



EuroDURG

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Patients, Medicines, Bytes:
Drug Utilisation Research and E-health



ABSTRACT BOOK

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Technology & Innovation Centre
University of Strathclyde, Glasgow UK



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European Drug Utilisation Research Group Conference 2017 Glasgow, UK

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P1W.1

The pattern of antibiotic use among Hungarian, Norwegian and Portuguese children

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Background: According to the European Surveillance of Antibiotic consumption (ESAC-net) network data for 2014, Norwegian and Hungarian ambulatory care antibiotic use has similar scale, but different pattern. Despite the high consumption data in Portugal, it has similarities with the Hungarian pattern of ambulatory antibiotic use. In the present work we aimed to focus on the paediatric population and examine if differences in the proportional use of different antibiotic classes exist.

Methods: A cross national cross comparison was performed to compare paediatric (0-19 years) antibiotic use. Ambulatory care systemic antibiotic use (ATC: J01) stratified by age-groups were retrieved from pharmacy claims data. Antibiotic use was expressed as number of packages per inhabitant per year. Population data were derived from Eurostat.

Results: Penicillins (ATC: J01C) were the most widely prescribed antibacterial class for children (in all paediatric age groups) in all countries, however, Norwegian and Portugese share of penicillins were much higher from total ambulatory antibiotic use (60.2% and 70.0 % vs. 42.7 % in Hungary). Moreover narrow spectra penicillins (ATC: J01CF, J01CE) were much commonly used in Norway than in the other two countries (41.8 % vs 4.6 % in Hungary and 4.6 % in Portugal). While for Hungarian children cephalosporins (J01D) (mainly cefuroxim) were widely prescribed (29.6%) its' use was lower in Portugal (8.3%) and quite rare in Norway (1.5%). Tetracyclines were commonly prescribed for Norwegian children (8.5 %) but not for Portugese and Hungarian ones (2.4 % vs. 0.4 %, respectively).

Conclusion: The pattern of paediatric antibiotic use in Hungary and Portugal were very different compared to Norway. The high consumption of broad spectra penicillins and the low consumption of narrow spectra penicillins begins in childhood in Hungary and Portugal. The responsibility of paediatrician, paediatrician GPs is outstanding to shape antibiotic use.

P1W.2

Measuring potential adverse consequences of restricting antibiotic treatment of respiratory tract infections in primary care: a population data linkage study using NHS Scotland's Infection Intelligence Platform

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Background

As antimicrobial stewardship interventions are leading to reductions in antibiotic prescribing in primary care, there are concerns about potential under-treatment of serious bacterial infections. The aim was to examine trends in prior antibiotic prescribing, and outcome, for patients admitted with complicated respiratory tract infections (RTI) over a time period of reducing primary care antibiotic use.

Method

Data on all hospital admissions in Scotland with community acquired pneumonia, mastoiditis and peritonsillar abscess, from April 2010 to March 2014, were identified within the NHS Scotland Infection Intelligence Platform (IIP) and linked at patient level to routine demographic and healthcare data, including all primary care prescribing in the previous year. The proportion of patients with an antibiotic prescription in primary care in the prior 30 days was calculated for each study month. Logistic regression analyses examined whether the likelihood of each prior antibiotic prescription measure was associated with time (study month) after adjustment for patient characteristics, and whether the likelihood of death within 30 days of admission was associated with time, patient characteristics and prior antibiotic prescription.

Results

Community acquired pneumonia was the most common study infection. Admissions rose for the first three years then levelled off, and were more common among older people. The proportion with any antibiotics, in the prior 30 days to admission increased over the study period, by 5% (4 to 6%) per study year. 30-day mortality reduced by 9% (6 to 12%) per study year.

Conclusion

This study provides reassurance that in a time period of reductions in overall primary care antimicrobial prescribing, there have been increases in prescribing rates among high risk patients. This analysis can be repeated with further decreases in antibiotic use and for other infections through NHS Scotland's IIP.

P1W.3

Characterisation of risk factors associated with antibiotic resistance in urinary isolates in the community: an exemplar of NHS Scotland's Infection Intelligence Platform

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Background

The threat from resistance to multiple antibiotics is growing. Multidrug resistance reduces treatment options and the potential for increased treatment failure. In the community urinary tract infections (UTI) are common and antibiotic treatment is usually empirical, often not taking account of patient characteristics, risks or previous treatments. This record linkage study used routine national data to characterise factors associated with antibiotic resistance in urine isolates.

Method

The NHS Scotland Infection Intelligence Platform was used to link data on urine isolates, collected from national surveillance data (January 2012 - June 2015), with national hospital activity and community prescribing datasets at an individual patient level. Patient and drug risk factors associated with resistant and multi-resistant isolates were assessed using multivariable multinomial logistic regression.

Results

Of the 40,984 isolates: 45% were resistant; 27% multi-resistant; and 28% susceptible to the antibiotics tested. Antibiotic exposure in the 6 months prior to a urine isolate was strongly associated with multi-resistance; those prescribed ≥ 4 different antibiotics had OR 6.09 (95% CI 5.16-7.19). Cumulative antibiotic exposure had a dose-response relationship - multi-resistance was observed in individuals with ≥29 DDD of any antibiotic (OR 6.54; 95% CI 5.88-7.27), nitrofurantoin (OR 8.56; 95% CI 6.56-11.18) or trimethoprim (OR 14.61; 95%CI: 10.53-20.27) in the 6 months prior to the isolate. The temporal effect of exposure to antibiotics on multi-resistant isolates remained in effect for up to 10-12 months for both nitrofurantoin (OR 2.31; 95% CI 1.93-2.76) and trimethoprim (OR 1.81; 95% CI 1.57-2.09) but not for any antibiotic (OR 1.16; 95% CI 0.99-1.34).

Conclusion

National data linkage capacity has allowed useful characterisation and quantification of risk factors for multi-drug resistance in urine isolates. This evidence base will inform the development of patient centred prescribing decision support tools for the treatment of UTI and enable improved antimicrobial stewardship.

P1W.4

Impact of the national intervention programme on parental knowledge, attitudes and practice of antibiotic use for respiratory infections

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Background

Children are prone to high rates of antibiotic use due to greater frequency of respiratory tract infections, and concerns about possible complications. Recent studies raised awareness of high resistance levels and inappropriate antibiotic use, including OTC sales of antibiotics across South-Eastern Europe. Nation-wide multifaceted interventions to improve antibiotic use were undertaken in FYR Macedonia in September 2014. This study aimed to assess the parental knowledge and attitudes about antibiotics, and self-medication practices in children, and evaluate the impact of interventions on these parameters.

Methods

Pre-post intervention surveys were conducted in May 2014, May 2015 and May 2016 in three administrative regions in the country. Data were collected by interviewing parents of children younger than 15 years of age through a questionnaire. The analysis of knowledge, attitudes and antibiotic use involved descriptive quantitative statistics. The effects of interventions were assessed by a logistic and linear regression analysis.

Results

Data from 1203 interviewees showed that 80% of parents knew that antibiotics could kill bacteria, while 40% believed antibiotics could kill viruses. One third of parents expressed potential dissatisfaction with doctors who would not agree with them on antibiotic use. More parents received information about not taking antibiotics unnecessary after the interventions, but the rates decreased one year later. At baseline, 20% of the parents and 10% of the children who received antibiotics in previous year, took them without prescriptions. Parental self-medication rates did not change over time, while children rates decreased only in 2015.

Conclusion

The insignificant and short-term effects of the interventions demonstrate that interventions need to be implemented for a longer period, at a large scale, with active health providers' engagement, and accompanied by inspections to promote appropriate antibiotic use and discourage self-medication. Future research should combine other methods (observations and pharmacy sales data studies) to validate self-reported data.

P2W.1

Analysis of risk factors for bacteraemia and subsequent mortality in Scotland: a national data linkage matched case-control study using NHS Scotland's Infection Intelligence Platform

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Background

Whilst some bacteraemia like MRSA have been in decline over the past few years in Scotland others such as E.coli have increased. This matched case-control study aimed to improve the understanding of the aetiological risks for acquiring bacteraemia other than MRSA and the risk factors that influence outcome.

Methods

Hospital-associated blood cultures positive with Streptococcus pneumoniae, Enterococcus faecalis, Enterococcus faecium, Escherichia coli, Klebsiella pneumonia and Pseudomonas aeruginosa were identified from the "Electronic Communication of Surveillance in Scotland" dataset for January 2010 to December 2014. Controls were assigned to each case from the national hospital activity dataset.

Using the NHS Scotland Infection Intelligence Platform all cases and controls were linked to national hospital activity data, patient-level community prescribing data and national mortality records. Risk factors associated with the development of bacteraemia were assessed using conditional logistic regression and risk factors for 30-day all cause mortality assessed using logistic regression.

Results

Measures of co-morbidity (Charlson score, previous hospitalisations and drug classes prescribed in the previous 12 months) were found to be associated with an increased risk of most types of bacteraemia, as was care home residence. Antibiotic exposure in the community in the three months prior to infection was not significantly associated with an increased risk for most types of bacteraemia. Risk factors for S.pneumoniae differed - immunosuppressant prescribing was associated with increased risk (OR=1.32; 95% CI 1.08-1.61), as was higher deprivation however antibiotic exposure was associated with a decreased risk (OR=0.83; 95% CI 0.69-0.99). Increased age, increasing morbidity and care home residence were found to be significant predictors of mortality across most types of bacteraemia.

Conclusion

Data linkage has enabled us to characterise risk factors for hospital-associated bacteraemia. These results will be used to enhance future studies and the development of clinical decision support tools in Scotland.

P3W.1

A snapshot of medication adherence across three European countries: application of common methodology.

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Introduction: Drug-utilization studies applies different methods to various data types to describe medication-adherence. Comparison of results of these studies is difficult due to differences in the methods applied, data sources and selected populations. This study, performed under the umbrella of Action-Group-A1 on adherence of European-Innovation-Partnership on Active-and-Healthy-Aging, evaluates medication adherence and persistence to chronic disease therapies across different European settings applying a harmonized method of data extraction and analysis.

