 billion. A common challenge in treating chronic pain conditions is accurate diagnosis and treatment.

Objectives: To assess the prevalence, pain intensity and disability associated with LBP in India.

Methods: A cross-sectional survey was conducted among the adult population of different strata of the community. Lifetime prevalence, point prevalence, recurrent prevalence, one-year prevalence and knowledge regarding LBP was collected. Numerical rating scale (NRS) and Oswestry low back pain questionnaire were employed to assess the pain intensity and disability among LBP subjects. Binary logistic regression test was conducted to determine the predictors of LBP prevalence.

Results: 1532 subjects were examined, among them 47.8% were males. Mean (SD) age and NRS was found to be 32 (10) years and 4.2 (2.6). Lifetime prevalence, point prevalence, and one-year prevalence were found to be 57%, 32% and 48% respectively. Females (65%) had a significantly higher lifetime prevalence compared to males (47%) ($p<0.001$). Oswestry disability index indicated 67% had moderate and 24% with a severe disability. 62% had poor and 38% had moderate knowledge sore. Increasing age (OR =1.03, 95% CI: 1.02-1.04, $P < 0.05$), being female (OR =0.5, 95% CI: 0.4-0.6, $P < 0.05$) and physical activity (OR=0.7, 95% CI: 0.6-0.9, $P < 0.05$) were most significant predictor of LBP.

Conclusion: LBP is highly prevalent in India, which results in an enormous disability. Therefore, it calls for action by health officials and professionals to plan for appropriate programs of prevention and management of LBP in society.

Keywords: Low back pain, Prevalence, disability, Oswestry low back pain questionnaire

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Association of diet and other risk factors among coronary heart disease patients.

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Background: Many western studies have revealed that the vegetarian diet has a lesser risk for developing coronary heart disease. However, very few studies on the impact of diet on developing coronary heart disease have been reported from India. Aim: The study aims to assess the association of diet and other risk factors among coronary heart disease patients.

Methods: A prospective observational study was conducted for one year among coronary heart disease (CHD) patients. Newly diagnosed coronary heart disease patients aged above eighteen years with or without the comorbid condition were included in the study. Patients with a past medical history of coronary heart disease and dyslipidemia were excluded. Patient's demographic details like education, socioeconomic status, age, gender, past medical history, personal history like alcohol consumption, smoking, and diet were collected. The association of vegetarian's diet and omnivorous diet on total cholesterol, Low-density lipoproteins (LDL), High-density lipoproteins (HDL), and Triglycerides (TG) were analyzed.

Results: Among 141 patients, 32 (23%) patients were found to be vegetarians, and 109 (77%) were found to be omnivorous. Compared to vegetarians, omnivorous group has shown a high level of LDL (p-value 0.003*), HDL (p-value 0.033*) and Total cholesterol (p-value 0.033*). Subgroup analysis among omnivorous patients even, non-smokers and non-alcoholic have shown the high level of LDL (p-value 0.001*) and Total cholesterol (p-value 0.003*). Vegetarians were having a healthy lifestyle compared omnivorous group. It was found that the omnivorous group has more likely to smoke and consume alcohol (p-value 0.007).

Conclusion: In our study, we found that vegetarians were associated with a healthy lifestyle and less coronary heart disease risk factors compared to the omnivorous group.

Keywords: Coronary heart disease, LDL- Low-density lipoprotein, HDL- High-density lipoproteins, Triglycerides (TG).

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Korean pharmacovigilance system based on EHR-CDM

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Aim/Objective: Our aim is to build nationwide, reliable data network and arrange a procedure to perform efficient simultaneous multi-center analysis using reusable, parameterized query tool without exposing any kind of private information out of the medical institutes.

Methods: In the Republic of Korea, the ministry of food and drug safety (MFDS) and Korea Institute of drug safety & risk management (KIDS) have developed an active pharmacovigilance system using CDM based on electronic health records (EHRs) since 2016. KIDS named this customized Korean model MOA(Medical record observation and assessment for drug safety)-CDM. During 2016-2017, MFDS constructed MOA-CDM on 9 hospitals in Korea. In 2018, KIDS selected five major hospitals including local representative drug safety centers as an attempt to expand the CDM. Also, KIDS developed MOA-NET, a web-based multi-directional portal service to network government and data partners. Through MOA-Net, hospitals participated in a pharmacovigilance study and confirmed the usability and adequacy of the CDM.

Results: In Korea, more than 11.7 million patient information from 14 national representative hospitals were acquired to construct a CDM database. The database converting EHR to CDM includes more than 127 kinds of clinical laboratory test, more than 7,000 drugs available in Korea. A total of 7 data partners participated in the phamacovigilance study. We found significant adverse drug reaction signal - allopurinol & TSH increase. We identified 10,663 cases of TSH increase and 42,631 matched controls. When all non-users were compared with users of allopurinol, the risk of TSH increase (unadjusted OR) was increased 3.52 fold (95% CI: 2.96-4.20).

Conclusion: We developed the Korean pharmacovigilance system based on MOA-CDM for active drug safety surveillance. It was possible to elaborate on research designs for adverse drug reaction using clinical information such as laboratory test results.

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The main position of medical and district health nurses in pharmacovigilance

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Aim/Objective: The reporting of assumed undesirable drug responses) is initializing to turn into practice to nurses. The objective of this review is to emphasize the position of clinical and district health nurses in pharmacovigilance and to endorse their effective contribution in ADR reporting in diverse countries and for patients of different ages.

Methods: The PubMed, Scopus and ISI Web of Science databases were investigated for research articles published between May 1990 and June 2016 by means of the search point "pharmacovigilance" AND "nurse; "district health nurse" AND "adverse drug reaction."

Results: An overall of 954 articles were acknowledged via our exploration strategy, of which 170 articles hang about after the exclusion of reproduction articles. Of these 170 studies, leading full review we recognized 22 which assembled the inclusion/exclusion criteria and integrated these in our review. ADR descriptions by medical nurses in some countries are similar in value and number to those proposed by medical doctors or pharmacists. Records on ADRs described by community nurses are presently not accessible. Nevertheless, several publications highlighted the challenges confronted by nurses in reporting ADRs and the requirement to comprise pharmacovigilance education in both medical and community health nurse university instruction.

Conclusion: Nurses are essential performers in pharmacovigilance actions, predominantly in categorizing ADRs which hang about remote the achievement of other healthcare suppliers and in being basic to the conservation of the health of patients and of the whole population, with awareness to the more susceptible patients, like children and the elderly.

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Impact of prevalence, sensitivity, specificity, and positive and negative predictive values from a validation study on planning of database studies

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Objective: Database studies are gathering increasing attention in recent years. This trend has accelerated with the 2018 revision of the Japanese good post-marketing study practice (GPSP) which introduced database studies as an additional mode of post-marketing safety studies. Thus, it is essential that all practitioners of database studies be aware of the knowledge of outcome validation and the impact of its results on planning and interpretation of database studies. We review basic setups in outcome validation studies and give informative results with a focus on the planning phase of a database study.

Methods: First, we describe the setup involving the "gold standard" and the database definition for an outcome of interest. In this setting, five parameters characterize the validation result, namely, prevalence, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Next, we examine the impact of these parameters on relative measures in a database study such as the risk ratio (RR) and the risk difference (RD) with a focus of deviation from its "true" value (i.e. bias). We also give some examples. Finally, we make some recommendations, including considerations for the acceptable range for the parameters such as PPV.

Results: The bias of the observed value of RR and RD from database studies depends on the parameters of validation study. A simple and elucidative expression for the bias of the observed RR is derived in the case of non-differential misclassification error. Similar expression is derived for RD. Graphical presentation of the results give useful information in planning of a database study.

Conclusion: Appropriate sensitivity analyses are critical components of any observational study during the data analysis phase. In addition, it is also instructive to examine possible types and degree biases during the planning phase of database studies.

Keywords: database, outcome, validation, Japan

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Effect of ICD-9-CM to ICD-10-CM coding system transition on prevalence of common diseases: an interrupted time series analysis

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Aim/Objective: Taiwan implemented the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) coding system on January 1, 2016. The purpose of this study was to evaluate the effect of coding system transition on the prevalence of common diseases recorded in its national claims database.

Methods: We used 2014-2016 administrative data from the National Health Insurance Research Database. We assessed published validated ICD-9-based and ICD-10-based diagnosis codes from other countries as well as the ICD-9-CM to ICD-10-CM mapping algorithm developed by Taiwan's National Health Insurance Administration. We estimated monthly prevalence of 19 diseases based on the ICD-9-CM diagnosis codes in 2014-2015, and the ICD-10-CM codes in 2016. For ICD-10-CM, we assessed two algorithms: the validated ICD-10-CM codes in the literature and the codes translated from ICD-9-CM using Taiwan's mapping algorithm. We used segmented regression analysis on time-series data to examine the changes in disease prevalence (both intercept and trend) before and after the ICD-10-CM implementation.

Results: For most conditions, we observed smooth (i.e., uninterrupted) transitions and similar disease prevalence based on the ICD-10-CM codes in the literature and Taiwan's mapping algorithm. However, significant changes in the intercept of prevalence (i.e., abrupt changes immediately after transition), with no or mild changes in trend, were found with ischemic stroke, kidney failure, and alcohol abuse when using the diagnosis codes in the literature. The estimated prevalence of metastatic solid tumor, psychosis, and drug abuse substantially increased when using Taiwan's mapping algorithm.

Conclusion: Most diseases had smooth transition with the ICD-9-CM and ICD-10-CM coding systems, and the ICD-10-CM codes in the literature and the Taiwan's mapping algorithm produced similar prevalence. However, researchers should pay attention to the conditions where the coding algorithms result in inconsistent estimates. The transition of diagnosis codes should be inspected before conducting studies that analyze both ICD-9-CM and ICD-10-CM data.

Keywords: ICD-9-CM, ICD-10-CM, disease prevalence, administrative database

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A novel software for efficient construction of datasets using health insurance claims database

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Aim/Objective: Administrative databases for health care are becoming popular for pharmacoepidemiologic study. However, since such databases generally only contain the data which are used for charging health insurance claims, contents of the data are insufficient for pharmacoepidemiologic study purposes; Thus, creating a dataset that is appropriate for specific analysis requires a great deal of technical efforts especially for those who are not familiar with database technique. The aim of our research is to create a software that allows researchers to create data set without expert data handling skills.

Methods: We used the JMDC claims database as source material. First, all CSV files obtained from JMDC were converted into database format. Second, variables commonly used in pharmacoepidemiologic study such as dose of drug (mg) etc. were added by using external master files obtained from the Medical Information System Development Center (MEDIS) and the Ministry of Health, Labour and Welfare (MHLW), to construct a Data Warehouse (DW). Finally, we developed a software that can create a per-patient data structure (data set) based on the DW.

Results: Consequently, we developed a software with simple graphical user interface that automatically converts all CSV files into a database structure, constructs the DW with SQL and MS-DOS commands. Using the DW, we published a short paper on drug epidemiology. In addition, by using software we developed, researchers can complement variables needed for their own pharmacoepidemiologic study in a per-patient data set without using SQL or other statistical analysis software.

Conclusion: The software we developed only supports cross-sectional studies and simple cohort studies, but we plan to expand the scope of study that can be further covered in the future. We believe our research can contribute to the further progress of pharmacoepidemiologic studies using real world data.

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Diabetic complications severity index and risk of mortality and hospitalization using National Health Insurance Database in Korea

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In Korea, the prevalence of diabetes mellitus (DM) is 14.4% over the age of 30 and 29.8% over 65 years old in 2016. In Korea's national burden study, diabetes is the leading cause of illness burden. The macrovascular and microvascular complications are contributing to morbidity and mortality in the long term. To evaluate whether the diabetes complications severity index are associated with increased risk of all-cause mortality and hospitalization. A retrospective cohort study was conducted using National Health Insurance Database (NHID) sample cohort 1,102,047 (2002-2015). Diabetic complications were evaluated at 2 years after new onset type 2 DM diagnosis. The type and severity of diabetic complications were converted to KCD-7 using the International Classification of Disease and ninth Revision (ICD-9 code) used in the Diabetes Complications Severity Index (DCSI). DCSI includes the following 7 categories of complications: nephropathy, retinopathy, neuropathy, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, metabolic disease. The complications index was based on a scale ranging from 0-2 for each complications abnormality and total score of 13 was possible for the DCSI. Cox proportional hazard and Poisson regression models were used to predict mortality and hospitalizations, respectively. The final subject were 27,871 patients. 9,130 had no complications, 9,015 had one complication, and 9,726 had two or more complications at 2 years after new onset type 2 DM diagnosis. Of these, 2,302 (8.26%) died, of which 490 (5.37%) had no complications, 659 (7.31%) had one complication, and 1,153 (11.85%) had two or more complications were found. The risk of mortality and hospitalization were with DCSI linear, HR 1.13 (95% CI 1.11–1.16), RR 1.04 (95% CI 1.03-1.06), respectively. The number and severity of diabetes complications in patients with type 2 diabetes in Korea has increased a statistically significant risk of mortality and hospitalization.

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Adverse Drug Reactions Evaluation in a Taiwan Hospital

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Objective: An adverse drug reaction (ADR) is an unwanted, undesirable effect when taking medicine during clinical use. Although some ADRs present as minor symptoms, others may cause a serious or fatal event. In order to let healthcare professionals to understand the importance of ADRs, we do ADRs analysis from our hospital.

Methods: This was a retrospective study which conducted in a teaching hospital. The study occurred from January 2018 to December 2018. Assessment of ADRs contains age, gender, occurring sources, the reaction mechanism of ADRs, management of ADRs and probability of calculating by Naranjo Score Scale. In addition, we also do an analysis regarding Anatomical Therapeutic Chemical (ATC) classification of suspected drugs and Adverse Effects in affected organ.

Results: The investigation included seventy-five ADRs reported. The average age was 66.2 year. Most of ADRs reported were occurring in outpatient department (78.7%). Majority of all ADRs reported were females (70.7%). Also, the major probability was possible (83.9%), which represents 1 to 4 points of Naranjo Score. According to ATC classification system, the major classification of suspected drugs were Sensory organs (30.7%) and Dermatologic Effects (52.0%) were the major adverse effects in affected organ.

Conclusion: ADR reporting undoubtedly is still a very important process to healthcare professionals. Therefore, we have put ADRs reporting information into our medical system which can remind a physician to consider prescribing medication. Consequently, it is truly a best way to improve medication safety by spontaneous reporting of ADRs by healthcare professionals for all patients.

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Assessment of record linkage using administrative claims data and antimicrobial susceptibility testing data

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Aim/Objective: To assess the association between antimicrobial treatment and antimicrobial resistance, both information is needed. The purpose of this study was to evaluate the validity of linkage between both data without using a common unique identifier.

Methods: We used administrative claims data produced under Diagnosis Procedure Combination (DPC) system and antimicrobial susceptibility testing data based on Japanese Nosocomial Infections Surveillance (JANIS) from 11 hospitals. We selected 9 variables (hospitals' identifier, hospitalization, year of birth, month of birth, age, sex, department, specimen reception date, and specimen sources) to link each dataset. Variables of specimen reception date and specimen sources were made from claims of "culture and identification of bacteria" and "detection of antigen in Escherichia coli" in administrative claims data. We then conducted deterministic linkage using combinations of variables to create 12 patterns of algorithms by multiple steps. To perform the linkage efficiently, the variable of hospitals' identifier and hospitalization was treated as a blocking variable. We evaluated the validity of the algorithm using sensitivity, positive predictive value, and f-measure using the dataset linked by the unique identifier.

Results: Linkage was performed for each hospital using the hospitals' identifier, and median (mix-man) of patients linked in each hospital was 4,999 (2,142-32,353). Median (mix-man) of sensitivity, positive predictive value, and f-measure at best algorithm showed 90.9 (15.7-98.3), 95.4 (89.6-99.9), and 93.1 (27.0-98.8), respectively. Especially, patients of 0 years old affected the number of false links. F-measure were improved slightly when that population was excluded.

Conclusion: The variables of specimen reception date and specimen source could be useful to link each dataset in the specific population; however, the results of linkage were extremely different among hospitals. Deterministic linkage depends on the completeness of variables, and data including many missing values showed very poorly f-measure.

Keywords: medical records linkage, administrative claims data, deterministic linkage, antimicrobial resistance

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Prevalence of significant lesions in Dyspepsia Patients by upper Gastrointestinal Endoscopy

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Aims & Objectives: To assess the outcome of gastrointestinal endoscopy in adult patients with dyspepsia.

Methodology: This is a Prospective Observational study conducted in the Department of Surgery at RMMCH for a duration of 3 months.

Results: In this study, majority of the patients affected by Dyspepsia was in the age group between 35-44 years accounting for 28.19% and among them, females were predominating (54%). Based on the age wise distribution in male and female subjects, 35-44 and 45-54 age frequencies comprised the majority in male subjects with Dyspepsia and 35-44 years comprised the highest in female subjects. Among the male subjects, significant lesions were found to be majority 64.71% and in female functional Dyspepsia comprised the majority of 59.32%. According to the distribution of endoscopic findings among the significant lesions, Esophagitis and Gastric erosions were more seen. In male's Esophagitis and Gastric erosions (21.21%) and in females Esophagitis (25%) were more seen. Normal study on endoscopy based on age showed that subjects between 35-44 years of age formed the majority of functional dyspepsia patients. Likewise, the normal study based on gender showed that functional dyspepsia was common between 35-44 years in females and 35-64 years in males.

Conclusion: According to the distribution of endoscopic findings in all subjects, significant lesions were found in 56.36% of dyspeptic patients. In this study, lesions like gastric erosions and esophagitis are relatively high. Dyspepsia declines with an increase in age and is more common in women's than males. Thus, for an initial evaluation in patients with dyspepsia upper gastrointestinal endoscopy plays a vital role.

Keywords: Endoscopy, Dyspepsia, Gastrointestinal tract, Gastric erosions, Esophagitis, Hiatus hernia.

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Liver enzymes during and after antimalarial therapy in Nigerian children with uncomplicated Plasmodium Falciparum infection

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Aim/Objective: To determine the effect of artemether-lumefantrine on plasma levels of four liver enzymes, namely; alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP] and gamma glutamyl transpeptidase [GGT] in children with uncomplicated Plasmodium falciparum infection.

Methods: We reviewed the records of all children who participated in a clinical trial of antimalarial drug in Ibadan, Nigeria and a sample of 102 children who met eligible criteria and with microscopically-proven Plasmodium falciparum infection treated with artemether-lumefantrine at recommended age-specific doses for 3 days. Study participants were followed up on days 3, 7, 14, 21, and 28 according to the World Health Organization recommendation for treatment of malaria research participants. Inclusion criteria included symptoms attuned with acute uncomplicated malaria, including parasite density of at least 1000/µL and absence of chronic illness or danger signs of severe malaria. The results of ALT (U/L), AST (U/L), ALP (U/L) and GGT (U/L) at baseline (day 0), on day 3, and day 28 post-treatments were extracted and compared using Friedman tests.

Results: The median age of participants was 25 months (range = 3 to 119), and 49% were male. The mean values of ALT and AST did not change significantly over the course of the 28-day follow-up from baseline (25.8 – 19.1U/L p= 0.0984 and 50.4 – 52.2U/L p= 0.1943 respectively). GGT decreased substantially between baseline 17.0 U/L (11.0 - 22.5) and day 28 15.0U/L (10.5-21.5) p= 0.0010 while ALP increased over time (baseline: 305.0U/L (216.0 – 403.5); day 28: 345.0 U/L (241.0 – 492.5) p=0.0303. Elevated ALT, AST, ALP and GGT were observed in 8.5%, 20.0%, 20.9%, and 14.8% of participants, respectively.

Conclusions: Considerable rise in plasma levels occurred in ALP which could be indicative of liver injury occurring during antimalarial treatment among Nigerian children. Further research is needed to identify the underlying mechanism responsible for this drug-induced liver toxicity.

Keywords: Liver enzymes, Artemether-lumenfantrine, Plasmodium falciparum

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Predicted population health impacts of heated tobacco products in Japan

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Objective: to predict the impacts of heated tobacco products on tobacco use and population health among Japanese adults, using a simulation model that follows US Food and Drug Administration (FDA) guidance for applications seeking authorization as a Modified Risk Tobacco Product.

Methods: The FDA encourages use of statistical models that predict the impact of new tobacco products, to ensure they are appropriate for protection of the public health. We used such a model to simulate the Japanese adult population through year 2100, using randomly generated tobacco product use histories including initiation, cessation, and switching between products and dual use. Although heated tobacco products may benefit smokers who switch completely to them, benefits are less certain for other groups, depending on uncertain transition rates and the Excess Relative Risk (ERR) experienced by heated tobacco product users relative to cigarette smokers. Sensitivity to each input was tested systematically. ERR was varied from 5% to 30%, and this range was compared to results from a published study of five-day changes in biomarkers of exposure and potential harm among Japanese smokers switching to a heated tobacco product. Biomarker changes were scaled between those for smokers who stopped smoking during the study and those for continuing smokers.

Results: Simulations suggested that heated tobacco products would provide net health benefits in all except extreme scenarios. Scaled biomarker changes ranged from 0% (representing smoking cessation) to 15.2%. The hypothetical "break-even" ERR, which would reduce a product's net population health benefit to zero (with base-case values for all other inputs), was over 50% relative to cigarettes.

Conclusion: Sensitivity analysis and comparison of biomarker changes to the estimated break-even ERR suggest that heated tobacco products would benefit the overall health of Japanese adults, despite uncertainties in ERR and other inputs.

Keywords: heated tobacco, cigarette smoking, population health, simulation model

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MEDICATION ERRORS ASSOCIATED WITH THE USE OF ANTIBIOTICS IN CRITICAL CARE UNITS

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Background: Iatrogenesis is an inevitable reality under the current complex healthcare framework. Medication errors (ME) jeopardizes patient safety. It is important to understand how often and why these errors are occurring and contributing factors. It is essential to reduce their occurrence in the limited resources scenario. Further, safer use of antibiotics will not only reduce the burden of antibiotic resistance, but also limits the patient from unnecessary exposures to the adverse effects.

Methodology: A descriptive cross-sectional study was conducted in inpatients of either gender, aged more 18 years who were admitted to critical care unit for more than 24 hours. All the required data were collected and documented. All the diagnoses and antibiotics were coded according to the International Classification of Disease 10 (ICD 10) and Anatomical Therapeutic Classification (ATC) codes respectively. Each prescription was subjected for review to identify the Medication errors associated with use of antibiotics.

Results: Of the 1162 antibiotic doses prescribed for 500 patients, 36 (7.2%) patients were presented with medication errors. A total of 47 medication errors were detected. The average number of medication error was 1.31 errors/ patient. Administration errors accounted for 21 (44%) MEs. Distractions [23 (48%)] and interruptions [16 (34%)] were the major contributing factors for these errors. A total of 14 individual antibiotics, under 4 different classes were implicated in the errors and Ceftriaxone (28%) was widely implicated. Most [27 (57%)] of the errors belonged to the category C as per the NCC MERP index.

Conclusion: The use of antibiotics was found to be high in the Intensive Care Unit. Of the total reported medication errors, Ceftriaxone was most commonly implicated. Clinical pharmacist plays an important role in the detection and management of MEs.

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Medication related hospital admissions to a tertiary care teaching hospital: A prospective cross-sectional study.

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Background: Increasing availability and usage of medicines can cause medication related problems (MRP) leading to hospitalisation and often affecting morbidity and mortality rates.

Objective: To determine the incidence, nature, and risk factors associated with medication related admissions and their severity and preventability.

Methodology: A prospective cross-sectional study design was adapted. All those patients admitted due to MRP to the departments of emergency, medicine, paediatrics and dermatology were enrolled over a period of six months. Hepler and Strand's classification of MRPs was adopted. All the required data were collected and analysed using standard descriptive analysis and the risk factors were assessed by using Chi Square test.

Results: of the 500 patients followed, 197 (39%) patients were admitted to the study site due to medication related problems. Males predominance was observed [n = 105 (53%)]. Majority of patients were presented with diabetes [n = 97 (49%)] and hypertension [n = 77 (39%)] as prevalent comorbid conditions. The most common type of MRP was failure to receive the drugs [n = 119 (60%)] followed by adverse drug reactions [n = 58 (29%)]. Metformin with glimepiride [n = 24 (9%)] followed by insulin [n = 18 (7%)] were most commonly implicated drugs. Majority [n = 102 (51%)] of these patients had a hospital stay of 3 – 5 days. The severity of MRPs was observed to be moderate [n = 189 (96%)] followed by severe [n = 8 (4%)]. Majority [n = 167 (85%)] of MRPs were preventable. Polypharmacy, non-adherence, comorbidities were found to risk factors.

Conclusion: The incidence of Medication related hospital admission was high due to polypharmacy, non-adherence, and comorbidities. While, majority of these problems were deemed to be preventable, appropriate use of medications can reduce the medication related hospital admissions.

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The effectiveness of a T2DM medication in lowering the risk of stroke: a cohort study using the MDV database

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We previously reported at the JSPE 2018 conference that sodium-glucose cotransporter 2 inhibitors (SGLT2i), a treatment for type 2 diabetes mellitus (T2DM) in Japan, lowered the risk of stroke compared to sulfonylureas (SU). In the report, we focused on the period for the first treatment, and censored any other T2DM treatments (oT2DMtd) that followed. In this report, we investigated the effectiveness of the treatment episodes in real-world practice.

Using data from the Medical Data Vision (MDV) database, accumulated from April 2008 to January 2018, we included patients prescribed SU, SGLT2i or dipeptidyl peptidase 4 (DPP-4) inhibitors, in the cohort. We set 3 reference groups: Group A as SGLT-2i, Group B as DPP-4 inhibitors and Group C as a combination of SGLT-2i and DPP-4 inhibitors. These reference groups were compared to the SU group. Hazard ratios (HRs) for stroke were calculated under the following 4 conditions;
Condition 1 -Any oT2DMtd treatments that were started after the first treatment were censored.
Condition 2 - Patients were followed until the end of the first T2DM treatment drug.
Condition 3 - We adjusted the oT2DMtd as time-dependent covariates.
Condition 4 - We adjusted the T2DM treatment as time-dependent exposures.

The upper one-sided 95% confidence interval (95 % CI) for stroke HRs under all 4 conditions showed less than 1.0 in Group A.

Taking into account real-world practice, we pursued the impact of add-on DPP-4 treatment in SU and SGLT2i groups (condition 3), and that of all episodes in which SU and SGLT2i initiation were eligible to be included (condition 4).
Our new approach provided further support for the hypothesis that SGLT2i is associated with significant risk reduction of stroke compared to SU.

Keywords: Database, SGLT-2 inhibitor, Stroke, Time-Dependent Confounding

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Validation study of medication adherence based on claims data in Japan

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Aim/Objective: It is very important to understand medication adherence of patients for appropriate medication behavior promotion. Proportion of days covered (PDC) is one of the way to measure medication adherence using claims data. However it is not clearly reported its accuracy of PDC calculated by claims data in Japan.
We try to figure out its accuracy and feasibility for detecting Non-medication adherence patients by PDC.

Methods: We randomly sampled 1,500 from 31,461 patients in claims data of Fukuoka branch of Japan Health Insurance Association, Japan, between May to July in 2017 and distributed questionnaire to them on March on 2018. The selection criteria were aged 40 to 74 patients taking seven or more oral medications prescribed only for 14 days or more, except for short-term prescriptions. Medication adherence score on questionnaire was measured by Ueno methods which is comprehensive score of medication adherence and including not only medication compliance but also other factors of it. We calculated PDC by claims data in between April 2017 to March 2018.

Results: We collected 471 answers. The mean of medication adherence (score is between 0-60) was 47.5(SD 6.0), medication compliance (0-15) was 14.4 (SD 1.4) respectively. The mean of PDC (0-100%) was 88.2% (SD 11.2%). Conclusion: We will report more detail correlations and accuracy between Medication adherence score and PDC on the day.

Keywords: Medication adherence, big data, health behaviour

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Epidemiology of heart failure in South-India: assessment of disease-specific prevalence, phenotypic classification, and risk factors from Manipal Heart Failure Registry

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Background and objectives: Heart Failure (HF) is a progressive disease and emerging as a high epidemiological burden. However, epidemiological data is very limited from low and middle-income countries, and all projections and estimations are based on the western data. This study is designed to assess the HF epidemiological burden and disease-specific estimates of prevalence in the South Indian adult population for three consecutive years in various cardiac and non-cardiac conditions.

Methods: The Manipal Heart Failure Registry [MHFR] is a prospective registry computed the detailed epidemiology of HF at a South Indian tertiary care center for consecutive three years.

Results: Out of 167,995 screened patients, 138,827 (82.6%) participants were found to be eligible for the study, and 1918 participants were diagnosed to have HF with a prevalence of 1.4% (14 per 1000). The mean age of the HF population was 64.3±12.8 years, and more than half of the HF cohort was diagnosed with HFrEF (50.5%; n, 969). Males showed higher prevalence of HF than females [0.8% versus 0.6%; p<0.002]. MHFR analyzed a large proportion of females and elderly (43% of patients had ≥75 years of age) as compared to other registries conducted in India.
HF was 4.8% of all the cardiac conditions. Disease-specific HF prevalence was maximum in hypertension (5.2%) followed by anemia (4.3%) diabetes mellitus (3.1%), renal insufficiency (3%) and in thyroid dysfunction (2.8%). Regression analysis was performed with multiple variables for risk factors prediction. Age group (61-80 years), female gender and ischemic heart disease were the significant (P, <0.05) risk factors associated with HF.

Conclusions: The cumulative HF prevalence was estimated 1.4% in eligible population in Southern part of India. HF was more prevalent in patients with hypertension and anemia than other cardiac and non-cardiac conditions. MHFR refined the risk factors and etiologies of HF; IHD and non-ischemic cardiomyopathies were significant contributors.

Keywords: Prevalence; Incidence; Proportions; Risk-factors

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Increased Risk of Allergic Reactions Associated with Xiyanping Injection: A Prescription Sequence Symmetry Analysis

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Background: Prescription sequence symmetry analysis (PSSA) is an effective signal detection method for adverse drug events based on electronic medical databases. Due to its easy application and effective control of time-invariant confounders, it can be used to identify unintentional drug effects of traditional Chinese medicine injections, such as estimating the association between xiyanping use and allergic reactions.

Objectives: To investigate the risk of allergic reactions associated with the use of xiyanping in a real-world setting. And to evaluate the feasibility of using PSSA to detect drug safety signal in a nationwide medical database in China.

Methods: A retrospective PSSA study was conducted by using data from the Chinese Basic Medical Insurance Database in 2015. The patients newly initiating both xiyanping (index drug) and antiallergic drugs (marker drug) were identified and selected as study subjects. Antihistamines, glucocorticoids, calcium gluconate and adrenaline were selected as the proxy of allergic reactions. The washout period was set as one mouth and the interval period was set as 3days. Adjusted sequence ratios (ASR) were calculated as the ratio of patients initiating xiyanping first (causal group) over those initiating an antiallergic first (non-causal group) adjusted for time trends in prescribing, which to investigate the potential association between xiyanping use and allergic reactions.

Results: There were 6 629 patients who newly initiated both xiyanping and an antiallergic drug in our study period. The ASR was 2.45 (95%CI: 2.33-2.59), which indicated an increased risk of allergic infections associated with the use of xiyanping. Signals were detected by each of the four kinds of antiallergic drugs.

Conclusions: The results of PSSA showed that there was a potential association between xiyanping use and allergic reactions. This signal detection method may be a fast and effective method in drug safety evaluation and can be used in the Chinese Basic Medical Insurance Database.

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Factors for Starting Biosimilar TNF Inhibitors in Patients with Rheumatic Diseases in the Real World

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Objective: To identify factors for starting biosimilar TNF inhibitors (TNFI) in patients with rheumatic diseases.

Methods: Using the national claims database, TNFI users with rheumatoid arthritis (RA) or ankylosing spondylitis (AS) since TNFIs were approved in Korea in 2004 were identified. We assessed changes in the proportion of each agent among all TNFI users between 2004 and 2017. Then, we selected new starters of TNFIs from 2013 to 2017 to identify factors for starting biosimilars.

Results: In RA (n = 4,216), biosimilars were much used at the clinic level [odds ratio (OR) 2.54] or in the metropolitan area (OR, 2.02), but were less likely to be used in general hospitals (OR 0.40) or orthopedics (OR 0.44). In AS (n=2,338), biosimilars were common at the hospital level (OR 2.20) and tended to increase over the years (OR 1.16), but to be used less in orthopedics (OR 0.07). In addition, RA patients were more likely to use biosimilars in combination with methotrexate (OR 1.37), but they were not used frequently in patients with higher comorbidity scores (OR 0.97) or receiving glucocorticoids (OR 0.67). In AS, the patient factors for biosimilar use were not clear.

Conclusion: In Korea, the proportion of biosimilar TNFIs has increased. The type of institution and the physician's specialty are more important than patient factors in affecting biosimilar use. In RA, biosimilar TNFIs tend to be used in combination with MTX and are less likely to be used in patients taking glucocorticoids or in those with high comorbidities.

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A retrospective database analysis to determine the number of patients using levonorgestrel intrauterine system (L-IUS) in estrogen replacement therapy (ERT)

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Objective: This study aims to investigate the number of patients using L-IUS for ERT and whether safety events of interest occurred during use of L-IUS in the real world setting.

Method: A retrospective cohort using two claims databases (Medical Data vision; MDV and Japan Medical Data Center; JMDC) was conducted to grasp the number of patients who met two following criteria. We judged that the patients who met either of the criteria were likely to use L-IUS for ERT purpose.
Criterion1. Of the patients who had already started using L-IUS for contraception, dysmenorrhea and hypermenorrhea, the patients were newly diagnosed with menopausal disorders and prescribed estrogen preparation for 14 days and more as ERT.
Criterion2. Of the patients who had already started ERT, the patients were newly prescribed L-IUS for prevention of endometrial proliferation.
Moreover, we investigated whether safety issues including pelvic inflammatory disease, uterine perforation, breast and ovarian cancer and ovarian cyst rupture occurred. Observational periods were April 2008 to June 2018 (MDV) and April 2008 to March 2018 (JMDC), respectively.

Results: The numbers of patients who have been prescribed L-IUS were 4,270 and 2, 052 in MDV and JMDC. As for MDV, there were 85 and 2 patients who met the criterion1 and 2. As for JMDC, there were 10 and 5 patients who met criterion 1 and 2. A total of 102 patients were estimated to use L-IUS for ERT purpose. Most patients (94%) were between 40 to 54 years of age, and the rest 5% and 1% were patients over 54 and under 40, respectively. No safety issue was found in all patients.

Conclusion: The study found there were patients who use/used L-IUS for ERT in the real world setting and most patients were aged over 40. There was no safety events of interest found.

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Comparison of laboratory threshold criteria in drug-induced liver injury detection algorithms for use in pharmacovigilance

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Aim: For the purpose of pharmacovigilance, we sought to determine the best performing laboratory threshold criteria to detect drug-induced liver injury (DILI) in the electronic medical records (EMR).

Methods: We compared three commonly used liver chemistry (LC) criteria from the DILI expert working group (DEWG), DILI network (DILIN), and Council for International Organizations of Medical Sciences (CIOMS), based on hospital EMR for years 2010 and 2011 (42,176 admissions), using independent medical record review. The performance characteristics were compared in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value, accuracy, F-measure, and area under the receiver operating characteristic curve (AUROC).

Results: For the 2010 cohort, DILIN had the highest PPV (11.5%, 95% CI: 8.1-15.8%), specificity (98.2%, 95 % CI: 97.9-98.4%), accuracy (98.9%, 95% CI: 97.7-98.2%) and F-measure (0.189). CIOMS had the highest sensitivity (73.0%, 95% CI: 60.3-83.4%) and AUROC (84.8%). A similar trend was confirmed in the 2011 cohort. Besides the laboratory criteria, including additional keywords in the classification algorithm improved the PPV and F-measure to a maximum of 41.3% (95% CI: 30.4-52.8%) and 0.504 respectively.

Conclusions: More stringent criteria (DEWG and DILIN) performed better in PPV, specificity, accuracy and F-measure. CIOMS criteria performed better in sensitivity, which is preferred for monitoring rarer events in pharmacovigilance. Requiring at least two abnormal LCs during hospitalisation and text-word searching in the discharge summaries decreased false positives without loss in sensitivity.

Keywords: Algorithm, drug-induced liver injury, electronic medical record, laboratory threshold criteria

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Practical issues of cohort and event definition in database research: Risk assessment of dyslipidemia by atypical antipsychotics using claim database

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Objective: To confirm issues of cohort study through practical examination using new user design, matching, composite event definition, and survival time analysis, trial survey was conducted on the already known risk of dyslipidemia by atypical antipsychotics.

Methods: Using JammNet claim database, newly prescribed cases of atypical and typical antipsychotics from April 2014 to March 2017, who met the selection criteria such as no antipsychotics prescription in the last 6 months, were defined as group A and B, respectively. Cases with no antipsychotic prescription matched by gender and age on the first dispensing day of group A were defined as group C, and observed for up to 1 year. Three event definitions were used; when anti-hyperlipidemic drugs were prescribed during the observation period (I), when disease names corresponding to dyslipidemia were given (II), or when both were applicable (III). As main analysis, hazard ratio before and after adjustment by covariate (age, gender, complication of hypertension, diabetes, etc.) using Cox proportional hazard model was calculated.

Results: When using event definition II, the number of events in groups A (n=939), B (n=269) and C (n=4691) was 66, 20 and 659, and the adjusted hazard ratio of group A to group B and C was 0.68 (0.40-1.14) and 0.88 (0.60-1.28), respectively. No increase in the risk was also observed when other definitions were used.

Conclusion; As non-treatment group, difficult to obtain from patients with the same target disease, is necessary to calculate the contribution risk, we used antipsychotics non-users regardless of the disease by simple matching. The higher number of dyslipidemic events in the non-treatment group than in the exposed group may be due to the inclusion of many patients with lifestyle diseases. It is considered difficult to set a neutral control group in the cohort study for the target event.

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Inventory of real-world data sources in Japan: survey results by JSPE Pharmacoepidemiology and Database Task Force

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Objective: Japanese Society for Pharmacoepidemiology (JSPE), Pharmacoepidemiology and Database Task Force has conducted an annual survey of databases available for clinical and pharmacoepidemiology researches in Japan since 2010. The objective of this survey was to update the database inventory as of October 2018 and to introduce newly developed website.

Methods: Using a web-based questionnaire, approximately 50 questions (e.g., data source, period, number of patients, age distribution, coding methods, presence of lab results) were asked directly to 22 data holders in October 2018. In addition to providing the summary table on the JSPE web site, we newly developed a user-friendly website that allows data filtering and comparison of the databases.

Results: In total, 19 data holders responded to the questionnaire. The study results are available on JSPE web site (http://www.jspe.jp/committee/020/0210/). There were 7 hospital-based databases, 5 insurance-claims databases, 5 pharmacy claims databases, and 2 other type of databases. The newly developed website allows data filtering based on set criteria.

Conclusion: To our knowledge, this is the only periodic survey of Japanese databases in the field. We expect our survey and the new website stimulate awareness and usage of database researches in Japan.

Keywords: Database, pharmacoepidemiology, Japan, inventory

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A study for incidence proportion of thrombocytopenia in herpes zoster patients using medical information data in Japan

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Objectives: For an acute-phase treatment of herpes zoster, an early-phase administration of anti-herpes virus drug is important and it is positioned as the first choice. While thrombocytopenia is listed in package insert as one of the significant adverse reactions in patients treated with those anti-herpes virus drugs, there are case reports to suggest that thrombocytopenia was caused by infections with herpes zoster virus. Since there are no previous studies to investigate the details that it is drug-induced or virus-induced, we investigated the incidence proportion and risk factors of thrombocytopenia in herpes zoster patients by using a medical database.

Methods: A cohort study was conducted by using the medical information database of Medical Data Vision. Co., Ltd. Out of patients with herpes virus infection in 2010 and onwards, a herpes zoster group was defined with ICD-10: B02 + anti-herpes virus drug, and with a control group of herpes simplex group (ICD-10: B00 + anti-herpes virus drug), the incidence proportion/onset odds ratio of thrombocytopenia was confirmed. Thrombocytopenia as an outcome was defined with a definite diagnosis (ICD-10), medical care procedures, and prescriptions of therapeutic drugs (The 24th Annual Conference of Japanese Society for Pharmacoepidemiology. October 2018. Abstracts. P122).

Results/Conclusion: With regard to the incidence proportion of thrombocytopenia in herpes zoster patients, crude incidence proportion was 1.74%. With regard to the odds ratio of thrombocytopenia, an adjusted odds ratio of the herpes simplex group against the herpes zoster group was 0.876 (95%CI: 0.801 - 0.957, p-value: 0.0035). According to the investigation of risk factors in the two groups, statistically significant differences were observed in “bone-marrow metastasis/blood cancer etc.”, “antimicrobial drugs”, “anticancer drugs” and “immunosuppressants” out of concurrent diseases/concomitant drugs. For these factors, the adjusted odds ratios of “Yes” against “No” were beyond 1, which showed that the factor increased the risk of thrombocytopenia.

Key words: medical information data, herpes zoster, thrombocytopenia

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Use of antihyperglycemic drugs and risk of colon cancer recurrence: a nested case-control study

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Aim/Objective: To assess the association between use of antihyperglycemic drugs and risk of colon cancer recurrence.

Methods: A nested case-control study was conducted using 2007-2017 data linkage of the Taiwan Cancer Registry and the National Health Insurance Research Database. Adult patients with type 2 diabetes who were newly diagnosed stage I-III colon cancer and underwent curative surgery between 2007/01/01 and 2015/12/31 were included. Cases with colon cancer recurrence were identified and controls were randomly selected by risk-set sampling. Exposure of antihyperglycemic drugs (in eight classes) was measured between surgery and 6 months prior to the index date. Conditional logistic regression was used to examine the risk of colon cancer recurrence associated with use of antihyperglycemic drugs. A sub-analysis was conducted in a subpopulation with known diabetes duration to investigate differential risks by diabetes duration. Sensitivity analyses with different case definitions, exposure measurement period, and external adjustment for controlling for unmeasured confounder were performed to test the robustness of study results.

Results: The study cohort consisted of 6,416 patients, with a mean age of 70.3 years and 53.9% of male. In total, 25.5% of patients had stage I colon cancer at diagnosis, and 38.7% and 35.8% were at stage II and stage III, respectively. After a median follow-up of 4.2 years, 412 cases and 1,378 controls were identified. Further analysis will be continued to examine if post-surgical use of metformin was associated with a decreased risk of colon cancer recurrence, while on the other hand, if the use of basal insulin could increase the risk. The effect of other antihyperglycemic drugs on colon cancer recurrence will be evaluated.