Methods: Information were retrieved from pharmacy-claims databases of three European countries: Spain (EpiChron-Cohort), Ireland (HSE-PCRS), Italy (Caserta-LHU). Subjects aged >65 years, newly initiated antidiabetics, statins, bisphosphonates (ATC III-level) between 7/1/2010 and 12/31/2010 were identified and followed over 12-months. The first dispensing defined the index-date and treatment group. Main outcome measures was adherence (medication possession ratio, MPR) and persistence on index treatment. MPR <80% was considered as non-adherence. Subjects were defined as persistent until discontinuation (gap >60 days between two subsequent index treatment refill). All country-specific datasets were prepared employing a common data input model. Outcome measures were calculated for each country and then pooled using random effect models.

Results: Total number of subjects analyzed was 33,490. Pooled estimates: i) antidiabetics cohort: 30.33% of subjects with MPR<80% (95%confidence interval: [25.53; 35.60], I²=95%, p<0.0001); rates of non-persistence 46.80% (95% C.I.: [36.40; 57.49], I²=98.7%, p<0.0001); ii) statins cohort: 52.45% of subjects with MPR<80% (95% C.I.: [33.43; 70.79], I²=99.9%, p<0.0001); rates of non-persistence 55.63% (95% C.I.: [35.24; 74.29], I²=99.9%, p<0.0001); iii) bisphosphonates cohort: 61.35% of subjects with MPR<80% (95% C.I.: [52.83; 69.22], I²=97.5%, p<0.0001); rates of non-persistence 60.24% (95% C.I.: [45.35; 73.46], I²=99.2%, p<0.0001).

Conclusion: Our study showed high degree of heterogeneity among countries in adherence and persistence rates. The extraction and aggregation of data into a common data model allowed to calculate the drug use parameters by means of a systematic and uniform approach.

P3W.2

Adherence Trajectories to Essential Medications and Clinical Outcomes after Acute Coronary Syndrome. A Population-Based Cohort Study

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Background: Treatment with antiplatelet, statins, beta-blockers, and ACEI/ARBs to reduce cardiovascular morbidity and mortality after an Acute Coronary Syndrome (ACS) is widely recommended. Our aim was to identify adherence patterns to the recommended medications after an ACS in the Valencia region and to assess their impact on clinical outcomes.

Methods: Population-based retrospective cohort of all patients discharged after hospitalization for ACS in the Valencia region (Spain) during 2009-2011. We created a subcohort with prescriptions from at least three therapeutic groups within the first month after discharge. We assessed monthly medication adherence during 360 days following initiation defined as having ≥ 24 days covered out of 30, and identified adherence patterns through group-based trajectory models. A composite clinical outcome (ACS, heart failure, stroke, and mortality) during the year after adherence assessment was evaluated. A multivariable Cox proportional hazards model was used to assess the association between adherence patterns and clinical outcomes.

Results: Among 15,797 patients discharged alive, 10,718 (67.85%) initiated treatment with 3 or 4 therapeutic groups. We identified six different adherence patterns: (I) nearly-always adherent (57.9%); (II) slow decline (7.7%); (III) fast decline (9.5%); (IV) early gap in adherence with a later recovery (9.7%); (V) moderate adherent with a later gap and recovery (6.0%); and (VI) non-adherent (9.21%). Compared to nearly-always adherent patients, slow decline (HR: 1.27, CI 95%: 1.01-1.60), and non-adherers (HR: 1.30, CI 95%: 1.06-1.60) had a greater risk of adverse outcomes.

Conclusions: Six adherence patterns to 3 or more essential medications after ACS were identified. Slow decline and non-adherence patterns were associated to a higher risk of adverse outcomes as compared to nearly-always adherent patients. The identification of adherence patterns associated to higher risk of adverse clinical outcomes may be useful to target interventions to improve medication adherence.

P3W.3

Introducing Adhere R: an R package for visualization of medication histories and calculation of adherence to medications using electronic healthcare data

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Background: Electronic healthcare data (EHD) are increasingly used to study adherence to medication and its role in drug effectiveness and safety, and to support clinical decision making. Recent theoretical work has established consensus on standardized definitions of the components of the adherence process. Yet, algorithms for estimating adherence from EHD have not been standardized and aligned to the new conceptual framework, and are not transparently reported on publication. As the Open Science movement gains momentum, standardized and transparent adherence algorithms have become indispensable for a solid evidence basis.

Methods: We developed AdhereR, a package for the statistical environment R, to facilitate computing EHD-based estimates of adherence to medications. Following a review of current adherence guidelines, definitions and operationalizations, we implemented several functions for calculating medication persistence (treatment episodes) and implementation (Continuous Medication Availability; CMA) and visualizing medication histories. We illustrate the use of AdhereR with an example dataset of 2-year records of 100 patients and describe the various analysis choices possible and how they can be adapted to different research contexts.

Results: Nine CMA variations can be computed for single intervals, multiple treatment episodes, and sliding observation windows. Different parameter choices result in different estimates (e.g. median 1-year implementation range 56%-83% in one simulation comparing single-interval CMAs). Separating persistence from implementation results in higher CMA estimates (e.g. median increased from 57% to 85% when comparing single with per-episode CMA). Interactive visualizations of medication histories will demonstrate the various parameters and their possible applications.

Conclusion: AdhereR facilitates transparent and replicable calculations of EHD-based medication adherence. Analysis choices impact calculations and need careful consideration. Visualisation of medication histories for individual cases can support communication between data analysts and clinical experts to guide parameter choices in individual studies. AdhereR can be easily integrated into more complex analysis protocols and clinical decision support systems.

P3W.4

Adherence to antiretroviral treatment amongst patients in Botswana: A multi-measure approach to guide future practice

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Introduction: Poor adherence rates are a concern as benefits of antiretroviral treatment (ART) to individuals and public health are adherence dependent. Currently, there is no "gold standard" for measuring ART adherence as the majority of adherence measurement tools cannot meet all features of an ideal tool. This study aimed to assess adherence to ART in routine clinical care using a multi-measure approach and identify factors contributing to non-adherence.

Methods: One objective and two subjective adherence measures were used in a quantitative descriptive study amongst 304 adult patients at Lesethana Clinic, Botswana. Three months' retrospective pill count data were collected from clinic records and mean medication possession ratio calculated/patient. Two self-report adherence measures (set of four questions; rating scale) and factors contributing to non-adherence were collected through interviews. A composite adherence score based on all three measures was calculated/patient. Calculated adherence scores/patient, and for each measure, were categorised as <95% or ≥95% adherent.

Results: Females predominated (66.1%), with mean age 40.4±9.3 years and mean duration on ART 52.5±33.9 months. Although mean (98.0±2.2%) and median (98.7%[97.7; 99.3]) pill count adherence (3 months) was high, lower proportions of patients were categorised as ≥95% adherent with the pill count (88.2%), self-report questions (80.6%) and rating scale (78.9%) methods. Proportion of adherent patients with the composite measure was significantly lower (60.9%; p<0.001). Challenges with adherence reported by 87(28.6%) patients, included arriving home late (33.3%), forgetfulness (23.0%), visiting or attending functions (19.5 %), alcohol (18.4%) and medication side-effects (16.1%).

Conclusion: Results illustrated the variability amongst different measures of adherence. Consequently, important when monitoring adherence to use more than one measure. Pill count adherence was high compared to other measures, while the composite adherence score was significantly lower. Using multi-method adherence measures would allow the strengths of one method to compensate for the weaknesses of another.

P4T.1

Trends of potentially inappropriate prescribing in early old aged people over a 5-year period

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Background

In Ireland, 30% of people aged 45-64 years and 60% aged ≥65 years use ≥5 daily medicines, similar to figures of other developed countries. High numbers of medicines and multimorbidity are major risk factors for potentially inappropriate prescribing (PIP) comprising potential inappropriate medications (PIMs) and potential prescribing omissions (PPOs). Recent efforts to improve prescribing appropriateness have focused on the older population (≥65 years). Whether there is likely to be benefit from earlier PIM and PPO intervention is unclear. This study therefore examined the patterns of PIP in an early old aged population.

Methods

A secondary data analysis of a primary care cohort of patients aged 60-74 years. Screening Tool to Alert doctors to Right Treatment (START) and Screening Tool for Older Persons' Prescriptions (STOPPP) criteria were used to identify PIMs and PPOs from medication data extracted from patient records over a 5-year period. Generalized estimating equations described the PIP patterns over time and adjusted for age, gender, number of medicines and new diagnoses.

Results

978 patients (52% female; mean no. medications: 2.1 (SD 3.1)) were included in the analysis. Those with a PPO increased from 31.2% at baseline to 42.2% at end of follow-up. For PIMs, the proportion increased from 39.7% to 45.6%. There were significant increases in the odds of receiving PPOs and PIMs comparing 5-year follow-up to baseline (OR 1.08, $p < 0.001$ and 1.04, $p < 0.001$, respectively). The increase in the odds was significantly associated with polypharmacy and number of new diagnoses, but not with age nor gender. Number of PPOs and PIMs were significantly correlated with number of medicines over the 5-year period.

Conclusion

PIP is highly prevalent in early old age and increases over a prospective 5-year period, indicating that PIP as a public health issue needs to be addressed before the onset of "old" old age.

P4T.2

Antihypertensive medication regimen intensity and incident dementia in an older population

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Background

Hypertension is associated with an increased risk of vascular dementia and Alzheimer's Disease. The potentially protective effects of antihypertensive medication regimens (number of antihypertensives, types of antihypertensive classes and total prescribed daily doses) on dementia remain uncertain. The aim of this study was to investigate the association between antihypertensive medication regimen intensity and dementia over a six-year period.

Methods

This was a prospective, longitudinal study of 1208 participants aged ≥ 78 years, free of dementia, and residing in central Stockholm at baseline (2001-2004). Participants were examined at 3- and 6-years follow-up to detect incident dementia. Data were collected through face-to-face interviews, clinical examinations, and laboratory tests. Antihypertensive use data were obtained by a physician through participant self-report, visual inspection or medical records. Cox proportional hazards models were used to compute hazard ratios (HRs) and 95% confidence intervals (CIs) for incident dementia associated with time-varying antihypertensive regimen intensity over the study period after adjusting for potential confounders.

Results

During the follow-up period, 125 participants were diagnosed with dementia. Participants who developed dementia were more likely to have vascular disease at baseline (66.4% vs 55.3%, $p=0.02$). In fully adjusted analyses, the number of antihypertensive classes (HR 0.81, 95%CI 0.66–0.99) and total prescribed daily dose (HR 0.80, 95%CI 0.66–0.96) were associated with reduced dementia risk. Angiotensin-converting enzyme inhibitors were associated with reduced dementia risk (HR 0.50, 95%CI 0.26 – 0.98), independent of other drug classes.

Conclusions

Increasing intensity of antihypertensive drug use among older people may be associated with reduced incidence of dementia over a six year follow up.

P4T.3

Prescription of futile and essential drugs in the last three months of life of older patients receiving palliative care

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Background

Near the end of life, reconsidering drug treatments is necessary. Priority should be given to drugs that are "essential" for the relief of distressing symptoms, while limiting the use of potentially "futile" treatments. Our objective was to assess the quality of prescriptions during the last three months of life of older adults receiving palliative care.

Methods

A retrospective observational study was conducted. It included patients aged ≥ 65 years, who died in a single university hospital between 1 January 2014 and 30 June 2014, and who received palliative care (ICD-10 code Z51.5). Prescriptions were collected during the last three months prior to death. Drugs were categorized as "futile" or "essential" to assess the quality of prescriptions 90 days before death (D90) and the day of death (D0).

Results

A total of 149 patients were included. The median number of drugs decreased from 7 (D90, n=995) to 5 (D0, n=841). Median duration of palliative care was 4 days. Between D90 and D0, the proportion of prescribed drugs described as "essential" increased from 32.8% to 64.9% while potentially "futile" drugs decreased from 47.7% to 15.6% during the same period of time.

Among "futile" drugs, antithrombotics and proton pump inhibitors were the most deprescribed (from 51.0%, 45.0% of patients at D90 to 11.5%, 18.8% of patients at D0, respectively). For "essential" drugs, midazolam, opioid analgesics, antiemetic and antiepileptic drugs were the most prescribed (1.3%, 16.1%, 0.7%, and 8.0% of patients at D90 to 75.2%, 79.2%, 26.8%, and 20.8% of patients at D0, respectively).

Conclusion

Drug use at the end of life remains high. It is characterized by the frequent introduction of essential drugs and the decrease of potentially futile treatments. This inversion occurs during the last week of life, which is probably related to the late implementation of palliative care.

P4T.4

Discontinuing Inappropriate Medication In Nursing Home Residents (DIM-NHR STUDY): A Cluster Randomized Controlled Trial

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Background: Inappropriate prescribing is a prevalent problem in nursing home residents that is associated with cognitive and physical impairment. Few interventions have been shown to reduce inappropriate prescribing. The aim was therefore to examine successful discontinuation of inappropriate medication.

Methods: A cluster randomized controlled trial was conducted. Fifty-nine wards were randomly assigned to the intervention or to 'care as usual'. The intervention was a Multidisciplinary Multistep Medication Review (3MR), consisting of an assessment of the patient perspective, a medical history, a critical appraisal of medication, a meeting between the elderly care physician and a pharmacist, and the execution of medication changes. The primary outcome was successful discontinuation of ≥ 1 inappropriate drug(s), without relapse or severe withdrawal symptoms. Secondary outcomes included neuropsychiatric symptoms, cognitive function and quality of life. Nursing home residents with a life expectancy of >4 weeks who did not refuse treatment with medication were included. Data were collected at baseline and at an average follow-up of 144 days.

Results: A total of 426 nursing home residents participated (intervention group: N = 233 and control group: N = 193). Generalized linear mixed models (logit link function) showed that for 91 (39.1%) of the residents in the intervention group ≥ 1 inappropriate drugs could be successfully discontinued vs. 57 (29.5%) of residents in the control group (adjusted odds-ratio: 1.57, 95%CI: 1.03 to 2.39). There was no deterioration on secondary outcomes.

Conclusion: The 3MR is effective in discontinuing inappropriate medication at the concerned medical units.

P5T.1

Psychotropic drug use and the differences between men and women: results from a household survey.

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Background: Although widely prescribed, psychotropic drugs are still controversial as to their use. Large-scale use refers to other dimensions of the problem, permeating areas of psychology and social sciences. Understanding the use of these drugs is, therefore, understanding the characteristics of the population that uses them.

Methods: Using data from the National Survey on Access, Use and Promotion of Rational Use of Medicines (PNAUM), a household survey conducted in Brazil in 2013-2014. The psychotropic drugs were grouped into four therapeutic classes: antidepressants; anxiolytics; antipsychotics and mood stabilizers. Prevalence estimates and their confidence intervals (95%) were calculated and Pearson's chi-square tests were used to assess the statistical significance (5%). The prevalence ratio between the sexes was calculated through a multivariable Poisson Regression, adjusted by polynomial age and by number of medicines, socioeconomical status and education as categorized variables.

Results: Psychotropic drugs were used by 8.0% of the adult population living in the Brazilian urban area. The prevalence use increased with increasing age. The adjusted prevalence ratio, considering men as a reference, in those who didn't use any other drugs was 2.43 [95%CI:1.90–2.96], 1.45 [95%CI:1.21–1.69] among those who used 1 to 4 and 1.49 [95%CI:1.04–1.94] for the ones who used 5 or more. Antidepressants and anxiolytics were the most commonly used therapeutic classes, being more prevalent among women, while antipsychotics and mood stabilizers were more prevalent among men.

Conclusion: The prevalence of psychoactive drugs use was 8%; among users, women stand out for their greater use. The historical-cultural context inherent to the genre; the social roles taken; the way conditions are diagnosed, the epidemiology and differentiated symptomatology between men and women seem to influence the occurrence of high prevalence of antidepressant use in women and the higher prevalence of antipsychotic use and mood stabilizers among men.

ion in nursing home residents whilst probably not compromising their wellbeing.

P5T.2

Concerns regarding the safety of combined hormonal contraceptives: influence of an EU risk assessment process on prescription patterns. An analysis of German claims data 2011–2015.

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Background: The composition of combined hormonal contraceptives (CHC) has changed over time for reducing side effects like cardiovascular and thrombotic events (VTE). Since several studies showed increased risk for newer combinations, a European referral process was initiated. EMA confirmed a higher risk for 3rd generation gestagens and for drospirenon, with no assessment given for some others. Manufacturers of 3rd/4th generation substances were required to document risks in the patient information. Risk classes (RC) have been defined, where the substances subject to the referral process are in classes I, III (higher risk of VTE) and X (no final assessment). The study answers the question whether the referral and the subsequent implementation led to changes in CHC prescription patterns.

Methods: German prescription data for 1.1m women below 20 were analysed descriptively. Effects of interventions were analysed with ARIMA-based models, potential influence factors were evaluated using logistic regression.

Results:

The shares of RC I and RC X recipients has risen substantially from 2011 to 2014, while the RC III recipient share shows a steady decrease (–64%). The analysis showed a slight enhancement of both the decrease in RC III and increase in RC X induced by the referral, whereas its implementation manifested no additional effect.

Conclusion:

The decrease in RC III share already observed before the referral process can be explained with the pre-existing discussion around CHCs. The effect attributable to the referral was statistically significant, though very small, both in RC III and RC X. However, it should be borne in mind that the evidence for a connection between interventions and prescription change is only indirect. Nevertheless, the analysis confirmed that routine data are suitable for impact analyses, and monitoring prescription patterns can be recommended as feedback after regulatory or political interventions. (BfArM grant V16770/68605/2016-2017)

P6T.1

Developing advices for safe drug use in patients with liver cirrhosis

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Background: Liver cirrhosis can have a major impact on pharmacodynamics and pharmacokinetics, but guidance for prescribing is lacking. The aim of this study is to develop advices for the safe use of drugs in patients with liver cirrhosis and to assess the clinical relevance of these advices.

Methods: Safety and dosing advices were developed by combining a systematic literature search with expert opinions. Safety advice was categorized as: drug can be used in liver cirrhosis; preferably use a safer drug; or avoid using this drug in patients with liver cirrhosis. Recommendations on dose adjustments were based on pharmacokinetic literature. Advices were, if applicable, sorted by severity of liver cirrhosis. All advices were implemented in the relevant clinical decision support systems in the Netherlands.

Results: We evaluated the safety and dosing of a total of 209 drugs in liver cirrhosis and formulated 218 advices. For nine drugs, two advices were formulated for different administration routes or indications. In 73% (n=159) of 218 advices an action is needed by the prescriber or pharmacist. This involves a safety action in 92 advices (42%), a dose adjustment in 31 (14%), or both in 36 (17%). The safety action is to preferably use a safer drug in 42 advices (19%) and is depending on the severity of liver cirrhosis in 56 (26%) of advices. The safety action in the remaining 30 advices (14%) is to avoid the drug because of large alterations in pharmacokinetics (n=9) or pharmacodynamics (n=21) in patients with liver cirrhosis compared to healthy controls.

Conclusion: Almost three quarters of 218 formulated advices need action by the healthcare professional and are therefore clinically relevant. A clinical decision support system can aid healthcare professionals to safely prescribe drugs in these patients.

P6T.2

Latent class analysis of anticholinergic and sedative medication use: a national population study

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Background

Anticholinergic/sedative medications are prescribed frequently to older patients, despite their negative effects on physical and cognitive function. Many different medications have anticholinergic/sedative effects, e.g. cardiovascular-, psychotropic- and alimentary tract medications. This study aimed to identify subgroups of anticholinergic/sedative medication use in patients with high cumulative anticholinergic/sedative drug exposure as measured by the Drug Burden Index (DBI).

Methods

A national population study of patients with high anticholinergic/sedative drug exposure. We used a nationwide sample of all anticholinergic/sedative medications dispensed in community pharmacies in November 2016 in the Netherlands. Data were provided by the Dutch Foundation of Pharmaceutical Statistics. We selected patients with high exposure to anticholinergic/sedative medications defined by having a DBI ≥ 2 (exposure to about 4 anticholinergic/sedative medications). A latent class analysis was performed on the top 5 used medications (grouped by ATC level 1) to identify subgroups of patients with specific medication combinations.