Conclusions: We expected that the findings of this study would help to guide the choice of antihyperglycemic treatment in patients with stage I-III colon cancer and improve the clinical outcomes of these patients.

Keywords: colon cancer, cancer recurrence, antihyperglycemic drugs, Taiwan Cancer Registry

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Systematic investigation on guidelines for real world study using observational designs

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Objective: Retrospective database is one important source of real-world data. We systematically investigated and analyzed the status and key methods of guidelines for real world study using observational designs, especial for retrospective database study to inform post-marketing drug evaluation.

Methods: We systematically searched Medline, EMBASE from inception to 15 January 2018. MeSH combined with free words terms were used to identifying potentially eligible studies. Two researchers independently screened titles/abstracts and full-text articles to identify eligibility and collected data. Eligibilities should be guidelines, standards or recommendations related to real world study using observational designs. Both prospective and retrospective observational designs were eligible. We collected information about year, issuer, purpose, study design for each eligibility. For retrospective database study informing drug evaluation, we further investigated key methods from six scopes including study planning, design, conducting, analysis, reporting and evaluation.

Results: 29 guidelines for real world study using observational designs proved eligible. These guidelines covered multi-faceted research questions, including treatment effects, safety, economy, and compliance. Of which, 12 (41.4%) guidelines were related to observational designs, 5 (17.2%) were exclusively prospective observational design, 6 (20.7%) exclusively retrospective observational design, 5 (17.2%) were both prospective and retrospective observational design. 19 guidelines were related to post-marketing drug evaluation using retrospective database. Of which, 10 (52.6%) guidelines involved study reporting, 7 (36.8%) involved study planning, 5 (26.3%) involved study design, 4 study involved implementation and 3 (15.8%) involved statistic analysis. On the scope of study planning, current guidelines discussed how to propose research question and choose suitable database. On design stage, guidelines proposed key methods regarding choosing optimal study design, defining important variable, and mitigating bias and confounding. Current guidelines, however, lack key technical standard regarding extracting data, cleaning data and structuring text information.

Conclusion: Real world study using observational design has recently received wide attention, especially retrospective database study. The current guidelines lacked key methods on study implementation.

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Statins or Thiazide Associated with New-onset Diabetes in Hypertensive Patients: Multilevel Random Effect Model

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Aim/Objective: To identify association between statins/thiazides with new onset diabetes (NOD) in patients with hypertension.

Methods: We used panel data of 4,505 newly diagnosed hypertensive patients prescribed with or without statins and were followed up within 6 years for NOD. Hypertension and NOD were identified by ICD10 and all relevant prescribed medications. NOD was modeled with both time-invariant and time-varying exposures and covariates by multilevel random effect model for self-controlling.

Results: Adjusting for other confounding factors and self-controlling, the model revealed that body mass index (95% CI of OR=1.04-1.69), cholesterol level (95% CI of OR =1.06-2.84), triglyceride level (95% CI of OR=1.07-2.18), and thiazides (95%CI of OR=1.32-2.99) are significant associated with NOD in hypertensive patients.

Conclusion: Thiazide was associated with NOD in hypertensive patients, but not statins. In addition BMI, cholesterol and triglyceride play pivotal role in NOD.

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Identification of Patient with Cardiovascular Diseases in EMR and Claim Databases in Chinese-Speaking Countries: An Extensive Review

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Objective: The PATCH (PATient identification in CHina) was initiated to explore challenges and develop solutions in identifying patients in EMR or claim databases in China. This sub-study aims to summarize CVD patient identification (CVD-PtID) methods and the development and validation of such methods in Chinese-speaking countries/regions.

Methods: A search strategy was applied in PubMed and CNKI (China National Knowledge Infrastructure) on studies on CVD. Studies were limited to Chinese-speaking countries/regions. We also conducted a quick review on studies (regardless of disease) reporting development and validation of PtID methods.

Results: Overall, 104 literatures were identified. Of the 82 relevant, 50% were in Taiwan, 44% in Mainland China, 4% in Singapore and 1% in Hong Kong. One-third reported PtID methods. Most studies (92%) in Mainland China used EMR, whilst 90% of studies in Taiwan used the National Health Insurance Research Database (NHIRD). Almost all studies using a claim database and 40% of studies using EMR used ICD codes for PtID. Only 2% used Chinese keywords and 19% used a combination of ICD codes and keywords. Other methods include chart review, lab testing, medication, and CT image. The positive predictive value (PPV) of NHIRD was over 70%. Other studies didn't report development or validation of PtID. A quick review found five studies reported development and validation of keywords. Development methods include random forest algorithm, Unified Medical Language System (UMLS), clinical Text Analysis and Knowledge Extraction system, Conditional random fields (CRFs) and Clinical Bayesian Network (CBN). Validation measures include sensitivity, specificity, accuracy, AUC and PPV.

Conclusion: As the need for using EMR to conduct RWE is growing, more efforts should be put into harmonizing and standardizing of ICD codes in China. Meanwhile, developing keywords using machine learning is highly recommended for studies on CVD patients using EMR or claim databases if ICD coding is not available or reliable.

Keywords: patient identification, CVD, keywords, Chinese

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Validation of heart failure diagnosis with International Classification of Diseases-10 and natural language processing in an electronic medical records database

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Background: Currently it is difficult to differentiate heart failure (HF) with reduced ejection fraction (HFrEF), mid-range ejection fraction (HFmrEF), and preserved ejection fraction (HFpEF) using only International Classification of Diseases-10 (ICD-10) codes in electronic medical records data research. This study aims to use ICD-10 and natural language processing (NLP) method to validate HF diagnosis.

Methods: We extracted HF patients (ICD-10: I50.xxx) from an existing electronic medical record database (National Healthcare Big Data in Fuzhou, China. 37 hospitals included). Ejection fraction (EF) values were extracted from medical records text utilizing NLP technology and a modified algorithm based on Patel YR 2018 approach for verification of HFrEF, HFmrEF and HFpEF: EF (<40%, 40%-50%, ≥50%) and either B-type natriuretic peptide (BNP) or aminoterminal pro-BNP (NT-proBNP) values recorded OR diuretic use within one month of diagnosis of HF. A random sample of cases, and of non-cases were selected, and the corresponding medical charts retrieved and reviewed for validation by pairs of trained, independent reviewers.

Results: Validation analysis of this method had a sensitivity/specificity of 82%/90% for HFrEF, 77%/84% for HFmrEF, and 86%/89% for HFpEF, respectively.

Conclusion: A sensitive and highly specific approach was developed using both ICD-10 and NLP to detect HF patients. A cohort of HFrEF, HFmrEF and HFpEF patients was established for further real-world study in Fuzhou, China.

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Considerations in Measuring Healthcare Resource Utilization Using Electronic Medical Record Databases versus Claims Databases in China: An Extensive Review

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Objective: Due to main limitations of EMR (disclosure and limited expense information) and claims databases in China (lack of comorbidity and test information), we aim to summarize the frequently used indicators of healthcare resource utilization (HCRU) in real-world evidence (RWE) and to discuss the advantages and limitations of the two types of data sources.

Methods: We searched CNKI (China National Knowledge Infrastructure) and PubMed (from January 2009 to May 2019) to identify studies using HCRU as an outcome and using EMR or claims as the data source in China. Full-text studies were reviewed.

Results: Overall, 51 studies were identified and screened. Twelve relevant studies cover seven disease areas with the top 3 being diabetes (25%), cardiovascular diseases (25%), and COPD (17%). Of studies used a multicenter EMR (50%), the most frequently reported HCRU indicators were the number of visits (by types of settings) and length-of-stay (LOS) (100% and 67%, respectively), corresponding proportions in studies using a claim database were 100% and 60%. Only the study on heart failure (1/12) evaluated surgery utilization. None reported the frequency of lab tests. None discussed potential bias using a multicenter EMR database to estimate these indicators.

Conclusions: The number of visits and LOS are the most frequently used indicators in current Chinese real-world data. Number of visits using claim databases may produce more reliable results as within a geographical area, a claim database in China can be considered as “closed” (i.e. all visits of a patient across hospitals can be captured). LOS is feasible in both EMR and claim databases. Detailed lab tests, surgery, and procedure in the EMR database provide great potential for HCRU evaluation for patients with certain conditions but haven’t been utilized.

Keywords: Healthcare Resource Utilization, Electronic Medical Record, Claims Databases, China

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Risk of Neuroleptic Malignant Syndrome Among Patients Exposed to Antipsychotics

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Background: Neuroleptic malignant syndrome (NMS), a rare but serious adverse reaction of antipsychotics. However, little evidence of risk and epidemiology of NMS is available.

Aim: To determine the risk of NMS associated with haloperidol, olanzapine, quetiapine, and risperidone. To characterise the incidence and case fatality risk of NMS in antipsychotic users.

Methods: We conducted a population-based cohort analysing health records of 297 647 antipsychotic users and measure the incidence and case fatality risk of NMS. We estimated the risk of NMS associated with exposure to antipsychotics, by comparing the exposure status during day 1-30, and day 91-120 preceding the diagnosis of NMS.

Results: After adjustment for time trends in exposure, concurrent medications, and medical conditions, diagnosis of NMS was associated with exposure to haloperidol (OR, 4.40; 95% CI 1.97-9.81), and quetiapine (OR, 4.32; 95% CI, 1.70-10.97). There was no observed association for risperidone (OR, 2.00; 95% CI, 0.93-4.32) or olanzapine (OR, 1.23; 95% CI, 0.47-3.18). NMS occurred with an incidence of 1.10 per 1000 persons. The case fatality risk of NMS was measured as 6.0%.

Conclusions: Patients had increased odds of exposure to, haloperidol and quetiapine but not risperidone or olanzapine, during the 30 days prior to the diagnosis of NMS, as compared with the earlier reference period. Clinicians who prescribe antipsychotics should weigh the acutely increased risk of NMS with the potential benefits of antipsychotic therapy, especially for haloperidol and quetiapine.

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The treatment patterns of patients with diabetic nephropathy in Songjiang District of Shanghai

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Aim/Objective: Diabetic nephropathy (DN) is one of the most serious complications of type 2 diabetes (T2DM), and an important cause of death. However, it is known little of the treatment for DN in China. The study was aim to investigate the treatment patterns of patients with DN in Songjiang District of Shanghai.

Methods: A population-based, cross-sectional survey of 37670 residents aged 20 to 74 was conducted in 7 communities that were randomly sample as a cluster from Songjiang District of Shanghai from June 2016 to December 2017. Face-to-face interview was done to collect data on personal demographic characteristics and diseases histories. Link the survey to the medical record system of Songjiang District to obtain all medical information. The Chi-square Test was used to compare differences in category variables.

Results: 106 (0.28%) DN patients were identified through the medical record system, and 78 (73.58%) of whom had relevant medication records. Of subjects, 22 patients (28.21%) were treated with antidiabetic drugs alone, and a substantial proportion used both antidiabetic drugs and ACEI/ARB or Calcium antagonists (43, 55.13%). In combination use of antidiabetic drugs and ACEI/ARB or Calcium antagonists, it was most common to have less than three kinds of antidiabetic drugs and ACEI/ARB or Calcium antagonists at the same time (35, 44.87%). Insulin injections and metformin HCL were the most frequently used antidiabetic drugs. 41 patients were treated with oral antidiabetic drugs, 8 patients treated with insulin injection, and 10 patients treated with both. Comparing the use of antidiabetic drugs with that of T2DM patients in Shanghai in 2013, the results showed no statistically significant difference ($\chi 2=5.138$, $P=0.077$).

Conclusion: Combination of antidiabetic drugs and ACEI/ARB or Calcium antagonists were popular under clinical guidelines among patients with DN in Songjiang District of Shanghai. Compared with insulin injection, oral antidiabetic drugs are more commonly among DN patients.

Keywords: Diabetic nephropathy; Treatment patterns; Drug combination

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Association between hepatitis B virus infection/anti-HBV agents and the risk of colorectal cancer

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Aim/Objective: Hepatitis B virus (HBV) infection has been associated with hepatocellular carcinoma. Two studies have shown that hepatitis B is associated with increased colorectal adenomas. We aimed to identify the association between HBV infection and the development of colorectal cancer (CRC), and further evaluated the effect of anti-HBV agents on the risk of CRC in patients with HBV.

Methods: A population-based retrospective cohort study was conducted using 2 million databases form National Health Insurance Research Database of Taiwan. A Cox proportional hazard model was used to calculate hazard ratios (HRs) and 95 % confidence intervals (CIs) for determining the association between HBV infection and colorectal cancer development. We also used HR to estimate the risk of CRC between HBV patients receiving anti-HBV agents and those without anti-HBV agents.

Results: During a 7-year follow-up period, we screened 34,553 patients diagnosed with HBV infection between 2001 and 2007 as the study group. A total of 137,508 age-, gender- and index-year (1:4) matched subjects without HBV infection were enrolled in the comparison group. After adjusting for age, sex, comorbidities of diabetes, hypertension, alcohol abuse, tobacco use disorder, obesity, adenomatous polyps, crohn's disease, ulcerative colitis and anti-HBV medicines, the risk of CRC was higher in study group compared to comparison group (aHR, 1.318; 95% CI, 1.172-1.484). For further examination, there was a lower incidence of CRC found in HBV patients receiving interferon compared to those without interferon (aHR, 0.744; 95% CI, 0.278-1.994). In contrast, uses of nucleos(t)ide analogues increased the risk of CRC in patients with HBV (aHR, 1.132; 95% CI, 0.779-1.644). However, both these two results did not reach statistical significance.

Conclusion: HBV infection may be associated with an increased risk of CRC. However, the significant effects of anti-HBV agents on CRC risk in patients with HBV were not found.

Keywords: Hepatitis B virus infection; Interferon; Nucleos(t)ide analogues; Anti-HBV agents.

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The effect of Rosmarinus officinalis L. on cognitive function and mood: a systematic review and meta-analysis

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Objectives: This study aims to summarize current evidence of rosemary on cognitive function and mood.

Design: A systematic review and meta-analysis was conducted in PubMed, Scopus, ThaiLIS, and Thai thesis database were searched from inception to December 2018. All randomized controlled trials which were conducted to determine the effect of R. officinalis on cognitive function or mood were included.
Intervention: Rosmarinus officinalis

Main outcome measures: Meta-analyses were performed under a random-effects model using standardized mean differences (SMD). All measures related to cognitive functions and mood found the eligible studies were included.

Results: Of 2,094 articles retrieved, thirteen studies were included in our systematic review with 806 subjects involved but only 11 studies were used in this meta-analysis. We found that rosemary in inhalation form could potentially improve cognitive function for sensitivity index of working memory for delayed word recognition test [SMD: 0.48 (95%CI; 0.08 to 0.89)]. Rosemary in oral form could improve prospective and retrospective memory [SMD: 0.59 (95%CI; 0.11 to 1.08)]. Rosemary in various forms could also improve moods including, confusion, vigor, alertness, motivation, anxiety, and contentedness.

Conclusion: Rosemary has the potential to be used as a supplement for improved cognitive function and mood. However, because of the limited number of studies and subjects, large high-quality clinical trials to determine such effect is needed.

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Epidemiology and Treatment Patterns of Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma (CLL/SLL) in Taiwan: 2007-2017

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Aim/Objective: Chronic lymphocytic leukemia/ Small Lymphocytic Lymphoma (CLL/SLL) is one of the most frequently seen leukemia in adult population in western countries. However, little is known regarding its epidemiology and treatment pattern in Asian countries. This study aims to estimate the incidence and treatment patterns of CLL/SLL using Taiwan Cancer Registry Database (TCRD) and Taiwan's National Health Insurance Research Database (NHIRD).

Methods: Patients with CLL/SLL were identified using the International Classification of Diseases for Oncology, the Third Edition (ICD-O-3 codes: 98233) reported by registries from the 2006-2015 TCRD. CLL/SLL treatments including chlorambucil (chl), bendamustine (B), cyclophosphamide, fludarabine, doxorubicin, vincristine, rituximab (R), and other antineoplastic agents were retrieved from the NHIRD. Number of incidence, prevalence, median age of diagnosis, and sex ratio were calculated and reported annually for patients with CLL/SLL. CLL/SLL treatments patterns were assessed for initial, refractory/relapse and intensive treatment stages, respectively.

Results: A total of 1497 patients aged 20 years or above and with newly-diagnosed CLL/SLL during 2006 - 2015 were identified. The age standardized incidence rates (0.36 and 0.54 per 100,000 persons in 2006 and 2015) of CLL/SLL increased during the 10-year period. Sex ratio ranged from 1.21 to 2.63 during 2006 – 2015. Overall, 72.8 % patients have received chemotherapy. Half of patients received initial treatment for CLL/SLL at less than a month following diagnosis (median: 27 days). Chl or B or cyclophosphamide monotherapy was the most commonly seen in initial treatment. During the study period, 45 % of our study population have encountered refractory/relapse of CLL/SLL. R-based chemotherapy accounted for 34.07 % of refractory/relapse regimens being chosen. Lastly, 32.28 % of patients enrolled have received intensive treatment (43.86 % were R-based chemotherapy).

Conclusions: This study is the first population-based study conducted in Asia providing comprehensive evidence of epidemiology and treatment patterns of CLL/SLL.

Keywords: epidemiology, treatment pattern, Chronic lymphocytic leukemia/ Small Lymphocytic Lymphoma (CLL/SLL)

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Korean Nationwide Registry of Severe Cutaneous Adverse Reactions 2010-2018

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Background: A life-threatening severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS), have a genetic risk factor and ethnic difference. A nationwide registry-based study was performed to assess culprit drugs and clinical characteristics including morbidity and mortality of SCARs in Korea.

Methods: SCAR cases which occurred from 2010 to 2018 were recruited to a nationwide Korean SCARs registry from 36 tertiary referral hospitals. Demographics, causative drugs, causality, and clinical outcomes were collected after a thorough retrospective review of medical records.

Results: A total of 1,075 SCAR cases by 207 drugs were registered; SJS or TEN (n=544, 53 ± 22 years), DRESS (n=531, 55 ± 18 years). Once diagnosed with SCAR, the overall mortality rate is 7.0% and two-times higher mortality of SJS/TEN than DRESS (9.6% vs. 4.4%). The mortality rate of SCAR is slightly higher but not significantly different from other countries. Predominant culprit drugs were relatively different depending on the phenotype. Allopurinol and carbamazepine were the most common culprit drugs similar to other countries. SCARs induced by abacavir, nevirapine, oxicams were rare, and vancomycin, anti-tuberculosis, antiglaucoma drugs were relatively common in Korea. Traditional Chinese medication could be a potential risk of SCARs in several Asian countries.

Conclusions: In Korea, the mortality and overall culprit drug distribution of SCARs were similar to that of other countries. However, there were also differences in culprit drugs due to genetic and social effect.

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Prescribed Medication for Identifying People with Dementia in Electronic Primary Care Records in the UK

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Aims: There has been concern regarding whether dementia is recorded well enough in a routine electronic primary care dataset. This study has explored this by conducting a systematic review to understand how dementia has been identified previously in primary care databases in the UK,and added to this by exploring additional terms and symptoms, and medications that might be helpful in identifying people with dementia.

Methods: The study estimated the prevalence and incidence rates of dementia in The Health Improvement Network (THIN) database and compared with other longitudinal studies using the comprehensive list of diagnostic codes.

Results: Four treatments of Alzheimer's disease listed in the NICE guidelines were selected as the Prescribed medication: Donepezil 64.8% (N=19,185), Galantamine 12.4% (N=3,681), Rivastigmine 12.1% (N=3,572) and Memantine 10.8% (N=3,188). Most of the patients 74.9% (N=22,197) who had received the first Prescribed medication had either the first QOF (Quality Outcomes Framework) or Other diagnoses. 2.1% (N=7,429) of people who had received the first Prescribed medication was uniquely identified among all the codes. The incidence rates of the Prescribed medication for the 60+ age group increased slowly and gradually: 0.1, 1.1, and 2.7 per 1,000 person-years in 1997, 2004, and 2015 respectively. The prevalence rates were 0.1, 1.7, and 6.1 in 1997, 2004, and 2015 respectively.

Conclusions: At least, using of the Other diagnoses (represented by dementia annual review, senile/presenile dementia, and dementia monitoring) in addition to the QOF defined codes, and the Prescribed medication were evidenced that will not missing out a number of people with dementia. Prescribed medications for a related illness would be one of the ways to verify or support the identification of people with dementia in addition to the diagnostic codes in primary care records.

Keywords: Diagnosis of dementia, Primary care records, Codes to identify dementia, Prescribed medication

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Evaluation of patterns of Tanreqing injection based on the real world study

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Objective: To investigate Tanreqing injection in the distribution of treatment symptoms, disease and syndrome, as well asthe status of syndrome differentiation treatment in the real world.

Methods: A total of 2837 cases with Traditional Chinese Medicine (TCM) diagnosis information were included, from the database of post-marketing surveillance of Tanreqing injection: a real world study (TReQS). Data was standardized first. The conformity of symptoms and diagnosis, as well as off-label indications, was further analyzed.

Results: Tanreqing Injection was mainly for the treatment of symptoms (77.90%) like cough with difficulty in expectoration, fever and swollen sore throat. It was widely used in the wind-warm pulmonary diseases, especially presenting syndrome as retention of phlegm-heat in the lung, together with its synonymous diagnosis (50.65%). There were 30.03% cases with inappropriate diagnosis or syndrome differentiation, including contraindications and irrelevant diseases. And it seems more likely to happen in those with reimbursement(OR=1.18，P=0.0778，$\chi 2$=3.11). Compared with the patients being diagnosed appropriately, those with inappropriate diagnosis had a prolonged length of stay（P <0.0001, Z=143.88）and higher total cost（P <0.0001,, Z=154.97）.

Conclusion: Tanreqing injection is predominately used for approved TCM symptoms, diseases and syndromes; however, the fact of diagnosing without accurate syndrome differentiation and using in off-label indications still exists. The standard of TCM diagnosis and treatment should be established.

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Incidence of bladder cancer in renal transplant recipients

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Aim/Objective: Malignancy is one of the most common causes of death in kidney transplant recipients. Immunosuppression is considered the most important risk factor, as it decreases the immunologic control of oncogenic viral infection and cancer immunosurveillance. Bladder cancer (BC) in the transplanted population can represent a challenge owing to the immunosuppressed state of patients and the higher rate of comorbidities. We reported on the incidence and types of BC in kidney transplant recipients, describing possible additional risk factors and outcomes in these patients.

Methods: We retrospective kidney transplant recipients diagnosed with de novo BC between 2003 and April 2019 in a single-center study in which all patients (n=247, 114 males and 133 females). We examined patient and tumor characteristics and 3-year survival rate. The risk of BC with time after renal transplantation and survival after diagnosis of BC were evaluated by Kaplan-Meier survival analysis.

Results: Seven patients were diagnosed with de novo BC during the study period, representing 3.6% of kidney transplant recipients. The mean interval between transplantation and diagnosis of bladder tumor was 11.3±3.2 years and mean age at the time of diagnosis was 48.1 ±8.5 years. Fourteen percent of the patients were male. The tumor types were all of the carcinoma in situ (7 patients), immunosuppressant exposure (7 patients). Two patients underwent radical cystectomy for invasive tumors. The mortality rate within the 3 years was 28.6%.

Conclusion: BC occurred more commonly in kidney transplant recipients with a predominance of aggressive tumors and high mortality. Prompt diagnosis and remedial treatment are vital to prevent graft loss. Early detection and therapy is the key to improving BC prognosis at present.

Keywords: Bladder cancer, Renal transplant recipients

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Effectiveness of Chinese herbal medicine in patients with hypertension

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Objective: To evaluate whether Chinese herbal medicine (CHM) treatment improves blood pressure control in patients with hypertension (HTN).

Methods: We performed a retrospective before-after study, in which all subjects serve as their own controls. We identified the patients from the electronic medical records of a medical center in Taiwan from 2014 to 2017. Patients with HTN diagnosed and with consistent antihypertensive agents treated for at least 28 days were included. All enrolled subjects had been added on CHM therapy for at least 3 months in managing their HTN in addition to their original antihypertensive agents. We adopted changes in number and dose of antihypertensive agents after three months as substitute indicators. Improvement was reached if the original medications were shifted to lower potency drugs or whether the number or the dosage of drugs was reduced after intervention of CHM. We employed descriptive statistics to analyze data and report percentage of improved patients while paired t-test was applied to evaluate the mean number and mean defined daily dose (DDD) of antihypertensive agents before and after 3 months.

Results: There were 45 eligible patients in this study. This population was aged 65±16 (mean±SD) years and 60% were male. 5 patients (11.1%) showed improved medication control of HTN after CHM therapy for 3 months. Mean number and DDD of antihypertensive agents increased non-significantly from 2.11±0.97 and 2.22±1.25 DDD to 2.16±0.79 and 2.26±1.22 DDD ($p = 0.53$ and $p = 0.74$) respectively, before and after CHM therapy.

Conclusion: Our findings showed limited effectiveness of combining CHM for decreasing the number and dose of original antihypertensive agents. This revealed that CHM therapy might not have roles in adjunctive treatment of HTN. However, this study was limited by small sample size, indirect outcome indicators and short observation period. Large-scale studies are required to further evaluate the impact of CHM therapy.

Keywords: Chinese herbal medicine; hypertension.

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Silymarin use reduces the risk of age-related macular degeneration in patients with chronic liver disease: a pilot study

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Aim/Objective: Age-related macular degeneration (AMD) is a medical condition which may result in blurred or no vision in the center of the visual field. The pathogenesis of AMD is not well known, and there are some theories have been put forward, including oxidative stress, mitochondrial dysfunction, and inflammatory processes. Silymarin is a flavonoid compound and it is usually used to treat chronic liver diseases (CLD) due to its antioxidant, anti-inflammatory, and anti-fibrotic properties. Therefore, silymarin might prevent AMD formation in CLD patients. We conducted a pilot study to assess the risk of AMD formation among CLD patients treated with silymarin.

Methods: A population-based retrospective cohort study was conducted from Taiwan's National Health Insurance Research Database with one million subjects from 2000 to 2013. We identified patients with CLD between 2001 and 2008. We used Cox proportional hazard ratio (HR) to compare the risk of AMD between CLD patients receiving silymarin (silymarin-use group) and those without receiving silymarin (nonuse group).

Results: We included 6,476 patients with CLD using silymarin and 26,326 patients without receiving silymarin. The mean age of silymarin-use group and nonuse group are 56.6 ±10.6 and 55.8 ± 11.1 years old, respectively. During a 5-year follow-up period, the cumulative incidence rate of AMD between the silymarin users and non-users was 2.01% and 2.44%, respectively. After adjusting for possible confounding factors, the adjusted HR was 0.76 (95% CI, 0.63-0.92) for silymarin-use group compared with nonuse group.

Conclusion: Our results demonstrated a decreased risk of AMD in patients with CLD who used silymarin.

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Risk study of rhabdomyolysis among users of statin, fibrate and statin-fibrate with and without impaired renal function using claims data.

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Objective: Concomitant use of statins and fibrates in patients with abnormal renal function values, listed previously in "Relative Contraindications" sections was moved to "Important Precautions" sections of package inserts of statin and fibrate drugs in 2018 in Japan. This study is to evaluate risk of rhabdomyolysis among users of statin, fibrate and statin-fibrate with and without impaired renal function using claims data in Japan.

Method: This study was a historical cohort study using database of health insurance claims in Japan from Jamm Net Co., Ltd. Users of statin, fibrate and statin-fibrate with and without impaired renal function were identified from the data of Aug 2012 to Jul 2017, and observed until Jul 2018. Risks of rhabdomyolysis adjusted using covariates were compared between groups using Cox proportional hazards models. We evaluated the impact of impaired renal function on rhabdomyolysis risk for groups of statin, fibrate and statin-fibrate using the models.

Results: Incidence ratios of six groups (statin without(A) and with(B) impaired renal function, fibrate without(C) and with(D) impaired renal function and statin-fibrate without(E) and with(F) impaired renal function) were 44/29803 (0.15%), 9/1507 (0.60%) 6/3899 (0.15%), 3/190 (1.58%), 2/971 (0.21%) and 2/41 (4.88%) for A-F groups, respectively. Hazard ratios [95% confidence intervals] for B-F groups relative to group A were 2.02 [0.89, 4.58], 0.87 [0.37, 2.05], 5.46 [1.66, 17.99], 1.14 [0.27, 4.72] and 15.58 [3.72, 65.25], respectively.

Conclusion: All groups of statin, fibrate and its concomitant users with impaired renal function showed a trend of increased risk of rhabdomyolysis compared to each corresponding group without impaired renal function. The different impact of impaired renal function on rhabdomyolysis risk between statin, fibrate and its concomitant group was indicated.

Key words: statin, fibrate, rhabdomyolysis, impaired renal function

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Exploring herbs that cause interstitial pneumonia using electronic healthcare record data

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Aim/Objective: Kampo medicines (traditional Japanese medicines) comprise various herbs. However, iseveral of these herbs, including ougon and hange, may cause interstitial pneumonia. To date, explanatory data analysis associating herbs with the occurrence of interstitial pneumonia using real-world data has not been performed. Thus, we investigated the causes of interstitial pneumonia using electronic healthcare record (EHR) data.

Methods: Research subjects included patients who were prescribed a herb or kampo medicine from 2008 to 2018 at the Kyushu University Hospital. For patients who developed interstitial pneumonia, all medicines prescribed within 30 days before the onset of the disease were considered as possible causes. We classified kampo medicines based on Kyoto Encyclopedia of Genes and Genomes. In addition, information about the herbs contained in each medicine was extracted from medical package inserts using a text mining method. We then calculated the incidence ratio of interstitial pneumonia for each medicine and each herb and evaluated their effects using a logistic regression with elastic net regularization.

Results: In total, 442078 patients were prescribed a herb or kampo medicine. Of these, 61 patients developed interstitial pneumonia. The number of types of medicines was 133, and 138 herbs were contained in the medicines or prescribed directly. Candidate drugs causing interstitial pneumonia were identified, such as jyuzentaitou or hangesyashintou. In addition, the herbs such as daiou, syakuyaku, maou, and hange were identified as the possible causes of interstitial pneumonia.

Conclusion: Although several limitations exist, real-world databases like EHR can be used to identify herbs that cause diseases.

Keywords: Kampo medicines, Intestinal pneumonia, Real-world database

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Investigating prescription patterns for kampo medicines using a latent dirichlet allocation model

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Aim/Objective: Kampo medicines (traditional Japanese medicines) have a long history of use in Japan. Each kampo medicine comprises several herbs. If multiple medicines are prescribed to one person, an overdose of herbs is possible. Although most of medical departments in Japan commonly prescribe kampo medicines, studies investigating actual prescriptions using real-world database are sparse. Thus, we investigated the prescription patterns for kampo medicines using electronic healthcare record data.

Methods: Research subjects were patients who were prescribed or kampo medicine from 2008 to 2018 at the Kyushu University Hospital. We classified the medicines based on Kyoto Encyclopedia of Genes and Genomes, and aggregated the prescribed medicines for each patient by month. Next, we applied a latent Dirichlet allocation model (LDA) to the aggregated data and extracted latent topics about the medicines that each patient was simultaneously exposed to. LDA is a machine learning method that can extract latent topics from words in documents and can be applied to prescription data to extract topics from medicines. We also aggregated the prescribed medicines by each medical department and then applied LDA to understand the prescription patterns for each department.

Results: Forty medical departments prescribed 133 types of kampo medicines to 267078 patients in total. LDA analysis extracted the following latent topics for kampo medicines: such as a topic composed mainly of Kamisyouyousan, Ninjinyoueitou, and Rikkousan and a topic composed mainly of Rokkunnshitou and Daikentyutou. Furthermore, the prescription patterns notably differed between medical departments.

Conclusion: We can understand which medicines are simultaneously prescribed as well as the prescription patterns of each prescriber using LDA. Thus, LDA may be useful for appropriate prescription of medicines.

Keywords: Kampo medicines, Latent Dirichlet allocation model, Electronic healthcare record data

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Drug utilization of CPM for patients with respiratory disease at community pharmacies in China: an analysis from 2014 to 2018

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Objective: This research aimed to investigate the situation of Chinese patent medicine (CPM) used for patients with respiratory diseases at community pharmacies in China.

Method: Using the China Health Industry Intelligence System Database that collected data from community pharmacies (n=11,450) in 185 cities over China, ranging from 2014 to 2018. In addition to overall trend analysis, further detailed analysis about indications and the leading over-the-counter and prescription drugs was conducted.

Results: Sales of CPM for respiratory disease increased from 34.7 billion CNY in 2014 to 49.5 billion CNY in 2018, with an average annual growth rate of 9.5%. In 2018, CPM accounted for 75% market share of respiratory disease at community pharmacies. Regarding the market concentration, the market share of the top 50 CPMs raised from 57.44% in 2014 to 59.27% in 2018. In terms of the indication, the leading three indications of CPM in 2018 were cold, pharyngitis and cough. OTC drugs were the main force of CPM, however the market share dropped from 85.60% (29.7 billion CNY) in 2014 to 83.83% (41.5 billion CNY) in 2018. The top 5 OTC leading drugs in 2018 were: (1) Ganmaoling Granules; (2) Nin Jiom Pei Pa Koa; (3) Pudilan Xiaoyan Tablets; (4) Huoxiang Zhengqi Oral Liquid; and (5) Lanqin Oral Liquid. The top 5 prescription drugs in 2018 were: (1) Pudilan Xiaoyan Oral Liquid; (2) Xiao'er GuYi Qingre Granules; (3) Bailing Capsule; (4) Suhuang Zhike Granules; and (5) Niuhuang Jiedu Tablets.

Conclusion: Complex interventions are needed to improve therapy management for CPM for patients with respiratory disease at community pharmacies in China. In particular, community pharmacists should pay special attention on the use of CPM prescription drugs for patients with respiratory disease.

Key words: Drug utilization; Chinese patent medicine; Respiratory disease; Community pharmacy

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Aspirin use and incidence of stroke in patients with diabetes treated with statins: A population-based cohort study.

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Aim/Objective: The effect of aspirin for primary prevention of cardiovascular disease was still controversial. The aim of the study was to investigate whether aspirin provides an additional effect for primary prevention of ischemic stroke in diabetes patients with statin using a real-world population-based cohort study.

Methods: We assembled a new user cohort of statin between 2001 and 2012 in patients with diabetes without prevalent cardiovascular diseases (CVD) from the Longitudinal Cohort of Diabetes Patients (LCDP) in Taiwan. Among the diabetes cohort, we identified subjects receiving aspirin within one year after the first prescription of statin as aspirin users; all other patients were considered as non-users. We calculated the crude stroke incidence rates per 1,000 person-years. Time-dependent Cox proportional hazards models adjusted for propensity score were used to estimate hazard ratios (HRs) with 95% confidence interval (CIs) of incident stroke associated with aspirin use. Subgroup analyses were performed by age, gender, and hypertension.

Results: A total of 18,815 patients were eligible and included in the final analysis, consisting of 6944 aspirin users and 111,871 nonusers. During a total of 603,166 person-years of follow-up, the incidence rate of stroke was 5.12 per 1,000 person-years, 95% confidence interval [CI] 4.94 - 5.30. Compared with nonusers, aspirin use was associated with an increased risk of ischemic stroke (HR 1.25, 95% CI 1.04-1.51).

Conclusion: In this study in Taiwan, aspirin use was associated with a 25% increased risk of ischemic stroke. Aspirin is used for primary prevention of CVD; however, among patients with diabetes treated with statins, aspirin did not provide additional benefit in prevention of ischemic stroke.

Keywords: primary prevention; ischemic stroke; aspirin; statin.

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The overview and perspective of pharmacoepidemiologic study based on medical database in China

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Object: To summarize the status of medical database and pharmacoepidemiologic study in China; to analyze the bottlenecks of pharmacoepidemiologic study based on medical database and propose strategies .

Methods: Systematically searching literatures related to pharmacoepidemiologic study based on medical database such as “CNKI” “Wanfang Database” and “PubMed”; comprehensively collecting Chinese guidelines on pharmacoepidemiology and real world study (RWS).

Result: Chinese medical database mainly includes Hospital Informatic System database, Medical Insurance Management Information System database, National Adverse Drug Reaction Monitoring database, and database established by researchers according to their investigation etc. Current research methods are mainly traditional pharmacoepidemiology methods. Besides, researchers have applied signal mining methods based on medical database to monitor drug safety, such as prescription sequence analysis and association rules analysis etc. In 2017 and 2019, the government issued the "Technical Specifications of RWS on Traditional Chinese Medicine (Draft)" and the "Guidelines on Methodology of Chinese Pharmacoepidemiology Study". Although China has issued a series of regulations so as to promote medical information sharing, its regulations and technical systems need to be established and improved. The bottlenecks of Chinese pharmacoepidemiology study are lack of regulation supports, “Information Island” and poor data quality.

Conclusion: China is still at the beginning of pharmacoepidemiologic study. It is not only the fundamentals of promoting Chinese pharmacoepidemiologic study but also an effective way to improve intelligent supervision level of National Medical Products Administration by strengthening policy support to promote information disclosure and data sharing, introducing regulations to ensure information security and protect patients' personal privacy, adopting internationally standardized codes for disease and drug names, establishing a common database model and continuously improving relevant guidelines in practice.

Keywords: medical database, pharmacoepidemiologic study, real world study

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Current status and consideration on the standard nomenclature and coding rules of Traditional Chinese Medicine Drugs

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Aim: To clarify the significance and the difficulties of coding rules of Traditional Chinese Medicine Drugs (TCMDs); to propose new ideas for optimizing the coding rules combined with the characteristics of TCMDs.

Methods: We went through documents related to the standardization and coding rules of TCMDs in the literature databases of "CNKI", "Wanfang database" and "PubMed". We also teased out Chinese drug standards and guidelines issued by National Medical Products Administration (NMPA). At last, by summing up the classification and characteristics of TCMDs lists commonly used in Chinese clinic, we made an analogy with Anatomical Therapeutic Chemical system.

Results: NMPA has promoted TCM products name standardizing by formulating NMPA Drug Regulatory Code. Chinese researchers have made exploration on the coding rules of TCMDs according to the characteristic of TCMDs, including two different coding rules for Chinese Medicine slices (CMSs) and the coding rule of TCM products proposed by China pharmacy pharm-info net (CPPN), the standard code of TCM products.

Conclusion: The standard code of TCMDs has not been widely used because of its disconnection and different application between regulatory and clinical practice. Therefore, based on the characteristics of TCM products and being appropriate for regulatory and clinical activities, we propose the following approaches to optimize the existing coding rules, including classifying based on the clinical division of diseases, separately coding TCM products containing toxic CMSs and Chinese-Western combination preparations, establishing coding rules for TCM products with the same prescription having various names or the same name belonged to different prescriptions. It will promote the global communication of drug clinical research and safety supervision, internationalization of TCMDs and integration of herbal medicine supervision in the worldwide.

Keywords: Chinese Medicine slices, Traditional Chinese Medicine Products, standard nomenclature, coding rules

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The relationship between calcium channel blockers use and risk of Parkinson's disease

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Aim/Objective: Parkinson's disease (PD) is a chronic, degenerative, and has an unpredictable disease process which makes it a big challenge for patients, doctors and caregivers. Antihypertensive drugs, especially calcium channel blockers (CCBs), have been suggested to modify the PD risk due to the neuroprotective effect. Several observational studies examined the association between CCBs use and PD risk were conducted in western countries with mixed results, thus, we aimed to examine the relationship between the CCBs use and risk of PD by using a large cohort extracted from the National Health Insurance Research Database (NHIRD) in Taiwan.

Methods: Based on data extracted from the NHIRD, we identified 20,132 incident PD cases and 80,517 age- and gender-matched non-PD controls from 2005 to 2010. CCBs user was defined as two or more CCBs prescriptions between 1999 and 2 years prior to the index data (i.e., the first date of PD diagnosis). Multivariate analysis with logistic models were used to estimate the associations between different types of CCBs and risk of PD.

Results: After controlling for urbanization, insurance premium, the Charlson comorbidity index, and the defined daily dosage of CCBs, we found no association between dihydropyridine used exclude amlodipine and PD risk (adjusted odds ratio, aOR = 0.98, 95% CI [0.92, 1.03]) compare with patients who did not use this type of CCBs. However, we observed those who used the type of amlodipine were associated with reducing risk of PD (aOR=0.90, 95% CI [0.83, 0.97]). Non-dihydropyridine CCBs were associated with increased risk of PD (aOR=1.14, 95% CI [1.06, 1.23]).

Conclusion: With this large population-based case-control study, we observed that those who used amlodipine type of CCB were less likely to develop PD compared with non-amlodipine users. Future studies are required to confirm our finding and more evidence is required to confirm which types of CCBs have protective effect on PD.

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Target identification and drug repurposing studies in Crohn's disease: An in silico approach

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Objective: To identify targets and determine off-label therapeutic possibilities for Crohn's Disease (CD)

Methodology: The dataset accession was done via GEO and extraction of DEGs through GEO2R, followed by enrichment analysis using the web-based DAVID tool. Then literature mining was done to identify well established genes implicated in CD, these genes were short-listed based on protein-protein interaction through STRING. The interacting gene products, with good scores, were concluded to be significant in CD, and were hypothesized as Potential Targets. These targets were then repurposed with NIH LINCS Repurposing hub, and Standard Drugs were identified. These standard drugs and their structurally similar counterparts were then screened through Schrödinger docking software to identify potential drugs for CD.

Result: This in silico approach has lead to the identification of potential therapeutic targets for CD, that is MAPK14, GSK3B, NRAS, NOS2, and PTAFR. Further, the repurposing study revealed new alternative drugs, and investigational drugs such as Losmapimod, Enzastaurin, rbt205 inhibitor, lonafarnib, Rupatidine, Miconazole, and Desloratidine, that could act on these targets and potentially aid in CD therapy.

Conclusion: Crohn's disease is a type of inflammatory bowel disease, which is a chronic auto-immune condition affecting any part of the gastro-intestinal tract. There is no abortive treatment addressing the root cause of the same. Therefore, these hypotheses serve as an excellent basis for further in vitro and in vivo studies.

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A target specific drug repurposing approach for Crohn's disease through molecular docking studies

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Objectives: To determine the potent drugs to repurpose for Crohn's Disease (CD).

Methodology: Literature mining was performed to retrieve the list of potential targets/genes. Drug Repurposing Hub, NIH-LINCS, was used to identify the drugs for the targets identified. Drug similarity search was done using Drug Bank Similarity search tool. Drugs possessing a similarity score 0.6 when compared with standards were shortlisted for docking studies. Standard and similar drugs were subjected to molecular docking using the Glide tool (v6.7) in Schrodinger. Pharmacokinetic and Physicochemical parameters were analysed using Qikprop.

Result: Over 14 gene targets were obtained through literature mining as potential targets for CD namely NOD2, IRGM, IL23R, LRRK2, ATG16L1, IL12B, STAT3, JAK2, TYK2, MUC2, HLA-DRB1, IL10, SLC22A4, SLC22A5. Out of which only JAK2 and TYK2 had reference drugs and PDB in the required form and were taken forward, JAK2 was found to have 6 standard drugs as a potential inhibitors of it and TYK2 with 3 drugs. For JAK2, around 15 similar drug molecules were found and docking was proceeded, out of which Decernotinib was better than the standard tofacitinib, and disulfiram was better than thiram, other 5 standards had no similar drugs with better docking scores. For TYK2 around 8 similar drugs were found for 3 standards, out of which for standard tofacitinib, fedratinib, and ruxolitinib were found to have good docking score.

Conclusion: Crohn's Disease (CD) is a chronic, relapsing and autoimmune Inflammatory Bowel Disease (IBD). The exact pathogenesis of CD is unknown, however various risk factors have been identified and specific theories for pathogenesis have been proposed. Exploring key pathogenic factors and drug re-appraisal would circumvent initial stages of drug discovery.

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Analysis of Potential Targets for Drug Repurposing in Cystic Fibrosis Through Microarray Profiles

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Aim/ Objective: The aim of the study is to explore the druggable targets of Cystic fibrosis (CF) using gene expression profiles and reappraise the indication of existing drugs towards the treatment of CF.

Methods: The dataset GSE15568 included the gene expression profile of 16 CF and 13 non-CF individuals, was downloaded from Gene Expression Omnibus (GEO) database. Differentially Expressed Genes (DEGs) were identified using GEO2R. Gene Ontology (GO) and Kyoto Enrichment of Genes and Genomes (KEGG) pathways were analysed using Database for Annotation, Visualization and Integrated Discovery (DAVID) tool. Protein-Protein Interactions (PPI) analysis was carried out using STRING. Homology modelling was done for Decorin (DCN). Drug for the shortlisted target was retrieved in Drug repurposing hub, NIH LINCS project. The drug was docked against target obtained from Protein Data Bank using Schrodinger Glide tool. Pharmacokinetic and physiochemical properties were analysed using Qikprop.

Results: Decorin (DCN) was identified as potential target for CF. The drug with possibility of therapeutic repurposing, targeting the protein was found to be Tromethamine and was found to comply with Lipinski's rule of five.

Conclusion: Cystic Fibrosis (CF), a progressive autosomal recessive disorder, caused due to deletion mutations in Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. Therapeutic options for the same are limited which poses a threat to the lives of these patients. Drug repurposing proposes a new window of hope which could help make their lives better.

Keywords: Cystic fibrosis, Drug repurposing, Decorin, Tromethamine

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In-silico Determination of Therapeutic Possibilities for Duchenne Muscular Dystrophy: A Gene Database Linked Analysis

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Aim: To determine off-label therapeutic possibilities for Duchenne muscular dystrophy.

Methods: Geo-databases were used to obtain a list of genes and proteins that are involved in the development and expression of Duchenne muscular dystrophy. The common genes and proteins involved in various pathways were then obtained and checked for their inter-cluster interactions using the David tool. The repurposing application was utilized to obtain possible drug targets for these genes, following which the drug targets and their structurally similar counterparts were analyzed through in-silico methods to screen out the drugs with the best docking scores.

Results: The genes and proteins that were found linked with Duchenne muscular dystrophy were DMD gene, Heat shock proteins (HSP), Matrix metalloprotease-2 (MMP-2) and Cathepsin S (CTSS). The drugs with possibility of therapeutic repurposing, targeting these proteins were found to be Amrubicin, Idarubicin, Daglutril, Doxycycline, Ozanimod, Tiludronate and Captopril.

Conclusion: Duchenne muscular dystrophy is a rare genetic disorder that leads to excessive muscle breakdown. Therapeutic options for the same are limited which poses a threat to the lives of these patients. Drug repurposing proposes a new window of hope which could help make their lives better.

Keywords: Duchenne Muscular Dystrophy, In-silico, Gene-linked analysis

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In-silico Identification of Potential Targets for Drug Repurposing in Cystic Fibrosis Using Gene Expression Profiles.

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Aim/objective: Cystic fibrosis (CF), is one of the most common fatal genetic diseases caused due to mutation in the chromosome 7q31.2 coding for Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, making the protein dysfunctional. The main objective is to find potential drugs for repurposing in the treatment of CF.

Methods: The dataset GSE15568 downloaded from GEO database and analyzed through GEO2R. Gene Ontology (GO) and Kyoto Enrichment of Genes and Genomes (KEGG) pathways were analysed using DAVID tool. The Protein- Protein Interactions (PPI) were studied using String and visualized using cytoscape. Drugs for the selected target were retrieved in Drug repurposing hub, NIH LINCS project. Drug similarity search for the standards was performed in Drug Bank. Standards and similar drugs were docked using Schrodinger Glide tool with the target obtained from PDB. Pharmacokinetic and physiochemical properties were predicted using Qikprop analysis.

Results: A total of 242 genes were obtained with both down-regulated (156) and upregulated (86) genes. PPI analysis revealed matrix metalloproteinase-13 (MMP13) with significant interactions. Ilomastat and Cipemastat were obtained as standards for MMP13. Golotimod, TT232, Relamorelin, Macimorelin and N-[(2R,3S)-1-[(2S)-2-[(cyclopentylcarbamoyl)amino]-3-methylbutanoyl]-2-(1-formylcyclobutyl)pyrrolidin-3- yl]cyclopropanecarboxamide had best docking scores comparable to standards. Drug N-[(2R,3S)-1-[(2S)-2-[(cyclopentylcarbamoyl)amino]-3-methylbutanoyl]-2-(1-formylcyclobutyl)pyrrolidin-3- yl]cyclopropane carboxamide was found to comply with Lipinski's rule of five.

Conclusion: Golotimod, TT232, Relamorelin, Macimorelin and N-[(2R,3S)-1-[(2S)-2-[(cyclopentylcarbamoyl)amino]-3-methylbutanoyl]-2-(1-formylcyclobutyl)pyrrolidin-3-yl]cyclopropane carboxamide were found to be potential and can be repurposable for Cystic fibrosis targeting MMP13 which further mandates in-vitro and in-vivo experimentations.

Keywords: Cystic fibrosis, drug repurposing, MMP13, molecular docking.

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A design to evaluate risk of intussusception after rotavirus vaccine based on active surveillance in China

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Aim/objective: To design a retrospective cohort study to investigate the relation between rotavirus vaccine-Lanzhou Lamp Rotavirus(LLR) and intussusception based on active safety surveillance.

Methods: The municipal health care information platform has integrated into various databases including vaccination, maternal and children health care, electronic medical records(EMRs), death registries, which is inherently linked by a unique identity. Linking the vaccination records with EMRs by unique identity, thus actively capture all the intussusception after LLR in this city. A substitue identifer will be created using deterministic linkage or pobabilistic linkage algorithm with combination of anonymized name, sex, birthday or address for missing identity.A self-controlled risk-intervals study and cohort study will design to estimate the risk of intussusception after 1 to 7 days and 1 to 24 days of LLR. The occurrence of intussusception will be validated with Brighton criteria by chart review. The study was approved by the Ethics Committee of Peking University.

Results: The primary analysis will use a self-controlled risk-interval design that includes only vaccinated children at least one dose of LLR who was first-ever diagnosed with intussuception. From January 1, 2011 to December 31, 2018, there were 141,748 first doses, 23,808 second doses and 3,506 third doses of LLR among the children aged below 5 years. Potential cases of intussusception were identified in line with ICD-10 K56.1 and a total of 16,494 intussuception were identified.

Conclusions: As a study that conducts an active surveillance after rotavirus vaccine through data linkage on basis of electronic healthcare records in China, it’s the first time to evaluate risk of intussusception after LLR and it will offer an opportunities or a paradigm for active surveillance following immunization in China.

Keywords: active surveillance, safety, rotavirus vaccine, intussusception

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Impact of changing reimbursement criteria on statin treatment patterns among patients with atherosclerotic cardiovascular disease or diabetes mellitus in Taiwan.

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Aim/Objective: Since August 1, 2013, the eligible cholesterol level for reimbursement of statin in patients with known atherosclerotic cardiovascular disease (ASCVD) or diabetes mellitus (DM) was changed from LDL-C ≥ 130mg/dL (or TC ≥ 200mg/dL) to LDL-C ≥ 100mg/dL (or TC ≥ 160mg/dL) in Taiwan, which may modify the prescribing behaviors of clinicians. Therefore, we aimed to evaluate the impact of changing reimbursement criteria on treatment patterns of statin.

Methods: A before-after cohort design was conducted using Taiwan's National Health Insurance Research Database. Difference of statin treatment patterns between the pre- and post-regulation periods were compared among patients with coronary heart disease (CHD), cerebrovascular disease (CBVD) and DM. Patients with prior use of statin before the diagnosis of CHD, CBVD or DM were excluded to guarantee new users of statin. Treatment patterns measured in this study included initiation, discontinuation, switching, dose increase, dose decrease, and dose maximization. We also explored the type and intensity of statin prescribed at initiation.

Results: The proportions of patients initiated statin during post-regulation period were higher than those during pre-regulation period (e.g. CHD patients, pre- vs. post-regulation: 41.23% vs. 48.25%). Atorvastatin was the most prescribed statin at initiation (e.g. CHD patients, pre- vs. post-regulation: 57.10% vs. 49.03%), followed by rosuvastatin (e.g. CHD patients, pre- vs. post-regulation: 33.54% vs. 37.45%). Moderate-intensity statins were the most prescribed statins at treatment initiation and the proportion of patients initiating them increased after the change of reimbursement criteria (e.g. CHD patients, pre- vs. post-regulation: 81.58% vs. 86.37%). The proportion of patients discontinuing statin use decreased after the change of reimbursement criteria (e.g. CHD patients, pre- vs. post-regulation: 59.07% vs. 52.75%).

Conclusion: Our study provides a 'real-world' example of how reimbursement criteria impact prescribing behavior of statin, and highlights future effort could be made to improve optimal use of statin.

Keywords: treatment pattern, statin, ASCVD, reimbursement scheme

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Economic burden of cancers in Taiwan: a direct and indirect cost estimates for 2007-2017

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Aim/Objective: Cancers have incurred significant economic burden to patients, health sectors and society. Reliable estimates of such burden, particularly with the considerations of both direct and indirect costs of cancers, will therefore help to guide resource allocation. This study aimed to conduct a nationwide cost analysis on direct and indirect costs of the top ten costly cancers in Taiwan.

Methods: Patients with newly diagnoses of top ten costly cancers (i.e. lung cancer, female breast cancer, colorectal cancer, liver cancer, oral cancer, leukemia, prostate cancer, non-Hodgkin lymphoma, gastric cancer, and esophageal cancer) between 2007 and 2014 were identified from the Taiwan Cancer Registry Database. Their direct medical costs were calculated from claims recorded in the National Health Insurance Research Database (NHIRD). Indirect costs, composed of productivity losses due to morbidity and mortality, were estimated from public data of life expectancy, average wage, and employment rate. Costs of the first three years after diagnosis were assessed in this study.

Results: A total of 545,635 patients were analyzed in this study. The sum of direct and indirect costs of cancer was highest in esophageal cancer (USD 86,268), while was lowest in prostate cancer (USD 16,401). Mortality cost accounted for over 50% of the total economic burden in most cancers, except for prostate cancer (31%) and female breast cancer (40%) due to lower mortality rate and older age at death. In the subgroup analysis, the direct medical costs of these cancers in year 2011~2014 were higher than those in 2007~2011. However, when considering both direct and indirect costs, the economic burden of cancers decreased in year 2011~2014.

Conclusions: This study demonstrates the comprehensive economic burden of the top ten costly cancers in Taiwan. The proportion of direct and indirect costs varied by different cancers. These discrepancies are valuable references to optimize healthcare resource allocation.

Keywords: cost-of-illness, cancer, economic, health policy

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Impact of medical fee restriction on multidrug prescriptions: A time-series analysis using real-world data

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Objectives: Multidrug prescriptions are common for elderly patients with multiple chronic health problems. In Japan, as part of institutional policies to optimize multidrug prescriptions, medical fee is restricted when seven or more types of drugs are prescribed, and when three or more types of psychotropic drugs are prescribed. The policy for multidrug prescriptions started in 2000, and multidrug psychotropic drugs was added around 2014. In this study, we evaluated the impact of the medical fee restriction.

Methods: We used national health insurance claim data of a university hospital. We assessed the number of patients who were charged hospital prescription fee "number F100" and outpatient prescription fee "number F400", that is, the patients who were prescribed seven or more types of drugs from 2008 to 2019. Moreover, the number of the patients who were charged the prescription fee of three or more types of psychotropic drugs was also assessed.

Results: Preliminary results indicated that the number of patients who were charged F100 was 41,047 and that of F400 was 233,396 from 2008 to 2019. The number of patients who were charged outpatient prescription fee of multiple psychotropic drugs was 570, and the number of hospital prescription fee was 5063. The number of patients who were charged F100 gradually decreased over the years, and the mean number by month changed from 497.3 in 2008 to 262.8 in 2018. On the other hand, the number of patients who were charged multiple psychotropic drugs fee increased over the years regardless of age categories and sex, and the mean number by month increased from 70.3 in 2014 to 133.8 in 2018.

Conclusions: The findings indicated medical fee restriction policy intervention was associated with the optimization of multidrug prescriptions, which warrants proper evaluation of clinical technology to prevent unintended outcomes of multiple psychotropic drugs prescriptions based on clinical guidelines.

Keywords: medication administration, multidrug use, psychotropic drugs

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Midodrine for Prevention of Intradialytic Hypotension in High Risk Patients at a Tertiary Referral Hospital: A Retrospective Study

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Background: Intradialytic hypotension (IDH) is the most common complication during hemodialysis procedure. Midodrine, an oral α-1 adrenergic agonist, is commonly used to prevent IDH. However, limited data is available to demonstrate midodrine effectiveness in the prevention of IDH in high-risk hemodialysis patients.

Objective: To describe the clinical outcomes of using midodrine in patients receiving hemodialysis concerning the incidence of IDH. Also, we aimed to explore the appropriate dose for midodrine use to prevent IDH.

Methodology: A descriptive retrospective cohort study was approved by IRB in January 2018. The data retrieved from BEST Care hospital information system, which included all the medical records for adult patients with end-stage renal disease on hemodialysis, who were placed on Midodrine for over a year. The variables that related to Midodrine dose, frequency, and IDH risk factors were recorded for each hemodialysis session. IDH is defined as a decline in SBP by ≥20 mmHg or a decline in MAP by ≥10 mmHg. Recurrent IDH labeled if the patient had at least three episodes of IDH.

Result: From a total of 68-screened patients' charts, 45 patients were included in the final analysis. 40% of the study population had an IDH that required additional interventions to restore the SBP and MAP. IDH occurred in 68% (n=23) of patients with hypoalbuminemia. Recurrent IDH occurred in 36% (n=16) of the patients during hemodialysis. Incidence of treatment failure and recurrent IDH was statistically significant higher (p=0.02) in patients who received midodrine three time per week (57%) in comparison to those who received more than three days per week (36%).

Conclusion: This exploratory study shows that a considerable proportion of patients receiving midodrine did not develop IDH or recurrent IDH. A long-term follow-up controlled study with larger number of patients would be useful to evaluate the effectiveness of midodrine in hemodialysis patients with high risk for IDH.

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Comparisons Empiric Antibiotics for Treatment of Patients Admitted with Pneumonia in a Regional Hospital in Taiwan: A Retrospective Cohort Study

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Aim/Objective: Research on the effectiveness of empirical antibiotics in patients with pneumonia in non-intensive care units (non-ICUs) in Taiwan is scarce. This study aimed to investigate the effectiveness of empirical antibiotics in patients with pneumonia in a regional hospital in central Taiwan.

Methods: We conducted a retrospective study comparing the treatment failure rates of different empirical antibiotics in a regional hospital in central Taiwan. Medical records of adult patients admitted to the hospital due to pneumonia diagnosis in the emergency department from January 2015 to March 2017. The primary outcome was treatment failure rate, and the secondary outcome was in-hospital mortality and length of hospital stay. Data were analyzed for descriptive statistics, chi-square tests, and risk analysis using SPSS 20.0.

Results: There were 584 non-ICU patients included in the analysis, including 243 (42%) community-acquired pneumonia (CAP) and 341 (58%) healthcare-associated pneumonia (HCAP). The mean age of the patients were 71.8 and 76.3 for CAP and HCAP, respectively. In the CAP group, 68% of the patients received fluoroquinolones as empirical therapy, while 28% received beta-lactams with or without macrolides. No difference between treatment failure rate between fluoroquinolones and beta-lactams [17.6% vs. 15.9% (P= 0.762)]. The mortality rates were also no statistical difference [3.6% for fluoroquinolones and 8.7% for beta-lactams (P= 0.110)]. In HCAP group, 43.6% received antipseudomonal-beta-lactams, 31.9% received fluoroquinolones, and 24.4% received non-antipseudomonal beta-lactams. The treatment failure rates were 36.8%, 40.5%, 45.9% (P =0.394) and the mortality rate were 17.1%, 11.1%, and 16.3% (P = 0.509) for antipseudomonal-beta-lactams, fluoroquinolones, and non-antipseudomonal beta-lactams, respectively. In CAP groups, Streptococcus pneumoniae was the pathogen detected most frequently (in 13.73% of all pathogens), followed by Mycoplasma pneumoniae (in 13.73%).

Conclusions: No statistical differences in treatment failure rate and mortality rate among empirical antibiotics in CAP and HCAP groups were observed. However, patients treated with fluoroquinolones seems to have the lowest mortality rate.

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Prescribing patterns of antiplatelet therapy in patients with ischaemic stroke and transient ischaemic attack in Malaysia

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Background: Antiplatelet therapy is the mainstay of treatment for secondary prevention in patients who have had a non-cardioembolic stroke or transient ischaemic attack (TIA). Several antiplatelet strategies are currently available and question remains about the selection of most appropriate antiplatelet agents for secondary stroke prevention. Gaining insight into treatment patterns of antiplatelet drugs against a background of evolving stroke treatment guidelines is vital. This study aims to characterise the prescribing patterns of antiplatelet drugs for newly diagnosed ischaemic stroke and TIA patients in Malaysia.

Method: Patients aged ≥18 years diagnosed with first ischaemic stroke or TIA from 2014 to 2017 were identified from stroke registry. Detailed information on antiplatelet treatment course was obtained through medical chart review and linkage to hospital pharmacy database. Baseline characteristics, clinical presentation, and medication prescribed over one-year follow-up were analysed.

Results: Of the 4739 patients discharged alive after an ischaemic stroke or TIA, 451 (9.5%) patients did not receive any antiplatelet therapy upon discharge. Among the 4289 patients on antiplatelet treatment, majority (90.3%) were treated with single antiplatelet therapy. Aspirin monotherapy was the most common (88.6%) regimen prescribed at discharge, followed by dual antiplatelet therapy (DAPT) of aspirin+clopidogrel (6.6%), and clopidogrel monotherapy (4.1%). The proportion of patients on aspirin monotherapy decreased from 92.9% in 2014 to 84.7% in 2017 whereas those receiving combination of aspirin+clopidogrel increased from 1.8% (2014) to 9.2% (2017). Factors influencing prescription of DAPT will also be discussed.

Conclusion: This analysis of a large patient cohort shows that most patients were treated with antiplatelet therapy after the first episode of ischaemic stroke or TIA. Aspirin monotherapy, despite showing a decreasing trend, remained as the most preferable antiplatelet regimen used for secondary stroke prevention. In view of increasing evidence on potential benefits of DAPT for secondary stroke prevention, more clinicians may consider such treatment for patients.

Keywords: antiplatelet; stroke; secondary prevention; drug utilisation

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Impact of antenatal steroids' use in pregnant mothers' on the severity of neonatal respiratory distress syndrome.

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Aim/Objective: The objective of the study was to evaluate use of antenatal steroids in pregnant mothers and its effects on Neonatal Respiratory Distress syndrome.

Methodology: A retrospective study was conducted in which, case files of 610 neonates were analysed based on inclusion and exclusion criteria of the study. Their relevant demographics, etiology, treatment patterns were documented. IBM SPSS version 20 was used for statistical analysis.

Results: A total of 610 neonates diagnosed with RDS were included in the study. With respect to use of antenatal steroids and severity of RDS, it was found that when mothers were given with antenatal steroids, occurrence of severe RDS was lower with majority of the cases having mild (46%) and moderate (23%) severity (p= 0.001). With respect to understanding the relationship between use of antenatal steroids and occurrence of death among neonates diagnosed with RDS; it was observed that 93.70% (p= 0.001) neonates had improved after the mother had received antenatal steroids while only 81.31% (p= 0.001) of neonates improved when no steroid was given. Mortality rate was found to be 6.299% (p= 0.001) in neonates who received antenatal steroids whereas it was 18.68% (p= 0.001) in neonates who did not receive antenatal steroids.

Conclusion: We found that there was a significant association between the use of antenatal steroids and reduction in neonatal mortality (p= 0.001). Hence from this study we can conclude that use of antenatal steroids can help reduce morbidity and severity of RDS in neonates.

Keywords: Antenatal steroid, RDS.

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Prescription patterns of medications for newly diagnosed adult patients with partial epilepsy from 2006 to 2017

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Aim: The study aimed to elucidate medical prescription patterns among adults who were newly diagnosed with partial epilepsy and evaluate the differences among different medical institutions and specialties.

Methods: We identified individuals aged between 20 and 65 years with a diagnosis of ICD-10-CM codes G40.1 and G40.2, and a prescription of ATC code N03A between 2006-2017, from a medical claims database. We selected each patient's first year of prescription or the whole period of prescription, if it lasted for less than one year, and recorded the most frequently prescribed medication in this period as that patient's prescription; the year of starting the prescription was denoted as the prescription year. We classified medical institutions based on the number of beds (0-19, 20-499, and 500+) and classified specialties into neurology, internal medicine, and others. We used the Cochran-Armitage trend test (CAT) and calculated the annual percentage change (APC) to elucidate prescription patterns and used logistic regression analysis to evaluate the differences.

Results: 1017 adults with partial epilepsy were selected from the database. From 2006, the prescription of new anti-epileptic drugs (AEDs) increased significantly (CAT, $p<0.05$; APC=10.21%) and until 2017, traditional and new AEDs were prescribed with almost the same frequency, while the guideline adherence rate was around 80% from 2010 to 2017, without significant change (CAT, $p=0.136$). Logistic regression analysis showed that medical institutions with 0-19 beds had the lowest odds of prescribing new AEDs [Odd's ratio (OR), 0.68; 95% confidence interval (CI), 0.48-0.95] and guideline adherence (OR, 0.16; 95% CI, 0.11-0.25). Internal physicians had the lowest odds of prescribing new AEDs (OR, 0.66; 95% CI, 0.47-0.92) and guideline adherence (OR, 0.49; 95% CI, 0.30-0.78).

Conclusion: The prescription patterns of patients newly diagnosed with partial epilepsy exhibit a shift from traditional to new AEDs from 2006 to 2017, with consistent guideline adherence.

Keywords: partial epilepsy, prescription patterns, newly diagnosed, guideline adherence

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Evaluation of Liraglutide Usage for Treatment of Type 2 Diabetes at a at a Hospital in Southern Taiwan.

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Aim/Objective: Guidelines recommend treatment with glucagon-like peptide-1 agonists, such as liraglutide after metformin that provide adequate blood glucose control. Clinical trials have shown that liraglutide offers well glycaemic control and body weight reduction.We aimed to assess the effectiveness of liraglutide in routine clinical practice.

Methods: Medical records of hospitalized geriatric patient who received liraglutide from January 2017 to December 2018 were reviewed.The medical records of the patients who received liraglutide were included. Clinical outcome development glycaemic, weight and side effect control were investigated six months after treatment initiation. Data collation hemoglobin A1c, Microalbumin, L.D.L Cholesterol, Triglyceride, Total Cholesterol, AST , ALT, and Creatinine.

Results: The study included 15 patients. Patients were male (73%), had a baseline HgbA1c of 10.02% , a baseline weight of 81.99 kgw .Average HgbA1c reduction of 1.79% was achieved in 86.7% of patients , Weight reduction of 2.45 kgw was achieved in 66.7% of patients. Microalbumin reduction of 57.08 mg was achieved in 66.7% of patients .

Conclusion: Significant reduction was demonstrated for liraglutide patients in HbA1c levels, microalbumin and weigh.

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Medication use for people with mild chronic obstructive pulmonary disease in community settings of Shanghai

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Aim: This study was aimed to understand current status of medication use for patients with mild COPD in Chinese community settings.

Methods: A cross-sectional study of 300 patients with mild COPD was conducted in 6 communities of the Pudong New Area in Shanghai, China in 2016. A face-to-face interview was done to collect data on personal characteristics, health conditions and medication use for COPD.

Results: There were a total of 275 participants with average age of 61.5±6.0 years and 51.3% of them were female. Average duration for their COPD was 11.3±14.1 years. Almost one third (35.5%) of them self-reported to have their medications for COPD timely and near half of them (46.9%) never used any medications for COPD in the recent year. Less than two fifth (38.6%) of them had bronchodilator agent, 11.6% had Chinese traditional medicine compound and 2.2% used glucocorticoid for COPD. There was no significant difference in COPD medication use between men and women.

Conclusion: There were a low proportion of medication use in patients with mild COPD in community settings of Shanghai, China. Guidance and surveillance programs on treatment for mild COPD should be improved for Chinese community settings.

Abbreviation: Medication; COPD; Chinese; Community settings

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Patterns and Predictors of Cardiac Specific Narrow Therapeutic Index and High Alert Medication Utilization

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Objectives: This study was conducted to assess the predictors and patterns of cardiac specific Narrow Therapeutic Index drugs (NTI) and High Alert Medications (HAM) used in the treatment of cardiac diseases.

Methodology: This was a prospective observational study conducted in inpatients of cardiology department for a period of 6 months. Patients were grouped into case or control based on the presence or absence of cardiac specific NTI/HAM in their prescriptions respectively. Binary logistic regression was applied to identify the determinants of NTI and HAM drug use among patients with cardiovascular disorder.

Results: 553 subjects were enrolled in the study (373 male and 180 female), 284 (51.36%) fell under case group and 269 (48.64%) under control group. The case group was found to show significantly longer duration of hospital stay (6.51 vs. 4.92; p <0.001) compared to control group. The most commonly prescribed class of NTI/HAM drugs were anti-platelets and anti-coagulants. Age >60 years [OR 2.552 (1.061-4.894) p <0.006], Length of hospital stay >5 days [OR 3.054 (2.577-5.704) p <0.001], presence of Coronary Artery Disease (CAD) [OR 3.823 (1.354-5.284) p <0.021] were identified as the significant predictors of NTI and HAM drug use.

Conclusion: The study revealed that age over 60 years, longer duration of stay and the presence on CAD warranted the use of NTI and HAMs. Moreover, presence of polypharmacy was found to further exaggerate drug related adverse outcomes.

Keywords: Narrow Therapeutic Index, High Alert Medication, Cardio-specific drugs

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Bacteriological study and antibacterial susceptibility of Ludwig's angina

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The knowledge of the local pattern of infection and antibacterial sensitivity in Ludwig's angina is essential to enable efficacious treatment for it. However, no previous studies in Bangladesh have investigated the pattern of bacteria responsible for developing Ludwig's angina and antibiotic sensitivity.

We aimed to evaluate the association between microorganisms responsible for Ludwig's angina and antibiotic sensitivity.

A prospective observational cohort study carried out from April 2016 to September 2016 in the Department of Otolaryngology & Head Neck Surgery (Dhaka Medical College Hospital, Bangladesh) and Department of Clinical Microbiology (International Centre for Diarrhoeal Disease Research, Bangladesh). A total of 100 patients with Ludwig's angina were included in the study. The responsible micro-organisms and antibiotics sensitivity test were performed for all patients. Data were analyzed using a logistic regression through SPSS.

The most frequently isolated organism in Ludwig's angina was Streptococcus (40%) followed bt Staphylococcus aureus (23%). The aerobic bacteria were found to be 60% resistant to doxycycline, 59% to penicillin-G and 59%% to ampicillin, whereas they were found to be 65% susceptible to ceftriaxone, 58% to ceftazidime and 56% to ciprofloxacin. The vancomycin was sensitive to 70% patients for Streptococcus, odds ratios (OR)=2.19 [95% confidence interval (CI): 0.90-5.42] and to 65% patients for staphylococcus aureas, (OR)=1.63 [(CI): 0.65-5.44]

Early diagnosis and treatment is essential to prevent complications. All patients must be treated initially with intravenous antibiotics, with treatment subsequently updated based on a culture and sensitivity report to reduce the mortality and morbidity.

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Comparing utilization of anti-tumor agents and survival outcome based on KRAS status among metastatic colorectal cancer patients using real-world data

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Objective: Metastatic colorectal cancer (mCRC) is about 20% of the diagnosed CRC cases. The KRAS gene mutation is speculated to have negative response to the cetuximab treatment. We conducted a retrospective cohort study to investigate utilization of anti-tumor agents and survival outcome among mCRC patients based on their KRAS status.

Methods: We extracted mCRC patients (ICD-O-3: C18~C20, stage 4 M1) with aged 20 years old or older, KRAS gene status and received systemic therapy between 2011 to 2014 from the Taiwan Cancer Registry database. The information of mortality and drug utilization was obtained from the Death Registry and National Health Insurance Databases. Four regimen groups were further categorized (FOLFOX + bevacizumab, FOLFOX + cetuximab, FOLFIRI + bevacizumab, and FOLFIRI + cetuximab).

Results: Among 3101 eligible mCRC patients (KRAS wild-type, WT, n=1804; KRAS mutation, MT, n=1297), the majority were diagnosed at 50~74 years old (WT: 63.91%; MT: 62.45%), and received operation in combination with chemotherapy and targeted therapy (WT: 54.71%; MT: 52.42%). The median survival time was significantly longer in patients with wild-type KRAS than in those with KRAS mutation (1.69, 95% CI: 1.59~1.76 year vs. 1.47, 95%CI: 1.39~1.54 year, $p<0.0001$). Among patients with wild-type KRAS, those receiving operation combined with chemotherapy and targeted therapy had the longest survival time (mean: 2.43 ± 0.05 year), while the smallest was in those receiving chemotherapy alone (0.62 ± 0.04 year). Regarding regimens, the FOLFIRI +cetuximab group had the longest median survival time among patients with wild-type KRAS. mutation, lower income and transverse colon tumor site were significant factors related to worse survival by using multivariable Cox regression analysis.

Conclusion: This study demonstrated that KRAS mutation is a significant factor associated with worse survival in mCRC patients, and the FOLFIRI +cetuximab regimen group had the best median survival time among patients with wild-type KRAS.

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Prescription of secondary preventive drugs after ischemic stroke in low- and middle-income countries: a systematic review and meta-analysis

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Aim/Objective: Stroke patients are at risks of developing further vascular events. Neither regular monitoring or comprehensive reviews are available to consolidate the prescription of guidelines-recommended secondary preventive drugs for stroke patients in developing regions. This review aims to quantify the prescription of secondary preventive drugs among ischemic stroke or transient ischemic attack (TIA) patients in low-and middle-income countries upon hospital discharge and explore factors that affect the prevalence estimates.

Methods: A systematic literature search was conducted in Pubmed/MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and Global Health Library to identify studies published between January 1996 to December 2016. Outcome measures include prescription of antiplatelet, statins, antihypertensive drugs and oral anticoagulants upon hospital discharge. Studies were assessed for risk of bias. Included studies were meta-analyzed using a random-effects model.

Results: Forty articles, comprising of 115996 ischemic stroke/TIA patients were included. The pooled prevalence was 81.0% (95% CI: 72.0 - 88.0%) for antiplatelet, 53.0% (95%CI: 44.0 – 63.0%) for statins and 65.0% (95% CI: 59.0 – 70.0%) for antihypertensive drugs. Only 25.0% (95% CI: 18.0 – 33.0%) of ischemic stroke/TIA patients with atrial fibrillation received oral anticoagulants. Temporal trends showed an increase in prevalence of antiplatelet between 2003 and 2015 (from 74.9% (95% CI: 50.0 – 93.2%) to 84.9% (95% CI: 68.4 – 96.1%)). Prescription of statins increased from 44.0% (95% CI: 26.4 – 62.4%) in 2006 to 63.7% (95% CI: 43.9 – 81.3%) in 2013 and for antihypertensive drugs, 58.9% (95% CI: 48.2 – 69.1%) in 2002 to 72.6% (95% CI: 58.9 – 84.4%) in 2014.

Conclusion: Prescription of secondary preventive drugs remains modest despite an increase of stroke burden in low- and middle-income countries. Regular monitoring on the uptake and effectiveness of secondary stroke prevention in this region should be established.

Keywords: Brain ischemia; Secondary prevention; Low- and middle-income countries

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Use of low-dose estrogen oral contraceptives among Japanese women: the Japan Nurses' Health Study (JNHS)

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Objective: In Japan, low-dose estrogen combined oral contraceptives (LCOCs) were approved for contraceptive use in 1999, and for dysmenorrhea in 2008. Although the reported number of LCOC prescriptions is increasing, there is little information on the actual use of LCOCs in Japan. In this study, we aimed to investigate the use of LCOCs using data from the Japan Nurses' Health Study (JNHS), a large cohort study.

Methods: The JNHS cohort consists of 15,019 female Japanese nurses, who were registered from 2001 to 2007. The study population includes women aged less than 60 years at the baseline survey. We used participants' 10-year follow-up data and estimated the prevalence of LCOC use. Furthermore, we conducted multivariable-adjusted logistic regression analysis to examine the characteristics of LCOC users.

Results: The prevalence of LCOC users among study participants was 6.0%; 16.1% were in their 20s, 9.0% in their 30s, 4.2% in their 40s, and 1.2% in their 50s. Younger age was significantly associated with LCOC use. Public health nurses and midwives were significantly more likely to use LCOCs than registered nurses. Similarly, single women, ever smokers, women who experience severe menstrual pain, or women diagnosed with endometriosis were significantly more likely to use LCOCs.

Conclusion: The prevalence of LCOC use in our 10-year follow-up of the JNHS was 6.0%. Our findings showed that use of LCOCs is associated with lifestyle factors such as marital status and smoking status, as well as gynecological diseases such as menstrual pain and endometriosis.

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Changes in medicine prescription before and after admission to long-term care welfare facilities in a city of Japan

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Aim/Objective: To examine (i) whether the number of prescribed drugs is increased or decreased after admission to long-term care welfare facilities (also called special nursing homes, or “tokuyo” in Japanese), and (ii) what types of drugs tend to be added or discontinued.

Methods: Using linked medical and long-term care data in a city of Japan, we identified people aged 75 or older (i) who received at least one outpatient prescription in the past two months, and (ii) newly admitted to long-term care welfare facilities. We excluded those who were in hospitals or other types of long-term care facilities in the past two months. We counted the number of prescribed drugs during periods of two months before and after the month of admission, and compared these using the Wilcoxon signed-rank test. We also conducted McNemar tests for individual drugs to identify which types of drug were added or discontinued.

Results: Among 234 study participants, the median number of prescribed drugs increased significantly from 8 (IQR 4–12) to 9 (IQR 6–13) (P=0.002). The proportion of people with 6 or more drugs (as a potential indicator for polypharmacy) increased from 67.1% (157/234) to 77.8% (182/234). We identified significant increases of laxatives, acid-suppressing drugs, antibiotics, and antihypertensives after admission.

Conclusion: We found that the number of prescribed drugs increased after admission to long-term care welfare facilities in a city of Japan. Generalizability of this finding to other cities and appropriateness of this change need to be assessed in future studies.

Keywords: polypharmacy, older people, nursing homes

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Comparison of surfactants used in the treatment of Neonatal Respiratory Distress Syndrome

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Aim/Objective: Compare the surfactants used in Respiratory Distress Syndrome(RDS) based on various factors.

Methodology: A retrospective study was conducted and casefiles of 610 neonates were selected on the basis of inclusion and exclusion criteria. Relevant demographics,etiology and treatment patterns were documented. IBM SPSS version 20.0 was used for statistical analysis.

Results: A total of 187 neonates out of 610 neonates were given surfactant therapy. 187 neonates were selected for further evaluation for comparison of surfactants. A two by two comparison of the three surfactants i.e. Survanta, Curosurf and Neosurf was done. A statistically significant difference was found between Survanta and Neosurf (p=0.005), which indicated that the neonates receiving Survanta required lesser NCPAP support as compared to Neosurf group. Neonates in the Curosurf group required significantly less NCPAP support than Neosurf(p=0.005). A significant reduction was seen within the group in Survanta and Curosurf for the parameter; partial carbon dioxide(p =0.003, p=0.002 respectively). A significant difference in pre and post values of base excess was also found in the Survanta group (p = 0.007).

Conclusion: From the results we could conclude that Survanta and Curosurf both are effective in reducing the need for NCPAP supports in neonates with RDS and both the surfactants reduced the partial carbon dioxide significantly. However, only survanta reduced base excess in neonates having RDS. Neonates receiving Neosurf did not show any statistically significant reduction for any of the factors when compared with Survanta and Curosurf.

Keywords: Survanta, Curosurf, Neosurf, Respiratory Distress Syndrome

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Early Conversion from Intravenous to Oral Medications: Assessment and Evaluation of Clinical Outcomes in Hospitalized Patients

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Objective: This study was conducted to evaluate the impact of early conversion of intravenous (IV) to oral antibiotic therapy w.r.t clinical outcomes.

Methodology: An ambispective study was carried out in the Department of General Medicine at a tertiary care hospital. This study constitutes two phases, Phase I (retrospective phase) in which IV to oral conversion was done before active involvement of the clinical pharmacist. Whereas clinical pharmacists were actively involved in recommending early conversion of IV to oral in Phase II (prospective phase).

Results: In this study 83 were in phase I and 88 in phase II. As per criteria for IV to oral switch, 71 (86%) of phase I and 84 (95%) in phase II were eligible for conversion. Out of which 13 (18%) of phase I and 66 (79%) of phase II were switched. The average length of hospital stay (LOHS) was found to be 6.0±1.5 days in phase I and 4.4±0.7 days in phase II and there was a statistically significant difference between two phases ($p<0.005$). The duration of IV therapy was 5.2±1.8 and 2.7±1.5 days in phase I and phase II respectively. The most common type of conversion was step down therapy (77%) phase I and (73%) phase II followed by sequential and switch therapy. The reinfection rate and readmission were similar among both the phases ($p>0.05$). The extra number of IV therapy days decreased from 112 (phase I) to 35 days in (phase II).

Conclusion: This study emphasizes that the practice of conversion from IV to oral antibiotic therapy has a considerable impact on clinical outcomes amongst hospitalized inpatients. This study demonstrates a decrease in LOHS if predefined switch criteria of IV to oral conversion are practised meticulously. There was no observed difference in readmission and reinfection after conversion to oral therapy.

Keywords: IV to Oral Conversion, Clinical Outcome, role of pharmacist

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Evaluation of drug utilization pattern among pregnant women in a tertiary care teaching hospital

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Aim/Objective: Objective of the study was to evaluate the drug utilization pattern in pregnancy.

Methods: A retrospective observational study was conducted among admitted pregnant women in a tertiary care teaching hospital. Institutional ethics committee approval was obtained prior to the study. Pregnant women admitted to Obstetrics & Gynaecology ward during January 2013 to December 2017 were identified using ICD-10 Code O00.0-O99.9 from inpatient medical records, based on the inclusion and exclusion criteria. Parameters like demography, gravidity, comorbid conditions, drugs prescribed and its utilization details, length of hospitalization and neonatal outcome were collected from the patient medical records. Drugs were classified according to FDA Pregnancy Categories and drug consumption was calculated using WHO defined daily dose (DDD) methodology.

Results: Study included 876 pregnant women. The mean age of the study population was 29.4±4.4 (mean±SD) years. Diabetes mellitus (33.6%) was the most common co-morbidity, followed by hypertension (28.3%) and thyroid disorders (18.3%). Most of the neonate born were alive and healthy (94.3%), 6 neonates expired during post-natal period and 1 had cleft lip. Folic acid (15.7%), calcium (15.2%), ferrous fumarate (7.1%), vitamin B12 (5.3%) and vitamin B6 (3.4%) were the most commonly prescribed drugs. In terms of DDD/100 bed days, levothyroxine (369.3), digoxin (53.6), dydrogesterone (27.4) and salbutamol (20.5) were the most commonly utilized drugs.

Conclusions: Levothyroxine was one of the most commonly utilized drug among the study population because 18.3% of pregnant women had thyroid disorders. It is essential to treat thyroid disorders during pregnancy. Study also reveals that FDA category X drugs were very rarely prescribed during the first trimester of the pregnancy in the study population. However it essential to monitor drug usage during pregnancy and correlate with neonatal out-come.

Keywords: Drug-utilisation, Pregnancy, Defined daily dose

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Utilization of intravenous ribavirin among reproductive age adults in 2010- 2017: a population-base study in China

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Background: Intravenous (IV) ribavirin is not approved in US and European Union, but it is authorized in China. Significant teratogenic and embryocidal effects of ribavirin have been found in almost all animal studies, it is critical to investigate the utilization of IV ribavirin among reproductive age population.

Objective: To evaluate the prevalence and trends of IV ribavirin use among reproductive age population in 2010-2017. Methods: We identified residents aged 18 to 44 years by using Yinzhou healthcare information database. A cohort of IV ribavirin users was identified through outpatient prescription records in 3 general hospital and 24 community health center from 2010 to 2017. We reported the number, proportion and prevalence of the exposure to IV ribavirin stratified by sex, age, marital status, education level, occupation, hospital level, calendar year, diagnosis, and dosage. The overall trends of IV ribavirin use, and the trends in different levels of hospital and common diagnoses were further analyzed and described in the study.

Result: During the study period, the prevalence of IV ribavirin exposure among reproductive age adults was 6.02% (48,287/801,667). Relatively higher prevalence was found in elder adults aged 40-44 (8.04%, 95%CI: 7.90 – 8.17) and adults with over 9 years of education (6.82%, 95%CI: 6.74 –6.90). The most common diagnoses were acute upper respiratory infections, accounting for 80% of the patients exposed to IV ribavirin. Overall, the prevalence of IV ribavirin users decreased from 1.72% in 2010 to 0.24% in 2017.