Results

Data were available from 1,773 pharmacies (89.5% of total community pharmacies). Overall, 493,753 patients had a DBI ≥ 2 . Patients (mean age 76.3 years (SD ± 7.5), 56.9% female) used on average 4.3 (SD ± 1.2) anticholinergic/sedative medications and had a mean DBI of 2.8 (SD ± 0.7), with a range of 2.0-10.9. Latent class analysis identified two subgroups of patients. Subgroup 1: "medium psychotropic use" (90.9%), subgroup 2: "high psychotropic use" (9.1%). In subgroup 1 patients often used a combination of cardiovascular- (98.2%), alimentary tract- (78.4%) and psychotropic medication (49.0%), whereas in subgroup 2 patients used psychotropic medication (95.1%), often only in combination with alimentary tract medication (81.8%).

Conclusion

Distinct subpopulations of patients with anticholinergic and sedative medication use were observed. We will develop targeted interventions for those subgroups to reduce overall anticholinergic and sedative drug burden.

P6T.3

Predicting rehospitalization in patients treated with antipsychotics: a prospective observational study

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Background

Prediction of rehospitalization in patients treated with antipsychotics is important to identify patients in need of additional support to prevent hospitalization. The aim of this study was to identify factors that predict rehospitalization in patients treated with antipsychotics at discharge from a psychiatric hospital.

Methods

In this prospective observational study, adult patients suffering from schizophrenia, psychotic or bipolar I disorders who had been hospitalized in a psychiatric hospital for ≥ 7 days and were treated with oral antipsychotics at discharge were included. The outcome of interest was rehospitalization within six months after discharge. A prediction model for rehospitalization using Cox proportional hazards was constructed including: patient/disease and medication characteristics, patients' beliefs about medicines, and health care professional's-rated assessment for all patients. The patients were stratified by diagnosis (schizophrenia and non-schizophrenia). Area under the receiver operating characteristic curve (AUCROC) was also assessed.

Results

87 Patients were included and 33.3% were rehospitalized within six months after discharge. The variables that predicted rehospitalization for all patients were duration of hospitalization, patients' attitude towards medicine use, and health care professional-rated assessment (such as whether the physician and the nurse discussed antipsychotic adherence during hospitalization, and whether the nurse asked the patient if he/she was adherent to medication). The model including these factors had an AUCROC of 0.82. Rehospitalization for patients with schizophrenia could be predicted (AUCROC=0.71) by GAF score, age, and harm score (from the patients' beliefs about medicines). Rehospitalization was predicted (AUCROC=0.73) for non-schizophrenia patients with GAF score, residential situation, adherence predicted by the physician, and rehospitalization predicted by the nurse.

Conclusions

Rehospitalization was predicted by a combination of variables from the patient/disease and medication characteristics, patients' attitude towards medicine use, and health care professional's-rated assessment. These variables can relatively easily be assessed at discharge to predict rehospitalization within six months after discharge.

P6T.4

Development and testing of the Side Effects Patient Assessment Tool (SE-PAST)

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Background

There are numerous methods for assessing causality of ADRs designed for use by professionals working in pharmacovigilance centres. However, there is limited research into similar tools to enable patients to assess causality. A mechanism for assisting them to do so may prove useful in encouraging reporting of suspected ADRs to regulatory authorities and empowering patients to discuss experiences with health professionals. This study set out to develop and test such a tool.

Methods

The SE-PAST was developed from results of a survey and interviews with patients' experiencing ADRs, a similar tool developed in Thailand and the Naranjo algorithm. It included 10 statements enabling causality to be assessed, covering timing, additional information sources and experiences, each with four possible options: yes/no/can't recall/not applicable. Responses were scored and weighted to arrive at four possible categories of causal association: highly probable, probable, possible, unlikely.

The instrument was validated by obtaining feedback from 11/15 interviewees whose experiences contributed to its development, plus a further 20 people known to have experienced an ADR. It was then evaluated by distributing an on-line version to the wider public through patient support groups.

Results

Validators found the instrument easy to read (31), to understand (27) and to complete (29). Of 761 people accessing it on-line, 303 completed some of the 10 statements. Of 184 with 10 fully completed statements, 38(20%) suspected ADRs were categorised as highly probable, 120(64%) probable, 19(10%) possible and 10(5%) unlikely.

Feedback was given by 240 respondents; of these 144(60%) found the SE-PAST useful; 146(70%) were encouraged to report their SE to relevant agencies and 170(75%) felt motivated to discuss it with a health professional.

Conclusion

The SE-PAST was easily completed and understood by the public experiencing ADRs and could be a useful tool to encourage patient reporting to agencies and health professionals.

P8T.1

Risks of specific major congenital malformations associated with prenatal exposure to antiepileptic drugs: a nationwide cohort study based on the French healthcare databases

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Background: Data on the risk of rare and specific major congenital malformations (MCMs) associated with maternal exposure to antiepileptic drugs (AEDs) is limited. The objective of the study is to assess the association between prenatal AEDs monotherapy exposure during the first two months of pregnancy and the individual risks of 26 specific MCMs.

Methods: This cohort study included pregnancies identified by their outcomes (live births, stillbirths and therapeutic abortion ≥ 20 weeks of gestation) between 2011 and 2015 in the French healthcare databases. Women were considered exposed if they were reimbursed for an AED from one month before up to 2 months after pregnancy onset. Reference group included pregnant women with no AED reimbursements. MCMs were detected up to 12 months after birth using child's hospital discharge diagnoses and/or specific medical procedures. Odds ratios were adjusted (aOR) for maternal age, deprivation, year of pregnancy and folic acid use, accounting for correlations within women with multiple pregnancies. Crude OR with exact confidence intervals were calculated for MCMs with fewer than five cases.

Results: The cohort included 1,897,359 pregnancies, of whom 3,035 were exposed to lamotrigine, 1,691 to pregabalin, 924 to valproate used as AED, 594 to levetiracetam, 521 to carbamazepine and topiramate, 140 to oxcarbazepine. Exposure to valproate was associated with increased risks of spina bifida (aOR=18.8[8.4-42.3]), heart defect (aOR=5.2[3.5-7.9]), cleft palate (OR=5.2[1.1-15.2]), anorectal atresia (OR=11.0[2.3-32.4]), hypospadias (aOR=4.7[2.3-9.7]), preaxial polydactyly (OR=10.8[1.3-39.5]); lamotrigine and pregabalin with an increased risk of heart defects (aOR=1.6[1.0-2.4] and 1.8[1.1-3.0] respectively); topiramate with an increased risk of cleft lip (OR=6.7[1.4-19.6]).

Conclusion: These results confirm the teratogenic profile of valproate and topiramate and suggest that maternal exposure to lamotrigine and pregabalin might be associated with an increased risk of heart defects. For some AEDs, the low number of certain MCMs should be kept in mind when interpreting the results.

P8T.2

Health care utilization and dispensed medicines among children in Stockholm, Sweden

Health Care Utilization And Dispensed Medicines Among Children In Stockholm, Sweden Elin Dahlén^{1,2}, Health Care Utilization And Dispensed Medicines Among Children In Stockholm, Sweden Björn Wettermark^{1,2}

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Background

Health care utilization among children is complex. Individual level data sources may be combined to provide an overview of health care utilization. The aim of this study was to assess the children's health care utilization including visits, telephone support and dispensed medicines in the region of Stockholm, Sweden.

Methods

A cross-sectional study including all children (0-17 years) living in Stockholm 2015. The regional database VAL (held by the Stockholm County Council) was used to collect number of visits and recorded diagnoses from inpatient care, specialized ambulatory care and primary care along with data on dispensed medicines. Also, data from the first line telephone support (1177, health care advices by experienced nurses free to dial 24 hours a day) for the study population was added to assess reasons behind calling health services.

Results

In total, 485 011 children lived in Stockholm 2015. Among them, 71% had at least one contact with healthcare. Visits in primary care were most common (292 202 children), followed by emergency hospitals (100 563 children) and paediatric clinics in specialized ambulatory care (60 575 children). The most common diagnosis for all visits was in respiratory medicine (ICD-10 chapter 10 J; 112 992 children). Over 3% (16 277 children) were hospitalized. One out of four children (or their guardian; 124 282 children) called 1177 with an average of 2.2 calls/child. The most common reasons for calling 1177 were fever, rash and cough.

Almost half of the children (223 646 children) were dispensed medicines, with antibiotics, asthma medicines, cough medicines and oral allergy medicines being the most common ones.

Conclusion

The first line telephone support is an important part of the children's health care utilization in Stockholm. To get an overall perspective of health care, also e-health such as telephone support needs to be included in future studies.

P9T.1

Modelling free-text prescription dose instructions to support daily dosage calculation

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Background

The NHS Scotland Prescribing Information System (PIS) receives around 100,000,000 electronic prescription messages containing, structured and unstructured, dose instruction (DI) fields annually from primary-care.

The aim, using Natural Language Processing (NLP), was to extract drug dosing information from DIs to calculate the intended treatment duration; facilitating conclusions about prescription frequency, treatment adherence, and impact upon prescribing safety and effectiveness.

Methods

NLP was used to develop an algorithm to transform DIs into DI variables. DIs issued from 2009 to 2014, for drugs in the British National Formulary (chapters 1-10), were sorted by frequency. The algorithm was developed incrementally using 1,000 DIs per development cycle until the algorithm could read the top 88% of DIs by volume. Further developments were made by randomly selecting >1000 DIs per development cycle from the remaining DIs until over 95% of the texts by volume were processed. For validation, all texts with a frequency count $\geq 1,000$ were selected along with 500 randomly selected texts from four frequency groupings. These texts were parsed by the algorithm and the output was checked by researchers in the FARR Institute.

Results

The NLP algorithm was applied to 456,684,974 DI texts consisting of 4,964,083 distinct DIs. The algorithm successfully populated the DI variables for 95% of DIs by volume. DIs containing “every 4 to 6 hours” proved problematic; assumptions are required when expressing the text as a dosing frequency. The data model was expanded to record the frequency information as either: ‘frequency per timing interval’ or ‘time interval between doses’.