Conclusion: Our findings demonstrate the high prevalence of exposure to intravenous ribavirin in Chinese reproductive aged population. Furthermore, we found IV ribavirin was mainly used for acute respiratory infection which suggests large amount of IV ribavirin use was probably irrational. Although the prevalence was decreasing over past eight years, clinicians and clinical pharmacists should continually avoid inappropriate use of IV ribavirin.

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Assessment of medication use and polypharmacy among pregnant women in the United States

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Aim/Objective: Taking medications while pregnant should be carefully evaluated as some drugs might affect pregnant women and their fetuses. Previous studies have indicated that many women take multiple medications during pregnancy. The purposes of this study were to: (1) characterize medication use, (2) estimate the prevalence of polypharmacy, and (3) identify factors associated with polypharmacy among pregnant women in the U.S.

Methods: We conducted a retrospective cross-sectional study using data from the 2013 and 2015 Medical Expenditure Panel Survey (MEPS), a nationally representative survey of the U.S. households. Pregnant women were identified if respondents self-reported that they were pregnant during the survey year. Medication classes used during pregnancy were first categorized by Multum Lexicon and then further revised based on the pharmacological classification and typical use. Polypharmacy was defined as taking at least five medications. Factors that may affect medication use and polypharmacy were selected using the Andersen's health behavior model. Multivariable logistic regression models were used to evaluate the association between factors and polypharmacy.

Results: Among pregnant women in 2013 and 2015, 78.7% and 72.4% took at least one medication during pregnancy, while polypharmacy occurred in 18.2% and 13.7%. The most commonly prescribed medications in 2013 and 2015 were analgesics (39.3%, 34.2%); followed by antibiotics (29.2%, 22.5%) and gastrointestinal/antiemetic agents (21.0%, 18.1%). Higher age (AOR=5.64, $p<0.05$, 95% CI=1.10-29.08), not being married (AOR=2.54, $p<0.05$, 95% CI=1.17-5.52), high income (AOR=5.39, $p<0.01$, 95% CI=1.69-17.21), poor health status (AOR=54.75, $p<0.01$, 95% CI=6.49-461.76), and having a job (AOR=2.53, $p<0.01$, 95% CI =1.27-5.05) were significantly associated with polypharmacy during pregnancy in 2015.

Conclusion: Medication use and polypharmacy were commonly reported among pregnant women in the U.S. Health care providers should be aware of the high prevalence of medication use and polypharmacy among pregnant women. Medication-related problems of polypharmacy during pregnancy need to be further investigated.

Keywords: Medication use, Polypharmacy, Pregnancy, Medical Expenditure Panel Survey

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Trends in antipsychotic use of newly treated schizophrenia patients

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Aim/Objective: This study aimed to describe the patterns in antipsychotic prescription of newly treated and diagnosed with schizophrenia from 2002 to 2012, and analyzed the trend in the first-year pharmacological treatment of newly diagnosed and treated schizophrenia patients. We also examined which baseline characteristic influenced the first antipsychotics prescription.

Methods: The data source was Taiwan National Health Insurance Research Database (2000-2013). The study identified all schizophrenic patients aged 18 years and older who were newly diagnosed between January 1, 2002 and December 31, 2012. We excluded subjects who had antipsychotics treatment before schizophrenia diagnosis. The following-up time for each patient was one year. Changes in the first year of treatment were assessed by multivariate logistic regression and Spearman's partial rank correlation. Multinomial logistic regression was used to analyze the relation between different antipsychotics and characteristics of the patients.

Results: The percentage of prescriptions of SGAs increased from 29.8% to 81.9%; however, FGAs declined from 77.8% to 32.9%. As a result of the change of the trend of antipsychotic prescription, the percentage of anticholinergic agents decreased from 78.9% to 49.7%. Different hospital level would influence prescription. The percentage of prescriptions of SGAs and FGAs were 57.6% and 29.1% in academic medical center respectively. With the declined of hospital level, the use of SGAs decreased to 36.0% but the use of FGAs increased to 59.6% in clinic. Besides, patients who used SGAs had lower hospitalization rate and average hospitalization days.

Conclusion: In the first-year treatment of newly treated patients with a diagnosis of schizophrenia between 2002 and 2012, SGAs replaced FGAs as the first choice for therapy. With the change of the trend of antipsychotics prescription, the percentage of anticholinergic agents decreased due to decreasing of FGAs. Hospital level played an important role in the selection of antipsychotics.

Keywords: schizophrenia, antipsychotic, utilization, trend

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The profile of antibiotic use and the economic burden in hospitalized patients with chronic obstructive pulmonary disease(COPD) in China

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Background: The number of patients with COPD in China has been approaching 100 million. Preventive use of antibiotics is very common, but currently, there is no national survey of the status of antibiotic use in COPD patients.

Aims: To describe the current status of antibiotic use and estimate the economic burden, so as to provide a basis for improving the treatment of COPD and effectively reducing the economic burden.

Methods: A cross-sectional study using all eligible patients in the National Urban Basic Medical Insurance (NUBMI) sample database in 2015 was implemented. We identified patients with COPD by diagnosis texts and International Classification of Diseases version 10 (ICD-10). Then the basic characteristics, clinical features and cost of the included subjects were extracted, descriptive analysis was used to describe the current status, and multiple linear regression model was used to analyze the economic burden and its affecting factors.

Results: A total of 24,229 patients were enrolled, including 15,734 males (64.94%) and 8,495 females (35.06%), average age (71.50±10.65) years. In the treatment of patients with COPD, the highest number of prescriptions was the third generation cephalosporin 12755 (42.58%), there were 1867 (6.23%) of the prescriptions for no antibiotics, 10474 (34.97%) for single drug, 10508 (35.08%) for the two drugs, 5161 (17.23%) for the three drugs, and 1943 (6.49) for three drugs or more. With age, hospital grade, use of β lactam, increased hospital stay will increase the cost of medication, and the results are statistically significant. The average cost for patients with COPD is 3,840.98 yuan, and this means if we do not control this disease, China will face a huge economic burden.

Conclusions: The use of antibiotics combination in hospitalized patients with COPD is very common and the economic burden of COPD patients is very heavy.

Keywords: COPD; Antibiotics; Economic burden

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Prescribing and dispensing of OTC analogue products in Japan: a review of real-world evidence

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Aim: In many cases, ethical pharmaceutical products may continue to be prescribed and dispensed in Japan even after they become available as over-the-counter (OTC) products in retail drug stores. These products are often described as OTC ruiji-yaku, or literally “OTC analogue” products. Moreover, when physicians prescribe those products they are reimbursed under the national health insurance system with a similar copayment rate as non-OTC analogue products. This research examined the prescribing and dispensing of OTC analogue products in Japan based on real world data.

Methods: The prescribing of 71 OTC analogue products in Japan was examined for 2018 using the Medi-Scope insurance claims database. The volume and prescribing characteristics for those products such as patient age, type of facility, region, and generic versus branded prescriptions was also examined.

Results: Nearly 20% of patients had been prescribed one or more OTC analogue product in 2018. 17 out of 71 OTC analogue products examined comprised over 75% of all prescription volume. Nonsteroidal anti-inflammatory drugs such as loxoprofen (19.6%) and diclofenac (4.3%), cough remedies such as ambroxol (9.6%) and dimemorfan (3.0%), and antihistamines such as fexofenadine (6.2%) and epinastine (5.3%) comprised a majority of OTC analogue prescriptions. Little or no difference was observed for OTC analogue products compared to all products in terms of prescribing characteristics. However, OTC analogue product prescriptions were somewhat more likely to be for generic agents.

Conclusions: Despite being available in retail drug stores, OTC analogue products are still commonly prescribed and dispensed for pain, coughs, allergies and other ailments in Japan. Further examination of prescribing and self-medication behavior is needed to understand the drivers and rationale for OTC analogue prescribing and dispensing in Japan.

Keywords: OTC analogue, OTC switch, self-medication, real-world evidence

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Prescribing Pattern of proton pump inhibitors in the department of general medicine of a tertiary care hospital

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Objectives: Utilization of Proton Pump Inhibitors (PPIs) has increased enormously as over the counter (OTC) drugs by the general public in India. Also, in current clinical practice, the majority of prescriptions include PPIs for gastric prophylaxis together with antibiotics and analgesics. Medical ignorance and underestimation of the adverse effects (like Clostridium difficile infection, nutritional deficiency disorders and fractures etc.) are the factors underlying such escalated PPI consumption. This scenario prompted us to look into the drug utilization pattern and the appropriateness in the utilization of PPIs in a tertiary care hospital.

Methods: This is a prospective observational study conducted in the Department of General Medicine for a period of 1 year from August 2017 to July 2018 to analyze the prescribing pattern of PPIs. The medication charts of both inpatients and outpatients of the General Medicine Department was reviewed. Core information such as demographic characteristics, diagnosis, and current medications was recorded. The patients were regularly monitored for drug-drug interactions.

Results: Of 1019 prescriptions, 908 (89%) prescriptions were found to have PPIs. Pantoprazole 749 (82.49%) was the most commonly prescribed PPI followed by esomeprazole 124 (13.66%). The indications for PPI therapy were acute gastroenteritis 103 (11.34%), gastric ulcers 7 (0.77%), gastroesophageal reflux disease 5 (0.55%), gastrointestinal bleeding 3 (0.33%), ulcerative colitis 2 (0.22%), IBD 1(0.11%), esophageal and gastric injury 1(0.11%), gastric erosion 1 (0.11%). PPIs were found to prescribe with antibiotics 681 (75%) followed by non-steroidal anti-inflammatory drugs 179 (19.7%).

Conclusions: The study showed inappropriateness in prescribing patterns of PPIs leading to increased therapeutic burden and treatment cost. This necessitates the formulation of standard therapeutic guidelines for rationalizing the utilization of PPIs.

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Benzodiazepine utilization pattern and adverse drug reactions amongst patients of Department of Psychiatry

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Aim: Benzodiazepines are commonly utilized for the treatment of anxiety and sleep disorders. The study aimed to assess the utilization pattern of Benzodiazepines (BZDs) among patients visiting psychiatry and evaluation of its adverse effects.

Methods: This was a prospective observational study carried out for a period of 7 months from August 2017 to February 2018 in the Department of Psychiatry, Ramaiah Hospitals, Bangalore, Karnataka, India. A total of 109 patients were recruited based on the inclusion criteria. The patient's demography, prescribing patterns and data regarding Adverse Drug Reactions (ADRs) were obtained from patient's medical records and by interviewing the patients. The observed ADRs were assessed for their causality, severity and preventability.

Results: Out of 109 patients, BZDs use was more prevalent among the age groups of 18-35 years and less prevalently used among 56-65 years. BZDs are more commonly utilized among males 62(56.8%) than females 47(43.11%). Clonazepam 35(87.5%) was the most frequently prescribed BZD followed by lorazepam 13(11.19%). Oversedation 16(14.7%), drowsiness 10(9.2%) and dizziness 9(8.3%) were the most regularly reported ADRs by patients. 2(3.5%) of the ADRs were definite, 33(58.92%) were probable and 21(37.50%) of the ADRs were possible. 44(78.57%) ADRs were mild and 12(21.4%) ADRs were moderate. 20(35.7%) of the ADRs were definitely preventable and 36(64.28%) ADRs were probably preventable.

Conclusion: BZDs use appears to be common and increases among middle-aged adults, despite its adverse effects. Inclusion of clinical pharmacists among health care team may rationalise and optimize the BZD utilization and minimize the incidence of ADRs.

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Study on the actual prescription practices of anti-influenza drugs in the pediatric field by using medical information databases

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Aim/Objective: Japan has a higher prescription rate of anti-influenza drugs than other countries. Unnecessary social demand for medical care is a cause for the collapse of the universal healthcare system. This study analyzed trends in anti-influenza drug prescription in medical facilities by using medical information databases, and examined the cost-effectiveness.

Methods: Using the data of outpatients diagnosed with influenza or those who received anti-influenza drug prescriptions during September 2015 to August 2016, which was extracted from the Pediatric Medical Data Collecting System Database (PMDCS DB) and the database of two university hospitals in the Medical Information Database Network (MID-NET), a meta-analysis of the institution type, age, sex, anti-influenza drug, and concomitant medication was conducted.

Results: The number of cases was 8,799, 1,245, and 122 at the pediatric clinics, children's hospitals, and university hospitals, respectively, and among those, 6,834 (77.8%), 460 (36.9%), and 99 (81.1%) received anti-influenza drug prescriptions, respectively. Regarding the type of anti-influenza drug, the mean ratios of oral medicines were 98.5%, 52.3%, and 8.10% for the age groups 0-4, 5-9, and 10-14 years, respectively; the ratios of oral medicines dropped with an increase in age (p value<0.05 by generalized Cochran–Mantel–Haenszel test). In contrast, the ratio of inhalant medicine was 1.02%, 47.3%, and 91.3% for each age category.

Conclusion: Prescription rates of anti-influenza drugs were higher in clinics and university hospitals than in pediatric hospitals. The high prescription rate in the clinic is considered to be due to social demands, whereas that in university hospitals is considered to be for co-morbidity management as per the US CDC guidelines. However, there was no tendency that the cases become severe in the non-prescription group. It would be worthwhile to analyze the effects of factors such as medical history and complications on the actual prescription practices in the future.

Keywords: Pediatric, anti-influenza drug, medical information database

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Effect of pro re nata medication usage on estimation of fragility fracture risk associated with concomitant central nervous system medications

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Aim/objective: People often use pro re nata (PRN; 'as needed') medications. This study analyzed the effects of PRN medication usage on estimation of fragility fracture risk associated with concomitant central nervous system (CNS) medications.

Methods: A case-crossover study was conducted using the National Database of Health Insurance Claims and Specific Health Checkups of Japan. Subjects were aged ≥65 years and had sustained a fragility fracture within the May, 2013 to September, 2014 period. The extent of concomitant use of PRN-CNS medications was measured by two indices: (1) the number of medications per day and (2) the cumulative standardized daily dose (SDD). The odds ratio (OR) of fragility fractures was estimated for each index for two populations, including or excluding PRN-CNS medication users.

Results: The risk of a fragility fracture tended to almost increase linearly for population including PRN-CNS medication users for either index. Conversely, the risk of fragility fractures for both indices virtually increased linearly for population excluding them: ORs for number and SDD=0, 0–1, 1–2, 2–3, 3–4, 4–5, and ≥5; ORs for number reference=1.2, 1.4, 1.7, 1.9, 1.9, and 2.2 (n=352,828); and ORs for SDD reference=1.2, 1.3, 1.4, 1.5, 1.4, and 1.7 (n=352,474).

Conclusion: The risk of fragility fractures increased in a near linear manner with increased concomitant use of CNS medications in elderly people in Japan, although the management of PRN-CNS medication use was integral to the association.

Keywords: fragility fracture, central nervous system, psychotropics, pro re nata medication

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Evaluation of prescription pattern in patients with Chronic Obstructive Pulmonary Disease in a tertiary care setting

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Aim/Objective: The study was aimed to evaluate the prescription pattern in chronic obstructive pulmonary disease (COPD) patients during hospitalization and assess the direct medical cost incurred by the patients.

Methods: A prospective study was conducted on in-patients diagnosed with COPD in pulmonary department of tertiary care hospital. The medication chart of the patients were reviewed to evaluate the prescribing pattern. The direct cost involved in the COPD therapy was calculated by assessing IP bills from finance department.

Results: A total of 100 patients were included for the study and was taken for analysis. 83% of the study population were male and 37.7% were smokers. The mean age of the population is 64±8 and the mean duration of hospitalisation in days was 5±2. 22% of the patients had a history of pulmonary tuberculosis. The total direct medical cost was USD 325. The major part of cost incurred was attributed to the cost of prescription medication.

Conclusion: It was found that majority of the patients included in the study were smokers and ex-smokers, which clearly indicates as the risk factor for disease. Hence interventions are required for smoking cessation program. The frequency of exacerbation leads to increased need for hospitalisation and subsequently increased health care cost and financial burden. The treatment should be individualized based on the micro-organism present in sputum, for the purpose of decreasing the duration of hospitalization and healthcare cost.

Key words: COPD, prescription pattern, direct cost

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Assessment of prescription pattern and estimation of clinical and economical outcome of management of gastroenteritis in paediatric population

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Background: Acute Gastroenteritis (AGE) causes significant mortality in developing countries and high economic burden to the developed countries.

Objective: To assess the prescribing pattern and determine the drug related problems (DRPs) in the management of AGE in a tertiary care teaching hospital. The study also aimed to estimate the clinical and economical outcome of AGE management.

Methodology: A prospective interventional study was conducted over a period of nine months in paediatric department of JSS Hospital. Subjects who met the study criteria were enrolled and required data was collected from their case sheets. Collected data was analysed and intervention was made by the researcher to the health care professional on identification of DRPs. The study population was followed until the recovery of AGE for the clinical and economical outcome.

Results: A total of 98 subjects enrolled, 39 from ambulatory setting and 59 from the wards. Most commonly prescribed drugs for AGE was Oral rehydration salt solution (90.82%) and probiotics (75.51%). Cephalosporins were the most commonly prescribed antimicrobial. The mean recovery period for hospitalized and ambulatory settings were 3.01± 1.07, 3.78±1.96 days respectively. The total median cost incurred for the management of acute gastroenteritis in the hospitalized and ambulatory settings was Rs. 4774 (68.79 US dollar) and Rs. 226.32 (3.26 US dollar) respectively.

Conclusion: Study found an appropriate use of ORS and Intravenous fluids which is rational as per the available guidelines. However a monitoring and change is required for the irrational use of antimicrobials and nutritional products for the management of AGE.

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Understanding of Medication Adherence and Patient Satisfaction in Low Socio-Economic Hypertensive Elderly Patients Visiting a Public Hospital in South India

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Background: Elderly populations in India are increasing at an alarming pace and are more prone for morbidity and mortality due to chronic diseases. Among elderly, hypertension is a common clinical condition and the prevalence of hypertension in India is increasing at a significant percent. Non adherence to anti-hypertensive medications may lead to development of life threatening complications in elderly.

Aim and Objectives: The study aimed at assessing the medication adherence and treatment satisfaction in the elderly hypertensive patients. And the study also assessed the prevalence and predictors for non-adherence among the elderly hypertensive patients.

Methods: This is a prospective, observational study conducted at a secondary care public hospital. Hypertensive patients of either sex aged > 60 years visiting outpatient department and hospital Pharmacy were recruited into the study. Morisky Medication Adherence Scale was used to measure medication adherence and Medication interview satisfaction scale was used to measure the treatment satisfaction.

Results: A total of 202 elderly hypertensive patients were recruited into the study. Majority of them were within the age group of 60-65 years belonging to lower and middle class of socio-economic status. The prevalence of non adherence was found to be 61.38%. Upon execution of bivariate analysis, elevated BP, polypharmacy and non-vegetarian diet were identified as predictors for non-adherence in the study population ($p<0.05$).

Conclusion: Multiple factors like patient's mental status, health literacy, co-morbidities and drug related problems affect the medication adherence behavior of elderly. As a special population, geriatric patients need to be specially addressed at hospitals regarding advantages of treatment adherence. There is an increased responsibility on all the health care professionals when dealing elderly patients with chronic diseases.

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Anti-diabetic drug utilization knowledge and glycemic index control in patient with uncontrolled diabetes mellitus

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Diabetes has become the seventh leading burden of diseases in South Asia. Roughly 1 in 13 achieves treatment targets to keep control the glycaemic index, one of the reasons may be lack of diabetic drug utilization knowledge. However, there is not much research done on the impact of drug utilization knowledge to achieve glycaemic control in Bangladesh.

We aimed to investigate the proper anti-diabetic drug use and glycemic control among uncontrolled diabetic patients. A prospective intervention study carried out from September 2017 to August 2018 in BIRDEM General Hospital, Bangladesh. After considering inclusion and exclusion criteria, a total of 100 patients aged 18 to 69 years with HbA1c > 7% were included. Structured diabetic education regarding the disease, medication adjustment (e.g. Metformin) and glucose monitoring including exercise management was provided to each patient separately and patients were followed in 3 months. Data were analysed using a logistic regression through SPSS.

Metformin was used for 47% patients and 59% patients took Metformin plus Insulin. For the intervention group, the average HbA1c significantly ($p < 0.001$) changed from baseline (11.59±2.48) to end of the follow-up (7.55±0.58). Similarly, Systolic Blood Pressure and Diastolic Blood Pressure changed from (138.31±15.73) to (126.90±11.15) and from (83.33±6.50) to (80.24±4.12), respectively ($p < 0.001$). Higher educated patients were more likely to have improve on glycemic control than lower educated patients [OR=1.5, CI=0.24-9.30,].
Proper knowledge on anti-diabetic drug utilization can help in glycemic control to include prevention of diabetes, improved quality of life and delaying of complications.

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Use of antibiotics and Xiyanping injection in Chinese children with bronchitis

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Aim: To understand the characteristics, treatment patterns and medical resources utilization of Chinese children with bronchitis.

Methods: All hospitalization records of children with bronchitis younger than 14 years old in Chinese 2015 National Urban Basic Medical Insurance Sample Database were included. Patients were identified by diagnostic texts and International Classification of Diseases version 10 (ICD-10). Antibiotics were classified by Anatomical Therapeutic Chemical Classification (ATC). Descriptive analysis was used to analyze the patient characteristics, treatment patterns and medical resources utilization. Patients were divided into exposed group and non-exposed group according to whether they used Xiyanping injection or not. Poisson regression was used to analyze the relationship between Xiyanping injection and readmission within 30 days. Additionally, sensitivity analysis was done by 1:1 matching according to age, sex, hospital level and hospitalization days.

Results: Finally, 13 695 patients (15 428 records) were enrolled, with an average age of 3.88 years.
The third-generation cephalosporins (n=5 631, 36.50%) was the most frequently prescribed. Among single-drug therapies, the third-generation cephalosporins was the most frequently used (n=1 544, 30.13%). The most common two-drug therapy was macrolides plus the third-generation cephalosporins (n=712, 12.62%). The most common three-drug therapy was penicillin plus macrolides plus beta lactam/enzyme inhibitors (n=278, 9.84%).
Both median hospitalization time of exposed group and non-exposed group were 6 days (Rank sum test: P<0.51). The median hospitalization costs of the exposed group and non-exposed group were 1 822.27 yuan per visit and 2 065.86 yuan per visit, respectively (Rank sum test: P<0.01). The incidence rate ratio (IRR) of use of Xiyanping injection for readmission within 30 days was 1.09 (95% CI: 0.84, 1.43). The result of sensitivity analysis was 0.93 (95% CI: 0.67, 1.29).

Conclusion: The most commonly used drugs for children with bronchitis were the third-generation cephalosporins and macrolides. The hospitalization costs of therapy with Xiyanping injection were higher.

Keywords: Bronchitis; Children; Antibiotics; Xiyanping injection

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Evaluation of Pharmacological interventions of Somatostatin and analogues for acute pancreatitis- A multi-center, real-world EMR database study in China

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Background: Acute pancreatitis (AP) is a common clinical condition with high mortality and known as with high disease burden. In 2017, more than 300,000 AP patients were hospitalized and 4 billion RMB were spent for treatment in China. Among treatment regimens, the usage of Somatostatin and analogues (SSTA) is the only difference between China and US/EU standard of care on AP.

Method: A retrospective study was performed to evaluate the effectiveness of SSTAs in hospitalized AP patients using existing data source from clinics. The data source came from 4 hospitals in different regions of China, which was structured into the standard data model by a leading healthcare big data company. All evaluation parameters were captured from the data-sets including Hospital Information System, Laboratory Information Management System, Electronic Medical Records (EMR), Picture Archiving, and Communication Systems. All in-patients diagnosed as 'Acute pancreatitis' from Jan 2016 to Dec 2017 (using ICD-10 code identification) were included. Medication usage were described with anatomical therapeutic chemical code. Artificial intelligence (AI) technology was applied to summarize and structure the useful information from the EMR progress note. Patients were grouped according to the different SSTA regimens. AP local or systemic complications and organ failure after treatment were evaluated.

Results: Totally 3,900 AP subjects were included, with 41% of which received Somatostatin, 22.9 % received Octreotide, 22.7% received somatostatin/octreotide, and 13.4% received supporting treatment only. Compared with the supporting treatment group, SSTAs (Such as somatostatin), with the significant high rate on continuous renal replacement therapy, group (9.4% VS 7.5%, $P<0.05$)), Local puncture drainage (6.4% VS 1.7%, $P<0.05$), Organ failure rate (7.6% VS 4.5%, $P<0.05$).

Conclusion: Compared with supporting treatment group, SSTA regimens, such as somatostatin, showed better effectiveness in terms of continuous renal replacement therapy rate, Local puncture drainage and organ failure in hospitalized AP patients in the real-world clinical settings.

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A comprehensive survey on drug dispensing in pharmacy for Japanese elderly patients dwelling in the community

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Aim/Objective: The Japanese regulatory authority has been making efforts to provide a guidance to facilitate safe use of drugs among the elderly and to reduce harms due to polypharmacy. The information is scarce regarding how often drugs to be prescribed with special caution in Japanese older people are prescribed. This study aimed to provide a basis on the use of drugs in pharmacies among the elderly dwelling in the community at the national level.

Methods: To describe the changes over time of drug use, a nationwide cross-sectional survey of drug utilization in October 2011 and October 2015, using the National Database of Health Insurance Claims and Specific Health Checkups of Japan, was conducted. The drug dispensing data of patients over 65 years were summarised and a subset over 75 years was chosen; predefined drug classes such as anticancer drugs were excluded thus patients with those drugs only were excluded. The survey described diseases and drugs as well as patients' demographics.

Results: The target elderly patients dwelling in the community increased from 14 million to 17 million approximately. Patients dispensed ≥5 drugs formed 12.7% of the elderly population in 2015 October. The mode number of drugs dispensed each month was two per each patient at each pharmacy. Medication problems were observed for patients dispensed ≥5 drugs in the same class such as for anxiety, diabetes, and diuresis.

Conclusion: Over 10% of the elderly population were those over 75 years dispensed more than five drugs at one or more pharmacies. The survey revealed many very elderly patients dispensed ≥5 drugs in a certain class and/or receiving drugs from multiple pharmacies. Appropriate medication management is to be encouraged especially to balance the risk of adverse reactions, drug interactions and changes in pharmacokinetics/pharmacodynamics with age.

Keywords: geriatric, drug utilization, screening tool for older persons' appropriate prescriptions for Japanese (STOPP-J), health insurance database

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Titration of topiramate in patients with epilepsy: a real-world database analysis

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Objective: Topiramate is a frequently used antiepileptic drug (AED). However, there was no study that described its titration process, which is very important to its safety and effectiveness in clinical practice. This real-world database analysis evaluated topiramate titration in patients with epilepsy.

Methods: This is a retrospective cohort study utilizing the largest claims database in Japan, Japanese Medical Data Center (JMDC), which has been processed into standardized format that can be used for research. All patients were included in the analysis if they were a) diagnosed with epilepsy, b) prescribed with topiramate between January 1, 2011 and December 31, 2016, c) enrolled in the database for at least 180 days after index date, and d) ≥ 2 years of age. Maintenance dose was identified when the dose was sustained for at least 8 weeks for the first time during follow-up period.

Results: Among 2218 eligible patients, 469 (21.1%) were of 2-16 years old and 1749 (78.9%) were at least 17 years. The mean (SD) initial dose was 86.0 (88.9) mg/day. 1487 (67.0%) achieved maintenance dose lasting for at least 8 weeks, the mean (SD) maintenance dose was 113.6 (106.3) mg/day. Patients took an average of 20.0 (SD: 38.3) days from initial dose to maintenance dose. Throughout titration, the mean (SD) dose increments was 53.1 (43.0) mg/day between unique doses. The medication frequencies per day in 1144 (76.9%) patients didn't change, while 184 (12.4%) patients increased 1 dose and 76 (5.1%) patients increased 2 doses every day during titration process.

Conclusion: The process of dose increments to achieve maintenance dose was mild and appropriate in this Japanese population, which was comparable with prescription guideline. However, the maintenance dose in this study was comparatively lower. Further analyses, such as subgroup analysis, are required to thoroughly delineate the topiramate titration process.

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Appropriateness of outpatient antibiotic prescribing in China: nationwide cross sectional study

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Objective To estimate the antibiotic prescription rates for common diagnosis categories and to assess the appropriateness of all outpatient antibiotic prescriptions in China.

Method: We used a data from a national monitoring network for rational use of drugs in China. The data consisted of outpatient prescriptions from 188 secondary and tertiary hospitals in all 31 provinces of China mainland. Antibiotic prescription rates for various diagnosis categories and proportions of inappropriate antibiotic use for different subgroups were estimated using a comprehensive diagnosis classification method. A post-hoc ecological association analysis was conducted for the association between appropriateness of antibiotic use and hospital-level characteristics.

Results: Among the 237920798 outpatient prescriptions, 10.8%(95%CI 10.8%-10.8%) contained at least one antibiotic. Almost for all diagnoses, visits in emergency department resulted higher antibiotic prescription rates than that in outpatient department. For conditions that antibiotic use is almost always appropriate, sometime appropriate, and almost always inappropriate, 42.2%(95%CI 42.1%-42.2%), 30.6%(95%CI 30.6%-30.6%), and 7.6% (95%CI 7.6%-7.6%) visits resulted in antibiotic prescriptions. Uncertain diagnoses were prescribed 5.8%(95% CI 5.7%-5.9%) less antibiotics. Among all antibiotic prescriptions, 51.4% (95%CI 51.4%-51.4%) were estimated as inappropriate, much higher than that in developed countries. Post-hoc regression analysis indicated that the inappropriateness of outpatient prescribing was associated with antibiotic prescription rate, level of hospitals, regions of hospital location, and age structure of patients. No positive association between inappropriate use of antibiotics and percentage of outpatient drug costs was observed.

Conclusions: In Chinese secondary- and tertiary-level hospitals, 10.8% of outpatient prescriptions were estimated to contain antibiotics, while over half of antibiotic prescriptions were inappropriate. Outpatient antibiotic stewardship aiming at reducing inappropriate antibiotic use is needed for China to achieve the goals set in the National Action Plan.

Key Words: Antibiotics; Prescription; Outpatients

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Referral system makes triple-win among patients, primary hospital and regional ART center: result from a pilot test

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Background: The majority of newborns being the second child in family in China in 2017. The assisted reproductive technology (ART) has been a useful method to help some infertile couples. Some primary hospitals are in lack of sufficient knowledge and technologies of diagnosis and treatment of infertility. It takes the infertility patients a long time to find appropriate and high-quality ART treatment by themselves.

Method: The medical alliance is a method to improve the overall medical service system capacity. Most of the current referral systems are offline, with low efficiency and poor operation capability. Several Online Referral Platform were developed by different agency. WeChat, QR code, SMS were used as client site of the online referral system that links online/offline, client /platform, primary hospitals and regional reproductive centers. The pilot test was carried out in one ART center in North East China and 10 primary hospitals within medical affiance region.

Results: Based on the results from the pilot test and focus group discussion, the referral system reduced at least three visits to different departments at various hospitals and 2-3 visits at the regional ART center before initiation of infertility treatment for patients. Besides save time and cost, patients also had better experience in whole treatment periods. More than 80% clinicians in primary hospital gained knowledge at diagnosis or treatment of infertility through following the patients' diagnosis and treatment at a high-level ART center in the referral system. More than 60% of the physician in the regional ART center appreciated the referral project save their time and made the treatment more efficient.

Conclusion: Using the referral system, patients can quickly and efficiently access the treatment of ART. The referral system improves the connection between the primary hospital and regional ART center within a alliance region. It also benefits infertility patients in receiving appropriate ART treatment in a more quickly and efficient manner.

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The study of the association between meteorological data and diseases using claims database

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Objective: It is widely known that there are diseases which symptoms appear in a specific season, such as hay fever, or become severe due to changes in weather. The aim of this study is to investigate if the association between weather and disease (medication) can be assessed by matching the claims database with the meteorological data.

Method: We match the meteorological data (temperature, atmospheric pressure, etc.) with claims database owned by JMDC. Meteorological data on a prefectural and daily basis provided by the Japan Weather Association is used. Among the 2,241,227 participants in claims data from April 2017 to March 2018, we consider the patients dispensed any drugs as 100% and compare the ratio of the number of patients dispensed the target drug by the temperature on the dispensing date.

Result: As the temperature decreases, the ratio of cold medicine tend to increase. This fact indicates that cold is often observed in winter. In addition, the ratio of some drugs such as asthma and COPD treatment is the highest when the temperature is about 14 °C and it tends to decrease regardless of whether the temperature is high or low. The reason would be that asthma and COPD tend to get severe at the turn of the season. Among Antibacterial drugs, the drugs increase in proportion as the temperature rises (cephalosporin type), increase as the temperature decreases (macrolides and similar types) and keep a certain proportion without being influenced by temperature (broad spectrum penicillin system) are observed. The reason could be the difference in antibacterial spectrum

Conclusion: This study suggests that the association between the weather and the disease can be observed by using matched meteorological data and the claims data.

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Treatment adherence and beliefs about medicines in autoimmune rheumatic diseases

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Objective: To determine treatment adherence and to assess specific beliefs and concerns that patients with autoimmune rheumatic diseases have about their therapy.

Methods: Rheumatoid arthritis (RA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE) and psoriatic arthritis (PsA) patients over 18 years, were opportunistically recruited from an outpatient clinic. Self-reported adherence was measured using a direct translation of the five items Compliance Questionnaire for Rheumatology (CQR5), and it was expressed as a dichotomous variable: high and low adherers. Perceptions about treatment were estimated by using the Belief about Medicine Questionnaire (BMQ). The BMQ was translated and adapted -by adding three extra questions to the BMQ-Specific section.

Results: Out of the total of 42 patients, 30 (71.42%) were high adherers. Similar percentages among RA and AS patients were found. The majority of the high adherers (25, 83.33%) were younger (age below 65), and two thirds had disease duration of more than five years. Most patients (37, 88.09%) held a high level of beliefs in the need for their medication while half (20, 47.61%) had increased concerns about their medication-related to worries about long-term effects of medicines (80.95%) and becoming too addicted to their medicines (47.52%). The extra questions showed that almost all patients had full understating of their prescribed treatment, followed recommendations without alterations depending on their current health status and had trust that the medicines were effective. 26 (61.90%) of the patients believed that medicines in general are beneficial and one third agreed that fewer medicines would be prescribed if doctors had more time with patients.

Conclusion: Results showed an overall high treatment adherence in patients with autoimmune rheumatic diseases. These patients held high beliefs in the necessity of their treatments, and although they had voiced some concerns they were adherent in a high percentage.

Keywords: adherence to treatment, beliefs and concerns, autoimmune rheumatic diseases

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Prevalence of opportunistic infections and their impact on healthcare cost among patients with HIV in a developing mixed economy country

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Objectives: To determine the prevalence and pattern of various opportunistic infections (OIs) among patients with HIV, and to assess the economic impact of OIs.

Methodology: A prospective observational study was conducted in a non-profit organization hospital for a period of 8 months. All patients admitted to hospital were reviewed intensively for the patients aged ≥ 18 Years, irrespective of gender gets admitted to hospital with at least one OI. All the required data were obtained from medical records and also by interviewing patients and their caretakers. Healthcare cost of OIs was assessed by calculating the direct medical cost.

Result: Among 353 patients assessed for eligibility, 177 (50.14%) patients with opportunistic infections were included in the study. Majority were males (64.40%), and in the age group of 40-49 years (44.63%). Majority (74.57%) of the patients were belonging to HIV stage four and having CD4 count less than 200 cells/µl (61.01%). Tuberculosis (50.84%) was the most common OI, followed by Pneumocystis Carinii Pneumonia (PCP) (18.64%) and candidiasis (18.64%). The average direct medical cost for tuberculosis was found to be 9428.52/- INR (range: 2450.64/- – 27817.06/- INR), for PCP 9504.32/- INR (range: 1977.76/- -21409.17/- INR) and for candidiasis 8575.95/- INR (range: 2259.16/- – 20376.35/- INR).

Conclusion: TB was found to be most common OI in our study. Even though patients are provided with free anti-retroviral therapy and anti-tubercular therapy drugs by public sectors, the amount patient spend for the management of various OIs is still a burden in contrast of their financial status.

Key words: Human Immunodeficiency Virus (HIV), Opportunistic Infection (OI), Acquired Immunodeficiency Syndrome (AIDS), Tuberculosis (TB), Pneumocystis Carinii Pneumonia (PCP).

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Heavy metals contamination in rice growth in Thailand: A systematic review for the past 10 years.

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Background: Numerous studies have revealed that there are heavy metals contamination in rice from both in Thailand and international. However, no evidence of overall heavy metals contamination in Thailand was reported. This study aims to systematically review the level of heavy metal contamination in rice growth in Thailand.

Method: A systematic search of studies published from 2009 – 2018 was conducted through electronic database including PubMed, Scopus, Web of Science, CUIR, ThaiLis, Thai index medicus, Thai thesis database and Thai Citation Index. Studies reported the quantity of metal in rice growth in Thailand were included in the study. Qualitative analysis was performed to summarize the existing evidence. The Thai food and drug administration (Thai-FDA) standard and the codex alimentarius international food standard (CODEX) were used as standards accepted level of metal in foods.

Result: Of the 1,263 studies identified, 26 studies were included. According to Thai-FDA standard, six studies (23.1%) found arsenic contamination, 2 studies (7.7%) found lead contamination, and 1 study found mercury contamination over the standard accepted maximum level. According to CODEX, 6 studies (23.1%) found cadmium contamination and 4 studies (15.4%) found lead contamination higher than accepted level. Arsenic contamination was found in the rice growth in lower north-eastern region of Thailand, while rice contaminated with cadmium was grown in the western region.

Conclusion: This study revealed that heavy metal contamination in rice is still an important problem in Thailand, especially arsenic, cadmium, and lead. Therefore, the government agency should consider strategies to prevent heavy metal contamination in Thai rice.

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Modelling the population health impact of introducing a reduced-risk product into asian markets, Japan and Singapore

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The Population Health Impact Model (PHIM) was developed to assess the impact of marketing a reduced risk product (RRP)* on population health within specific countries, including Japan and Singapore.
The PHIM uses publicly available data on smoking prevalence and smoking-related disease-specific mortality, together with estimates of the exposure from using the RRP relative to smoking a cigarette. The model was developed to explore different scenarios of RRP introduction in order to assess the prevalence of cigarette and RRP use patterns (including combine product use). By comparing scenarios with and without the introduction of the RRP during the same time period (1990–2010), the model predicts the change in smoking attributable deaths (SAD) and life years saved from the major smoking-related disesases (lung cancer, ischemic heart disease, stroke, and COPD).
In Japan, heated tobacco products were marketed nationally in 2016 with multiple products entering shortly thereafter. Using the initial data on the uptake of these products between 2016-2018 we modeled an RRP uptake base-case scenario where ten years after marketing the RRP, 55% of the smokers switch to the RRP (heated tobacco products such as IQOS). Although, in Singapore these products are banned, to understand the impact that marketing these products could have on the population health we modeled scenarios of similar uptake, in the Singapore population. The results demonstrate that within 20 years Japan could see 0.96 million life years saved (75,820 SAD reduction), while Singapore could observe 0.03 million live years saved (2,100 SAD reduction).
Tobacco Harm reduction, the introduction of RRPs as a replacement to cigarettes, as a supplement to tobacco control policies can lead to significant net positive health benefit in countries such as, Japan and Singapore even with very different smoking habits and regulatory enviroments.

Population Health, Modeling, Reduced-Risk Products, Asia

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Timing of pediatric labeling and clinical trial evidence supporting approval of pediatric drugs in Japan, the US, and the EU

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Aim/Objective: To characterize the timing and frequency of the pediatric labeling change, and to evaluate the strength of clinical trial evidence supporting regulatory approval of pediatric drugs in Japan, the United States (US), and the European Union (EU).

Methods: This study included novel therapeutics approved in Japan, the US, and the EU from 2005 through 2014. We identified pediatric labeling changes between approval date and April 30, 2018 using the review reports and labels available on each authority's website. Next, we investigated the design of pediatric studies (i.e., randomization, blinding, comparator) supporting regulatory approval using publicly available regulatory documents and websites.

Results: A total of 319, 263, and 242 novel therapeutics were approved in Japan, the US, and the EU, respectively. During the follow-up period, there were 33 pediatric labeling changes affecting 29 (9%) novel therapeutics in Japan, 72 changes affecting 54 (21%) in the US, and 55 changes affecting 43 (18%) in the EU. The number of pediatric efficacy studies submitted per approval was greater in Japan than in the US and the EU (median, 2 [interquartile range, 1-3] vs 1 [1-2] vs 1 [1-2]; p=0.001). However, these pediatric efficacy trials were less likely to be randomized (36% vs 66% vs 56%; p<0.001), double-blinded (26% vs 52% vs 39%; p<0.001), and placebo controlled (24% vs 43% vs 35%; p=0.015) in Japan compared to the US and the EU.

Conclusion: The US and the EU experienced post-approval pediatric labeling change more frequently than did Japan. In addition, the US and the EU tended to approve pediatric drugs based on fewer but higher quality global studies; while Japan's approvals tended to be based on more but lower quality local studies. These differences might be attributed to the different legislative systems on pediatric drug development between the regions.

Keywords: off-label use, pediatric drug development, pediatrics, regulatory science

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The Recent Landscape of Observational Studies Initiated by Pharmaceutical Companies in Japan: Implication from Literature Search

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Aim/Objective: The surroundings of pharmaceutical industry is changing (e.g. HTA implementation and Clinical Trial Act). The value-based medicine has gained attention, and the evidence generation through observational studies becomes more important to explain the value of the products. However, the landscape of the observational studies initiated by pharmaceutical industry in Japan has been unclear. The objective of this study is to describe the recent changes in the number of industry-initiated clinical studies and to investigate the design and topics of the observational studies through literature search.

Methods: Articles of clinical studies from 2007 to 2017 were searched with prespecified keywords and filtered by article type in PubMed. The number of the articles published per year was identified. The articles of observational studies from July to December 2017 were extracted using the prespecified keywords and reviewed to be classified by study design and topics. The impact factor of the journals was also identified.