Conclusions

Representing DIs using a dose amount, unit, and frequency data model requires assumptions to be made that are not globally valid. A zero assumption data model resolves this restriction by providing researchers with a machine readable version of the DIs containing the dosing information from the text.
present population. This is particularly important with increasing numbers of medications prescribed.

P9T.2

Dynamics of discontinuation in new metformin users in the first year of treatment

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Background

Adherence to pharmaceutical therapy is a complex behaviour. We sought to describe the patterns of discontinuation in users of metformin for type 2 diabetes (T2D) during their first year of treatment and identify factors associated with discontinuation.

Methods

Data were obtained for T2D patients who initiated metformin monotherapy from 2007 to 2013 inclusive from the Groningen Initiative to Analyze Type 2 Diabetes Treatment (GIANTT) primary care database. Information on prescriptions, demographics, laboratory tests, and co-morbid conditions was obtained. Discontinuation was defined as a gap of at least 180 days between the end of metformin supply from one prescription and the subsequent metformin prescription or end of follow-up. Patients were followed-up for 545 days (one year plus the minimum discontinuation gap) to identify discontinuations in the first year of treatment. Generalised linear mixed models were used to identify factors associated with discontinuation in those who continue metformin beyond the first 90 days.

Results

Of the 8499 study patients, 160 (2%) discontinued metformin within 90 days, with 130 (81%) restarting treatment with any antidiabetic during follow-up. Another 496 (6%) discontinued within a year of starting metformin, with 57 (11%) restarting any antidiabetic treatment. Mean time to discontinuation was 215 days (SD: 76). Being aged between 45 and 74 at metformin initiation (all OR < 1 and p < 0.05), or diagnosis one to five years prior (OR = 0.72, 95% CI: 0.55-0.94), were associated with reduced odds of discontinuation. A HbA1c ≤ 7.0 prior to initiation was associated with increased odds (OR = 1.43, 95% CI: 1.16-1.77).

Conclusion

Discontinuation was low in the first year of treatment, but appears to occur especially in initially well-controlled patients. Further analyses of adherence and reinitiation patterns will be performed to identify clusters of patients who might benefit from early targeted interventions.

P9T.3

Measuring polypharmacy in the elderly on a French national health database: impact of calculation method on prevalence and therapeutic classes

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Introduction. Polypharmacy is defined by World Health Organization as "the administration of many drugs at the same time or the administration of an excessive number of drugs". Neither the calculation method nor the number of molecules that defines polypharmacy are included in this definition. In this study, we compare two definitions of polypharmacy (cumulative versus continuous) in terms of prevalence, targeted therapeutic classes and associated factors.

Method. The analysis was performed on a sample of 43.619 persons aged 75 and over extracted from a representative sample of the population covered by health insurance in France (EGB) for year 2013. Cumulative polypharmacy was defined as the number of therapeutic classes reimbursed per quarter and continuous polypharmacy as the number of therapeutic classes reimbursed at least three times in the year. In addition, we measured the impact of counting fixed-dose combinations as one or two drugs and the impact of taking into account quarterly packs. A threshold of 10 was chosen to define polypharmacy. Medicines were identified according to the 5th level of their ATC code.

Results. For elderly over 75, prevalence of polypharmacy ranges from 27% for the continuous indicator without taking into accounts combination drugs and quarterly packs to 40.5% for the cumulative indicator including combination drugs. Taking into account combination drugs and quarterly packs increases the prevalence by 7 points for each indicator. Continuous polypharmacy underlines medicines for temporary conditions whereas indicators taking combinations into account bring in focus medicines that are frequently combined in single dosage forms, such as diuretics. Socio demographic factors do not differ according to the indicators.

Discussion. Our study confirms the major impact of the calculation method on the prevalence of polypharmacy. It clarifies the calculation method to be used in different circumstances and stresses the importance of selecting similar definitions when comparing studies.

P9T.4

National monthly standard-reports of incidence-rates of drugs in Sweden - development process, validation and results

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Background

Individual-level data over dispensed prescription drugs facilitate both research and enhanced descriptive data sets. The Swedish Prescribed Drug Register covers all drugs dispensed to inhabitants of Sweden (linked by the personal identification number) since July 2005. An important, but underutilized, new measure for longitudinal follow-up is incident-rates for different time periods.

The aim of the current project was to develop and validate standards for measuring and continuously reporting different incidence-measures (new on drug; on therapeutic group; on both drug and group; on drug but not on group) for age, sex, and area of residence.

Methods

Positive predictive value, PPV, of different run-in periods were analyzed based on golden standard as true incident user defined as 10 years of ru-in. Based on this a standard run-in period of 480 days were chosen, corresponding to an estimated at least 365 days without treatment in Sweden.

Extractions of datasets for several therapeutic drug groups were performed and the results analysed. Automated routines for monthly data updates were developed.

Results

Within statins the PPV was not only highly dependent on the run-in period but also on the substance studied. Positive predictive values for 18, 15, and 12 months of run-in varied between substances within a therapeutic group. For example statins: simvastatin (68-62-54%), pravastatin (87-84-77%), atorvastatin (91-89-86%), rosuvastatin (89-86-81%).

Actual up-to-date incidence-rates for different therapeutic groups, including trends, will be presented in an interactive manner.

Conclusion

The PPV of incident-rates will vary not only by the run-in period, but also significantly between substances in the same therapeutic class with the same run-in. The extraction of standardized and validated incidence rates was possible to perform and to automate. Further studies on the usability of the data sets are needed.

P9T.5

Doing the right thing: Factors influencing GP prescribing of antidepressants and prescribed doses

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Background: Antidepressant prescribing continues to increase. Partly due to increased long-term use, greater selective serotonin re-uptake inhibitor (SSRI) use and the use of higher SSRI doses. Evidence does not support the use of higher SSRI doses for depression treatment, and factors influencing the use of such doses are not well known. This study aims to explore factors influencing GP's use of antidepressants and their doses to treat depression.

Methods: Semi-structured interviews with a purposive sample of 28 practising GPs; sampled by antidepressant prescribing volume, practice size and deprivation level. A topic guide drawing on past literature was used with enough flexibility to allow additional themes to emerge. Interviews were audio-recorded and transcribed verbatim. Framework analysis was employed. Constant comparison and disconfirmation were carried out between transcripts, with data collection being interspersed with analysis by three researchers. Thematic framework was then systematically applied to the data and modelled.

Results: Depression treatment involved ethical and professional imperatives of 'doing the right thing' for individuals by striving to achieve the 'right care fit', involving medicalised and non-medicalised patient-centred approaches. Factors influencing prescribing and doses varied over time from first presentation, to antidepressant initiation and longer-term treatment. For moderate to severe depression GPs were confident prescribing SSRIs which they considered safe and effective medicines, and ethically and professionally appropriate. However, many were unaware that higher doses lacked greater efficacy and onset of action occurred within 1-2 weeks, preferring to wait 8-12 weeks before increasing or switching. With ongoing pressures to maintain prescribing, few perceived continuation problems or lack of proactive medication review combined to further drive antidepressant growth over time.

Conclusion: GPs strive to 'do the right thing' to help people. Antidepressants are only a single facet of depression treatment. However, increased awareness of drug limitations and regular proactive reviews may help optimise care.

P9T.6

Off-label use of oral morphine sulfate for opioid maintenance purpose in France: results from the 2009-2015 UTOPIA study

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Background: In France, high-dosage buprenorphine (HDB) and methadone (MTD) are the only drugs approved for opioid maintenance treatment. However, oral morphine sulfate (OMS) prescription is tolerated in some specific cases. Data on this off-label use are scarce. We aimed to quantify and characterize patients treated with OMS for opioid maintenance.

Methods: Yearly repeated cross-sectional study (2009-2015) on data from the French National Health Insurance database. For each year considered, all affiliates to the general scheme were included. Ad hoc algorithms were developed to identify prevalent users of slow-release OMS for opioid maintenance based on i) diagnoses of hospitalisation and severe chronic diseases, and ii) reimbursement for OMS and analgesics.

Results: In primary analysis, 548 OMS maintenance users were identified in 2009, representing 1.1 per 100,000 affiliates. They represented 1.5 per 100,000 affiliates in 2015 (+37.5%), with 805 OMS maintenance users. Of note, around 150,000 subjects used MTD/HDB for maintenance each year over the period. In 2009, 72% of users were men; this was 76% in 2015; median age was constant (40 years). Complementary coverage for low-income was found in 42.5 and 42.7% of OMS maintenance users in 2009 and 2015, respectively. During the period, median average daily dose decreased from 345.1 to 328.6 mg/d. A total of 19.7% and 23.9% OMS maintenance users concomitantly used immediate-release OMS in 2009 and 2015, respectively. In 2015, 29.3% of OMS maintenance users presented with schizophrenia and related disorders, 21% with hepatitis B or C, and 6.5% with HIV (vs. 18.6%, 8.7%, and 2.6% of MTD users and 17.9%, 7.8% and 2.6% of HDB users, respectively).

Conclusion: The prevalence of OMS use in opioid maintenance was very marginal compared to that of MTD/HDB. OMS users appeared with poorer health and more precarious situation. Their use of immediate-release formulation appeared far from negligible.

P10F.1

Effect of tobacco cessation policies in the consumption of anti-smoking medicines in Portugal

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Background: Smoking is one of the worst public health problems worldwide, especially in Europe, where 30% of the population uses tobacco. In Portugal, smoking is on the top of avoidable morbidity and mortality causes, leading to the implementation of several tobacco cessation policies in the last years. In 2007, the main legal document addressing the prevention and control of tobacco use was implemented in Portugal (Law 37/2007, 14 Aug).

Methods: We performed a time series analysis of the use of tobacco cessation medicines containing nicotine (OTC drug), bupropion and varenicline (both prescription-only). Consumption was expressed in DID obtained between Jan-2003 and Dec-2016. Statistical descriptive analysis was conducted in SPSS and geographical characterisation of consumption was also performed.

Results: Nicotine is the most used substance varying between 0.012 DID (Aug-2003) and 0.154 DID (Jan-2006). The global consumption curve has shown an erratic pattern between Oct-2005 and Mar-2008, with peaks matching the dates of implementation of legal documents on the prevention and control of tobacco use. Since Mar-2008 consumption has declined reaching similar values to the beginning of the series. The south of Portugal has a higher use (peak at 0.194 DID in Jan-2006) of anti-smoking medicines compared to national use (0.160 DID in Jan-2006). Time series analysis revealed seasonality, with a peak each year in January, probably reflecting New Year's resolutions of smokers on tobacco use.

Conclusions: A similar pattern of consumption of anti-smoking medicines was found in all regions, the south with the highest consumption, in line with the highest prevalence of tobacco use in that region (20.7%). Nicotine is the most used substance, probably because it is the only OTC tobacco cessation drug in the Portuguese market. Apparently the legal approach to tobacco control did not have a sustained effect on the consumption of anti-smoking medicines in Portugal.

P10F.2

Changes in pharmaceutical expenditures with massive price cuts

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Background : Pharmaceutical reforms have been implemented in order to slow down the increasing trend of drug spending in Korea. The Drug Expenditure Rationalization Plan(DERP) has launched in 2007 by introducing the positive list system and price negotiations. Equal medicine pricing(EMP) has taken in effect on April 2012, which was to cut prices of the off-patented medicines(brand-named and generics). This study aimed to examine the effect of these cost-containment policies on pharmaceutical spending in Korea.

Methods : The National Health Insurance claims data for a 168-month period between 2003 and 2016 were analysed. A segmented regression analysis was conducted with two major reforms : DERP(January 2007) and EMP(April 2012).

Results: Although DERP has an objective of rationalization of drug spending, the trend of drug spending decreased by KRW 671.47 million(USD 578,180.57) per month($p=0.0728$). A increased level of KRW 48,140.00 million(USD 41,451.76 thousand) in drug spending was shown($p=0.012$). The EMP significantly curved down the trend of drug expenditure by KRW 1,331.30 million(USD 1,146,338)($p<0.0001$). Also, the trend in volume decreased by 10,668.71 after the EMP($p=0.004$). The level of volumes after the EMP increased by 1,210,200,000($p=0.0058$). The trend in the unit prices decreased by KRW 0.79(USD 0.00068) after the DERP($p=0.0317$) but showed a steady trend after the third price cut. The level of unit price decreased by KRW 60.96 (USD 0.05) with the EMP but not significant.

Conclusion: Recent cost containment reforms have a great impact on pharmaceutical expenditures in Korea. In particular, the EMP with a substantial price cuts curved down the increasing trend of drug spending. However, the volume and unit price have little been influenced by these reforms. In the long-run, it is questionable whether the effects of these reforms will continue.

P10F.3

Analysis of out-of-pocket payments for medicines in Kyrgyzstan

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Background

Government and patients expressed concerns about rising pharmaceutical expenditure and large out-of-pocket payments (OOP) for medicines in Kyrgyzstan in recent years. The aim of this research was to analyse the extent and possible causes of OOP for outpatient medicines in Kyrgyzstan and to develop policy recommendations to reduce them.

Methods

We analysed data of reimbursed medicines under the 'Additional Drug Package' (ADP) programme provided by the Mandatory Health Insurance Fund and of imported medicines provided by the National Medicines Regulatory Agency. The data referred to the years 2013 till 2015. We also did a literature review and conducted twelve face-to-face interviews with key stakeholders in Kyrgyzstan (May/June 2016).

Results

Prices of outpatient medicines, both reimbursed and not reimbursed, are not regulated in Kyrgyzstan. The ADP list includes 76 items for which patients are reimbursed 50% of a calculated tariff. Between 2013 and 2015, the number of prescriptions dispensed under the ADP decreased by 14% while the average amounts reimbursed per prescription increased for nearly all therapeutic groups. Compared to 2013, co-payments for medicines dispensed under the ADP increased by 20% in 2015. Following a depreciation of the Kyrgyz som, the imports of medicines in 2015 were at around the same level as in 2013 in terms of volume, but Kyrgyzstan had to pay nearly 20% more.

Conclusion

Kyrgyz patients have been suffering from higher co-payments due to increased medicine prices. The price increases were partly attributable to the currency devaluation but they also resulted from the lack of price regulation. It is thus recommended to establish a legislative framework for the regulation of medicine prices. Furthermore, Kyrgyzstan should increase the efficiency of lower-priced medicines by enforcing measures such as generic substitution and building trust into generics via improved regulatory practices.

P10F.4

Out-of-tender medicines procurement in a Brazilian reference cancer institution

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Background: Tender procedures are essential for obtaining lower prices and for guaranteeing transparency and accountability in procurement. In Brazil, public procurement is regulated by law (number 8666/1993), with tender as a rule. Out-of-tender medicines procurement is a possibility, but in a very limited number of situations. The study examined out-of-tender drug acquisitions, by waiver or sole source, in the Brazilian National Cancer Institute (INCA), a Ministry of Health nationwide reference center.

Methods: A quantitative exploratory study examined data from January 2007 to December 2014. Data were provided by the federal procurement system. Unit prices were deflated to December 2014 using the National Price Index (IPCA) and values were converted to equivalents in US dollars. Medicines were classified according to ATC. Providers and justifications for out-of-tender procurement were analyzed. Trends of out-of-tender acquisitions were calculated by the minimum-squares method.

Results: During the period 605 out-of-tender purchases occurred in INCA (14.4% of total purchases), with expenditures of US\$ 20,688,094.70 (3.8% of total). First Level ATC groups V, L, N and J accounted for approximately 60% of out-of-tender purchases. Radiopharmaceuticals concentrated the largest proportion of out-of-tender purchases (19%) and the largest financial amount (45%). Trends showed a rise in out-of-tender procurement over time, mainly due to increases in sole source acquisitions. Justifications for this result were problems stemming from the procurement process and those of legal nature, covered by law.

Conclusions: INCA registered a fair quantity of out-of-tender procurement in spite of the legal requirements for tender. Trends for out-of-tender procurement rose in the period, and were linked to sole source providers, which may signify a greater number of purchases of medicines under monopoly. The study indicates the possibility of specific interventions to enhance quality of drug procurement in Brazil.

P11F.1

Parents' and guardians' perceptions on availability and pricing of medicines and healthcare for children in eThekweni, South Africa – A qualitative study

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Background: Inadequate access to affordable essential medicines poses a challenge to achieving Universal Health Coverage. Access to essential medicines for children is emphasized in recent research. However, information from end users of medicines i.e. patients, is scarce. Obtaining information at a household level is integral to understanding how people access and use medicines. This study gathered opinions/perceptions from parents/guardians on availability, affordability and quality of medicines and healthcare for children in South Africa (SA).

Methods: Eight Focus group discussions were held with 41 individuals in eThekweni, SA, from September–November 2016. Participants were parents/guardians of children up to 12 years from different ethnic and socio-economic backgrounds. Key informants recruited participants using snowball sampling. Focus group discussions were recorded, transcribed verbatim, coded, verified, reconciled for consensus, and analysed in NVIVO.

Results: Medicines and healthcare facilities are accessible in urban and peri-urban areas in eThekweni. Medicines may not always be available in public sector facilities due to medicine shortages, compelling the purchase of medicines from private sector pharmacies. Common medicines were perceived as affordable for most socio-economic groups except the 'Poor' group. Quality of medicines was perceived as 'good' when obtained from the private sector but sometimes perceived as 'poor' when received from public sector clinics. Quality of healthcare was perceived as 'good' but required improvement for both sectors.

Conclusions: This is the first study in SA to report on parent/guardian perceptions on availability, affordability and quality of medicines and healthcare for children. It has the potential to be up-scaled to a country-wide investigation and will allow for patient input into pharmaceutical and healthcare policy governing access and availability of essential medicines and services in SA. The study recommended that patient input be sought to assess the impacts of policies on the intended target groups in SA to ensure policy objectives are achieved.

P11F.2

Media attention for drug safety issues. A survey of newspapers and social media in the Netherlands (2001 – 2015)

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Background

Media attention may amplify the way drug risks are perceived by the public. Major scares were e.g. SSRI's and suicidality and thrombosis and oral contraceptives.

Objectives

To assess to what extent drug safety issues as communicated through Direct Healthcare Provider Communications (DHPCs) are covered in paper-based newspapers and by social media in the Netherlands.

Methods

We retrieved newspaper articles reporting on drug safety issues as reported in 379 DHPCs issued from 2001 to 2015 from the Lexis Nexis AcademicTM repository. Articles were retrieved when they were published 1 year before to 1 year after the DHPC was issued. Social media postings were retrieved with the CoostoTM repository for 213 DHPCs that were issued from 2010 to 2015, as earlier postings are not captured. Web-postings were retrieved from 7 days before to 7 days after the DHPC was issued, when mentioning the drug name for which the DHPC was issued. Descriptive statistics were used.

Results

In total, 88 (23%) safety issues mentioned in DHPCs were covered in newspaper articles. Social media covered 193 (91%) of the drugs for which a DHPC was issued. Newspapers covered most frequently safety issued with Diane-35TM ('13; n=588), rofecoxib ('04; n=395), 3rd generation contraceptives ('14; n=262); rimonabant ('07; n=180); and celecoxib ('04 and '05; n=109). The drugs implicated in DHPCs most frequently discussed in web-postings were ibuprofen (PediaTM '13; 912 posts), levothyroxine ('14; 515 posts); diclofenac ('13; 430 posts), NovomixTM ('13; 372 posts) and Diane-35TM ('13; 304 posts).

Conclusions

Our overview indicates that a quarter of drug safety issues is picked up by newspapers. Beyond the well-known safety issues (oral contraceptives, coxibs and Diane-35) few issues were picked up in the news media. Almost all drugs implicated with a safety issue were discussed on social media.

P11F.3

Which patients and healthcare professionals are interested in an app for reporting adverse drug reactions and receiving drug safety information?