Results: The number of articles of clinical studies increased from 208 to 1380 for the past ten years. In the second half of 2017, 36 articles of the observational studies extracted. Among those, nine “cross-sectional”, nine “database”, seven “prospective”, five “retrospective”, and six “other” studies were included. Of the nine “cross-sectional” studies, six were “QOL/PRO”-related. Of the nine “database” studies, there were three studies in each of “epidemiology and public health” and “economic evaluation”. The classification by topics was as follows; 10 “QOL/PRO”, eight “economic evaluation”, seven “epidemiology and public health”, six “clinical outcomes”, and nine “others” (double-counting included). Of the six “clinical outcomes”-related, three were “prospective” studies. The median (range) impact factor of the 36 observational studies was 2.7 (0.7-27.1).

Conclusion: The number of articles of clinical studies has been increased. “Cross-sectional” study and “QOL/PRO”-related was the most frequent design and topic respectively in the observational studies.

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A bibliometric and text mining analysis of the publications using Taiwan's National Health Insurance claims data: Rise and fall?

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Aim/objective: Taiwan's National Health Insurance (NHI) claims data have been widely used for clinical and health services research since the public release of the data in 2000. However, with the growing research output, the use, and perhaps misuse, of NHI claims data has incurred criticism and even litigation. In this study, we updated the bibliometric profile of the literature using NHI claims data and attempted to identify the most popular topics and to classify the types of studies by text mining analysis.

Methods: Bibliometric and text mining analyses of articles published in English and entered PubMed between Jan 1, 1996 and Dec 31, 2017.

Results: We included a total of 4473 articles published between 2000 and 2017 in the analysis. A rapid growth of publications has been witnessed from 2000 to 2015, followed by a plateau thereafter. Diabetes, stroke and dementia were the top three most popular research topics whereas statin therapy, metformin and Chinese herbal medicine were the most investigated interventions. While almost all of these studies were published in Journal Citation Report-indexed journals, approximately one third of them were published in open access journals. Studies with two or more medical conditions, but without any intervention, mentioned in the article title were the most common study type. Studies of this type tended to be contributed by prolific authors and published in open access mega journals.

Conclusion: We will discuss the reasons behind these findings and propose future directions for improving the impact of research based on NHI claims data. Despite the controversies, the analysis of secondary data, such as NHI claims data, may still have its place in the production of scientific knowledge to inform medical decisions and policy making.

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Performance of Charlson Comorbidity Index and Elixhauser Comorbidity Index to predict mortality with cancer in Korean national health insurance cohort

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Objective: This study aims to evaluate validity of the CCI and ECI in predicting mortality in patients with cancer including gastric cancer, liver cancer, colon cancer using Korean National Health Insurance data.

Methods: We identified patients aged ≥25 years who were firstly hospitalized with gastric cancer, liver cancer, colon cancer between January 2006 and December 2010 using the Korean National Health Insurance System National Sample Cohort (NHIS-NSC). The study population divided into four groups according to their age (25-54, 55-74, 75-84, and ≥85 years). We categorized patients by using their CCI and ECI score (0, 1-2, 3-4, ≥5). Cox proportional hazards models adjusted for sex were used to estimate hazard ratios (HR) with the comorbidity score 0 group as reference to compare the risk of mortality after hospitalization by cancer. Area under the receiver operating characteristic curve (AUC) was used to compare the predictive power of the comorbidity scores in each age group.

Results: Of the 8,250 cancer patients, 28.2%, 53.6%, 15.2%, and 3.0% were aged 25-54, 55-74, 75-84, ≥85 years, respectively. In 25-54 and 75-84 years group, only HR of CCI score ≥5 were significantly higher compared with CCI score 0 group (HR 3.46 (95% CI 2.61-4.60), 1.63 (95% CI 1.29-2.07)). In 55-74 years group, HRs of CCI score 3-4, ≥5 were significantly increased (HR 1.36 (95% CI 1.15-1.62), 2.89 (95% CI 2.46-3.39)). In ≥85 years group, all of the HRs were not significant in each CCI score group. When adjusted for sex and CCI, AUC was 0.604 in ≥85 years group and less than 0.6 in other groups (0.590, 0.585, and 0.560). It showed a poor discrimination capacity to predict mortality. The results of ECI were similar with the CCI results.

Conclusion: This study showed that the conventional comorbidity scores were not fully reliable in predicting mortality in Korean patients with cancer.

Keywords: mortality, comorbidity index, Korean

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Introducing Patient Flow Concept to Analyze Pneumonia Care Experience in a Regional Hospital

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The patient-level indicator is an important source of mastering big data at present. Considering the hospital attributes and patient population, the detailed registration and current situation analysis of pneumonia, it is planned to obtain the experience of future care quality.

The top ten diseases of inpatients in this hospital were pneumonia, and the conditions were excluded: 1.18 years old 2. Transferred from other hospitals 3. Inpatients within 48 hours of chest X-ray showed no pneumonia in the lung 4. Inclusion in clinical trials Subject 5. Transfer or discharge within 24 hours after admission 6. Death within 24 hours after admission 7. Automatic discharge from non-disease, including gender, birthday, arrival time and discharge day, admission method, discharge situation, risk factors, each Bacterial culture and strains, antibiotic use, to build a complete patient flow system.

According to the data of hospitalized pneumonia patients, males accounted for 55.7%, females accounted for 44.3%, and the average age was 78 years old. X-ray examination was performed within an average of 43 minutes after admission, with an average of 126 minutes of antibiotic treatment. The average length of hospital stay was 9 days. The mortality was 5.7%; the past history found that hypertension was 59%, stroke was 45.3%, dementia was 37.7%, diabetes was 32.1%, chronic renal failure was 27.4%, COPD was 27.4%; blood culture 9% of the strains were cultured, belonging to "Methicillin resistant Staphylococcus aureus", "Coagulase-negative Staphylococcus species", "Corynebacterium species", "Proteus mirabilis; 29% of sputum culture, Pseudomonas aeruginosa 32.3%, Klebsiella pneumoniae 25.8%,Acinetobacter baumannii total 16.1%.

Among the medical care groups in this hospital, the proportion of senior citizens is high, mostly from the maintenance institutions. ER is the entrance for medical treatment. The pneumonia patients are established through the rapid chest X-ray diagnosis and antibiotic use to establish the hospital patient community experience therapy; whether in patient safety or quality Improvement can have better benefits.

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Developing an integrated real-world data ecosystem to enhance care delivery for chronic obstructive pulmonary disease patients in Singapore

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Objective: To develop a real-world data ecosystem (RWDE) allowing for effective capture, aggregation and analysis of electronic medical information for patients with chronic obstructive pulmonary disease (COPD). This abstract describes the creation of data pipelines, source data verification and data validation steps in the creation of the RWDE within a large academic medical centre in Singapore.

Methods: A public-private partnership was formed for this project. Information from various clinical and operational databases, including electronic medical records, clinical documents and radiology databases, were linked and managed using an enterprise data warehouse (EDW). Back-end data retrieved was matched with the front-end data captured at the point of care to ensure fidelity. As part of the data validation process, descriptive analyses for patient demographics and clinical characteristics were generated for a sample of COPD patients who visited the hospital and had their data captured in the specialist COPD clinical documents between October 2012 and October 2017.

Results: We included 198 COPD patients. Mean age was 74.9 years and 96.0% were males. 82.8%, 7.1%, 6.1% and 4.0% were of Chinese, Malay, Indian and other ethnicities, respectively. Among the 79 patients who were smokers, about one-third received smoking cessation counselling. The majority had their results for the COPD Assessment Test documented at each clinical encounter (82.3%). Modified Medical Research Council Dyspnea Scale (78.3%) and spirometry (83.3%) were also captured. Among the 67 patients due for influenza vaccination (over the past year), 34.3% were eligible and received vaccination. For pneumococcal vaccination, 29.8% were both eligible and agreeable for administration.

Conclusion: The development and application of a COPD RWDE enabled the analysis of real-world tertiary data. The COPD RWDE offers a reliable and timely source of tertiary data that can facilitate quality improvement, outcomes measurement, clinical research, and the design of clinical decision support systems to improve patient outcomes.

Keywords: chronic obstructive pulmonary disease, data ecosystem, real-world

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Health-related quality of life in type-2 Diabetes Mellitus patients: A cross-sectional study in South India

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Aim/Objectives: The study aims to understand the health-related quality of life in patients with type II diabetes mellitus.

Methods: A prospective, cross sectional study was conducted in patients above 20 years of age and diagnosed with type II diabetes mellitus who attended Endocrinology department from September 2018 to March 2019. EuroQo-5 dimension (EQ-5D-5L) scale was used for the assessment of health-related quality of life.

Results: A total of 252 subjects from in-patient department, who satisfied criteria were recruited. The mean age of the cohort was 58.76 ±12.5 of which a male preponderance was observed (61.9%). EQ-5D index and EQ-VAS scores (Visual assessment scale) were 0.416± 0.26 and 53.61±18.09 respectively.

Conclusion: HRQoL is one of the most important goals of all health interventions. The findings from this study indicated that diabetes patients has lower score of health-related quality which entails the need to intervene beyond the provision of standard treatment to improve the HRQoL of patients with diabetes. Health care professionals play a pivotal role in improvement of HRQoL in diabetic patients and clinical pharmacists' being a part of it, can improve glycemic control, empower patients to self-management, increase patients' satisfaction and quality of life through various interventions.

Keywords: Type II diabetes mellitus, Health-related quality of life, EQ-5D-5L.

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Real world data in drug discovery: Approach for understanding diseases and their unmet medical needs

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In recent years, the target disease of drug discovery tends to focus on symptoms with low therapeutic satisfaction and intractable diseases with a small number of patients. Under these circumstances, it is essential to understand the disease itself and unmet medical needs (UMNs) of patients in drug discovery research. To achieve this, in this study, we used JMDC Inc.'s database (JMDC DB) of health insurance receipts, and selected Parkinson's disease as an example of a putative indication. JMDC DB contains information on a total of approximately 4 million patients, with more than 3,000 PD patients

First, an analysis of the past histories of PD patients revealed that many patients had symptoms characteristic of PD, such as constipation, insomnia, and depression. In addition, information on antiparkinsonian medications indicates that not all patients receive levodopa which is the gold standard of treatment for PD, and that anticholinergic medications with a risk of dementia are the third most commonly prescribed.

Next, we then analyzed the symptoms and medication information obtained above in detail. As an example of the results of the analysis, many patients who were not receiving levodopa or dopamine agonists had a diagnosis of depression or schizophrenia, and these patients were found to be receiving anticholinergic medications as antiparkinsonian agents. This suggests that the treatment of PD patients with psychiatric symptoms has become an UMN, with fewer treatment options. In this presentation, we introduce some examples of UMNs that have been obtained by utilizing JMDC DB. The results support that real-world data is a useful tool for predicting patient pathology and UMNs in drug discovery research.

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Cost-Effectiveness of Evolocumab in Treating Cardiovascular Disease

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Aim of the Study: To compare the cost-effectiveness of evolocumab with traditional statin therapy since PCSK9 inhibitors are very costly when used for cardiovascular disease.

Methods: The databases used for searching were Pubmed search index and EBSCOhost and articles were only chosen from 2010-2018. Keywords used include “pharmacoeconomics” or “cost,” and “PCSK9 Inhibitors” or “evolocumab.” Of the 76 results that were presented, 7 studies were included in our systematic review. The inclusion criteria was any study that described the cost-effectiveness of evolocumab or PCSK9 inhibitors.

Findings/Results: The cost of the drug would have to be reduced per patient for PCSK9 inhibitors like evolocumab to be cost effective at <$100,000 per QALY. For the studies that were done in the U.S., the researchers found that four out of the seven studies that were analyzed found PCSK9i to be cost-effective.

Conclusion: Evolocumab was cost-effective when compared to statins for the treatment of major adverse cardiovascular events but more research needs to be done.

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Optimal drug master that enhances real world data analysis and improves medical safety

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Objective: A wide range of Real World Data (RWD) has been accumulated; however, each medical data has a limited coverage or granularity and is not self-sufficient.
Therefore, in order to broaden RWD utilization, information gathered from multiple data sources must be combined. The optimal “master data” would be an important key in achieving this objective.
This study focused on the “drug masters” to enhance RWD analysis.

Methods: This study investigated the drug masters publicly released by the Ministry of Health, Labor and Welfare, and the Medical Information System Development Center (MEDIS) in terms of collected data, data comprehensiveness, and consistency. Near miss incident reports submitted to the Japan Council for Quality Health Care were also analyzed and the relevance between those reports and the master data was scrutinized.

Results: Two main issues on the drug masters have been extracted:
1) Deficiency in data comprehensiveness and consistency
2) Inconsistent granularity and composition of the master source information

1) Incomplete information of the pharmaceutical ingredients is one instance. The problem lies in extracting the proper set of drug components to be analyzed.

In the clinical sites, it has been implied that the absence of comprehensive drug masters, which must cover complete ingredient information, may be the primary cause of medical errors.

2) Inconsistent granularity and composition can be exemplified by the inconsistent NHI price listing unit between original and generic products as seen in the case of the Aripiprazole Liquid, which may cause misinterpretation in the analysis of the generic product’s volume of penetration.

Conclusion: The study confirmed the necessity to develop the ideal drug master in order to maximize its benefits in implementing RWD analysis. Further, it has been concluded that establishing an effective system with the optimal master to prevent medical malpractice is also imperative.

Keywords: Real World Data, drug master data, drug safety

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Impact of sleep and stress on pregnant woman: A cross sectional study

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Objective: To assess the quality of sleep, stress on pregnant women in and around a small village.

Methods: A Prospective cross sectional observational study was conducted at SVR hospitals and Government hospitals located in a rural areas of southern India in outpatient department from June 2018 to January 2019. Data was obtained regarding patient demographic details, past medical history, social history, current therapy, gestational age and fetal weight and identified potential risk factors by patient interview using a pre validated questionnaire. Quality of sleep and stress were assessed by using questionnaires Pittsburgh sleep quality index (PSQI) and perceived stress scale. Descriptive statistics of demographic and clinical variables included percentages, mean and standard deviation. Mann Whitney U test and Pearson correlation was used to determine the significance between the objectives and parameters.

Results: A total of 1200 pregnant women were enrolled in to the study with consent. Amongst whom only 480 (30%) pregnant women had scored less than 5 on PSQI thus reflecting sleep disturbances. These women lived in joint families. Further, primigravida women (OR: 4.988) experienced more sleep disturbances, when compared to multigravida women (OR: 4.922). Around 941 (78%) women were graded to have mild stress followed by moderate depression [99 (8%)] during their pregnancy across all the trimesters. Stress was commonly noted in all the women who lived in an urban nuclear family compared to rural joint families (OR: 10.29 vs. 5.273; $P < 0.0001$). Further, the stress was associated with the progression of the trimester age and passive smoking, alcoholism, socioeconomic status, and type of parity respectively.

Conclusion: We found a significant effect of stress and lack of sleep on their newborns, who were considerably under when compared to control group. Sleep hygiene practices should be emphasized for high risk women. Sleep and stress were interrelated hence, both factors should be addressed at the earliest in pregnant women.

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Comparative effectiveness of unicompartmental and total knee replacement for patients with comorbidities

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Aim/Objective: We have previously shown propensity score (PS) stratification and inverse probability weighting (IPW) to emulate a surgical RCT comparing partial (PKR) to total knee replacement (TKR). We here study the effectiveness of PKR vs TKR for multi-morbid patients ineligible for the same RCT.

Methods: Patients undergoing a PKR or TKR in 2009-2016 identified in the UK National Joint Registry and ineligible for the TOPKAT RCT were included, and data linked to hospital inpatient (Hospital Episode Statistics) and patient reported outcome measures (PROMs). Revision, previous cruciate ligament injury or inflammatory arthritis were excluded. Logistic regression was used to calculate PS for PKR using 28 covariates including demographics, preoperative PROMs, comorbidity, and procedures within 3 years before surgery. Different analyses were conducted: 1) stratification based on the entire cohort's PS (PSScohort); 2) stratification based on the PS of patients with PKR (PSSexposure), and 3) IPW. Linear regressions with clustering by surgical units were used to derive average treatment effect (ATE) estimates of difference in postoperative Oxford Knee Score (OKS) between groups with adjustment for imbalanced covariates (absolute standardized mean differences (ASMD) >0.1).

Results: 151 PKR and 24,542 TKR patients were included. PSSexposure and PSScohort resulted in excellent covariate balance (all ASMD<0.1 and only one covaiate with ASMD>0.1, respectively) while half of 28 covariates remained imbalanced in IPW. Postoperative OKS ATE was 2.00 (95%CI: 0.28, 3.74) in favour of PKR in PSSexposure. Smaller and non-significant ATE were seen in PSScohort (1.25; -0.49, 2.98) and IPW (1.30; -0.04, 3.03).

Conclusions: Post-operative PROMs following PKR are better than post-TKR for patients with comorbidity in PSSexposure analyses. However, smaller and non-significant ATEs were seen in PSScohort and IPW.

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Incidence of Community-acquired Pneumonia in China: a Nationwide Claims Database Analysis

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Objectives: To estimate the incidence rate of community-acquired pneumonia (CAP) in China by using a nationwide insurance claims database.

Methods: A retrospective study was conducted by using the Urban Basic Medical Insurance (UBMI) database from January 1, 2016, to December 31, 2016. The data of patients diagnosed with CAP in 23 provinces were identified and extracted. The incidence rates were calculated and compared among different groups of populations.

Results: A total of 427.52 million enrollees were covered in the UBMI of 23 provinces in 2016. Among this population, 1.42 million patients were identified as having a CAP episode by having at least one claim record of CAP diagnosis, and finally a sum of 1.48 million CAP episodes was counted. The overall incidence rate of CAP was 7.96 (95% CI: 7.95-7.97) per 1 000 person-years in 2016, in males 8.04 (95% CI: 8.03-8.05) and females 7.87 (95% CI: 7.86-7.88) per 1 000 person-years, respectively. The insured population covered all ages, in the youth population, the incidence rate was 60.83 (95% CI: 60.67-60.98) per 1 000 person-years in children (under 5 years old) and 18.84 (95% CI: 18.80-18.87) per 1 000 person-years in adolescents (under 18 years old); in adults, the incidence rate was 7.55 (95% CI: 7.53-7.56) per 1 000 person-years in patients aged 40 years and older, increased to 10.28 (95% CI: 10.25-10.31) per 1 000 person-years in patients aged 60 years and older, and the highest rate of 14.70 (95% CI: 14.62-14.79) per 1 000 person-years was observed in patients aged 80 years and older.

Conclusions: This study shows a relatively high level of CAP incidence in China. The rates appeared a U-shaped curve with the highest incidence in children and elder population, and higher rates were observed in males than in females. These findings suggest that youth and elder population (especially males) are relatively more susceptible to CAP.

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Impact of medical conditions and medication use during pregnancy on adverse birth outcomes: a hospital-based case-control study

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Objective: To identify the impact of medical conditions and medications received during pregnancy on the development of adverse birth outcomes (ABOs).

Methods: A case-control study was conducted at the Obstetrics and Gynecology Department of a tertiary care hospital over a period of three years (July 2015 to June 2018). Liveborn & stillborn neonates and their mothers were included in the study. Neonates were categorized into cases and controls based on the presence or absence of composite ABOs respectively. Binary logistic regression analysis was used to identify the risk factors for ABOs among medical conditions and medications received by mothers during the current pregnancy.

Results: A total of 1214 neonates and their mothers were included in the study. About 556 (45.80%) neonates were identified with composite ABOs, 320 (26.36%) were born low birth weight, 300 (24.71%) were born preterm, 12 (0.99%) were macrosomic and 54 (4.45%) were identified with some form of congenital abnormalities. Hypertension (12.03%), hypothyroidism (8.24%) and diabetes mellitus (7.74%) were the common medical conditions, levothyroxine (7.58%), nifedipine (5.93%), labetalol (4.94%) and magnesium sulphate (3.62%) were the common medications received by mothers during the current pregnancy. After adjusting for confounding factors, it was identified that the hypertension [aOR 7.28 (95% CI 1.66-31.90); P=0.008], oligohydramnios [aOR 3.88 (95% CI 1.23-20.58); P = 0.011], nifedipine [aOR 10.01 (95% CI 2.92-21.87); P<0.001], nicardipine [aOR 5.32 (95% CI 1.35-24.18); P=0.026] and magnesium sulphate [aOR 5.31 (95% CI 1.93-11.68); P=0.001] were the risk factors for overall ABOs, and specifically for preterm birth and low birth weight.

Conclusion: Hypertension and the use of nifedipine during pregnancy were identified as the most important risk factors for ABOs like preterm birth and low birth weight. It was also identified that the early detection and management of hypertension with antihypertensives like labetalol and methyldopa can reduce the risk of ABOs.
Keywords: Adverse birth outcomes, Medications, Medical conditions, Pregnancy.

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Impact of preterm birth and low birthweight on medical conditions, medication use and mortality among neonates: a prospective observational study

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Objective: To assess the impact of preterm birth and low birthweight on medical conditions, medication use, and mortality among neonates.

Methods: A prospective observational cohort study was conducted at the neonatal intensive care unit (NICU) of a tertiary care hospital over a period of one year from July 2016 to June 2017. Neonates admitted in NICU for more than 24 hours and who received at least one medication were enrolled in the study. Perinatal and demographic data of neonates, reason(s) for NICU admission, diagnosis, medications prescribed, medication-related problems, discharge status, and the direct medical cost were documented and analyzed.

Results: A total of 405 neonates were included in the study; 254 (60.49%) were boys, 179 (44.20%) were born low birthweight, 132 (32.59%) were born preterm and 75 (18.52%) were either small or large for gestational age. Neonatal sepsis [125 (30.86%)], unconjugated hyperbilirubinemia [83 (20.49%)] and respiratory distress syndrome [62 (15.31%)] were the most common medical conditions and were significantly higher among preterm and low birth weight neonates. Nearly half of the medications prescribed were anti-infectives for systemic use [1310 (47.45%)]. The mean number of medications received by neonates increased from term to extremely preterm (5.21 to 15.00), normal birthweight to extremely low birthweight (4.97 to 14.90) and >30 days age to 1-10 days age (3.78 to 8.89). The mortality rate was significantly higher among extremely preterm (66.67%) and very preterm (15.22%) neonates compared to term (2.93%) neonates. The median direct medical cost for NICU admission was INR 21430 (USD 331).

Conclusion: Medical conditions, medications prescribed and the mortality rate was significantly higher among preterm and low birthweight neonates admitted in NICU.

Keywords: Low birthweight, Medical conditions, Medications, Mortality, Preterm birth

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A Natural Language Processing algorithm for pulmonary nodule identification from chest CT imaging report in Chinese free text

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Objective: Electronic medical records (EMR) may provide extraordinarily granular information about healthcare services, compared to claims-based data. However, large volumes of text-formatted fields in EMR data prevent efficient analytics for RWE generation. AI development such as Natural Language Processing (NLP) and Machine Learning enable systematic and objective utilization of text data, which we applied to identify patients with pulmonary nodules (PN) from chest CT imaging text reports in a large hospital in China.

Methods: From a training set extracted from the hospital CT report database, we developed a customized NLP scheme with two automated AI identification systems: a practice-based classification (PBC) algorithm system and a supervised text classification (STC) modelling system. The PBC was developed through unsupervised PN text-profiling with theme and feature discovery combined with expert radiologist review. The STC primarily relied on computer-profiled PN-text commonalities. To validate the custom-built NLP schemes and compare with the traditional keyword search, we randomly extracted 991 chest CT image reports as test set from the same hospital.

Results: There were 891 PN positive and 100 PN negative reports confirmed by radiologists in the test set. The PBC identified 858 PN positive and 99 PN negative reports with a sensitivity of 96.3% and accuracy of 97.0%. The STC identified 866 PN positive and 96 PN negative reports with a sensitivity of 97.2% and accuracy of 97.1%. For comparison, the sensitivity and accuracy yielded from traditional keyword search were 82.3% and 84.0%, respectively (733 PN positive and 99 PN negative reports). With NLP schemes, an additional 17-18% of PN patients could be identified and perhaps treated earlier.

Conclusions: Both NLP schemes yielded highly satisfactory results. The sensitivities and accuracy rates in identifying PN using the NLP scheme were >10% higher compared to the traditional keyword search. AI technology has the potential to enrich EMR data and will greatly empower its use for further analysis.

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Major drivers of pharmaceutical costs in state sector health care institutions of Sri Lanka

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Aim/Objective: This study was conducted to identify the major cost drivers of pharmaceuticals in the state sector health care institutions from 2014 to 2018 and to determine whether it is consistent with the most prevalent diseases.

Methods: An ABC analysis was conducted on the costs of all utilized pharmaceuticals by the state sector health care institutions from year 2014 to 2018 by analyzing the aggregated data collected from the Medical Supplies Division (MSD), Ministry of Health, Sri Lanka. Costs were expressed in Sri Lankan Rupees (LKR).

Results: The total number and costs of medicines in the MSD formulary had increased from 2014 to 2018 with the addition of 60 new items and 1.8 fold increase in total expenditure. The total expenditure for year 2018 was 26 billion LKR. Percentage of medicines reduced for 'group A' (17.22% to 15.96%) and increased for other groups from 2014 to 2018 (group B, 17.82% to 18.19% and group C, 64.95%.to 65.85%). The medicine with the highest unit cost was rituximab in 2014 and trastuzumab in 2018. Among pharmaceuticals accounting for 25% of the total expenditure, biologics were predominant. The highest percentage of total expenditure was for trastuzumab in the years 2016 and 2017 (3.6% and 4.8% respectively) and in 2014, 2015 and 2018, sodium chloride (2.69%), human immunoglobulin (2.7%) and bevacizumab (5.5%) were the highest. Excluding biologics, the other medicines included in the top 25%, were medicines for Non communicable diseases (NCDs) which increased from 3.63% in 2014 to 4.28% in 2018. Percentage cost decreased for antibiotics from 5.27% in 2014 to 1.53% in 2018.

Conclusion: The main driver of cost was NCD medicines with the highest driver being biologics and it is consistent with the prevalent diseases in Sri Lanka.

Keywords: Cost, Pharmaceuticals

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Comparative study between isophane protamine Biosynthetic human insulin injection and other antidiabetic drugs for the treatment of diabetes mellitus

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Objective: To comprehensively evaluate the effects between Isophane Protamine Biosynthetic Human Insulin Injection (IPBHI) and other antidiabetic drugs for the treatment of diabetes mellitus.

Methods: We conducted a comprehensive literature search of Cochrane Library, EMBASE, CBM, PubMed, CNKI, and WanFang databases to identify randomized controlled trials (RCTs) that assessed the efficacy/effectiveness and safety of IPBHI against other antidiabetic drugs in the treatment of type 1, type 2, and gestational diabetes mellitus. Paired reviewers independently screened for eligible studies, assessed risk of bias, and extracted data. We pooled data from included studies using mean differences (MDs).

Results: 88 RCTS (at moderate or high risk of bias) were included in the study. Compared with the control group (oral hypoglycemic agents, other human insulin, animal insulin, and blank control group), the mean differences of changes in fasting blood glucose [MD=-0.65, 95%CI (-0.93, -0.37), P<0.00001], postprandial blood glucose [MD=-0.64, 95%CI (-1.03, -0.25), P=0.001] and glycosylated hemoglobin [MD=-0.65, 95%CI (-0.94, -0.36), P<0.00001] from baseline were statistically significant. Subgroup analysis also showed similar results, such as the mean differences of changes in fasting blood glucose were statistically significant [IPBHI vs oral hypoglycemic agents MD=-1.00, 95%CI (-1.40, -0.60); IPBHI vs other human insulin MD=0.12, 95%CI (-0.10, 0.35); IPBHI vs animal insulin MD=-1.16, 95%CI (-2.25, -0.08); IPBHI vs blank control group MD=-1.34, 95%CI (-1.78, -0.90)]. We assessed the safety of IPBHI against other antidiabetic drugs, and found that general hypoglycemia events [RR=1.25, 95%ci (0.96, 1.64), P=0.10], severe hypoglycemia events [RR=2.25, 95%ci (0.55, 9.15), P=0.26], edema events [RR=1.48, 95%ci (0.62, 3.54), P=0.26], body mass index [MD=1.14, 95%ci (0.19, 2.46), P=0.09] were not statistically significant.

Conclusion: Compared with oral hypoglycemic agents, other insulin, and animal insulin, IPBHI may reduce fasting blood glucose, postprandial blood glucose, and glycosylated hemoglobin in type 2 diabetes, type 1 diabetes, and gestational diabetes.

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A Study of Knowledge, Attitude and Practice about Nosocomial Infections among Healthcare Workers in a Tertiary Care Teaching Hospital

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Objectives: The main aim of the study was to assess healthcare professionals knowledge, attitude and evaluate their practice regarding infection control standard practices.

Methodology: A cross sectional study was carried out at tertiary care teaching hospital in a developing country. The data was collected by a pre designed questionnaire. The study population included specialists, doctors, post graduates, interns, staff nurses and student nurses. The study included 180 participants from different cadres of healthcare workers selected by random sampling technique covering the intensive care unit of the hospital. The data collected was analyzed by using descriptive analysis. Chi –square test was done to find the association between the categorical variables.

Results: Knowledge Score: The mean knowledge score was 9 out of 12 among all the participants in the study. The specialists had good knowledge when compared to other groups. The knowledge among nursing students was of significant importance and a matter of concern for the management.
Attitude score: The mean attitude score was 6.79 out of 8 among all participants in the study. The post graduates and interns had good attitude towards nosocomial infections.
Practice score: The mean practice score was 7.32 out of 10 among all the participants in the study. The specialists, doctors, post graduates and interns had poor practices which are of significant importance in this study.
The female participants (61.7%) had good knowledge, attitude and practice about nosocomial infections when compared to males (38.3%).
The participants with age group 25-35(85%) had good knowledge, attitude and practice on nosocomial infections.

Conclusions: Education has a positive impact on retention of knowledge, attitudes and practices in all the categories of staff. In order to reduce the incidence of nosocomial infections, compliance with regulations and timely interventions are mandatory.

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Direct comparison of statins and fibrates on important efficacy and safety outcomes: systematic review and meta-analysis

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Objective: To synthesize the evidence directly comparing statins and fibrates on major clinical efficacy and safety outcomes.

Methods: Ovid MEDLINE (plus PubMed for recent non-indexed records), Ovid Embase, Cochrane Library, ClinicalTrials.gov, and International Clinical Trials Registry Platform were systematically searched from inception to November 2018, using keywords, subject headings, and spelling variants for all statins and fibrate drugs and efficacy and safety outcomes of mortality, cardiovascular disease, cerebrovascular disease, coronary artery disease, musculoskeletal disease, and hyperlipidemia. We included randomized controlled trials which directly compared statin monotherapy with fibrate monotherapy, with a minimum follow-up duration of at least 28 days in participants ≥ 18 years of age, that reported any outcome of cardiovascular mortality, all-cause mortality, coronary artery disease, myocardial infarction, angina pectoris, and stroke. Safety outcomes included the number of participant withdrawals due to adverse effects, number of serious adverse effects, and myopathy. We estimated summary risk ratios (RR) with 95% confidence intervals (CI) using a random effects model and the Mantel-Haenszel method, with pooled effect estimates less than zero favoring statins.

Results: The literature search identified 3560 records. Nineteen studies with 7608 participants were included. There was no detectable effect of statins compared with fibrates on cardiovascular mortality (RR 1.39, 95% CI 0.68-2.84), all-cause mortality (RR 1.43, 95% CI 0.73-2.81), cardiovascular events (RR 0.97, 95% CI 0.68-1.39) and myocardial infarction (RR 0.71, 95% CI 0.44-1.15). Statin therapy reduced the risk of participant withdrawal from the study due to adverse effects (RR 0.74, 95% CI 0.56-0.98) and the occurrence of serious adverse effects (RR 0.51, 95% CI 0.32-0.82), but had no effect on myopathy (RR 1.29, 95% CI 0.93-1.79).

Conclusion: There was limited direct evidence to support differences in efficacy between statins and fibrates. However, statins appear to be better tolerated than fibrates.

Keywords: Statins, fibrates, efficacy, safety

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Bone targeting agent utilization in breast and prostate cancer patients with bone metastasis: a nationwide population cohort in Taiwan

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Objective: We aimed to describe bone targeting agent(BTA) utilization among breast cancer (BC) and prostate cancer (PC) patients with bone metastases (BM) in Taiwan in recent decade.

Methods: A retrospective cohort of incident BC and PC patients with BM from 2004 through 2015 was identified from Taiwan Cancer Registry and their reimbursed treatment retrieved from Taiwan National Health Insurance data. Diagnosis codes of International Classification of Disease 9th revision (ICD-9: 198.5) and ICD-10 (C79.51 and C78.03) were used to define BM. We ascertained demographic information and BTA use among these patients. The initiating BTA regimen and time from BM to first BTA were described. Zoledronic acid (ZA) and clodronate were approved for reimbursement in 2004 and denosumab received coverage approval in 2013.

Results: A total of 16,474 BC patients and 12,800 PC patients had BM diagnosis during the study period. Median age at the time of BM diagnosis was 55 years and 77 years for BC and PC patients respectively. Seventy-one percent (11,723) of BC patients received at least one BTA and 64% (7,465) of BTA users initiated treatment after BM diagnosis. Among BC patients who initiated BTA after BM diagnosis, 55%, 19%, 15% and 11% initiated with ZA, clodronate, denosumab and other BTAs, with a median time of 3 weeks from BM diagnosis to BTA initiation. Half of PC patients (n=6499, 51%) received at least one BTA and 71% (4,604) of BTA users initiated treatment after BM diagnosis. Among the PC patients who initiated BTAs after BM diagnosis, 54%, 25%, 13% and 8% initiated with ZA, clodronate, denosumab and other BTAs, with a 3-month median time from BM diagnosis to BTA initiation.

Conclusion: In Taiwan, most BC patients received BTA shortly after BM diagnosis, while less PC patients received BTA and initiated at a later time after BM diagnosis.

Keywords: Bone Metastasis(BM), bone targeting agents (BTA), breast cancer(BC), prostate cancer(PC)

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Accuracy of commercial molecular diagnostics for the detection of pulmonary tuberculosis in China: A systematic review

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Objectives: This systematic review aimed to assess the accuracy of different molecular diagnostic methods for the detection of pulmonary tuberculosis in Chinese.

Methods: Based on comprehensive searches of the China National Knowledge Infrastructure (CNKI), Wanfang database, SinoMed, VIP Information (VIP), Pubmed, Embase, and Cochrane Library, we included studies that assessed the accuracy of molecular diagnostic for pulmonary TB in China. For each index test, a summary estimation for sensitivity and specificity were calculated with the bivariate random-effects model.

Results: A total of 59 studies were included in our analysis. LAMP (6 studies; pooled sensitivity 90%, 95%CI 78-95%; specificity 93%, 85-97%), LPA (1 study; 87%, 84-90%; 94%, 92-95%) and PCR (4 studies; 90%, 55-99%; 93%, 71-99%) showed good diagnostic performance in the meta-analysis. The highest pooled sensitivity was Xpert MTB/RIF (20 studies; pooled sensitivity 91%, 95%CI 87-94%). The highest pooled specificity was CPA (6 studies; pooled specificity 97%, 95-99%). The lowest pooled sensitivity and specificity were from SAT-TB (3 studies; 79%, 66-88%; 72%, 48-88%). In subgroup analysis, molecular diagnostics demonstrated higher sensitivity for pulmonary TB detection on smear-positive specimens.

Conclusions: Xpert MTB/RIF, LAMP, LPA, CPA and PCR demonstrated high accuracy overall for pulmonary tuberculosis detection, while SAT-TB had poor performance.

Keywords: Systematic review; Molecular diagnostics; Pulmonary tuberculosis

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Real-world outcomes associated with the use of companion diagnostics in advanced NSCLC, Flatiron Health 2011–2018

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Aim/Objective: Companion diagnostic testing (CDx) identifies patients with molecular targets likely to respond better to particular therapies; however, not all cancer patients receive CDx in the real-world setting. This study evaluated factors associated with CDx testing in the real world and the clinical value of CDx associated with survival among patients with non-squamous advanced (Stage IIIB/IV) non-small cell lung cancer (aNSCLC).

Methods: Patients diagnosed with aNSCLC between January 1, 2011 and May 31, 2018 from the de-identified Flatiron Health electronic health-derived database; those who received CDx with their first line of treatment were compared with those who did not. Logistic regression using components of the modified Lung Cancer Prognostic Index (LCPI; age, sex, stage, actionable mutation(s), smoking, respiratory comorbidity; Alexander et al. Br J Cancer. 2017) and other clinical factors were used to predict factors associated with receiving CDx. Overall survival was evaluated using Kaplan-Meier analysis. Unadjusted and adjusted Cox proportional hazards models were used to evaluate the association between CDx and overall survival.

Results: A total of 17,143 patients (CDx, n=14,389; no CDx, n=2754) were included in the analysis, patients who were female, Asian, non-smokers, diagnosed after 2014, treated in an academic center, receiving multiple lines of therapy or had advanced stage at diagnosis were more likely to receive CDx. Patients receiving CDx lived longer than those not receiving CDx (median survival 14 vs 7 months). Reduced mortality associated with CDx remained after adjusting for clinical factors included in the modified LCPI (unadjusted [95% CI] =0.54 (0.52, 0.57); adjusted HR [95% CI] =0.78 [0.75-0.82]).

Conclusions: Among patients with non-squamous aNSCLC, use of CDx was associated with reduced risk of mortality compared with no CDx, highlighting the value of patient access to precision medicine programs.

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Validity and reliability of patient section of evidence-based medical records about doctor-patient building through integrated therapy to gastrointestinal diseases

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Background: We developed an evidence-based medical record for doctor-patient relationship building through an integrated therapy of traditional Chinese and Western medicine (DPEBMR) to assess the efficacy in patients with digestive system diseases. The instrument was categorized into a doctor section and a patient section. In this article, our main goal was to test the validity and reliability of the patient's section for DPEBMR (DPEBMR-P).

Methods: One hundred patients were recruited. Doctors and patients used a predefined format to jointly record the illness. Cronbach's α and factor analysis were used to evaluate the reliability and structure validity, respectively.

Results: Cronbach's α of all 12 items from DPEBMR-P was 0.906, which demonstrated high reliability. The Kaiser-Meyer-Olkin value was 0.811 and Bartlett's spherical test value was 452.2 ($P<0.05$), which meant it was suitable for performing factor analysis. A total of 3 items were identified as factors, and each had high loading: items of mental status (0.584 to 0.833), items of therapeutic effect (0.518 to 0.797), and items of appetite (0.857 to 0.882).

Conclusions: The DPEBMR-P indicated substantial reliability and structure validity.

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Effectiveness of prevention of influenza infection with green tea catechins; A systematic review and meta-analysis

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Objective: Influenza viruses can spread easily from person to person, and seasonal influenza epidemics are serious public health worldwide. Although several clinical evidence studies have reported that green tea catechins (GTCs) prevent influenza infection by drinking, gargling, and taking GTCs supplements, the effectiveness of each method has remained uncertain.

Methods: We searched PubMed, SCOPUS, Cochrane Library, and reference lists of studies. Databases were collected from their inception to March 2019. Both randomized controlled trials (RCTs) and prospective cohort studies were assessed the effect of GTCs on the prevention of influenza infection. Two authors independently reviewed each study, assigned quality scores and extracted data for all outcomes using a standardized form. Pooled effect estimates (risk ratio; RR) were obtained using a fixed and random effects model.

Results: A total of 8 studies which involved 5,048 participants selected from 364 articles identified including 2 studies by drinking, 4 studies by gargling, and 2 studies by taking GTCs supplements (aged, 6-70 years). The participants who treated with GTCs had statistically significant effects on the prevention of influenza infection than did participants who no treated; fixed effects model (RR, 0.59; 95% confidence interval [CI], 0.47-0.74); random effects model (RR, 0.62; 95% CI, 0.49-0.77). Moreover, the participants who consumed GTCs by drinking and taking GTCs supplements showed similar effectiveness (RR, 0.54; 95% CI, 0.37-0.8; RR, 0.54; 95% CI, 0.26-1.13, respectively). It is important to note that a sensitivity analysis of gargling [RR, 0.3; 95% CI, 0.08-1.14] with green tea everyday (100 mg/day GTCs, approximately) showed similar preventive effects with taking GTCs supplements [RR, 0.31; 95% CI, 0.11-0.93] in high concentration (2,200 mg/day GTCs, approximately).

Conclusion: The meta-analysis results indicated that GTCs consumption have effective prophylaxis for influenza infection. However, RCTs studies of drinking green tea are needed to confirm the findings.

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The impact of selected biomarker levels changes on serum tumor marker levels elevation among Chinese lung cancer patients

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Objective: To evaluate whether biomarker levels changes were associated with elevated tumor marker levels in lung cancer patients

Methods: A case-control study using one hospital database in Shandong province, China. All lung cancer patients tested at least twice of serum tumor markers between January 2013 and December 2017 were studied. Cases were subjects with elevated tumor marker levels from baseline to end of follow-up and controls were those without elevation. Baseline and follow-up biomarker levels were considered as the first biomarker test value within 180 days after first discharge and average test values after 365 days of first discharge. Logistic regression models were used to adjust for age, gender, pathology types, and lab biomarkers. The selection rule of studied lab biomarker was that increased proportions of biomarker test value were larger than 75% quantile of all biomarkers test value increased proportions from baseline to end of follow-up.

Results: Patient numbers with and without elevated tumor marker levels were 275 and 101 in CEA, 115 and 86 in SCC, 216 and 124 in NSE, 233 and 111 in Cyfra211, and 63 and 36 in Pro-GRP. No statistically significant association was observed between selected biomarkers and rising CEA. TBIL increase was associated with rising SCC (adjusted OR, 1.90 95%CI 1.01-3.61). AST and Na increases were associated with rising NSE (adjusted ORs of 2.26, 95%CI 1.04-5.07 and 0.43, 95%CI 0.20-0.89). ALB and CEA increase was associated with elevated Cyfra211 (adjusted ORs, 0.41, 95%CI 0.23-0.69 and 3.32, 95%CI 1.90-5.88). HGB and TBIL increases were associated with ProGRP elevation (adjusted ORs, 3.65, 95%CI 1.42-9.95 and 0.22, 95%CI 0.06-0.67).

Conclusion: Increasing levels of some biomarkers were associated with significantly increased odds of elevated tumor maker levels. The findings might provide real world evidence on making more meaningful clinical use of biomarkers in tumor marker management.

Keywords: biomarker level change, tumor marker level elevation, lung cancer

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Serum tumor markers utilization pattern among Chinese lung cancer patients in routine clinical practice

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Objective: To explore the trends in usage of tumor markers of CEA, SCC, NSE, CYFRA211, and Pro-GRP among Chinese lung cancer patients in the real world setting.

Methods: A retrospective descriptive study was conducted using one hospital database in Shandong province, China between January 2013 and December 2017. Utilization trends were analyzed by first discharge year of lung cancer, by serum sample test year, and by subtypes of lung cancer. Distribution of combined usage of these tumor markers was explored. Focused analysis of utilization rates within different durations before and after first discharge was conducted.

Results: Among 6053 lung cancer patients, these tumor markers had increased utilization by first discharge year of lung cancer and by serum sample test year from ~15% in 2013 to ~30% in 2017 except ProGRP increasing from 17% in 2015 to 50% in 2017. Around 50% patients regardless of subtypes of lung cancer had combined five or six tumor markers tests before first discharge date of lung cancer during the study period. However, around 60% patients were with no tumor markers testing after first discharge date. Utilization rates of CEA, NSE, SCC, and Cyfra211 within 30 days before first discharge date of lung cancer was ~50% during 2013-2014 and ~70% during 2015-2017 in NSCLC, and ~67% and ~80% in SCLC. But utilization rates after first discharge date decreased sharply from ~25% in CEA, ~20% in NSE, SCC, and Cyfra211, ~10% in ProGRP during 90 days after first discharge to ~5% in all these biomarkers after one year of first discharge in NSCLC, and from ~40% to ~10% in SCLC.

Conclusion: This study suggests tumor marker of lung cancer in Chinese routine clinical practice might have low utilization rates after discharge. The reasons for low utilization and its impact on outcomes deserve further investigation.

Keywords: tumor marker utilization, lung cancer, real world

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ETV combination with IFN-α is superior to ETV monotherapy in reducing hepatocellular carcinoma in chronic hepatitis B patients

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Aim: To assess whether ETV adding or switch to INF-α could reduce hepatocellular carcinoma (HCC) in chronic hepatitis B (CHB) patient.

Methods: In a cohort with 465 patients treated with ETV combination with IFN-α and 3729 patients with ETV monotherapy, we analyzed the HCC incidence after adjusting clinical parameters.

Results: Liver cirrhosis diagnosis algorithm were established to validate cirrhosis diagnosis. By multivariate cox regression analysis, the risk of hepatocellular carcinoma in ETV combination with IFN-α group was 40% lower than that in ETV monotherapy (HR = 0.6, 95% CI: 0.3-0.9, P=0.0487). The conclusions were consistent using propensity score matching and propensity score-based inverse probability weighted adjustment. The complete virological suppression rates and HBsAg serological rates were significantly higher in combination therapy group compared to monotherapy. After adjusting virological suppression and HBsAg seroclearance, ETV combined with IFN-α is superior to ETV monotherapy in reducing HCC.

Conclusion: ETV combination with IFN-α therapy had a lower risk to develop HCC than ETV monotherapy for CHB patients, whether or not adjusting complete virological suppression and HBsAg seroclearance. Considering that ETV being the preferred antiviral drug for patients with CHB in China, it is necessary to add IFN-α to the population at higher risk of hepatocellular carcinoma.

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Efficacy and safety of anti-cancer biosimilars compared to reference biologics in oncology: a systematic review and meta-analysis

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Aim/Objective: Many biosimilars of monoclonal antibodies (mAbs) are becoming increasingly available in in anticancer therapies, such as the rituximab, bevacizumab, and trastuzumab biosimilars. However, no comprehensive summary of their efficacy and safety is available. This study synthesized current evidence on the efficacy and safety of mAb biosimilars relative to their reference biologics among cancer patients.

Methods: We searched PubMed, Embase, the Cochrane library, ClinicalTrials.gov, the ISI Web of Science, and several Chinese databases from their inception dates to December 31, 2018, for randomized controlled trials (RCTs) or comparative observational studies that compared the efficacy and safety of biosimilars with reference biologics used in oncology. The binary outcomes were pooled using risk ratio (RR) with 95% confidence intervals (CIs), continuous outcomes using weighted mean difference (WMD) with 95% CIs, and time-to-event outcomes using hazard ratio (HR). Subgroup and sensitivity analyses were conducted following this. We used the GRADE approach to rate the quality of the evidence.

Results: We did not find any comparative observational studies that fit the criteria. Only 23 RCTs were identified for biosimilars of three monoclonal antibodies, of which 8 RCTs examined rituximab biosimilars (total N = 1534), 6 RCTs were for bevacizumab biosimilars (total N = 1897), and 9 were for trastuzumab biosimilars (total N = 4953), respectively. The quality of the GRADE evidence for efficacy and safety outcomes was moderate or low. The findings were robust for all pre-specified subgroup and sensitivity analyses.

Conclusion: The existing evidence suggests highly comparable efficacy and safety profiles between mAb biosimilars and their reference biologics in oncological drugs.

Keywords: Anti-cancer biosimilars, efficacy, safety, meta-analysis

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Safety of rapid deployment versus conventional bioprosthetic valve: a systematic review and meta-analysis

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Objectives: This meta-analysis was conducted to compare the mortality and postoperative complications of aortic valve replacement using rapid deployment valves (RDVs) with conventional bioprosthetic valve (CBVs).

Methods: Ovid-Medline, Embase, Web of science, ClinicalTrials.gov, and the Cochrane Library databases were searched from January 2000 to March 2019. Randomized controlled trials (RCTs) and comparative matched studies using propensity-score were included. The primary outcomes were early mortality and all-cause mortality during follow-up and the secondary outcomes were postoperative complications. Data was summarized as relative risk (RR) or hazard ratio (HR) and 95% confidence intervals (CI).

Results: Three RCTs involving 264 patients, and 14 matched studies involving 5311 patients were included in the meta-analysis. There was no significant difference in early mortality (RR: 1.03, 95% CI: 0.18-5.73, for 2 RCTs; and RR: 1.12, 95% CI: 0.79-1.59, for 9 matched studies) and follow-up mortality (RR: 1.27, 95% CI: 0.55-2.94, for 2 RCTs; and HR: 0.99, 95% CI: 0.68-1.43, for 5 matched studies) between patients who received RDVs compared with CBVs. For the analysis of 9 matched studies, the incidence of permanent pacemaker (PPM) implantation was significantly higher in the RDVs group than in the CBVs group (RR: 2.26, 95% CI: 1.78-2.88), but there was no significant difference in two RCT studies (RR: 0.69, 95% CI: 0.09-5.38). Compared with CBVs, RDVs showed no significant difference in PPM implantation, stroke, any cerebrovascular accident, any aortic regurgitation, major bleeding, reoperation, myocardial infarction, and respiratory failure in RCT and matched studies.

Conclusions: There was a higher incidence of PPM implantation with RDVs than CBVs, but no difference in early mortality, follow-up mortality and other postoperative complications between RDVs and CBVs.

Keywords: Rapid deployment aortic valve replacement; Aortic valve replacement; Bioprosthesis; Meta-analysis

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Long-term outcomes of bioprosthetic versus mechanical mitral valve replacement: a systematic review and meta-analysis

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Objectives: This meta-analysis was conducted to compare the long-term outcomes of mitral valve replacement using bioprosthetic valve (MVRb) with mechanical valve (MVRm).

Methods: Ovid-Medline, Embase, Web of science, ClinicalTrials.gov, and the Cochrane Library databases were searched from January 2000 to January 2019. Eligible randomized controlled trials (RCTs) and cohort studies followed patients after MVR for at least five years were included. The primary outcome was long-term any cause mortality and the secondary outcomes were long-term complications. Data was summarized as hazard ratio (HR) and 95% confidence intervals (CI).

Results: Two RCTs involving 442 patients, and 11 cohort studies involving 24497 patients were included in the meta-analysis. For the primary outcome of death from any cause, MVRb when compared with MVRm was associated with a significant relative risk increment (HR: 1.18, 95% CI: 1.07-1.31). In subgroup analyses for study type, MVRb showed a survival harm over MVRm for patients in 9 cohort studies (HR: 1.18, 95% CI: 1.07-1.30), but not significant in two RCT studies (HR: 1.13, 95% CI: 0.55-2.32). In subgroup analyses for age group, MVRb showed a survival harm over MVRm in patients younger than 65 (five studies, HR: 1.28, 95% CI: 1.06-1.55), but not significant in patients aged or older than 65 (three studies, HR: 1.02, 95% CI: 0.98-1.09). For the secondary outcomes, MVRb showed lower risk for bleeding (six studies, HR: 0.78, 95% CI: 0.70-0.88) and stroke (three studies, HR: 0.84, 95% CI: 0.76-0.93), higher risk for reoperation (six studies, HR: 2.73, 95% CI: 1.92-3.88), and similar risk for endocarditis and major adverse prosthesis related events.

Conclusions: Compared with MVRm, MVRb is associated with a significant survival harm over 5 years of follow-up, but not significant in patients aged or younger than 65. Additionally, MVRb shows lower risk for bleeding and stroke but higher risk for reoperation.

Keywords: Mitral valve replacement; Mechanical valve; Bioprosthesis; Meta-analysis

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Effects of a newly-design antiviral-drug teaching kit used in people living with HIV (PLHIV) in a Taiwan regional teaching hospital.

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Aim/Objective: To enhance drug safety, compliance, and education satisfaction in people living with HIV (PLHIV) by using a newly-design antiviral drug teaching kit.

Methods: An infectious disease specialist and pharmacists designed an antiviral drug teaching kit in January 2017. The kit can show drug size, appearance, information, Chinese and English trade names, pharmacological classification. The kit was commenced on 1st of March 2017. A satisfaction survey conducted on both patients and medical professionals during March.

Results: During the investigation period, a total of 30 patients and 28 professionals were surveyed. The education level of interviewed patients was 6 in high school, 22 in universities, and 2 in graduate institutes. The average age was 31.3-year-old. Among them, 12 were newly diagnosed. 84% of patients thought it was helpful to learn the drug appearance, 74% of patients thought the drug appearance help them to confirm whether they took the right drug or not.
The interviewed professionals were 8 doctors, 13 pharmacists, and 7 case-managers. The professionals thought the kit had advantages: 89% professionals affirmed that this was convenient to educate patients, 82% considered they could save teaching time, 71% said that the kit could improve the correctness of education, and 61% thought it could confirm the correctness of drug.

Conclusions: Using drugs correctly can ensure the efficacy of the drug and prevent drug resistance. The kit not only improved the convenience of education, saved time, but could help both professionals and patients confirm the correct use of antiviral drugs and prevent medication errors. From the results, it can also be found that higher educational level and new patients had the higher demand for understanding drugs. This is a good sign and helps shared decision making in medicine. Meanwhile, the kit is very suitable for promotion to other countries to enhance medication safety and make relationship between patients and medical professionals better.

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Integrated the pharmacist clinical monitoring practices and decision-guide order entry system to reduce the antibiotic dosing errors and cost

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Background: Computerized physician order entry systems can reduce prescription writing errors; however, the wrong typing of the dose or the medical error caused by the lack of professional knowledge cannot be avoided. The decision-guide order entry system can really reduce these errors. Although the clinical monitoring work of pharmacists can effectively prevent medical malpractice.

Material and methods: First step of the antibiotic dosage decision-guide calculators which have 9 antibiotics related renal functions was implemented into CPOE system. The antibiotics where been prescribed and the appropriate dosage regimen can provide automatically. Second step of the clinical pharmacist was visit in patients' antibiotic dosage by antibiotic dosage monitoring system of the hospital to further provide appropriate dosage recommendations for the physician. Third step of the compared the risk of inappropriate antibiotic doses and related renal function damage before and after the integration of the above two methods, and describe the acceptance of the dose recommendations by the descriptive analyst and use the antibiotic expenditure of evaluation.

Results and discussion: The two way were integrated for 3 years, the inappropriate antibiotic dosing errors were decreased about72%, the relative risk (RR) were within 0.33-0.24. The physician acceptant rates in dosage decision function were increased from 42.5% in 2015 to 91.4% in 2018, and 93.0% in pharmacist dosage recommendations. The use of alternative cost-effective antibiotics with an equivalent spectrum and instructed them on the appropriate time for using such antibiotics and replaced expensive antibiotics with cheaper alternatives with similar efficacy and activity. From 2015 to 2018 of the implementation of these measures, the mean expenses incurred per month for antibiotics administered to hospital inpatients reduced from 6,662,000 NT dollars to 4,825,000 NT dollars.

Conclusion: This study explores the effectiveness of integrating computerized medical decision-making functions with the clinical monitoring of pharmacists to improve antibiotic doses and cost.

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Patient safety attitudes of pharmacy students in an Indian Medical University: a cross-sectional study

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Introduction: Patient safety is a major health care concern and is not being included in the Pharmacy curriculum except some aspects of patient safety, Pharmacovigilance. HCPs needs to know about the patient safety, as it plays a major role in lessening harm to the patients. Therefore, we aim to assess patient safety attitude of pharmacy students.

Methods: A cross-sectional study using a self-administered questionnaire containing 21 items was conducted at the Pharmacy College of Jagadguru Shri Shivarathreeshwara Academy of Higher Education and Research (JSSAHER), Mysuru campus. Students studying various pharmacy courses were the study population. Data analysis was performed to calculate mean, standard deviation, percentages and logistic regressions using SPSS software version 22 (licensed to JSSAHER). A P value of <0.05 were considered as statistically significant with 95% confidence interval.

Results: A total of 442 pharmacy students were enrolled into the study with a response rate of 93.77%. 64.43% of the study population possess adequate patient safety attitude. A higher patient safety attitude was observed in students of fifth and 6th year Pharm.D (80.00 and 83.33% respectively). Most of the respondents (73.07%) agree or strongly agree that after an error occurs, an effective strategy is to work hard to be more careful. Most of them (83.03%) believe that pharmacists should routinely spend part of their professional time working to improve patient care. About half (68.77%) of pharmacy students disagree or strongly disagree that pharmacists should discuss and report errors to an affected patient and their family even if the patient is not harmed. Statistically significant association between the attitude of pharmacy students toward patient safety and their age, year of study and the course they studied.

Conclusion: Pharmacy students have the overall good attitude to patient safety. Standardised patient safety course would be considered in the curriculum for junior pharmacy students to improve their attitude toward patient safety.

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Improving medical safety by preventing medication errors with information management system intervention in Taiwan

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Aim: To evaluate the effectiveness of pharmacy intervention and ensure patients have safe and effective mediations.

Method: This was a retrospective study between January 2014 and April 2016 in a regional hospital in Taipei. Health Information System (HIS) is system that physicians prescribe medications on a computer. Pharmacists give recommendations to physicians and analyze the types of medical problems monthly. After careful consideration, three HIS system changes were used to reduce medication errors.

Result: A total of 511 medication errors were discovered during January 2014 to April 2016.
The top five categories of medication error were:

- Over dosage (n=142; 28%),
- Under dosage (n=75; 15%),
- Repeat with the same pharmacological effects of medications (n=65; 13%)
- Inappropriate formation (n=62; 12%)
- Medications do not meet the diagnoses (n=37; 7%).

Among these errors, over dosage, repeat with the same pharmacological effects of medications, and medications do not meet the diagnoses, could be reduced by altering the factors in HIS.
First, over dosage (n=142; 28%): set the maximum daily dose on HIS. Ever after, there was significant reduction of prescribing over medication's maximum daily dose. For example, after setting on August 2015, there was no case of cough syrup overdose (5% vs 0%).
Second, repeating medications with the same pharmacological effects (n=65; 13%): use warning window while prescribing. Compared to 2011-2013, the proportion of repeating medications reduced by 49% with the warning window.
Last, medications do not meet the diagnoses (n=37; 7%).After the analysis, we found out medication errors often caused by look-alike, sound-alike brand names. Therefore, we modified brand names in HIS to avoid doctor being confused.

Conclusion: After evaluation of system, it effectively improved medical safety. Through the precautionary approach in computer system, medication errors have been significantly reduced. Above all, pharmacists should regularly analyze prescription problem data to find the way to prevent them.

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Assessment of Prescribing pattern and source of prescription of Histamine 2 receptor antagonists and Proton pump inhibitors.

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Aim: To evaluate the prescribing pattern and determine the source of procurement of H2RA and PPIs among the patients.

Methods: It is a prospective observational study carried out for a duration of 7 months from October 2018 to April 2019 in the Department of Gastroenterology, M.S. Ramaiah Hospital, Bangalore, India. Patients aged >18 years, consuming H2RAs and PPIs > 4 weeks were included. The sociodemographic details, medication history, information about usage and source of procurement of H2RA and PPIs usage obtained by conducting a personal interview with patients and caregivers.

REesults: Among 367 patients, 200 patients consumed PPIs (29 rabeprazole, 34 omeprazole, 43 esomeprazole, 94 pantoprazole) and 167 consumed H2RA, ranitidine. Source of prescription for H2RA and PPI was found to be 122(33.24%) physician, 213(58.03%) pharmacist, 21(5.72%) by nurse and 11(2.99%) others.

Conclusion: The usage of PPIs is more compared to H2RA among patients and source of prescription seems to be more with the pharmacist, therefore, knowledge regarding the medication use seems to be poor in the patients.

Keywords: Histamine2 receptor antagonist, Proton pump inhibitors, prescribing pattern, source of prescription

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Variation in medication regimen complexity in Australian residential aged care

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Aim/Objective: To explore variation in medication regimen complexity in residential aged care facilities (RACFs) according to resident age, length of stay, comorbidity, dementia severity, frailty, and dependence in activities of daily living (ADLs).

Methods: Cross-sectional analysis of baseline data from the SImplification of Medications Prescribed to Long-tErm care Residents (SIMPLER) cluster randomized controlled trial. There were 242 residents prescribed at least one regular medication recruited from 8 RACFs in South Australia. Medication regimen complexity was assessed using number of daily administration times and the Medication Regimen Complexity Index (MRCI). Comorbidity was assessed using the Charlson Comorbidity Index (CCI). Dementia severity was assessed using the Dementia Severity Rating Scale. Frailty was assessed using the FRAIL-NH scale. Dependence in ADLs was assessed using the Katz ADL scale.

Results: The median age of participants was 87 years (interquartile range 81-92). Over one-third of participants (n=86, 36%) had 5 or more daily medication administration times. The number of daily administration times and MRCI scores were positively correlated with resident length of stay (rs=0.19; 0.27), FRAIL-NH score (rs=0.23; 0.34) and dependence in ADLs (rs=-0.21; -0.33) (all $p<0.01$). MRCI was weakly negatively correlated with CCI score (rs=-0.16; p=0.013). Medication regimen complexity was not correlated with age or dementia severity. In multivariate analysis, frailty was associated with number of daily administration times (OR: 1.13, 95% CI: 1.03-1.24) and MRCI score (OR: 1.26, 95% CI: 1.13-1.41). Dementia severity was inversely associated with both number of daily administration times (OR: 0.97, 95% CI: 0.94-0.99) and MRCI score (OR: 0.95, 95% CI: 0.92-0.98).

Conclusion: Residents with longer lengths of stay, who were dependent in ADLs and most frail had the most complex medication regimens. Residents living with more symptoms of dementia were less likely to have complex medication regimens. These findings will help target strategies to reduce medication regimen complexity.

Keywords: Aged; nursing homes; medication regimen complexity; frailty.

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Domperidone Prescribing Practices for Insufficient Lactation in Mothers at a Mother and Child Hospital

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Aim/Objective: Our aim was to describe the rational domperidone prescribing postpartum in women to promote lactation.

Methods: We conducted a retrospective cross-sectional analytical study using data from an inpatient and outpatient services at a hospital. We random sampling women with live births from October 2013 to September 2015, excluding those with nonlactation indications for domperidone. We collected data of 394 mother-child pairs from electronic medical records to collect prescribing and additional clinical data. Domperidone prescribing data were also collected in those mothers who continued visiting the outpatient breastfeeding clinic after delivery. Data collection included prescribing of domperidone to promote lactation, high dose initiation of domperidone (>30 mg/day), early initiation of domperidone (within 10 days postpartum), and long-term use of domperidone (> 30 days). Potential mother and child predictors of domperidone prescribing were analyzed by multivariate logistic regression.

Results: Domperidone was prescribed to promote lactation in 35 women (8.9%) postpartum. Among women prescribed with domperidone, 80% had records of adequate lactation. Most women (82.3%) were prescribed high dose domperidone in their first prescription (20 mg 4 times/day). Early initiation of domperidone was founded in 28.6% of the women (within 2 days after delivery). Among 326 women who visited the outpatient clinic after delivery, domperidone was initiated in 12 women (3.7%) in outpatient clinic, where every woman received high dose. The median number of days prescribing domperidone in the outpatient clinic was 64 days. Multivariate logistic regression did not find any significant association between the preselected predictors and domperidone prescribing.

Conclusion: We observed prevalent high dose domperidone and long-term domperidone prescribing practices postpartum, which potentially increased risk of sudden cardiac death.

Keywords: Domperidone, prescribing, insufficient lactation, postpartum

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Assessment of quality of life amongst knee osteoarthritis patients deprescribed of analgesics

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Objectives: To assess the Quality of Life (QoL) among knee Osteoarthritis (OA) patients deprescribed of analgesics.

Method: Prospective interventional study was conducted for 8 months in the Department of Orthopedics, Ramaiah Hospital, Bangalore, India. Patients >18 years with mild to moderate knee OA pain and consuming at least one analgesic, seeking alternative pain reduction therapy, and patients allergic to analgesics were included. The demographic details and medication history of patients are collected from case sheets and interview. After reviewing the collected patient details, based on pain intensity and acceptance of patients for dose reduction, frequency of analgesic intake and cessation of medicines, deprescribing was suggested and Physiotherapy (PT) was taught by a physiotherapist. WOMAC questionnaire is a validated tool based on pain, stiffness and physical function was employed to evaluate the QoL at baseline and after the 4th week of PT.

Results: Almost 230 patients were included and 10 patients didn't accept deprescribing intervention, though the physician suggested. Of the remaining 220 patients accepted intervention, 162 were completely deprescribed and 37 were dose tapered and also continued with PT. Comparing the QoL based on WOMAC, 162 patients continued PT and showed improvement in QoL. Other 37 patients, who were dose tapered and continued PT showed a slight improvement in QoL. Because analgesics reduced the pain in patients for a short period of time and the pain relapsed. Mc Nemar's test showed a significant reduction in pain grade after the 4th week of PT ($p<.000$). The long term analgesic administration may lead to side effects and delay soft tissue formation. But, soft tissue formation is possible in case of patients deprescribed of analgesics and continued PT.

Conclusion: WOMAC score showed better improvement in QoL among patients completely deprescribed of analgesics and continued with PT compared with that of patients dose tapered and followed PT.

Keywords: Deprescribing, Analgesics, WOMAC, Quality of Life.

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Study the Prevalence of significant Microbial changing pattern in Diabetic foot ulcer patients at tertiary care teaching Hospital

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Aim & Objective: To study microbial changing pattern and finding the significant prevalence in diabetic foot ulcer patients

Method: This is a Retrospective and comparative analysis conducted at 1800 bed tertiary care teaching hospital for the duration of 6 months and a total of 96 patients were involved in this study. The necessary data were collected from the medical record department of a particular hospital by using the specified data collection forms. Finally, all the collected data were organized and analyzed using SPSS statistical tool to calculate the clinical signs of a microbial changing pattern.

Results: The gender distribution table shows male is the highest participants with 66 in number (68.75%) and age distribution shows that the 41-50 age group was higher with 32 patients (41.55%). The culture sensitivity comparison table indicates the higher prevalence of E.coli and Klebsiella with 23 patients (25%) in 1st time culture test, Where in the second time culture shows the higher prevalence E.coli about 18 Patients (23.07%) and second highest is Streptococcus Aureus in 17 patients (21.79%). On the other hand, the Anti-microbial resistance comparison shows the higher use of Amikacin about in 44 patients (32.83%) as the 1st time definitive therapy and 2nd-time culture test indicates the higher prevalence of Ciprofloxacin-Resistant in 8 patients (29.62%). Also the second highest 1st time definitive therapy of ciprofloxacin in 24 patients (17.91%) became higher resistant.

Conclusion: from this study, we concluded that there is clinical significant microbial changing pattern while in hospital has observed. (P>0.05) is considered as significant. And also the study shows the increasing risk of 1st-time definitive therapy of ciprofloxacin and Amikacin Resistant in the aftermath days of hospitalization. Finally, the reason for microbial changing is maybe nosocomial infection and to reveal the appropriated cause for this dispute needs more studies to concentrate on this topic.

Keywords: Anti-microbial changing, Nosocomial infection

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Assessment of Clinical & Economic Impact of Clinical Pharmacist -Initiated Drug Therapy Management among General Surgery Patients

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Objectives: To assess the clinical pharmacist interventions in general surgery and to identify its impact in clinical and economic outcomes.

Methodology: A prospective interventional study was conducted for a period of 9 months in the General Surgery wards of a tertiary care hospital. All the patients admitted were reviewed on daily basis and those who met the study criteria were enrolled into the study and were followed till discharge. All the necessary data were obtained from medical records. All the necessary data was collected and reviewed to identify DRPs (Drug Related Problems) and categorized as per Hepler and Strand classification. An independent panel was convened to assess the clinical outcome of pharmacist-initiated drug therapy management. Economic outcome was assessed taking into account the direct medical cost.

Result: 471 DRPs were observed from 301 patients. Males (72.09%) were more in the study population and majority (32.23%) belonged to the age group of 60 –89 years. Suggestions were provided for 469 DRPs. Drug use without indication and improper drug selection accounted for 16.35% and 12.53% respectively. DRPs other than those in Hepler and Strand were identified wherein inappropriate duration of drug use was highest [55 (11.68%)]. The acceptance rate of pharmacist intervention was 100% and the change in drug therapy was made in 97.23%. It was found that there was 1.33% reduction in probability of readmission, 8.97% reduction in frequency of performing laboratory investigation/medical procedure and 19.6% reduction in length of stay. Clinical pharmacist interventions resulted in a net saving of Rs.2,07,134.7 in terms of direct medical cost.

Conclusion: Our study findings suggest that, clinical pharmacist as an active member of healthcare team has an enormous role to play in optimization of drug therapy and thereby improve clinical outcomes and reduce the healthcare cost.

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The influence of a short-term physicians' training course on adherence to long-term statin therapy

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Aim: To assess the effect of a training course based on recent ESC guidelines, on physicians' and patients' adherence to statin treatment and the efficacy of this therapy.

Methods: The study was multicenter prospective observational. 298 patients (pts) of high and very high cardiovascular risk were included in the study. Before study initiation, a physicians' training course based on ESC guidelines was conducted. Patients were monitored for 12 weeks with 3 visits: inclusion (V0), 1 and 3 months after V0 (V1 and V3). Initial treatment with statins at V0 and its changes at V1 and V3 were assessed. Low-density-lipoprotein cholesterol (LDL-C) levels were registered at each visit. A special questionnaire was used at V1 and V3 to assess pts' adherence.

Results: Initially, 112 (37,6%) of 298 pts did not take statins. At V0 statins were recommended to all patients. According to the special questionnaire at V1 13 pts did not start prescribed statin therapy, 7 pts started therapy, but stopped it due to various reasons. At V3 another 25 pts stopped taking prescribed statins, however, 12 pts, who initially refused to take statin therapy, started it. Overall, 262 pts were adherent and took statins from V0 to V3. Target LDL-C levels were achieved at V0 only in 11 (3,7%) pts, at V1 in 47 (15,8%) pts, at V3 in 121 (40,6%) pts. Physicians appreciated LDL-C levels as target in 16 (5,4%) pts at V0, in 67 (22,5%) pts at V1 and in 142 (47,7%) pts at V3. Dose titration was performed only in 56 pts at V1.

Conclusion: A special training course, in general substantially improved physicians' adherence to clinical guidelines. It also has a positive effect on patients' adherence to treatment. However, a number of doctors misinterpreted target LDL-C levels and showed clinical inertia in dose titration.

Keywords: a training course, physicians' and patients' adherence, statin therapy

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Effectiveness of Educational Intervention on Knowledge and Counseling Practice on Common Cold Management among Community Pharmacists

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Objective: This study aims to assess effectiveness of educational interventions on knowledge and counseling practice among community pharmacists on common cold management at Hue, Vietnam.

Methods: Thirty eight community pharmacists were invited to educational interventions including in–class training and providing of a printed pocket handbook. Knowledge was measured before and after interventions by paper test, and actual practice were assessed by pseudo customer method after intervention a week.

Results: The interventions resulted in significant improvements in knowledge of management of common cold of pharmacists ($p<0.05$). In pre – test, only 15.8%-63.2% of pharmacists had correct answer that increased to 71.1%-97.4% in post – test. By pseudo customer method, pharmacists focused on asking about identification, age and symptoms of patients (93.3%, 80.0% and 80.0%, respectively) but not about medical and medications history, and allergies (less than 20%); all pharmacist advised dosage while only about a half told about the name and indication of drugs and a third counseled drug interaction; less than 20% pharmacists conducted counseling ending. Inappropriate dispensing practice of drug included wrong drugs or selling prescription-only drugs without prescription.

Conclusion: Educational interventions were effective in improving pharmacy staff's knowledge and counseling practice. There was still a big gap between knowledge and actual practice of pharmacists.

Keywords: educational intervention, community pharmacist, knowledge, counseling, practice

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Study protocol of electronic health record nested pragmatic randomized controlled trial of reminder system for serum lithium level monitoring

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Aim/Objective: The weaknesses of classical explanatory randomized controlled trials (RCTs) include limited generalizability, high cost, and time burden. Pragmatic RCTs nested within electronic health records (EHRs) can be useful to overcome such limitations.
Serum lithium level monitoring has often been underutilized in real-world practice in Japan. This trial aims to evaluate the effectiveness of the EHR-nested reminder system for serum lithium level monitoring in the maintenance of therapeutic lithium concentration and in the improvement of the quality of care for patients on lithium maintenance therapy.

Methods: The Kyoto tOyooka Nested cOntrolled Trial Of Reminders (KONOTORI trial) is an EHR-nested, parallel-group, stratified permuted block randomized controlled trial. Screening, random allocation, reminder output, and outcome collection will be conducted automatically by the EHR-nested trial program. Patients with a mood disorder (major depression disorder and bipolar disorder) taking lithium carbonate for maintenance therapy will be randomly allocated to the two-step reminder system for serum lithium level monitoring or to usual care. The primary outcome is the achievement of therapeutic serum lithium concentration between 0.4 and 1.0 mEq/L after 18 months after informed consent. The trial was registered at the University Hospital Medical Information Network (UMIN) Clinical Trials Registry. (UMIN000033633)

Conclusion: The KONOTORI trial uses EHRs to enable the efficient conduct of a pragmatic trial of the reminder system for lithium monitoring. This may contribute to improved quality of care for patients on lithium maintenance therapy.

Keywords: electronic health record, pragmatic trial, mood disorder, lithium carbonate

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Prevalence of antiplatelet drug resistance using thromboelastography and major adverse cardiac events after coronary intervention in acute coronary syndrome patients

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Background: Patients undergoing percutaneous transluminal coronary angioplasty (PTCA) with drug eluting stent (DES) for the acute coronary syndrome (ACS) are recommended dual antiplatelet drugs (APs) for a minimum of 12 months after the procedure to prevent stent thrombosis. However antiplatelet effect may not be identical. Some patients show non-responsiveness to APs and therefore may be at risk of catastrophic events. Lab assessment of platelet response may identify patients at higher risk.

Aim/objectives: Assessment of prevalence of antiplatelet drugs resistance using thromboelastography and its correlation with major adverse cardiac events (MACE) up to 90 days.

Methods: We conducted a prospective observational cohort study in a tertiary care center in South India including adult patients with ACS who underwent primary PTCA with DES and started on dual antiplatelet therapy. Whole blood thromboelastography (TEG) with platelet mapping using arachidonic acid (AA) and adenosine diphosphate (ADP) as reagents was performed to assess the platelet response to aspirin and ticagrelor respectively within 24 hours after PTCA. MACE were observed for up to 90 days.

Results: Fifty-six patients with a mean age of 58.8±10.9 years were included of whom 72.4% were male. Nine (16.1%) patients showed a low response or no-response to ADP and 4 (7.1%) patients showed a low response or no-response to AA. Clinical MACE was seen in 6 (10.7%) of the patients, out of which 4 (66.7%) events occurred in those with abnormal platelet response to ticagrelor. Only one patient was not compliant to medications but no MACE occurred in that patient. Association between the occurrence of MACE and abnormal platelet response to ticagrelor was significant (P= 0.002). However, the association between MACE and platelet response to aspirin was not significant.

Conclusions: TEG is a relatively new investigational approach to assess the ticagrelor non-responsiveness. Abnormal platelet response detected by TEG-platelet mapping was associated with major adverse cardiac events.

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Evaluating Drug Safety of Benzodiazepine and Non-benzodiazepine Medicine with Chronic Obstructive Pulmonary Disease

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Objective: To evaluate the risk of exacerbation of chronic obstructive pulmonary disease (COPD) symptoms by benzodiazepine receptor agonists (BZRA).

Methods: This was a retrospective cohort study, national population, based on data from Taiwan's National Health Insurance Research Database for the years 2002 to 2016.From approximately 82,700 patients newly prescribed BZRA drugs after a COPD diagnosis, propensity score matching was used to create three groups according to the patient's initial prescription: benzodiazepine (BZD), non-benzodiazepine BZRA drugs (Non-BZD) and both (Mix). Each group included 2856 patients. A fourth group of patients not prescribed BZRAs (Non-user) was created for comparison. Events related to the exacerbation of COPD in the 30 days following the index date were collected, including outpatient visits for respiratory exacerbation, admission for COPD acute exacerbation admission for respiratory exacerbation, emergency department attendance for COPD or pneumonia and all-cause mortality. Poisson regression analysis was performed to evaluate the incidence rate ratios (IRRs) for the outcomes in the groups.

Results: The Non-BZD group experienced significantly fewer outpatient visits for respiratory exacerbation than the BZD group did (IRR = 0.84, 95% confidence intervals (CI) = 0.72–0.97). Compared to the Non-user group, the BZD, Non-BZD and Mix groups experienced significantly more outpatient visits because of respiratory exacerbation, with IRRs of 2.57 (95% CI, 2.13–3.10), 2.40 (95% CI, 1.97–2.94) and 3.38 (95% CI, 2.74–4.17), respectively. Similarly, they experienced more emergency department for COPD or pneumonia than the Non-user group did, with IRRs of 2.11 (95% CI, 1.48–3.02), 2.12 (95% CI, 1.46–3.09) and 1.87 (95% CI, 1.33–2.64), respectively.

Conclusions: The patients administered non-benzodiazepine BZRAs experienced 0.84-fold fewer outpatient visits for respiratory exacerbation than those administered benzodiazepine did. All the patient groups administered BZRAs showed a higher risk than non-users for COPD-related exacerbation did.

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Analysis of Individual Case Safety Reports of Drug-induced Anaphylaxis in Korea Adverse Event Reporting System Database

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Background: Drugs are the major cause of anaphylaxis especially in adults. However, little is known about the characteristics of drug-induced anaphylaxis (DIA) in Korea.

Objective: To identify causal drugs of the drug-induced anaphylaxis by using the Korea Adverse Event Reporting System (KAERS) in Korea and to check labeling information of causative agents.

Method: Among Individual Case Safety Reports (ICSRs) in KAERS from January, 2008 to December 2017, cases of drug-induced anaphylaxis were analyzed for demographics, causative agents and fatal cases resulting in death. The domestic drug labeling, Micromedex® and United States FDA (USFDA) drug package insert were reviewed to check that the labeling information of suspected causative agents contains anaphylaxis.

Results: A total of 5,873 cases of DIA were analyzed. The mean age was 49.77±18.55 years, 3,234 patients (55.1%) were females. Among 513 kinds of drugs reported as causative agents, antibiotics (27.7%) accounted the largest portion, followed by non-steroidal anti-inflammatory drugs/aspirin (18.5%), contrast media (10.8%), and antineoplastic agents (8.5%). Cephalosporins accounted for majority (60.1%) of antibiotic-induced anaphylaxis, followed by penicillins (19.3%) and quinolones (7.5%). There were 43 fatal cases (0.7%); antibiotics (8 cases), antineoplastic agents (4 cases) were the major causative drug category of mortality. Of 513 drugs reported as suspected causative agents, 103 drugs (20.1%) did not reflect anaphylaxis in domestic drug labeling and 16 drugs (3.1%) did not reflect anaphylaxis in any of three adverse drug information. In 2.5% of reported drugs, ADR information about anaphylaxis was reflected in FDA drug package insert but not in domestic labeling.

Conclusion: Analysis of KAERS 10-year data showed that antibiotic was the main cause of DIA and mortality rate was 0.7%. In 3.1% of suspected drugs, there was no mention of anaphylaxis in any of the drug labeling and in 2.5% of suspected drugs, anaphylaxis was mentioned in FDA drug package insert but not in domestic labeling information

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Drug-stimulated nephrotoxicity

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Background: Risk features of drug-stimulated nephrotoxicity comprise drug overdose, drug-drug contacts and drug-correlated undesirable effects. Since the usage of some nephrotoxic drugs is still inevitable in the medical setting, considering the pathogenic devices of their nephrotoxicities is significant to reduce the incidence of kidney damage. Early recognition of drug-stimulated nephrotoxicity and decrease of the therapeutic part effects are pragmatic approaches to evade the end stage of renal failure.

Method: In this review, we recapitulated the devices and prevention approaches for some drugs that were frequently used clinically and had the opportunity of suggesting acute and chronic kidney harms. We discussed the benefits and disadvantages of presently obtainable biomarkers for representing kidney injury. In vitro and pre-clinical in vivo models for evaluating the nephrotoxicity through the drug developmental phases were also assessed.

Results: Currently, an escalating quantity of biomarkers were found out for the premature diagnosis of kidney impairment. Besides, different types of in vitro and pre-clinical in vivo patterns were expanded and exploited to reduce the probable nephrotoxicity through the drug progress.

Conclusion: The recognition of the early biomarkers and extension of accurate diagnostic methods are competent prevention strategies for drug-stimulate kidney injury.

Keywords: Drug-stimulated nephrotoxicity; kidney function.

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Drug - stimulated Nephrotoxicity

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[1]*University of Medicine, Tirana, Albania*

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Conclusion: The recognition of the early biomarkers and extension of accurate diagnostic methods are competent prevention strategies for drug-stimulate kidney injury.

Keywords: Drug-stimulated nephrotoxicity; kidney function.

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Diabetic ketoacidosis induced by SGLT2 inhibitors

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Objectives: Diabetic ketoacidosis (DKA) is a serious adverse reaction of sodium-glucose cotransporter 2 inhibitors(SGLT2i) which may lead to life-threatening consequences. The aim of this study was to evaluate the risk of DKA in reported patients treated with SGLT2i.

Methods: We retrospectively review outpatients with drugs of the 5th ATC code (A10BK) during Jan 2016 to Dec 2018 in Chimei mendical center in Taiwan. And ADRs case in our hospital during the 2016-2018 period were collected. Descriptive analysis the reported adverse event of treated with SGLT2i.

Results: A total of 2,125 patients were treated with SGLT2i in our hospital from 2016 to 2018. And total 7 ADR cases treated with SGLT2i were collected in the study period. Futher analysis, the incidence of diabetic ketoacidosis was 0.23%(n/N=5/2125) in SGLT2i users, and the incidence of skin rash was 0.09%(n/N=2/2125).

Conclusions: The incidence of SGLT2i-associated Diabetic ketoacidosis in type2 DM is rare, but which cannot be ignored. However, frequencies of prescribing SGLT2i much increased plus DKA remains a medical emergency needed to be treated in a quick manner. Thus patients should be monitored for renal function regular in order to ensure safe use of medications.

Keywords: Type 2 diabetes, SGLT2 inhibitor, ketoacidosis, serious adverse events

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Impact of deprescribing and counseling on quality of life amongst chronic H2 Receptor Antagonists and Proton Pump Inhibitors consuming patients

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Aim: To evaluate the impact of patient counseling and deprescribing on quality of life amongst chronic H2RA and PPIs consuming patients.

Method: A prospective interventional study was carried out for a duration of 7 months from October 2018 to April 2019 in the Department of Gastroenterology, M.S. Ramaiah Hospital, Bangalore, India. Patients >18 years and consuming histamine2 receptor antagonist (H2RA) and proton pump inhibitors (PPIs) >4 weeks were included. Patient assessment of upper gastrointestinal disorders questionnaire was employed for comparing the quality of life (QoL) of patients at baseline and after 8 weeks of deprescribing. The patient assessment of upper gastrointestinal disorders (PAGI) questionnaire consists of five domains such as daily activities, clothing, diet and food habits, relationship, psychological well-being, and distress. The results obtained are compared and analyzed accordingly.

Results: Among 367 patients analyzed, there was significant improvement among the QoL of patients at baseline and after 8 weeks of deprescribing. Based on daily activities, at baseline, 124(39.28%) patients responded saying they depend on others for daily activities. After counseling for deprescribed patients, the dependency of patients reduced to 110(29.97%). Similarly, the 181(49.31%) patients experienced poor concentration at baseline and increased to 250(68.11%) after counseling. The desire of patients for participating in social events increased from 217(59.1%) at baseline to 300(81.74%) at 8th week of follow–up. The level of discomfort in constricted clothes among patients at baseline and after deprescribing is 239(65.1%) and 315(85.8%) respectively. Satisfaction at choosing desired food at baseline and after deprescribing was 241(65.66%) and 315(85.8%). Assessment of psychological disturbances among patients was found to be 315(85.8%) at baseline and it declined to 127(34.6%) after counseling.

Conclusion: QOL among deprescribed patients increased with counseling compared with baseline scores. Chronic H2RA and PPIs consumers should be monitored and counseled to improve the QoL of patients.

Keywords: PAGI-QOL, Psychological disturbances, Deprescribing, Proton Pump Inhibitors.

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Antipsychotic drugs and the risk of diabetic complications: a systematic review

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Aim/Objective: Antipsychotic drugs (APDs) are prescribed to treat psychotic disorders and other conditions. In recent years, case reports and epidemiological studies have reported a potential association between APDs and diabetic complications, namely diabetic ketoacidosis (DKA) and hyperglycaemic hyperosmolar state (HHS). The objective of this systematic review is to examine the association between typical and atypical APDs and the risk of DKA and/or HHS.

Methods: A systematic literature search was conducted in MEDLINE, EMBASE, PsycINFO and the Cochrane Central Register of Controlled Trials databases to identify case reports and epidemiological studies that assessed the association between APD use and at least one of the outcomes of interest among all ages. Two reviewers independently screened articles for inclusion using a two-stage process. Only studies published in English or French were eligible for inclusion.