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Background

Previously, an app has been developed for people to report adverse drug reactions (ADRs) to the national agency and receive drug safety information. This study aimed to determine which patient and healthcare professional (HCP) characteristics are associated with interest in the app.

Methods

In this cross-sectional study, European patients and HCPs were asked to complete a web-based survey developed in the context of the Web-Recognizing Adverse Drug Reactions (Web-RADR) project. Responders were asked whether they were interested in the app. This outcome measure was used as binary variable (not/somewhat interested versus very interested). A separate logistic regression analysis was conducted for patients and HCPs. For the patients, the following predictor variables were included: Age, gender, educational level, number of prescribed medicines, specific diseases, use of health apps in general, being aware of the possibility to report ADRs, and experience of an ADR. For HCPs, the included variables were: Age, gender, profession, use of health apps in general, and whether the HCP ever reported an ADR to the national agency.

Results

The study included 636 patients and 390 HCPs. Older patients were less often 'very interested' than younger patients (OR 0.98; 95% CI 0.97-0.998). Patients sometimes using an health app were more often 'very interested' than those never using these type of apps (OR 1.67; 95% CI 1.21-2.31). Finally, patients who experienced an ADR were more often 'very interested' (OR 1.54; 95% CI 1.01-2.35). For HCPs, it was shown that those sometimes using a health app were more often 'very interested' than those never using these type of apps (OR 3.71; 95% CI 2.04-6.76).

Conclusions

Patients, especially younger ones, and HCPs who use health apps in general may be more receptive to using an app for two-way risk communication. Interest in the app is influenced by patient and HCP characteristics.

P11F.4

Patients with type-2 diabetes attending a community health centre in Pretoria, South Africa: Do they know how to manage their chronic condition to improve future care?

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Introduction: Diabetes mellitus is a growing problem in South Africa (SA) and the second leading underlying cause of death in SA. It is also the most prevalent chronic condition at Laudium Community Health Centre (CHC) in SA. Patients' knowledge about their disease and the management thereof plays an important role in the self-management and care of chronic conditions, especially given concerns with current adherence rates. This study aimed to assess the knowledge of type-2 diabetes patients about their medicines and self-care practices for their condition to guide future initiatives.

Methods: Descriptive, quantitative study conducted at Laudium CHC among 217 conveniently sampled adult type-2 diabetes patients. Patients were interviewed with a structured questionnaire on exit from the clinic, after consultation with the medical practitioner and their collection of medication. Ethical clearance was granted for the study and participants provided written informed consent.

Results: Of the 217 participants, females predominated. 65.5% were >60 years and 51% were from the Indian racial category. Two thirds of the patients had been diagnosed and been on anti-diabetic medication for ≥5 years. Most patients did not know how their medication controls their diabetes, 83.9% were not aware of the side effects of their medicines and just under half could explain how to take metformin. Upon questioning about what to do if a dose is missed, 67% indicated that they would wait for the next dose. More than a third indicated they were not practicing any form of self-care, and of those practicing self-care (n=126), exercise (58.7%) and diet (54.8%) were most common.

Conclusion: Knowledge of type-2 diabetic patients regarding their medication and self-care was sub-optimal. Behavioural change counselling should be integrated into routine practice to improve patient care given rising prevalence rates in SA. This should be part of ongoing strategies to improve chronic disease management.

P12F.1

NSAIDs utilization in a large cohort of Italian elderly with cerebro/cardiovascular disease

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Background

Non-steroidal anti-inflammatory drugs (NSAIDs) should be generally avoided in patients at high cerebro/cardiovascular (CCV) risk. The aim of this study was to describe the NSAID utilization in the Italian elderly population with CCV disease.

Methods

Italian administrative data collected from Caserta (South), Lazio, Toscana (Center), Lombardia and Treviso (North) between 2008 and 2012 were used. Patients hospitalized for CCV events between 2008 and 2011 (cohort entry) were selected. Those aged <65 and with <2 years of look-back at cohort entry were excluded. During one year after cohort entry we observed: prevalence of use; amount of NSAIDs dispensed to users, measured by Defined Daily Doses (DDD)/1000*user*day; distribution of the Received Daily Dose (RDD) among patients with ≥2 dispensings (RDD= between first and last dispensings:[dispensed DDD]/[days of follow-up]). Among new users (no NSAID dispensing during two years before cohort entry), the first dispensed NSAID was observed.

Results

Among 511,987 selected patients, prevalence of use ranged from 48% in Caserta to 21% in Treviso. Overall prevalence of use by cohort entry decreased from 34% in 2008 to 27% in 2011. Amount of dispensed NSAIDs ranged from 30 DDD/1000*user*day in Treviso to 67 in Lazio. Overall amount dispensed increased from 45 to 75 DDD/1000*user*day between 2008 and 2011. Nimesulide and diclofenac had the highest prevalence of use, 12 and 9% respectively. The highest amount of dispensed DDDs was observed for nimesulide and coxibs, i.e. 10 and 9 DDD/1000*user*day respectively. Around 10% of patients had an RDD ≥1. Between 2011 and 2012, 35% of new users received diclofenac or coxib as the first NSAID prescription.

Conclusions

The utilization of NSAIDs varied considerably across geographic areas. Active substances associated to the highest thrombotic risk, such as coxibs and diclofenac, were the most used even in new users. Interventions to improve appropriateness of use are warranted.

P12F.2

Co-prescribing of renin-angiotensin system (RAS) acting agents is decreasing in Estonia

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Background

Regardless of beneficial effects on certain surrogate endpoints, recent studies have shown that dual blockade of renin-angiotensin system (RAS) is associated with an excessive risk of adverse events (hyperkalaemia, hypotension, and renal failure) and not being beneficial compared to monotherapy with an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB). Therefore dual RAS blockade therapy is not recommended.

Methods

We inquired from the Prescription Centre of Estonian Health Insurance Fund data on patients who had purchased at least two prescriptions (presumably a four month treatment course) of both – ACEI and ARB or their combinations with diuretics during a half-year period from 2013 - 2016. Direct renin inhibitors were left out of the study as they haven't been used in Estonia.

Results

In the first half of 2013 there were nearly 6500 patients who received ACEI and ARB concomitantly. Within 4 years it decreased 50% and there were slightly over 3000 patients in the second half of 2016. The decrease is statistically significant and the mean annual decline rate was 18%. The decline can be seen in combination of all groups. The concomitant use of ACEI and ARB monopreparations has decreased the most (60%), while ACEI and ARB combination preparations the least (31%). The decrease was smallest in patients 85 and older (21%) although the risk of adverse events resulting from combining RAS medicines is highest in this patient group.

Conclusion

Considering the wide use of RAS-acting agents, the amount of patients who receive combined therapy is low (1%) and decreasing. Still, the combination should be avoided. In those for whom dual blockade is considered absolutely necessary, it must be carried out under specialist supervision with close monitoring of kidney function, fluid and salt balance and blood pressure.

P12F.3

Factors predicting the addition of a second antihypertensive drug in treating hypertension - a longitudinal retrospective cohort study in the UK primary care setting

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Background

People with primary hypertension often require a second antihypertensive agent to be added to achieve optimal blood pressure (BP) control; attributed mainly to the ineffectiveness of the initial/solo treatment. However, apart from the patient's baseline BP value, little is known about what influences the addition of a second antihypertensive drug. This study aimed to identify how often a second additional antihypertensive treatment is initiated and investigate the factors associated with it.

Methods

This study used a UK primary care database – the Clinical Practice Research Datalink from April-2006 to March-2012. Adults with primary hypertension were followed from their initial antihypertensive prescription date (index date) to the earliest of the first add-on prescription, study end, patient leaving the database or death. Cox regression was used to investigate the independent association between time to the first add-on date and baseline patient characteristics: age, gender, initial antihypertensive drug class, incident or prevalent hypertension (had a hypertension diagnosis ≥ 1 year before index date), BP, Charlson Comorbidity Index (CCI), and Townsend deprivation score.

Results

Of the 176,835 included patients, 42% received add-on antihypertensive drugs; of which 23.5% happened six months posterior to the initiated treatment. Baseline hypertension stage-III (HR: 3.5, 95%CI: 3.3, 3.7), deprivation (HR: 1.09, 95%: 1.07, 1.12), CCI ≥ 2 (HR: 1.11, 95%: 1.08, 1.14), and older age were associated with a higher probability of add-on treatment. Angiotensin-converting enzyme inhibitors use (HR: 0.74, 95%CI: 0.72, 0.76), female (HR: 0.92, 95%CI: 0.91, 0.94), or a prevalent patient (HR: 0.96, 95%CI: 0.93, 0.98) were associated with a lower probability of add-on treatment.

Conclusion

Adding a second antihypertensive drug happened mostly after six months of therapy and was more common in patients with higher baseline BP, older age, multiple comorbidities and low socioeconomic status. These patients are likely to need closer monitoring for side effects and drug interactions

P12F.4

Adherence to evidence-based drug therapies after myocardial infarction: is geographic variation related to hospital of discharge or primary-care providers? Methodological challenges and policy perspectives

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Background. Benefits of polytherapy after myocardial infarction (MI) have been shown. However, observational studies reported poor adherence to medication. From current evidence, it is not possible to quantify how much of the gap from guidelines is attributable to the patient, the hospital of discharge (HoD) or primary care providers (Local Health Districts - LHDs). The objectives were: to measure adherence to polytherapy after MI; to identify determinants of adherence; to compare the amounts of variation attributable to HoDs and LHDs.

Methods. This was a cohort study of patients hospitalized with incident MI in 2007-2010. Data were retrieved from Information Systems of the Lazio Region, Italy. The outcome measure was adherence to polytherapy in the two years following MI, defined as "MPR>0.75 for at least three of the following drugs: antiplatelets, β -blockers, ACEI/ARBs, statins". Cross-classified models were applied to analyze geographic variation and compare the amounts of variability attributable to HoDs and LHDs. Variation was expressed as Median Odds Ratio (MOR). A MOR of 1.00 stands for no variation between clusters, a large MOR indicates considerable variation.