Results: The research strategy identified 1,171 potentially relevant references. In total, 108 case reports, 13 observational studies and 2 randomized controlled trials (RCTs) were included in the systematic review. Of the case reports, 88 cases of DKA and 20 cases of HHS potentially linked to the use of APDs were noted. Overall, 94 cases were known to be treated with an atypical antipsychotic, of which 42% used olanzapine monotherapy. In total, 12 observational studies and 2 RCTs found evidence of an association between the use of APDs and different outcomes, including DKA and HHS. For epidemiological studies, detailed summaries of the findings will be presented. Results will also be stratified by exposure, outcome and patient population.

Conclusions: Initial analyses of included studies suggest a potential association between APDs and diabetic complications. A critical appraisal of case reports and detailed findings of epidemiological studies will provide a better understanding of existing risks and will contribute to the need for informed clinical decisions when using APDs in certain patient populations.

Keywords: Antipsychotic drugs, Diabetic ketoacidosis, Hyperglycemic Hyperosmolar State

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Investigation of drug-induced hearing loss using the Japanese Adverse Drug Event Report database

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Aim/Objective: Hearing loss causes language delays in children and is considered a serious issue. Moreover, it has been identified as a potentially modifiable risk factor of dementia in midlife. Administration of drugs accounts as one of the reasons for hearing loss. This study aimed to investigate drug-induced hearing loss through analysis of the data reported in the Japanese Adverse Drug Event Report (JADER) database.

Methods: Data reported in the JADER database from April 2004 to March 2018 were extracted. Preferred Terms (PTs) that belong to "Hearing and vestibular disorders" (Standardised MedDRA Queries (SMQ): 20000170; MedDRA/J version 22.0) were used as terminology associated with drug-induced hearing loss. Patient background, outcomes, number of adverse event reports, and reporting odds ratio (ROR) of drugs were aggregated and/or calculated.

Results: A total of 1,773 cases included PTs associated with drug-induced hearing loss. Regarding patient background, the male-female ratio was balanced (42.7% for men vs 52.3% for women) and the frequency of reports was high in elder patients (18.1% for patients in their 60s and 18.0% for those in their 70s). For the outcomes reported, "unknown" and "recovery" were confirmed with high frequencies of 36.3% and 23.8%, respectively. Drugs with large report number as "suspect drug" and high ROR value were detected as follows: Ribavirin (80 cases, ROR 2.6 [95% confidence interval: 2.1–3.2]), Furosemide (74 cases, ROR 9.2 [7.3–11.6]), Cisplatin (69 cases, ROR 2.6 [2.1–3.4]), and Recombinant bivalent human papillomavirus vaccine (69 cases, ROR 5.2 [4.1–6.6]).

Conclusion: The detected drugs were expected to induce hearing loss; therefore, attention should be paid to use these drugs carefully. Owing to the incomplete outcome, this study did not clarify whether this drug-induced hearing loss is transient or curable. Further research is needed to investigate other data, including those from a hospital information system.

Keywords: JADER, Hearing loss

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Evaluation of warfarin usage and INR control in a hospital in Taiwan: A retrospective study.

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Objective: With the development of novel oral anticoagulants, there is more anticoagulants choice in the clinic, but warfarin still has its role in treatment. This study is to understand the usage of warfarin and INR control for outpatients in a regional hospital in Taiwan.

Methods: This retrospective study analyzed gender, age, diagnosis, INR control and the frequency of monitoring INR by descriptive statistics in Microsoft Excel. The study further analyzed for patients with abnormal INR.

Results: The study included 62 outpatients over a six-month survey period based on study criteria. There were 53 % (n=33) male and 47 % (n=29) respectively. The mean age of 62 patients was 69.8 year-old. Among the patients we surveyed, the most common diagnoses were atrial fibrillation and atrial flutter. During the survey period, the most monitor frequency of INR were 3 times (27.42%, n=17) and 4 times (24.19%, n=15) respectively. The average of INR was 1.82 ± 1.05. 43.84% remained INR range<1.5. 29.56% remained INR range of 1.5-2.0. There were 13 INR abnormal events (INR>3), with an average of 5.1 drugs use at the same time. Analyzed all the drugs combined with warfarin. 7 drugs had drug-drug interaction with warfarin. 3 of them would increase the bleeding rate or increase INR, 3 would decrease anticoagulant function, and 1 had nothing to do with coagulation.

Conclusion: This study revealed that although most of the patients monitor INR regularly, still 73.4% of patients with atrial fibrillation control INR lower than international guideline instructions. This might be due to population, age, weight, diet, etc. All care givers should pay more attention on effectiveness to avoid under-dosing and therapeutic failure. Pharmacists should also adjust the dosage of warfarin person by person and give complete patient education to enhance medication safety.

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Risk of malignant lymphoma in patients with rheumatoid arthritis treated with biological disease-modifying antirheumatic drugs and methotrexate

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Objective: Malignant lymphoma is one of the serious adverse drug reactions of methotrexate therapy. Additionally, increased risk of malignant lymphoma is of particular concern in patients with rheumatoid arthritis treated with biological disease-modifying antirheumatic drugs (bDMARDs) because of their immunosuppressive effect. The combined use of bDMARDs and methotrexate is recommended in the world. However, it is unclear if bDMARDs further increase the risk of malignant lymphoma in patients with rheumatoid arthritis treated with methotrexate. This study investigated whether using bDMARDs further increase the risk of malignant lymphoma in patients with rheumatoid arthritis undergoing methotrexate therapy using spontaneous adverse reaction databases in different countries.

Methods: Patient data were acquired from the US Food and Drug Administration's Adverse Event Reporting System (FAERS), the Japanese Adverse Drug Event Report (JADER), and the Canada Vigilance Adverse Reaction Online Database (CVARD) from the first quarter of 2004 to the end of 2015. Data subset analysis was performed to investigate whether the use of bDMARDs further increased the risk of malignant lymphoma in patients receiving methotrexate therapy. The reporting odds ratio (ROR) and information component (IC) were used to detect spontaneous report signals.

Results: The FAERS subset data indicated a significant association between Hodgkin lymphoma and methotrexate with infliximab [ROR: 8.28. 95% CI: 5.70–12.02; IC: 2.04, 95% CI: 1.59–2.49]. In addition, signal scores suggested that methotrexate with infliximab (ROR: 3.26. 95% CI: 2.68–3.98; IC: 1.31, 95% CI: 1.04–1.58) was significantly associated with non-Hodgkin lymphoma (NHL). The CVARD subset data also indicated a significant association between NHL and methotrexate with infliximab (ROR: 22.82. 95% CI: 5.02–103.78; IC: 1.77, 95% CI: 0.13–3.41). However, the JADER subset data revealed no significant associations.

Conclusion: The present study shows that using infliximab further increases the risk of malignant lymphoma in patients receiving methotrexate therapy.

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Identification of Background Factors Affecting the Risk of Specific Adverse Drug Reactions in Patients Receiving Dipeptidyl Peptidase 4 Inhibitors

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Aim/Objective: Spontaneous reporting is widely used to identify adverse drug reactions (ADRs), but relatively little is known about the relationships between specific ADRs and background factors of affected patients. Currently, nine dipeptidyl peptidase 4 (DPP-4) inhibitors are marketed in Japan as anti-diabetic agents. Since the differences in their ADR profiles are unclear, the aim of this study was to apply latent class analysis (LCA) to identify background factors that might be associated with adverse events in patients taking DPP-4 inhibitors.

Methods: We selected all cases of patients using only a DPP-4 inhibitor who encountered adverse events that were reported in the Japanese Adverse Drug Event Report (JADER) database up to April 2019 (N=3577). LCA was adopted to classify these cases based on underlying diseases and lifestyle factors (alcohol, tobacco, diet, and exercise) and to identify characteristic ADRs in each class. The number of classes was decided by selecting the model with the lowest value of the Bayesian information criterion (BIC).

Results: A model with six classes had the lowest BIC and was selected as the best, at least for this dataset. The classes were characterized by specific background factors and ADRs. For example, one class included diabetes complications, while another class included exercise and diet as background factors. Increased risk of a specific ADR(s), such as pancreatitis or pemphigoid, was found in each class. The nine DPP-4 inhibitors were not uniformly distributed among the classes, though individual classes included patients receiving different inhibitors.

Conclusion: Our methodology grouped DPP-4 inhibitor users who encountered ADRs into six classes based on their background factors, and each class was associated with distinct ADR(s). Thus, it should be possible to estimate the risk that patients who are receiving a certain DPP-4 inhibitor will encounter a specific ADR by analysis of the patients' background factors.

Keywords: Spontaneous reporting, latent class analysis, JADER, background factors

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Patterns of spontaneous adverse event reporting following HPV vaccination in Korea and the United States

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Objective: To compare the adverse event following immunization (AEFI) reporting patterns of human papilloma virus (HPV) vaccines.

Methods: We analyzed Korea adverse event reporting system (KAERS) and vaccine adverse event reporting system (VAERS) database involving HPV vaccines between 2008 and 2017. The demographic characteristics of individual case safety reports (ICSRs) and proportion of serious AE reports were compared between KAERS and VAERS. Patterns of AEs were categorized into (1) vaccine reaction, (2) immunization error-related reaction, and (3) immunization anxiety-related reaction according to the report of CIOMS/WHO. We defined anxiety-related reactions as preferred terms (PTs) related to syncope or hyperventilation (46 PTs in WHO-ART for KAERS, 21 PTs in MedDRA for VAERS). Chi-square tests were performed to examine differences in proportions of characteristics or AEs between KAERS and VAERS.

Results: The number of ICSRs including HPV vaccines was 3,124 and 38,466 for KAERS and VAERS, respectively. Reports for male were 1.2% and 15.0%, and reports for cases aged under 19 years were 13.0% and 52.5%, in KAERS and VAERS. HPV vaccine and all other vaccines had similar serious AE proportions in ICSRs in both Korea (7.8% vs. 8.3%) and the US (27.3% vs. 29.3%). Of the three AEFI types, error-related and anxiety-related reactions were more reported in VAERS (7.0%, 9.1%) than in KAERS (3.2%, 5.7%) (both of $p<0.0001$). The most frequently reported system organ classes were injection site reactions, nervous system disorders, and skin disorders in both KAERS and VAERS. Reproductive disorders were reported more frequently in KAERS (4.7%) than in VAERS (1.3%) ($p<0.0001$).

Conclusion: Although the demographic characteristics of the KAERS and VAERS reports were different, patterns of reported AEs related to vaccine reaction were similar. However, immunization error-related or anxiety-related reactions were reported less in Korea. Differences of AE terminology system and AEFI reporting system should be considered.

Keywords: Vaccine, Human Papilloma Virus Vaccine, Adverse event following immunization, Pharmacovigilance

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Selective serotonin reuptake inhibitor use and brain hemorrhage: systematic review and meta-analysis

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Background: The use of antidepressants has been steadily increasing worldwide. The Selective Serotonin Reuptake Inhibitor (SSRI) has become one of the most broadly used medications in psychiatry. SSRI may have an impact on hemostasis related to serotonin, and thus increase the risk of brain hemorrhage. However other antidepressants were also regulated by serotonin. A number of cerebral hemorrhage have been reported, however, study results have not been consistent. In addition, comparative studies between antidepressants are very limited.

Objectives: To investigate the association between SSRI use and brain hemorrhage.

Methods: We identified relevant articles from the databases (MEDLINE, EMBASE, CINAHL, and PsycINFO). Observational studies comparing SSRI with non-use and other antidepressants. We assessed methodological quality based on ROBINS-I. Pooled effect estimates were obtained by meta-analysis using random-effects model. Heterogeneity of results was evaluated by Higgins statistics. Publication bias was also examined by funnel plot and Egger test.

Results: Seventeen relevant studies were finally included in this study. In case of SSRI compared to non-use, the result was statistically significant (adjusted RR (aRR) 1.43, 95% CI 1.09-1.88). The aRR was 1.17 (95% CI 1.02-1.34) between SSRI and brain hemorrhage compared to tricyclic antidepressant (TCA). The brain hemorrhage was increased compared using serotonin reuptake inhibitors and non-use (aRR 1.36, 95% CI 1.11-1.68). And brain hemorrhage also associated with high/intermediate serotonin inhibition groups compared to low inhibition group (aRR 1.45, 95% CI 1.05-1.99).

Conclusions: SSRI use showed increased risk of brain hemorrhage compared to non-use and TCA. And relative risk increased according to the serotonin reuptake inhibitors. For patients with high risk of brain hemorrhage prescribing antidepressants other than SSRI and higher 5-HT reuptake inhibition groups can be recommended.

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Association between methylphenidate/atomoxetine use and long-term cardiovascular risk in pediatric patients with attention-deficit and hyperactivity disorder.

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Aim/Objective: Evaluate whether methylphenidate and atomoxetine use is associated with long-term cardiovascular risk.

Methods: We included newly diagnosed ADHD patients aged 3 to 18 years between 2004 and 2017 from the Health and Welfare Database in Taiwan. All patients were required to have at least 3 years of follow-up duration. Patients who were pregnant or had cancer during study period were excluded. Patients were separated into three groups: methylphenidate users, atomoxetine users, and non-ADHD-medication users. Two exposure status were assessed: initial treatment ≥ 7 days and ≥ 180 days. Methylphenidate and atomoxetine users was compared to non-ADHD-medication users respectively by one-to-one propensity score matching.

Studied outcome included acute cardiovascular events, which were acute coronary syndrome, stroke events, cardiogenic shock, cardiogenic death and all-cause mortality. We also evaluated the risk of chronic CV disease including hypertensive disease and coronary artery disease. Cox proportional hazards model and Kaplan-Meier Method were used to estimate cardiovascular risk. We performed both of the intention to treat (ITT) and as treated (AT) analysis. Patients were censored in the AT analysis if they discontinued their initial treatment for more than 90 days, switched medications, or reached the end of the study (December 31st, 2017). We also performed a subgroup analysis in patients with congenital heart disease. Association between the cumulative doses within 180 days after treatment initiation and cardiovascular risk will also be evaluated.

Expected results: Compare to non-ADHD-medications users, we expect patients who exposed ADHD treatment for more than 7 days have higher risk of acute CV events. For patients who exposed for more than 180 days, we expect to detect the tendency of higher chronic CV disease risk.

Conclusion: Several studies have evaluated the association between ADHD medications and the risk of acute CV events. More evidence on long-term ADHD medications uses and chronic CV disease remains needed.

Keywords: methylphenidate, atomoxetine, ADHD, cardiovascular safety

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Antiretroviral Therapy and Lactic acidosis: Risk Quantification using Disproportionality analysis in USFDA Adverse Event Reporting System (FAERS)

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Aim: Lactic acidosis is a serious condition with poor prognosis. Antiretroviral drug class has previously been attributed to lactic acidosis. This study aimed to quantify the risk of lactic acidosis associated with individual antiretroviral drugs using disproportionality analysis of USFDA Adverse Event Reporting System (FAERS).

Methods: An analysis was performed using publicly available FAERS data from January 2010 through May 2019. Rates of lactic acidosis were calculated for each antiretroviral drug. Reporting Odds Ratios (ROR) and Proportional Reporting Ratios (PRR) with 95% confidence intervals (CIs) were computed.

Results: A total of 10,088 reports for lactic acidosis have been reported in the FDA database. Amongst which 702 (6.95%) reports were associated with antiretroviral drugs. The antiretroviral drugs with the highest risk estimates were Stavudine (ROR 30.15, 95% CI 18.28-44.92; PRR 29.29, 95% CI 17.93-43.04), Didanosine (ROR 29.04, 95% CI 12.42-47.74; PRR 28.19, 95% CI 12.09-45.76) and Saquinavir (ROR 22.40, 95% CI -0.165-54.14; PRR 21.78, 95% CI 0.60-49.27). Nevirapine had a ROR of 9.03 (95% CI 5.81-17.77) and PRR 9.0 (95% CI 5.76-17.70). Efavirenz (ROR 7.2, 95% CI 4.13-14.13; PRR 7.2, 95% CI 4.14-14.06), Lamivudine (ROR 5.21, 95% CI 2.98-10.43; PRR 5.24, 95% CI 2.96-10.62), Abacavir (ROR 5.70, 95% CI 3.06-11.10; PRR 5.7, 95% CI 3.07-11.04) and Ritonavir (ROR 3.01, 95% CI 2.49-5.92; PRR 3.03, 95% CI 2.51-5.99) had lower risk for lactic acidosis when compared to other antiretroviral drugs.

Conclusion: Among antiretroviral drugs, Stavudine, Didanosine and Saquinavir have a higher risk for lactic acidosis. Increased awareness of this risk among healthcare professionals, particularly variations in risk among different antiretroviral drugs may help reduce the severity and number of adverse events.
Keywords: Antiretroviral Therapy, Lactic acidosis, FAERS

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Incidence of proton pump inhibitors induced fundic gland polyps based on endoscopic findings: a prospective study

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Aim: To assess the frequency of Proton Pump Inhibitors (PPIs) induced fundic gland polyps among patients with Functional Dyspepsia (FD)

Methods: A prospective observational study was conducted in the Department of Gastroenterology, M.S. Ramaiah Memorial Hospital for a period of 8 months from August 2017 to March 2018. The study was conducted in accordance with the permission granted by the Institutional Ethics Committee. All patients consuming PPI for functional dyspepsia, aged more than 18 years and visited the outpatient clinics for the upper gastrointestinal endoscopy procedure were included in the study. Fischer's exact test and odds ratio were used to find the association between the long term use of PPI and the occurrence of polyps.

Results: A total of 745 patients underwent upper endoscopy were included in the study. Among them, 113 (15.1%) patients were on PPI for varied durations. Regardless of diagnosis, the patients were interviewed about their past medical and medication history. Among them, 113 (15.16%) were on PPI therapy. The endoscopies revealed that 6 (5.3%) out of 113 patients on PPI, had FGPs. In contrast, only 5 (0.79%) out of 632 without PPI use had FGP. Fischer's exact test revealed a significant association of FGP with PPI use and female gender and no significant association was found with age and duration of therapy. Amongst the 6 PPI induced polyps cases, 5 (83.33%) were found to be females. The average age distribution was found to be 52 years and average PPI consumption was 6.3 years (Mean = 1.83 years, SD = ± 0.84). The commonly used PPI included pantoprazole, omeprazole, and esomeprazole respectively. The odds ratio revealed seven times more risk of FGP in PPI users.

Conclusions: Long term use of PPI more than 12 months and female gender is a risk factor for the development of FGP.

Keywords: Proton Pump Inhibitors, Fundic gland polyps, Functional Dyspepsia, Endoscopy.

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Attitude and willingness of residents towards deprescribing to minimize drug related problems

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Objectives: Deprescribing is a newly emerging concept which helps to reduce drug-related problems, Adverse Drug Reactions (ADRs), pill burden and polypharmacy. Though the concept of deprescribing is beneficial to older adults, the attitude of old age home residents towards deprescribing is essential to implement it in clinical practice. The current study aimed to identify the attitude of old age home residents on deprescribing.

Methods: The study included 560 patients belonging to 24 old age homes located at Bangalore and Mangalore, Karnataka, India. It is a questionnaire based observational study carried out from October 2017 to April 2018. A 10-item Patients' Attitude Towards Deprescribing (PATD) questionnaire was employed for the study.

Results: Among the 560 prescriptions analyzed, 67 patients had prescriptions with polypharmacy. 271 (48.75%) were males and 289(51.6%) were females. Of all, 85(15.1%) residents strongly agreed and 190(33.9%) residents agreed to reduce one or more medications consumed to be deprescribed if their physician ensures it to be possible. 11(1.9%) strongly agreed and 12 (2.1%) agreed that the side effects they experienced may be due to one or more of their medications. 45(67.1%) individuals were willing to stop one or more of their medications due to financial constraints.

Conclusion: Deprescribing interventions were likely to be acceptable by the old age home residents, with a high willingness to discontinue medicines, if doctors say it is possible. The study emphasizes the residents' belief towards their physicians and the responsibility of physicians towards the process of deprescribing.

Keywords: Deprescribing, Old age home residents, Attitude, PATD questionnaire

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The study of local anesthetics` safety in electronic database of adverse drug reactions reports occurred in Crimea Republic in 2010-2018.

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The effectiveness and safety of surgical treatment depend largely on the painlessness of the interventions. Local anesthesia, which allows to prevent pain without turning off the consciousness and keep contact with the patient, is the most convenient and safe method of pain control.

The aim of the study was to study the adverse reactions (ADR) associated with the use of local anesthetics (LA) occurred in patients living in the Crimea in 2010-2018.

Materials and methods: In this work, we used the data of ADR reports received by local Pharmacovigilance office of the Republic of Crimea.

Discussion: There were 124 cases of ADR recorded for the LA group. Most often, the LA ADRs were associated with the injection of Lidocaine - 69 cases (55.7%) and Articaine in the combinations - 36 cases (29%). More rarely, ADRs were associated with the use of Procaine - 9 cases (7.3%), Bupivacaine - 8 cases (6.4%) and Mepivacaine - 2 cases (1.6%). The main clinical manifestations of ADRs were immediate-type hypersensitivity reactions (34 cases, 27.4%), among which there were 13 cases of anaphylactic shock and 2 cases of angioedema. In 29 cases, the use of LA caused disturbances of the cardiovascular system and hemodynamic disorders (weakness, dizziness, and pallor), in 19 cases resulted in central nervous system disturbances. It is important that the administration of LA in 2 cases caused the death of patients, in 34 cases it caused life-threatening ADRs, and hospitalization or prolongation of hospitalization was observed in 7 cases. It is worth noting that in most cases (85 cases, 68.5%), the development of ADRs required medical correction.

Conclusion: The results of our study confirm previous findings that the use of LA is quite often associated with the development of vasovagal reactions, which mistakenly perceived and then reported by doctors as allergic reactions.

Keywords: adverse reactions, local anesthetics, allergy.

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Adverse effects of Fluoroquinolones: a retrospective cohort study in a tertiary health-care facility

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Objective: The purpose of the study was to investigate the incidence and risk factors for Fluoroquinolones induced adverse drug reactions in comparison with other antibiotics use.

Method: A retrospective cohort study was conducted over 7 months; patients who were prescribed with Fluoroquinolones were selected as study cohort (SC; n= 482) and those without Fluoroquinolones were reference cohort (RC; n=318).

Results: The results showed 41 (8.5%) patients developed adverse drug reactions in the SC, whereas 13 (4.1%) patients developed adverse drug reactions in the RC. With oral and parenteral routes of administration, almost similar number of adverse drug reactions was observed. Levofloxacin caused highest number of adverse drug reactions and were reported especially with 750 mg dose. Based on multiple logistic regression model, Fluoroquinolones use (OR:2.27; 95% CI: 1.18-4.39; p=0.015) and concomitant steroid use (OR:3.19; 95% CI:1.31- 7.79; p= 0.011) were identified as independent risk factors for development of adverse drug reactions among antibiotic users, whereas, age was found to be protective (OR:0.98; 95% CI:0.97-1.00; p=0.047).

Conclusion: The study concludes a harmful association between Fluoroquinolones use and development of adverse drug reactions. Moreover, Fluoroquinolones are not safe compared to other antibiotics, hence, use of Fluoroquinolones should be limited to the conditions where no other alternatives are available.

Keywords: Adverse effects; Drug safety; Fluoroquinolones; Pharmacovigilance

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Feasibility assessment of a study for hepatitis-C patients using MID-NET as an early experience of the new database.

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Aim/Objective: MID-NET (Medical Information Database NETwork), a hospital-based database in Japan, has been accessible since APR-2018 to facilitate the evaluation of drug safety. Little is known about the specific data available in MID-NET, such as sample size, representativeness, completeness of variables, etc. We plan to perform a descriptive analysis before conducting a formal study on hepatitis-C virus (HCV) infected patients using MID-NET.

Methods: MID-NET is structured from electronic medical records, containing information on procedures, drugs, laboratory results, and claims data from both inpatient hospitalizations and outpatient encounters/visits to hospital clinics. Data from 21 participating hospitals captured from 01-SEP-2013 to 31-DEC-2018 will be used. The study population includes patients diagnosed with HCV, aged 18+ years and new initiators of interferon (IFN)-free direct acting antivirals (DAAs), including grazoprevir/elbasvir, from SEP-2014 to 31-DEC-2018. DAA index date will be defined as the first prescription written. Patients with a recorded prescription for DAAs within 360 days prior to the index date will be excluded. Evidence of hepatitis B virus (HBV) infection screening test within 360 days prior to the index date will be assessed. Data will be descriptively summarized for patient demographics (gender, age, BMI, etc.) and clinical characteristics (hepatic and renal conditions, etc.). A trend of a performance assessment for a HBV screening test prior to DAA index date will be conducted.

Results: It is estimated that N=5,000 HCV patients will be included in this analysis. As the data are now being analyzed, summary information will be presented on the analytical cohort. Descriptive results will assess the quality and completeness of MID-NET for use in a future pharmacoepidemiologic study.

Conclusion: This analysis will descriptively assess the feasibility of using the MID-NET data source to evaluate IFN-free DAA use among HCV-infected patients, and therefore there will be no conclusive findings.

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Improving diabetes drug adherence using accurate information delivery to patients using drug dispensing history while securing patient's identity anonymity

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Aim/Objective: Harmo, electronic medicine notebook, was built as a tool to obtain information while maintaining anonymity of patients

Methods: Not only just a single direction of display medicine information to patients but also enable patients to feedback to Harmo while the system keeps sending information in a form of anonymity.
In order to investigate the implementation possibility, it grasps the descriptive statistical actual condition of the Harmo smartphone application users (patients).

Results: As a result of the physically separation of personal data storage and medicine information storage built in system design, an interactive questionnaire is possible while anonymity is still maintained.
As a QoL pilot survey targeted to patients who registered has condition of atopic, diabetes and allergic diseases, 5% of patients responded to pilot survey within 12 hours, and the next phase can be implemented.

Conclusion: Although patient’s personal information is retained as anonymity, Harmo system allowed communication with targeted patients directly via its smartphone application.
As a post-implementation attempt, we plan to publish the findings on diabetes drug adherence improvement.

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Novel adverse events of Bedaquiline: a disproportionality analysis in USFDA Adverse Event Reporting System database (FAERS)

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Aim/Objective: Signal detection is one of the most advanced and emerging field in pharmacovigilance. It facilitates early Adverse Drug Reaction (ADR) detection. The US Food and Drug Administration (FDA) on 28 December 2012 approved bedaquiline for multidrug-resistant tuberculosis. It is that first FDA-approved tuberculosis drug in 40 years. This study aimed to identify the signal strength for bedaquiline associated Adverse Events (AEs) using data mining technique in FAERS.

Methodology: Publicly available FAERS database was used for analysis. Most commonly used data mining algorithms, Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR) were selected for the study. A value of ROR-1.96SE>1 and PRR≥2 were considered as positive signal.

Results: The database had a total of 399 reports for bedaquiline. Amongst which 41% of reports were associated with females and 59% with males. 74.7% of reports were reported by physician, 16.8% by other health care professionals, 4.3% by pharmacists and 4.3% by consumers. Positive signals were obtained for ototoxicity (PRR: 218.96; ROR: 220.81), blood disorder (47.03; 47.87), hypomagnesemia (26.80; 27.23), optic neuritis (25.83; 26.17), psychotic disorder (12.67; 12.93), hypokalemia (12.46; 12.80), anemia (10.73; 12.02), mental disorder (6.90; 6.98), acute kidney injury (4.48; 4.56), seizure (4.24; 4.30), pulmonary embolism (2.52; 2.54), sepsis (2.50; 2.52) and renal failure (2.02; 2.03).

Conclusion: The present study suggests that bedaquiline may be associated with these AEs, although a causal relationship cannot be definitively established. Further pharmacoepidemiologic studies are necessary to confirm this conclusion and to improve the precision of the prevalence and/ or the risk factors of AEs.

Keywords: Bedaquiline, FAERS, Adverse events

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When the safety profile of the drug is well-characterized?

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Aim: International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) released the E19 draft guideline “Optimisation of Safety Data Collection” in 2019. The draft guideline provides an optimized approach to safety data collection (selective safety data collection) in some late-stage pre-approval or post-approval studies when the safety profile of a drug is sufficiently characterized. The objective of this study is to evaluate the reasonable number of patients to conduct selective safety data collection in a clinical trial based on simulations.

Methods: We performed Monte Carlo simulations to evaluate the empirical power of 95% confidence interval by increasing sample size from the view point of incidence rate or risk difference of adverse events (AEs), respectively. In the simulations, we assumed that incidence rates were 1, 3, or 5% as the common AEs, respectively.

Results: The simulations based on incidence rate showed that when a sample size exceeds 1000 patients, further accrual of data did not yield more information for the safety profile. The simulations based on risk difference showed similar results of those based on incidence rate. Moreover, we graphically displayed relationships between sample sizes and 95% confidence intervals in incidence rates or risk differences, respectively.

Conclusion: Our study found that applying the simulations can contribute to estimate the optimum sample size for the use of selective safety data collection. However, it is important to pay attention to the fact that the optimum sample sizes were depended on the assuming situations, e.g. the character of a drug, the population in clinical trials. Furthermore, not only the amount of data accumulation but also qualitative issues should be considered when deciding on the transition to selective safety data collection.

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The potential beneficial effects of low-dose aspirin on gastrointestinal cancers: a population-based cohort study in Hong Kong

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Aim/Objectives: The study aimed to evaluate the association between the long-term use of low-dose aspirin and the risk of colorectal cancer (CRC), gastric cancer (GC) and esophageal cancer (EC) in Hong Kong. In addition, to examine the case-fatality of CRC, GC and EC cases among the study cohort.

Methods: A retrospective population-based cohort study was conducted using the Clinical Data Analysis and Reporting System (CDARS) to investigate the association between the long-term use of low-dose aspirin and gastrointestinal (GI) cancers. Patients prescribed low-dose (75-300mg/daily) aspirin between January 2004 and December 2008 were compared to non-users. The primary outcome was the first diagnosis of GI cancer (either CRC, GC, or EC). Secondary outcome was the case-fatality for all three types of cancer mentioned above. Propensity score matching in a 1:1 ratio was used to control for potential confounding including; demographics, comorbidities, and medications. Poisson regression was used to calculate the incidence rate ratio (IRR) with 95% confidence interval (CI).

Results: The median (IQR) follow-up was 9.8 (6.7) years for aspirin users and 10.4 (6.5) years for non-users. The incidence rate of CRC, GC, and EC was 20.16, 5.53, and 2.07 per 10,000 person-years respectively for aspirin users. Aspirin use was associated with a reduced risk of all three types of cancer (CRC: IRR = 0.87 [0.81-0.93]; GC: 0.82 [0.76-0.96]; EC: 0.79 [0.65-0.95]). The case-fatality of CRC, GC, and EC was 28.63%, 44.91%, and 56.79% respectively for aspirin users. As for the non-user group, case-fatality was 30.97%, 51.06%, and 51.95% for CRC, GC, and EC respectively.

Conclusion: The long-term use of low-dose aspirin was associated with a reduced risk of CRC, GC, and EC among the study cohort. Further investigation in the safety of long-term use of low dose aspirin is warranted for a benefit-risk assessment.

Keywords: Aspirin, gastrointestinal cancer, cancer prevention, drug repurposing

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How much evidence is needed before we conclude against the use of oxygen therapy in acute myocardial infarction?

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Background: Oxygen therapy (OT) has often been used for the treatment of patients with acute myocardial infarction (AMI). However, the evidence from randomized control trials (RCTs) on the use of OT in AMI is conflicting and many recent systematic reviews have explored to summarize the evidence.

Aims: To synthesize the evidence from systematic reviews published in the last five years assessing the benefit and harm associated with OT for the treatment of AMI.

Methods: We searched the PubMed, Embase, Cochrane, and Epistemonikos databases (for last five years) for systematic reviews assessing OT for AMI patients. Reviews including Acute Coronary Syndrome (ACS) population were excluded; reviews specifically focusing on AMI population were included. Two researchers independently performed the assessment for inclusion, quality assessment (AMSTAR), and data extraction.

Results: Eight systematic reviews (7 non-Cochrane, 1 Cochrane) qualified for inclusion. The included systematic reviews comprised 4-8 RCTs, of total nine unique RCTs included across the systematic reviews, with a patients population ranged 871-7998. Included RCTs were published from 1976 to 2017. Majority of the reviews (5) were of medium or high quality. Across reviews, OT did not show improvement in key outcomes of all-cause mortality, recurrent ischemia/MI, and pain. In contrast, OT was associated with an increased rate of recurrent MI, longer average hospital length of stay, and a trend in increased mortality.

Conclusions: Evidence from the recent systematic reviews, and constituting primary studies, unanimously confirms the uncertainty around the perceived beneficial effect of OT while its harmful effect cannot be ruled out for the patients with AMI. The finding support retiring the use of OT in AMI, until a well-conducted, high-quality RCTs suggests otherwise.

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Data sources supporting food and drug administration drug safety communications

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Objectives: Drug safety communications (DSC) are the primary tool used by the Food and Drug Administrations (FDA) for conveying important new safety information to patients and healthcare professionals. We aimed to describe the sources of initial safety signals triggering DSCs. A secondary aim was to explore potential associations between DSC source and characteristics of trials supporting the label, regulatory approval pathways and subsequent drug label changes.

Methods: We reviewed all DSCs posted on the FDA website between January 2010 and December 2018. Associations between sources of initial safety signals and initial approval regulatory pathways, time between initial approval and DSC posting, number, design and sample size of clinical studies included in the most recent drug labels prior to DSC publication, subsequent safety-related drug labels modifications and requirement for Risk Evaluation and Mitigation Strategy were explored using Fisher's exact test for categorical variables and T-test for continuous variables. Trend for the number of DSCs published each year was assessed using Pearson's correlation.

Results: A total of 259 DSCs were included. The median time from initial approval to DSC posting was 14.2 years (interquartile range 5.3-27.2). The most frequent sources of initial safety signals were the FDAs Adverse Event Reporting System (FAERS) (n=110, 42%) and post-marketing randomized controlled trials (RCTs) (n=82, 32%). The most frequent subsequent drug label changes were additional warnings and precautions (n=116, 45%) and boxed warnings (n=43, 17%). There were no statistically significant associations DSC source and trial characteristics supporting approval, approval pathway and subsequent label changes. The number of DSCs decreased over time (correlation -0.78, p=0.01).

Conclusions: The most frequent sources leading to DSCs were the FAERS and post-marketing RCTs highlighting the importance of post-marketing RCTs for identification of previously unrecognized safety issues and reporting to pharmacovigilance programs.

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Effect of interaction between tacrolimus and mammalian target of rapamycin inhibitors on risk of non-Hodgkin lymphoma and non-melanoma skin cancer

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Objective: Tacrolimus and mammalian target of rapamycin inhibitors (mTORis) are immunosuppressive drugs widely used to prevent graft rejection after transplantation. However, patients receiving immunosuppressive therapy have increased risks of non-Hodgkin lymphoma (NHL) and non-melanoma skin cancer (NMSC). Tacrolimus is associated with higher NHL and NMSC risks. Meanwhile, mTORis are also used in anticancer therapies and are expected to prevent NHL and NMSC. However, whether mTORis decrease the risk of NHL and NMSC in patients treated with tacrolimus remains to be clarified. This study investigates the association between mTORis (sirolimus and everolimus) and NHL or NMSC in patients treated with tacrolimus using data mining of the spontaneous adverse reaction database.

Methods: Patient data were acquired from the US Food and Drug Administration's Adverse Event Reporting System from the first quarter of 2004 to the end of 2017. Reporting odds ratio (ROR) and information component (IC) were used to detect spontaneous report signals.

Results: Significant associations were detected between tacrolimus and NHL (ROR: 8.61, 95% CI: 7.91–9.38; IC: 3.01, 95% CI: 2.88–3.13) and between tacrolimus and NMSC (ROR: 4.40, 95% CI: 3.99–4.84; IC: 2.09, 95% CI: 1.95–2.22). In the subset data analyses using the adverse event report of tacrolimus, no significant associations were observed between NHL and sirolimus (ROR: 0.92, 95% CI: 0.63–1.34; IC: −0.11, 95% CI: −0.64–0.42) and between NHL and everolimus (ROR: 0.86, 95% CI: 0.51–1.44; IC: –0.20, 95% CI: −0.92–0.52). However, significant associations were observed between NMSC and sirolimus (ROR: 3.15, 95% CI: 2.41–4.10; IC: 1.43, 95% CI: 1.06–1.81) and between NMSC and everolimus (ROR: 1.89, 95% CI: 1.25–2.86; IC: 0.82, 95% CI: 0.24–1.41).

Conclusion: The present study shows that use of mTORis further increases the risk of NMSC in patients receiving tacrolimus therapy.

Keywords: Tacrolimus, mammalian target of rapamycin inhibitors, non-Hodgkin lymphoma, non-melanoma skin cancer

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Proton pump inhibitors and infection-related hospitalizations among residents of long-term care facilities: a case-control study

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Aim/Objective: To investigate the association between use of proton pump inhibitors (PPIs) and infection-related hospitalizations among residents of long-term care facilities (LTCFs).

Methods: We conducted a case-control study of residents aged ≥65 years admitted to hospital between July 2013 and June 2015. Residents admitted for infections (cases) and falls or fall-related injuries (controls) were matched for age (±2 years), sex, and index date of admission (±6 months). Conditional logistic regression was used to estimate crude and adjusted odds ratios (aOR) and 95% confidence intervals (CI) for the association between PPI use and infection-related hospitalizations. Analyses were adjusted for age, sex, polypharmacy, diabetes, heart failure, chronic obstructive pulmonary disease, myocardial infarction, cerebrovascular accident, and concomitant use of cancer and immunosuppressant medications. Sub-group analyses were performed for high and low/moderate intensity PPIs and for respiratory and non-respiratory infections. Logistic regression was used to compare the odds of infection-related hospitalizations among users of high vs. low/moderate intensity PPIs.

Results: Overall, 181 cases were matched to 354 controls. Pre-admission PPI use was associated with infection-related hospitalizations (aOR=1.66, 95%CI 1.11-2.48). In sub-group analyses, the association was apparent for respiratory infections (aOR=2.26, 95%CI 1.37-3.73) and for high intensity PPIs (aOR=1.93, 95%CI 1.23-3.04) only. However, risk of infection-related hospitalizations was not significantly higher among users of high vs. low/moderate intensity PPIs (aOR=1.25, 95%CI 0.74-2.13).

Conclusion: Residents who use PPIs may be at increased risk of infection-related hospitalizations, in particular respiratory infections. Our results provide further support for initiatives to minimize unnecessary PPI use in the LTCF setting.

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Evaluation of adverse drug reactions in Taiwan regional hospital

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Aim: The importance of post-marketing surveillance should not be estimated, because it might be the way to know the risk of special populations, such as elderly and pregnant woman, and to know the off-label use of drugs, the unknown risks of drug in the real world needs us to collect the data of adverse drug reactions(ADRs) which leads to morbidity and mortality. We analysed the ADRs from January 2016 to December 2017 to know the safety of post-marketing drugs in regional hospital in Taipei.

Method: This was a retrospective study for 2 years i in a regional hospital in Taipei. All the outpatients and inpatients admitted hospital were included for ADRs monitoring. The study show the of causality, severity and preventability of ADRs was done as per standard algorithms.

Results: A total of 190 ADRs were reported from patients during Jan 2016 to Dec 2017, elderly patients (39.1%) are the largest populations of ADRs and females(59%) are more likely to ADRs than males. Central nervous system agent (25.8%) and anti-infective agent (22.1%) contributed to the majority of the ADRs. Among the ADRs, etodolac (8.4%) was found to cause the number of ADRs followed by aceclofenac (5.3%) and tramadol (4.7%). The most commonly reported ADRs were skin and subcutaneous tissue disorders (52.5%) and, gastrointestinal disorders (11.6 %). In 145(76%) ADRs, the drug was withdrawn and 39(20.5%) reactions were treated.

Conclusion: The more ADRs in regional hospital were discovered and report by hospital pharmacists, doctors or others, the more we can identify and prevent from drug-induced safety risk, therefore, anticipating better health outcomes.

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Effect of coffee consumption and nonalcoholic fatty liver disease: umbrella review and systematic review and meta-analysis

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Objectives: To evaluate the effectiveness of coffee consumption to nonalcoholic and fatty liver disease (NAFLD) and the effectiveness of coffee consumption to liver fibrosis of NAFLD.

Method: This study consisted of two part. The first part is umbrella review and the second part is systematic review and meta-analysis. Searches were made from PubMed, EMBASE, Cochrane, Scopus and CINAHL databases of all language articles published up to 15 December 2018. The first analysis included studies comparing the risk of NAFLD in participants who did and did not drink coffee. The second analysis included studies comparing the risk of liver fibrosis between NAFLD patient who did and did not drink coffee. Pooled risk ratios (RR), Odds ratio (OR) and 95% confidence interval (CI) were calculated.

Results: The umbrella review identified 4 systematic and/or meta-analysis. The quality assessment using the Amstar2 was high quality review. The systematic review and meta-analysis identified 13 observational studies fulfilled our eligibility criteria and included in the analysis with 74,871 subjects (mean age 50.68±7.74 years old). The meta-analysis compared between <1 cup and 1-2 cups or >2 cups of coffee consumption per day were not significantly associated with NAFLD occurrence, and RR were 0.95 (95%CI: 0.83-1.10, p <0.001) and 0.90 (95% CI: 0.68-1.11, p <0.001), respectively. Interestingly coffee consumption was significantly reduced liver fibrosis with OR 0.63 (95%CI: 0.49-0.78, p <0.001)

Conclusions: Although coffee consumption is not associated with the incident of NAFLD, but it might associate with liver fibrosis progression. Whether consumption of coffee could be considered a preventative measure against NAFLD needs further investigations

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Epinephrine for The Treatment of Anaphylaxis: A Systematic Review

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Background: Epinephrine is recommended as the first-line therapy in treating anaphylaxis by most of clinical guidelines. However, some systematic reviews performed several years ago did not find convincing evidence about its efficacy and there has no overall picture of clinical evidence lately.

Objective: To evaluate the comprehensive therapeutic efficacy of epinephrine for anaphylaxis.

Design: Systematic review and meta-analysis.

Methods: PuMed, Embase.com, the Cochrane Library, Web of Science, ClinicalTrial.gov and three Chinese databases were retrieved with highly sensitive search strategies on 27th December 2018. Clinical trials, cohort studies and case-control studies reporting efficacy and safety of epinephrine in treating anaphylaxis were included. Literature screening and data extraction were performed independently by two reviewers. Studies were pooled using random effects models and presented as risk ratio, or odds ratio, with 95% confidence interval.

Results: 1 cohort studies and 12 case control studies indicating epinephrine's efficacy were finally included. The cohort study showed that anaphylaxis patients who received epinephrine before reaching emergency department (ED) had significant lower risk of hospitalization than those who got epinephrine after arrival to the ED. One case-control study found that using epinephrine before ED was associated to decreased risk of multiple ED epinephrine dose. Meta-analysis of 11 case control studies showed that using epinephrine to manage anaphylaxis did not relate to lower incidence of biphasic anaphylaxis (odds ratio 1.08, 95% confidence interval 0.82 to 1.44, I2=59%).

Conclusions: Two observational studies with negative confounding bias demonstrated that epinephrine did show standout curative effect in managing anaphylaxis, although there is no high-quality clinical trial. For patients encountering anaphylaxis, epinephrine should be rationally used as soon as possible.

Keywords: anaphylaxis, epinephrine, treatment

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Assessment of knowledge, attitude and practice on drug allergy amongst in-patients in a tertiary care hospital

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Background: Drug allergy refers to immunologically mediated drug hypersensitivity reactions which maybe either immunoglobulin E (IgE)–mediated (immediate) or non–IgE-mediated (delayed) hypersensitivity reactions. Understanding the perceptions of patient and creating awareness is important to ensure patient safety.

Objective: To assess the knowledge, attitude and practice (KAP) of drug allergies among in-patients in a tertiary care hospital.

Methodology: An interventional study was conducted in a tertiary care hospital with a predesigned questionnaire focusing on assessing the KAP of patients about drug allergies. The validated questionnaire was administered at pre and post intervention phases of the study. Patient information leaflet (PILs) and counseling about drug allergies were used as the interventional tools to create awareness. Median split method was employed to categorize participants into adequate and inadequate knowledge groups.

Results: Interviewer based KAP questionnaire (22 questions) administered to a total of 750 patients (87%, n= 853 eligible patients) in a phased manner. The mean average age of the participants was 55 ± 7.6 years. Majority [(338, 45%)] of the participants were illiterates, were intervened by direct pharmacist counseling. Among the respondents, 488 (65.4%) had an inadequate knowledge about drug allergies (KAP scores 2.4 ± 2.4) in the pre interventional stage. In the post interventional stage, there was significant increase in both adequately [(428, 57%)] and inadequately [(323, 43%)] knowledge patients with score ranging 4.9 ± 1.54 at p value < 0.005. The study results showed a statistical significant improvement in the knowledge in the post interventional phase.

Conclusion: Our study draws a conclusion that there is a high requirement for creating awareness about drug allergies among patients and public which helps them in preventing and managing the drug allergy consequences effectively.

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Efficacy of pharmaceutical care at hospital setting in China: systematic evaluation of evidence from randomized clinical trials

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Objective: In China, pharmaceutical care in the hospital setting is fast-developing but the evidence about the efficacy is still unfolding. This review aimed to evaluate the quality of evidence from randomized controlled trials (RCTs) about the efficacy of pharmaceutical care provided in the hospitals in China.

Methods: Six databases (Pubmed, ScienceDirect, Web of Science, Scopus, Embase and China National Knowledge Infrastructure) were searched for related RCT studies dated since 2013. The quality of reporting was assessed using the CONSORT 2010 checklist statement.

Results: Eighteen studies (8 Chinese reports and 10 English reports) were included in this study. The study targets were disease-specific including patients with diabetes (n=6), cardiovascular disease (n=5), respiratory disease (n=3), cancer (n=3) and peptic ulcer (n=1). The study sample size ranged between 44-542 allocated to either 2-arm or 3-arm studies with duration of study ranging from 1 to 12 months. The most commonly tested interventions included integrated pharmaceutical care (n=15). The primary outcome of pharmaceutical care as an intervention was measured in terms of medication compliance (n=11), treatment success rate (n=5) and prevention of ADE (n=3). Changes in patients' knowledge (n=4), satisfaction (n=2) and quality of life (n=5) were measured as the secondary outcomes. All study findings demonstrated clinical improvement with statistical difference. None of the studies fully complied with the CONSORT guideline. Major discrepancies identified were (1) a lack of explanation about how the sample size was determined, and how randomization and blinding were performed; (2) a lack of participant flow to analyze the losses and exclusions after randomization; and (3) a lack of reporting about possible harms possibly associated with the intervention.

Conclusion: This study shows that there is some clinical evidence for the efficacy of pharmaceutical care pharmacists provided at hospital setting in China, but the overall quality of reporting warrants further improvement.

Keywords: Pharmacists; Pharmaceutical care; Randomized clinical trials; China

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Severity classification and estimating of ulcerative colitis (UC) patients using Japanese clime database

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Background: Ulcerative colitis (UC) is a diffuse nonspecific inflammatory disease that recurs repeatedly, and the cause of the outbreak has been unclear. Japanese UC patients are increasing, the prevalence was about 100 per 100,000 people according to the survey in 2013 (Japan Intractable Diseases Information Center). However, knowing the severity of the patient is very important to consider the treatment, the number of patients by severity was about 90% or less in moderate disease in 2005, but there are no recent survey results. Current medical treatments are mainly prescription or surgery, these are determined by each severity according to the diagnostic criteria of the Japanese guidelines for UC. So we estimated the severity of UC patients using prescriptions and medical procedures record.

Objective: To estimate the number of patients by severity of Japanese UC patients.

Method: Using Japanese claim database (provided by JMDC), patients who onset UC between January 2014 and November 2017 were observed to for one year and classified using prescription and medical procedure records at onset as follows, 1)Fulminant or severe: High doses(>=80mg/day) of corticosteroids, or other UC treatment drug excluded 5-ASA, or resection or Blood cell component removal therapy, 2) Moderate: Middle doses(<80mg/day) of corticosteroid, 3) Mild: 5-ASA treatment only.

Results: 2,876 UC patients included (male: 65.0%, mean age (S.D): 39.4 (13.1)) in this study, the proportion of young people was lower than the published data. Among them, 2,386 patients (83.0%) were mild, and 296 patients (10.3%) were identified moderate severity. 194 patients (6.7%) were identified to fulminant or severe, among them 13 patients (6.7%) had underwent surgery. Patients under age 20 had higher rates of moderate or more compare to other patients.

Conclusion: Severity of UC patients were roughly identified using claim databases and guidelines, so it was useful for future analysis.

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The use of isoproterenol for ventricular fibrillation in Brugada Syndrome

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Introduction: Brugada syndrome (BrS) is an inherited arrhythmic disease associated with ventricular fibrillation (VF). The specific characteristics of BrS are marked ST-segment elevation in right precordial leads without evidence of ischemia, electrolyte imbalance, and other structural heart diseases. The prevalence of BrS has been evaluated in several different populations and was determined to be more common in Asian populations by approximately five times more than Caucasians and 32 times more than Hispanics in a pooled analyzed prevalence. The use of intravenous isoproterenol in BrS has been reported in suppressing VF thereby improving quality of life of the patients.

Method: The search was conducted in PubMed to identify relevant studies of major medication isoproterenol in BrS. A total of 77 articles and case reports were screened. Of the articles and reports, 17 were assessed for eligibility with a total of 12 being candidate to be included. A total of 8 articles and case reports discussed effectiveness of isoproterenol for VF in BrS.

Result: From the selected articles, total of 37 patients with BrS were treated with Isoproterenol for ventricular fibrillation. Isoproterenol was administrated as a bolus injection intravenously at a dose of 1-2 microgram, followed by continuous infusion of 0.15 – 0.30 microgram/min until baseline heart rate is stabilized. Out of 37 patients, 32 patients were stabilized, which is about 86.4% treatment success rate. The rest of the 5 patients also were stabilized after being treated with combination therapy of isoproterenol plus quinidine.

Conclusion: Studies were limited to low sample sizes and no truly randomized controlled environment because of the disease's uncommonness. However, all the studies concluded with consistent effectiveness of isoproterenol for treating ventricular fibrillation in BrS. Isoproterenol should be considered as drug of therapy for VF in BrS.

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The association between partner bereavement and new melanoma diagnosis and subsequent mortality of melanoma: population-based cohort studies

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Aim/Objectives: Partnership status is important for early melanoma detection, and consequently improved survival. However, it is unclear whether a partner's death affects new melanoma diagnosis and subsequent mortality. We aim to evaluate associations between partner bereavement and: 1) incident melanoma; and 2) mortality in patients with melanoma.

Methods: Two cohort studies using the Clinical Practice Research Datalink (1997-2017). Study 1: Matched cohort study using stratified Cox regression to estimate hazard ratios (HR) comparing new melanoma diagnosis in bereaved to matched (age, sex and general practice) non-bereaved individuals. Study 2: Restricting to individuals with melanoma who were eligible for linkage with Office for National Statistics (ONS) death data, we used Cox regression to estimate HRs comparing hazard of melanoma-specific and all-cause death in those whose partner died to those whose partner was alive. All analyses were adjusted for Charlson Comorbidity Index, smoking, body mass index, alcohol and deprivation.

Results: In Study 1, we included 170,002 bereaved and 1,599,260 matched non-bereaved persons. we observed lower melanoma risk (HR:0.86;95%CI:0.79–0.94) in bereaved compared to non-bereaved people. In Study 2, (n=3,233 patients with melanoma), we found evidence of increased mortality (HR:1.23;95%CI:0.98–1.54 for all-cause mortality; HR:1.28;95%CI:0.88–1.86 for melanoma-specific mortality) in those whose partner died compared to those whose partner was alive, possibly due to limited power. In a sensitivity analysis of Study 2 where we did not restrict to those with ONS linkage (n=8,373 individuals with melanoma), we showed increased all-cause mortality associated with bereavement (HR:1.31;95%CI:1.15–1.50).

Conclusions: We found a decreased melanoma diagnoses, but increased mortality associated with partner bereavement. These findings may be partly explained by delayed melanoma detection as a result of the bereaved not having a partner to notice skin changes. Results from a parallel Danish registry study are pending and will be presented.

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An analysis of reports for conventional synthetic disease modifying antirheumatic drugs (csDMARDs) in EudraVigilance

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Objective: To characterize adverse events (AEs) reporting patterns for csDMARDs.

Methods: We performed a descriptive analysis of Individual Case Safety Reports (ICSRs) and suspected adverse drug reactions (sADRs) from EudraVigilance (EV). Data was extracted by active substance for azathioprine (AZA), cyclosporine (CYC), hydroxychloroquine (HCQ), leflunomide (LEF), methotrexate (MTX), methylprednisolone (MET) and sulfasalazine (SSZ). We collected all reports available up to August 2018. Data elements retrieved from EV included age, gender, seriousness of sADR, geographic origin, reporter group, reaction group -System Organ Class (SOC).

Result: A total of 149,190 ICSRs was submitted for the csDMARDs included. These reports contained 356,698 sADRs, of which 337,894 (94.72%) were serious. The majority of the sADRs were reported by healthcare professionals (HCP) [132,552 (88.84%)] and originated from non- European Economic Area (non-EEA) [87,951 (58.95%)]. Non-HCP reporting varied in-between csDMARDs from 5.85 to 20.18%. Within the EEA a quarter of the total ICSRs originated from France (14,148, 23.13%) followed by Germany (8,074, 13.2%), United Kingdom (7,232, 11.82%), Italy (1,731, 2.83%) and the Netherlands (1,729, 2.82%). MTX and CYC accounted for the most ICSRs submitted to EV, for 59,661 (40%) and 29,992 (20%). Overall most of the sADRs reported were for the “General disorders and administration site conditions” SOC type (46,224, 12.95%), followed by “Infections and infestations” (35,877, 10.15%) and “Gastrointestinal disorders” (22,763, 6.38%). Most frequently AEs (SOC) categories, as well as the proportion of serious and fatal cases varied widely between the seven substances.

Conclusion: Although, four of the seven substances (AZA, MTX, CYC, and LEF) are pharmacologically related, they had slightly different sADRs reporting patterns for the five most reported SOC categories, which underlines once again the importance of active vigilance and “real-time” monitoring. EV, one of the biggest spontaneous reporting systems in the world is an important tool in the detection and analysis of new risks.

Key words: adverse drug reactions, post-marketing safety, csDMARDs

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Non-steroidal anti-inflammatory drugs and the risk of nephrotic syndrome: A case-control study

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Aim: Non-steroidal anti-inflammatory drugs (NSAIDs) have been associated with acute renal failure. However, the association between NSAIDs and nephrotic syndrome (NS) has not been systematically studied. This study aimed to assess the risk of NS for NSAIDs, including its duration of use.

Methods: A case-control study was performed among adults in the UK Clinical Practice Research Datalink, a primary health care database. Data were collected from October 1989 until November 2017. Cases were patients with a first diagnosis of NS and controls were those without NS. Up to 5 controls were matched to a case for age, sex, general practitioner practice, and diagnosis date. NSAID exposure (grouped as conventional NSAIDs, selective COX-2 inhibitors, or chemical groups) was classified as current, recent, or past use. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated using logistic regression analysis.

Results: We included 2,620 cases and 10,454 matched-controls. Compared to non-use, current use with duration 1-14 days, 15-28 days, or >28 days, recent use, and past use (discontinuation between 2 months-2 years or >2 years) of conventional NSAIDs showed the following associations with NS: adjusted OR 0.78, (95%CI, 0.46-1.31), 1.34 (1.06-1.70), 1.42 (0.79-2.55), 1.55 (1.11-2.15), 1.24 (1.07-1.43), and 0.96 (0.85-1.09), respectively. Selective COX-2 inhibitors were not associated with an increased risk compared to non-use. Categorization based on chemical groups showed that acetic acid derivatives (AADs) and propionic acid derivatives (PADs) were associated with an increased risk compared to non-use.

Conclusion: Current use of conventional NSAIDs was associated with an increased risk of NS starting from 2 weeks of exposure onwards. Likewise, recent and past exposure up to 2 years of conventional NSAIDs before NS diagnosis were associated with an increased risk. This increased risk appeared attributable to AADs and PADs. The increased risk disappeared after 2 years of discontinuation.

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The use of antibiotics in adult patients with chronic bronchitis and the influencing factors of readmission

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Aim: To describe the use of antibiotics in Chinese adults with chronic bronchitis, and to further explore the factors that influence the treatment effect and patient's recovery.

Methods: We used a data from a national health insurance database in China. The data consisted of people participating in health insurance from 61 cities in China. A total of 23912 inpatients from Jan 1, 2015 to Dec 31, 2015 were included in our study. A descriptive analysis of inpatient antibiotic use was performed. Logistic regression analysis was used to assess the impact of different types of antibiotics and other characteristics of patients on the 30-day readmission risk.

Results: 26614 cases from 23912 patients were included in this study. Third generation cephalosporins were the most widely used antibiotic, accounting for 37.96% of all cases (n=10103). The third generation of cephalosporins were the most common in monotherapy (n=3152, 33.67%). The combination of fluoroquinolone and the third generation of cephalosporins was the most common in the case of combination therapy with two drugs (n=1858, 21.07%). The combination of penicillin, fluoroquinolone and beta-lactamase inhibitors was the most common in the case of combination therapy with three drugs (n=387, 10.31%). Logistic regression showed that getting older, having coronary heart disease and male sex significantly increased the risk of 30-day readmission, whereas treating with broad-spectrum penicillin significantly reduced the risk of 30-day readmission. The effects of other factors on the 30-day readmission risk were not statistically significant.

Conclusion: Third generation cephalosporins were the most widely used antibiotics in Chinese adults with chronic bronchitis. Getting older, having coronary heart disease and male sex were risk factors for poor treatment effect and recovery in Chinese adults with chronic bronchitis, while the treatment with broad-spectrum penicillin was a protective factor.

Keywords: Chronic bronchitis; Antibiotics; Readmission

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Analysis on drugs triggering allergic reactions in the combination with Xiyanping injection: a nested case-control design

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Objective: To explore the drugs that may trigger allergic reactions when combined with Xiyanping injection.

Methods: A nested case-control design was used in the study. Data was from the 2015 National Urban Basic Medical Insurance Sample Database. Patients prescribed both Xiyanping injection and anti-allergic drugs in the database were extracted. The case group was defined as the casual group in prescription sequence symmetric analysis part of previous study. Two case groups were set up by including and excluding patients who were prescribed Xiyanping injection and anti-allergic drugs on the same day. The control group was selected by a 1:1 match from the database using propensity score matching method by age, sex, types of visit and hospital levels. 25 drugs were selected as combined drugs according to frequency of prescription on the same day as Xiyanping injection. Conditional logistic regression was used to estimate the ORs.

Results: In the group 1 which excluded patients who were prescribed Xiyanping injection and anti-allergic drugs on the same day, 1898 patients were included in the study. There were 949 patients in case group, including 504 males and 445 females, average age was 33.99±29.56 years old. In the group 2 which included those patients, 4876 patients were included in the study. There were 2438 patients in case group, including 1335 males and 1103 females, average age was 36.06±27.62 years old. Most patients were hospitalized and visited in secondary hospitals in two groups. Among two groups, the ORs of combined use of aminophylline, ribavirin, lidocaine, vitamin C, potassium chloride, and gentamicin were greater than 1. The OR of cephalosporin was less than 1.

Conclusions: The combination of Xiyanping injection and gentamicin may increase the risk of allergic reactions, and the combination with cephalosporin may reduce the risk of allergic reactions.

Keywords: Xiyanping injection; Allergic reaction; Nested case-control design

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Adverse events of TGP in patients from rheumatology and dermatology departments: a multi-center, non-intervention register study

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Objective: To observe the adverse events and safety of total glucosides of peony (TGP), and to evaluate risk factors associated with these adverse events.

Methods: 1422 patients from 5 hospitals in China were included in the study during October 2017 and December 2018. All the patients were from rheumatology and dermatology departments and were the new user of TGP. Descriptive analyses on TGP medication, adverse events, serious adverse events, and incidence of adverse events were conducted. And the risk factors were analyzed by single factor and multivariate logistic regression analysis.

Results: A total of 193 cases of adverse events were observed, more than 90% were diarrhea. 73.00% of adverse events were mild, 69.76% occurred within two days after taking TGP, and 84.37% of cases recovered within 10 days. No serious adverse events occurred. The incidence of adverse events at the end of 1 week was 10.48% (95% CI: 8.92%~12.22%) and was 3.66% (95% CI: 2.71%~14.83%) at the end of 1 month. In addition, for Sjogren syndrome patients, the number of cases with constipation was gradually decreased. As for medication, most patients took 0.6g/time and 3 times/day. Univariate analysis showed that past medication history of TGP was related to the occurrence of adverse events at the end of 1 month ($P<0.05$). Multivariate logistic regression analysis showed that diarrhea occurred before taking TGP was independent risk factor for the occurrence of adverse events in the study period (OR=11.652, 95%CI:4.244~31.990).

Conclusion: TGP has good safety, the main adverse event is diarrhea. In clinical prescription, TGP should be avoided for patients who have developed diarrhea. Taking TGP may improve dry stools in Sjogren syndrome patients.

Keywords: Total glucosides of peony; Safety; Adverse events; Risk factors

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Safety profile of Thalidomide: Is it still Worth discussing?

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Background: Despite its history as a human teratogen, thalidomide is emerging as a treatment for cancer and inflammatory diseases. Thalidomide was approved by the US Food and Drug Administration (FDA) in 2006 for the treatment of multiple myeloma. This study aimed to identify the signal strength for thalidomide associated Adverse Events (AEs) using disproportionality analysis in the FDA Adverse Event Reporting System (FAERS) database.

Method: Data were obtained from the public release of data in FAERS. Most commonly used data mining algorithms, Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR) were used in the study. A value of ROR-1.96SE>1 and PRR≥2 were considered as a positive signal.

Results: Thalidomide had a total of 26,795 reports in the FDA database. Amongst which 56.1% of reports were associated with males and 42.4% with females. The mean age was 55.87 (95% CI, 52.21- 59.52). 50.81% of reports were reported by the physician, 24.76% by other health care professionals, 16.34% by consumers and 7.99% by pharmacists. The most common indications were multiple myeloma (n=8,246) and plasma cell myeloma (n=7,363). Positive signals were obtained for peripheral neuropathy (PRR:11.35; ROR:11.52), osteonecrosis (9.76; 9.67), bone disorder (9.27; 9.15), deep vein thrombosis (6.39; 6.45), pancytopenia (5.09; 5.09), febrile neutropenia (4.05; 4.05), sepsis (4.00; 4.03), thrombocytopenia (3.87; 3.90), renal failure (3.46; 3.50) and pneumonia (3.18;3.27). Serious adverse events included death (35.43%), hospitalization (27.80%), life-threatening (2.85%), disability (2.40%) and others (31.50%).

Conclusion: The present study identified a positive signal for these AEs, although a causal relationship cannot be absolutely established. Health care professionals should be cautious about the possibility of encountering serious adverse events associated with thalidomide and should be reported to the regulatory authorities. Further pharmacoepidemiologic studies are necessary to confirm this conclusion.

Keywords: Thalidomide, Adverse Events

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Neurodegenerative Diseases Global Epidemiology Network (NeuroGEN)

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Aim/Objective: Research using administrative data is important for understanding medication safety and effectiveness in groups of people often excluded from randomised controlled trials. The Neurodegenerative diseases Global Epidemiology Network (NeuroGEN) is a new international initiative to optimise the use of administrative data for improving health outcomes.

Methods: NeuroGEN was established at a meeting of 30 researchers from eight countries in October 2018. The meeting involved research priority setting and discussion of the data strengths and limitations in each country. A common study protocol will be developed for each analyses performed within NeuroGEN. Using this protocol, investigators in each country will analyse their own data and report the results to the principal investigator. Data will be presented separately for each country, and where possible, data will be pooled using meta-analyses.

Results: Initial funding has been secured for analyses related to the use of guideline-recommended medications for stroke and type 2 diabetes among people with dementia. Common study protocols related to adherence and persistence to cholinesterase inhibitors and survival among people with dementia have been developed in Australia and Hong Kong, respectively. Work is underway to develop an international common data model for medication research among people with dementia.

Conclusion: Development of common data protocols and a common data model will facilitate timely analyses and internationally generalisable results using multiple national administrative databases. This will improve the evidence base for medication use in people with dementia and other neurodegenerative diseases.

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Assessment of severe events in influenza outpatients treated with baloxavir marboxil: an observational database study

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Aim/Objective: Influenza is a common cause of acute respiratory infection. For most cases, symptoms of influenza are relatively mild and self-limiting. Complications of influenza, however, can lead to hospitalization or death. Baloxavir marboxil (BXM) is a selective inhibitor of influenza cap-dependent endonuclease. The objective of this study is to compare the frequency of hospitalization and death in outpatients treated by BXM with other anti-influenza drugs.

Method: We confirmed the demographics of outpatients prescribed anti-influenza drugs (BXM, Oseltamivir (OTV), Zanamivir (ZNV), Laninamivir (LNV)) using Japanese acute hospital-based claims database. Patients with age ≥1 years old who had the starting date of influenza medical care (Day 1) between 1 October 2018 and 15 February 2019 were eligible for this study. We calculated the proportion of hospitalization which occurred during Day 2 to Day 14 and estimated odds ratio (OR) and 95% confidence intervals (CIs) by adjusting imbalanced demographics factor among drugs. In addition, we calculated the proportion of in-hospital death.

Results: The demographics of the patients were similar except for age category. The proportion of hospitalization in patients with BXM (1.29% (139/10769)) was comparable with that in OTV (1.24% (376/30388)), and slightly greater than that in ZNV (0.75% (12/1603)) and LNV (0.84% (127/15193)). Adjusted OR (vs BXM, as denominator) and 95% CIs by age category was 1.103 [0.901, 1.350], 1.299 [0.709, 2.382] and 0.943 [0.737, 1.207] for OTV, ZNV and LNV, respectively. In addition, the proportion of death in patients with BXM (0.05%, n=5) was comparable with that in OTV (0.05%, n=15), LNV (0.03%, n=5), and there were no deaths in ZNV.

Conclusion: In an observational study of Japanese acute hospital-based claims database, the frequency of severe events in influenza outpatients was comparable among anti-influenza drugs during the 2018-19 influenza season; however, and further studies are needed to confirm the findings.

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Skeletal Muscle Relaxant Associated Renal Disorders: Exploration of Novel Adverse Event using Disproportionality Analysis

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Objective: Among skeletal muscle relaxants, only succinylcholine is previously known to cause renal disorders. This study aimed at the identification of renal disorders associated with skeletal muscle relaxants using disproportionality analysis in the FDA Adverse Event Reporting System (FAERS) database.

Methods: Public release of data in FAERS was used for analysis. The MedDRA terms searched were “Renal injury”, “Renal impairment”, Renal failure” and “Renal failure acute”. The data mining algorithms used were Reporting Odds Ratio (ROR) and Proportional Reporting Ratio (PRR). A value of ROR-1.96SE>1, PRR≥2 were considered as a positive signal.

Results: The FAERS database had a total of 1,56,112 reports associated with renal disorders. Pancuronium had 65 reports for renal injury (PRR: 234.61; ROR: 308.89), 58 reports for renal impairment (58.94; 75.12), 99 reports for renal failure (50.34; 79.83) and 27 reports for renal failure acute (23.95; 26.54). The number of reports for Vecuronium was 87 for renal injury (43.0; 44.59), 105 for renal impairment (14.60; 15.33), 141 for renal failure (9.80; 10.47) and 76 for renal failure acute (9.22; 9.54). Rocuronium had 56 reports for renal injury (12.34; 12.42), 55 reports for renal impairment (3.41; 3.44), 105 reports for renal failure (3.26; 3.31) and 56 reports for renal failure acute (3.04; 3.05). Atracurium had 11 reports for renal failure acute with PRR: 5.90 and ROR: 6.03.

Conclusion: This study concluded that all the drugs in the class, skeletal muscle relaxants, are associated with renal disorders. Although a causal relation cannot be definitively established, the number of cases reported suggests that there might be an association. Health care professionals should be cautious about the likelihood of encountering these adverse events and should be reported to the regulatory authorities.

Keywords: Skeletal Muscle Relaxant, Renal Disorders, Disproportionality analysis

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Efficacy and safety of febuxostat in kidney transplant recipients

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Aim/Objective: The association of hyperuricemia with kidney allograft outcomes remains controversial. Febuxostat insufficient to provide evidence in kidney transplant patients. We aimed to assess the effects and safety of Febuxostat in post-renal transplant recipients, focusing on evaluating the urate-lowering effect and recovery of allograft renal function.

Methods: A Single-center retrospective study in which all patients (n=247, 114 males and 133 females) transplanted between 2003 and April 2019.The efficacy and safety results of febuxostat after 3, 6, 9, 12 months in transplant patients were evaluated. The initial dose of febuxostat was 40-80 mg/d depending on serum uric acid level and body weight. Adverse events, patient and renal allograft survival were recorded throughout the follow-up period.

Results: Forty-six patients were included in this study. The initial serum uric acid (UA) of 8.96 ± 2.24 mg/dl decreased to 4.96 ±1.76 mg/dl($p<0.01$) after 3 months of febuxostat. No other adverse events were reported. In addition, at 12 months, mean serum UA were 5.85±1.45mg/dl ($p<0.01$), no apparent effect on estimated glomerular filtration rate ($p=0.316$). All patients and renal grafts survived during the follow-up period.

Conclusion: Hyperuricemia is a common complication after kidney transplantation, and Febuxostat is considered the treatment of choice for renal transplant recipients with hyperuricemia and no effect of graft function. Febuxostat is effective and safe in the treatment of hyperuricemia in renal transplant recipients.

Keywords: Febuxostat, Renal transplant recipients

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Bisoprolol compared with carvedilol for sudden cardiac arrest prevention among individuals receiving maintenance hemodialysis

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Introduction: Sudden cardiac arrest from ventricular dysrhythmias is the leading cause of death in patients receiving hemodialysis (HD). Studies suggested β-blockers use was associated with lower risks of sudden cardiac arrest. However, the prevention effect of sudden cardiac arrest in different β-blockers remains to be elucidated. Using Taiwan National Health Insurance Database, we compare cardiac arrest outcome associated to carvedilol or bisoprolol use, the two most commonly prescribed β-blockers in patients with HD.

Methods: We conducted a retrospective study of 9,305 HD patients who initiated bisoprolol and 11,171 HD patients who initiated carvedilol treatment between 2004 and 2011. We compared the risk of sudden cardia arrest between carvedilol and bisoprolol new users during a 2-year follow-up using Cox proportional hazard regression adjusting for age, gender, comorbidities, and concomitant drugs. Falsification end points were used to detect residual confounding and bias due to unobserved confounders. In the primary analysis (intention-to-treat approach), all patients were followed within their initiation groups until the study end, disregarding any changes in treatment status over time. Sensitivity test of as-treated analysis was defined as censor index β-blocker treatment switching to a nonindex β-blocker during follow-up.

Results: Compared with carvedilol initiators, bisoprolol initiators were older, more male, more comorbidities with hypertension and hyperlipidemia, and more concomitant drugs used with statins and antiplatelets. In contrary, fewer heart failure and less digoxin treatment in bisoprolol users. Bisoprolol (vs Carvedilol) initiation was associated with lower sudden cardiac arrest risk (adjusted HR, 0.72; 95% CI, 0.53-0.98) in intention-to-treat analyses. Similar results were found in auxiliary as-treated analyses (adjusted HR, 0.72; 95% CI, 0.52-0.99) after controlling for confounders. Analyses of the falsification end points showed no association between two β-blockers veins and risk of traffic accidents or cataract surgery.

Conclusion: Relative to carvedilol, bisoprolol initiation among HD patients was associated with a lower 2-year risk of sudden cardiac arrest.

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Adverse drug events: data sources and difficulties in collecting of information in a framework of outpatient registry

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Aim: To compare the possibilities of collecting information on adverse drug events (ADEs) according to the data of a patient survey and on the registration cards of the outpatient register.

Methods: Data of 1531 patients were collected for the period from January 2011 to August 2015 in a framework of outpatient register. The information about ADEs was collected from two sources. The first of them was a registration card, which was filling by a physician. The card includes information about the drugs taken by patients, doses of drugs, and the regularity of taking and availability of AE. The second data source was a patient questionnaire, including questions on the assessment of tolerability of drugs, determined by the patients themselves. The survey involved 487 patients included in the outpatient registry.

Results: According to the data of cards, a total of 301 ADEs were registered in 223 patients. According to the survey data, there were 139 ADEs in 115 patients. Various allergic reactions and symptoms of gastrointestinal disorders were leaders in the structure of ADEs both in register cards and the survey data. Only 46 patients had the same data in both sources of information. When analyzing the data on ADEs of statins in patients who filled in the original questionnaire, doctors reported 13 such cases of ADEs, patients noted the occurrence of 14 ADEs, but the coincidence of the data was consistent with both registration cards and questionnaires for only 3 patients.

Conclusion: The results of the study demonstrate a similar structure of ADEs according to the doctors (register card) and patients (questionnaires), however, a significantly smaller number of ADEs are observed according to the results of the survey.
Keywords: adverse drug events, an outpatient register, registration cards, patients' survey

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The interrelationship of aspects of medication adherence and therapy safety in patients of outpatient register

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Aim: To study the interactions between pharmacotherapy safety, medication adherence in patients (pts) with chronic cardiovascular diseases (CVD) and their risk factors in the framework of outpatient prospective register.

Materials: The data of outpatient register, supplemented by two original questionnaires for assessing medication adherence and for obtaining the history of adverse events (AEs), were used. The survey was conducted during the period from September 1, 2017, to May 31, 2018. A total of 162 pts filled in the questionnaire forms: 80 females, 82 males, mean age of pts was 67.2 ± 11.1 years.

Results: In 46 (28.4%) of 162 pts, the AEs of pharmacotherapy varied, half of the pts (88 people; 54.3%) denied the presence of AEs, and 34 pts found it difficult to answer. Practically all pts (158 of 162 pts, 97.5%) were given medical recommendations (MR) for taking medications, but only 117 pts (74.0%) were fully adherent to MR, 13 pts did not take medicines at all, the rest of patients were partially non-adherent. Regular consultations with the attending physician during which pts were provided information about their treatment, including information about drugs AEs, were associated with the increased odds (odds ratios (OR)=3,8; 95%CI [1,2; 12,6], p=0,03) of adherence to MR. Among pts who changed the treatment regimen, dosage or discontinued taking medications by their own, AEs were registered significantly more often: OR=3,3 95%CI [1,5; 7,1], p=0,003. The absence of AE fivefold increases the chances of the pts being adherent to MR: OR=5,2; 95%CI [1,2; 22,9], p=0,028.

Conclusion: The close interrelation of the aspects of drug therapy safety and treatment adherence determine the most promising directions (optimization of doctor-patient relations, rational use of medicines, etc) in breaking the "vicious circle" of the relationships mentioned above.

Keywords: drug therapy, adverse events, treatment adherence.

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Pharmacovigilance and Risk Management Plan at Pre-authorization: A comparative study to medicine decision making

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Introduction: Prescribing the drugs uses the balance between benefits and harms. Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects (AEs) or any other medicine-related problem. Pharmacovigilance and Drug Risk Management Plan (DRM) at pre-authorization are considered a new concept in Thailand. The new pharmacovigilance legislation, Volume 9A of the European Union (EU), contains pharmacovigilance guidelines for drugs. The additional monitoring status is particularly important when granting marketing authorization for drugs containing a new active substance and for all biological products, including biosimilar for which there is limited post-marketing experience. Recently, Thai Food and Drug Administration (Thai-FDA) has been implemented of the new drug legislation for ensuring proper DRM through the suspected AEs. The pre-authorization DRM has been effective with this post-marketing data collection.

Objectives: The study is aimed to review and compare the activities of pharmacovigilance and risk management plan at pre-authorization made by Thai–FDA with the European guidelines.

Methods: A comprehensive review of the current activities of pharmacovigilance and DRM at pre-authorization made by Thai–FDA is presented. An analysis of post-marketing scheme, the practice guidelines or any guidance are elaborated and compared with the European's.

Results: Our review shows that intense efforts by regulators in the new drug or biosimilar application have been implemented for pharmacovigilance and drug risk management plan at pre-registration in two years recently. The need for collection of safety data through effective post-approval safety is important for 12 biologic approval determination. Thai-FDA has followed the EU guidelines for decision processes with patient involvement. The practice guidelines have not been implemented but robust regulations were involved.

Conclusions: Pharmacovigilance and DRM are similarly in the EU. Various stakeholders play important roles to enhance patient safety. Thai-FDA needs to establish guidelines to support medicinal decision making.

Keywords: pre-authorization, pharmacovigilance, drug risk management

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Trend in method for statistical sample size calculation of the post-marketing surveillance in Japan.

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Objective: The submission of Risk Management Plan (RMP), including Post-Marketing Surveillance (PMS) plans, has been required since 2013 to ensure drug safety. When planning PMS, it is important to clarify the research questions that are the subject of the survey and implement them appropriately. However, in the past PMS, the surveillance with 3000 cases has been frequently conducted when research questions were not clear. Therefore, this study investigated the types of statistical sample size calculation and their trend of recent years for PMS.

Methods: We investigated the method for statistical sample size calculation of the PMS in more than 300 RMPs in Japan that have been published on the Pharmaceuticals and Medical Devices Agency (PMDA) website between 2013 and 2019. We classified the typical method for statistical sample size calculation of the PMS and summarized the yearly frequency and proportion of methods used for sample size calculation.

Results: Method for statistical sample size calculation of the PMS could be classified into four methods: Rule of three, Confidence interval, Binomial test, Chi-squared test. The trend in method for statistical sample size calculation was shown to decrease in Rule of three, and to increase Confidence interval and Binomial test.

Conclusion: In recent years, a PMS based on research questions has been required, and the guideline has also been issued from PMDA in Jan 2018. Out study demonstrated the trend in method for statistical sample size calculations before the publication of guideline. The change of recent trend is considered to accelerate in the future.

Keywords: Risk Management Plan, Post-marketing surveillance, Statistical sample size calculation

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Feasibility Assessment of Post-marketing Surveillance of Vaccine Safety and Effectiveness Using Reginal Health Information Platform in China

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Aim/Objective: This study aimed to assess the feasibility of using population-based electronic health records in China for post-marketing safety and effectiveness of vaccine.

Methods: Ningbo Regional Health Information Platform (NRHIP) in Zhejiang Province was evaluated in this study. Self-administered questionnaires and face-to-face interviews were conducted with custodians of NRHIP. Data collected included health policies, medical services, a description of the various data sources available and the linkage possibility between them, as well as the completeness of the data.

Results: The NRHIP has built a lifespan healthcare information system including databases on maternal and neonatal health, vaccine registry, general electronic medical records (EMR), chronic diseases and death registries, covering all residents of the Ningbo city since 2013. The vaccine registry captures detailed data on all pediatric and adult vaccinations. EMRs capture most health outcomes of interest for vaccine safety, including related to pregnancy exposure. Records from these different sources could be linked through personal identifiers. As is often the case in large linked healthcare databases, information related to lifestyle and health status were not captured well. Furthermore, some population-based preventive programs were handled separately and not linked to the individual EMR system or vaccine registry, including systematic neonatal screening (for some pre-specified metabolic conditions) and free cervical cancer screening.

Conclusion: This feasibility study confirmed the quality of the vaccination registry and the ability to link it with other healthcare databases, including EMR. The assessment suggested that NRHIP could be used for vaccine safety surveillance. The ability to use NRHIP for vaccine effectiveness evaluation depends highly on the availability of the efficacy outcome and potential confounding variables in the database, and may not always be feasible.

Keywords: Post-marketing surveillance; Electronic health records; vaccine

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Evidence-based evaluation of benefit and risk for incretin-based therapies: a protocol

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Aims/Objective: For the treatment of type 2 diabetes mellitus (T2DM), incretin-based therapies, including dipeptidyl peptidase-4 inhibitors (DPP-4Is) and Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been on the market for more than ten years and steadily gaining clinical popularity. Although the benefits and risks of DPP-4Is and GLP-1 RAs have been reported separately by many studies, yet to our knowledge no previous study has been conducted synthetically considering both sides. So the aim of our study is to give a comprehensive benefit–risk assessment of DPP-4Is and GLP-1 RAs for adult patients with T2DM.

Methods: Medline, Embase, the Cochrane library and www.clinicaltrials.gov were searched from inception through March 29, 2019 to identify randomized clinical trials on the DPP-4Is or GLP-1 RAs versus placebo or other anti-diabetic drugs including metformin, insulin, sulfonylurea, thiazolidinediones, alpha-glucosidase inhibitor, and sodium-Glucose co-Transporter 2 in T2DM. Next, the literature will be filtered. Then, the Delphi method will be used to selected the significant indicators and the corresponding information of literature will be extracted. Network meta-analysis will be used to synthesize data for each indicator. After that, multiple criteria decision analysis (MCDA) model will be constructed to get the comprehensive evaluation values of benefits and risks. In addition, sensitivity analysis and uncertainty analysis will be conducted for quality control.

Results and conclusion: The results will constitute evidence on the benefit-risk balance of DPP-4Is and GLP-1 RAs.

Keywords: DPP-4Is, GLP-1 RAs, MCDA, benefit-risk assessment

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A feasibility assessment framework for conducting comparative effectiveness research (CER) using electronic medical record (EMR) database in China

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Objective: EMR databases, as a cost-saving and efficient way to access patient-level data, may be utilized to conduct CER studies. However, country-specific data issues, including poor data linkage and unstructured variables, may present as barriers. This study aims to propose a framework that can be adopted as a basis for feasibility assessment of conducting CER using EMR in China.

Methods: An inductive approach, retrieving 8 literatures and synthesizing 2 empirical cases.

Results: A framework with four domains focusing on CER evaluating long-term exposure is proposed:
Patient identification: To assess the possibility of identifying new drug users or patients without pre-existing conditions (in CER to address confounding and selection bias). Full medical history is usually not available due to poor data linkage and unstructured medical history. Patient classification is often based on assumptions, which need to be justified. Potential risks of misclassification need to be assessed.
Exposure measurement: To define concomitant medication and continuous exposure. Due to country-specific prescription patterns (e.g. concomitant medication not on the same prescription, no patient-referral system, refilling in community hospitals), reported frequencies of prescription and gaps between two prescriptions must be assessed to facilitate the definition of window periods.
Outcome measurement: To assess the feasibility of measuring different types of outcomes. Due to poor data linkage, count-of-events and time-to-event in a long-term are more likely to be affected by information bias. Short-term outcomes such as events during each hospitalization may be more feasible.
Confounding adjustment: To assess the availability and granularity of potential confounders. Potential confounders such as medical history and disease severity, remain unstructured in Chinese EMR. The availability of alternative variables should be considered.

Conclusion: The framework covers essential domains to be assessed in a CER feasibility assessment. Adaptive designed RWE studies, careful evaluation of potential biases, and sensitivity analyses are recommended.

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Study Feasibility Assessment for Total Joint Replacement Surgery, Comparing Japanese and United States Databases: A Retrospective Cohort of Osteoarthritis Patients

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Aim/Objective: Osteoarthritis (OA) progresses gradually over months or years. Among patients with advanced OA, total joint replacement surgery (TJR) may be an ultimate option to alleviate severe pain by replacing damaged joints, and is indicative of severe OA. However, information regarding TJRs in the Japanese real-world settings is limited. Thus, the objective was to assess the feasibility of identifying TJRs using a Japanese hospital based receipt database, compared with output from a United States (US) healthcare claims database.

Methods: A retrospective cohort study was conducted using the databases between 2013 and 2017 in Japan and US. TJRs were identified with ICD-10 codes (K082) in the Japanese database, and with CPT, ICD-9 and ICD-10 codes in the US database. The incidence of TJRs in OA patients and descriptive characteristics of TJR cases were summarized.

Results: 60,158 patients with OA in the Japanese database and 67,838 with OA in the US database were identified as new initiators of NSAIDs or opioids during the period. The incidence rate (cases and proportion) of TJR in Japanese OA patients was 86 per 1,000 person-years (3,263 cases, 5.4%), compared to 47.9 per 1,000 (5,113 cases, 7.5%) in US. The Japanese OA patients were older at the time of their TJRs, compared with the US OA patients (means: 73 vs. 53 years). Opioid use in the 1 year prior to TJR was much more common in the US (45%), than in Japan (1.4%).

Conclusion: Feasibility assessment suggested that a sufficient number of OA patients and TJR events in OA patients can be identified in the Japanese database as well as the US database. However, differences in age and TJR incidence are likely due to different age distributions for the populations captured in the data sources. Given the output of this feasibility assessment, outcome validation is warranted.

Keywords: Osteoarthritis, Total Joint Replacement, Real-World Evidence, Study Feasibility Assessment