Results. We enrolled 9,606 patients. About 63% were adherent to polytherapy. Adherence was higher for patients discharged from cardiology wards (OR=1.56 versus other wards, 95%CI: 1.26-1.92) and for patients with general practitioners working in group practice (OR=1.14 versus single-handed, 95%CI: 1.08-1.29). A relevant variation in adherence was detected between LHDs (MOR=1.24, $p<0.001$). When introducing the HoD, the variation between LHDs decreased (MOR=1.13, $p=0.020$) and the variability attributable to the HoD was significantly higher (MOR=1.37, $p<0.001$).

Conclusion. Adherence to pharmacotherapy after MI is not consistent with clinical guidelines. The relevant geographic variation raises equity issues in access to optimal care. Adherence is influenced more by HoDs than by primary care providers. Cross-classified models proved to be a useful tool for defining priority areas for intervention.

P12F.5

Factors associated with physician adherence to prescribing guideline-recommended medications for acute coronary syndrome in Vietnam

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BACKGROUND

Prescribing according to guidelines improves patient outcomes. We aimed to identify factors associated with physician adherence to prescribing guideline-recommended medications for patients with acute coronary syndrome in Vietnam.

METHODS

We conducted a cross-sectional study in two public hospitals in Vietnam. We included patients with acute coronary syndrome. We defined guideline adherence as prescribing guideline-recommended medications for eligible patients at both hospital admission and discharge. We performed multivariable analyses using logistic regression models to identify factors associated with guideline adherence.

RESULTS

Overall, 610 patients were included. Of those, 282 patients (46.2%) were in the guideline adherence group and 328 patients (53.8%) in the non-adherence group. Physicians were less likely to prescribe guidelines for patients with social health insurance (OR, 0.50; 95% CI, 0.32-0.80), prior heart failure (OR, 0.43; 95% CI, 0.26-0.74), or atrial ventricular block II-III (OR, 0.14; 95% CI, 0.02-0.90). Physicians were more likely to prescribe guidelines for patients who underwent percutaneous coronary intervention (OR, 2.23; 95% CI, 1.44-3.46); or who with systolic blood pressure < 100 mmHg (OR, 9.87; 95% CI, 4.76-20.47), Killip class II-IV (OR, 10.10; 95% CI, 4.93-20.69), or ejection fraction < 40% (OR, 9.93; 95% CI, 4.77-20.67).

CONCLUSIONS

Physicians prescribed guideline-recommended medications for less than half of the patients with acute coronary syndrome in Vietnam. Under-prescribing in patients who have social health insurance, prior heart failure, or atrial ventricular block II-III should be investigated further to determine the nature of the association and develop appropriate interventions to improve the prescribing.

P12F.6

Use of direct oral anticoagulants in patients with atrial fibrillation in Scotland: Applying a coherent framework to drug utilisation studies

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Background: Information regarding adherence to treatment with direct oral anticoagulants (DOACs) is still limited. Drug utilisation research is commonly conducted to analyse the usage of drugs in clinical practice, but drug utilisation studies make use of various conceptual definitions and a diverse set of measurements. The aim of this study was therefore two-fold: to report on DOAC use in Scotland; and to advocate the standardisation of drug utilisation methods.

Methods: Retrospective cohort study using linked routinely collected administrative data. Patients include those with a diagnosis of atrial fibrillation (AF) who received a first prescription for a DOAC (dabigatran, rivaroxaban, apixaban) from September 2011 to June 2014. In order to give a valid representation of patients' drug taking behaviour, this study comprises measures of both discontinuation/persistence and adherence.

Results: 5398 patients (mean CHA₂DS₂-VASc score 2.98 [SD 1.71], 89.7% with ≥ 5 concomitant medicines) were treated with DOACs for a median of 228 days (IQR 105 – 425). Of 35.6% who discontinued DOAC treatment, 11.0% switched to warfarin and 48.3% re-initiated DOACs. Persistence after 12 and 18 months were 75.9% and 69.8%, respectively. Differences between DOACs were observed: discontinuation rates ranged from 20.4% (apixaban) to 60.6% (dabigatran), and 12 months persistence from 60.1% (dabigatran) to 85.5% (apixaban). Adherence to treatment with all DOACs was good: overall DOAC median medication refill adherence (MRA) was 102.9% (IQR 88.9% - 115.5%), and 82.3% of patients had an MRA > 80%.

Conclusions: In Scotland, adherence to DOAC treatment was good and switching from DOAC to warfarin was low. However, discontinuation and persistence rates were variable – although treatment interruptions were often temporary.

To decrease the inconsistencies in drug utilisation methods and facilitate meaningful study comparison, the use of a coherent framework – combining discontinuation, persistence and adherence – and the standardisation of measurements is advocated.

P13F.1

PROMs in cancer care – examination of the current evidence of collection and use in routine clinical practice

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Background

Cancer medicines account for the highest proportion of medicines introduced within NHS Scotland, yet currently patient reported outcome measures (PROMs) are not routinely captured. The Cancer Medicines Outcome Programme (CMOP) aims to: test the feasibility of PROMS collection in routine clinical practice, commencing with prostate cancer (PC) and melanoma; to inform patient-clinician decision making and support broader population-level analysis of PROMS. This study presents an initial examination of the evidence for PROMs in applied to clinical practice globally.

Methods

A literature search utilising “quality of life” or “QoL” in Springer journals and PubMed in English in the last 5 years produced results on PROMs tool type, development and testing. Results were then limited by prostate cancer and melanoma. PROMs applications in clinical practice were identified and organised by location, population and tools used.

Results

PROMs applications in clinical practice were categorised i.e. early-stage disease versus survival/post-intervention, and pilot versus service-embedded. Most studies utilised a combination of QoL tools. The few examples of PROMs collection as part of service were not routinely embedded in practice or used to inform patient care.

Reporting of PROMs application in routine cancer care was limited. In PC, studies detailed PROMs collection at pilot-stage only. One application in surgical patients saw PROMs well-embedded in (private) service. Service-embedded melanoma PROMs applications were not found.

Conclusions

The literature details PROMs tool development and testing, while examples of PROMs applied in clinical care are limited to pilot studies, non-cancer cohorts, or, where service-based, were not collected routinely. Service-embedded PROMs may be challenging as current applications have failed to reach spread. Given the limited evidence base, next steps will involve patient and clinician engagement to identify priorities for PROMS application, followed by an analysis against current tools to derive a tool for testing (output to be presented at conference).

P13F.2

Enabling daily monitoring of chemotherapy toxicity: The Daily Chemotherapy Toxicity self-Assessment Questionnaire (DCTAQ)

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Purpose: Close monitoring of chemotherapy toxicity is instrumental to ensuring prompt symptom management, quality care, maximum treatment benefit, and improved patient outcomes. We developed a brief clinical tool to enable daily assessment of chemotherapy toxicity, and investigated its content validity, feasibility/applicability, internal consistency and stability.

Methods: Development of the Daily Chemotherapy Toxicity self-Assessment Questionnaire (DCTAQ) was based on an initial pool of items generated from two scoping reviews. Expert panel review (n=15) and cognitive debriefing with patients with cancer (n=7) was used to establish content validity. Feasibility/acceptability, applicability (self-report v. interview-like administration), internal consistency (Kuder-Richardson Formula 20; KR-20) and test-retest reliability (at 1-hour intervals) of the DCTAQ were field-tested with 82 patients with breast or colorectal cancer, who received chemotherapy at eight hospitals across the UK.

Results: Initial development/content validity stages enabled item revisions and re-wording to ensure comprehension and relevance of DCTAQ items. This work led to a final, 11-item version of the DCTAQ that comprised 10 core symptom items plus one open-ended 'any other symptom' item. Feasibility and acceptability were demonstrated through absence of participant withdrawals, absence of missing data and no complaints about tool length. The DCTAQ was found to have modest internal consistency (KR-20=0.56), but very good test-retest reliability, with Cohen's kappa coefficients for the total sample and cancer type subgroups exceeding cut-offs for excellent agreement (>0.80) for 8 out of 10 core items and regardless of type of cancer, age, or gender.

Conclusions: The DCTAQ is a brief clinical tool that enables for rapid and accurate daily assessments of chemotherapy toxicity in clinical practice. The DCTAQ (available in English and translated/linguistically validated for German, Greek and Norwegian languages) is in the core of the Advanced Symptom Management System (ASyMS), an electronic platform that enables remote patient monitoring through use of mobile phones.

P13F.3

Long-term Exposure To Anticholinergic And Sedative Drugs And Cognitive And Physical Function In Later Life

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Background: Anticholinergic and sedative drugs from various therapeutic classes are frequently prescribed to older people. These drugs are known to impair cognitive and physical function in the short-term. However, long-term exposure to these drugs remains less examined.

Methods: Data from the Longitudinal Aging Study Amsterdam, a Dutch nationally representative cohort study, collected over twenty years (1992-2012) at seven occasions, were analyzed. On each occasion, cumulative exposure to anticholinergic and sedative drugs was quantified with the Drug Burden Index (DBI), a linear additive pharmacological dose-response model. The relationships between the DBI and outcomes of cognitive function (MMSE, Alphabet Coding Task, 15-Words Test) and physical function (Walking Test, Chair Stands Test, Cardigan Test, and Functional Independence Scale) were examined using linear mixed models adjusted for sex, marital status, age, education, smoking status, drugs not included in DBI, body mass index, depression, and co-morbidities.

Results: At baseline, there were 2896 individuals (52% women; mean age 70 ±9 years). Of them, 62% had no exposure to anticholinergic and sedative drugs (DBI=0), 24% moderate exposure (DBI=0-1), and 14% high exposure (DBI>1). Significant independent associations were found between the DBI and physical function (Walking Test log transformed: B = 0.02 [95%CI:0.01;0.03], Cardigan Test log transformed: B = 0.02 [95%CI:0.01;0.03], Chair Stands Test B = 0.48 [95%CI:0.20;0.76], and Functional Independence: B = -0.89 [95%CI: -1.22;-0.55]). No associations were found between the DBI and cognitive function.

Conclusion: Over 20 years, higher anticholinergic and sedative exposure is associated with poorer physical but not poorer cognitive function.

P13F.4

Complexity of medicine regimens and patient perceptions of medicine burden

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Background

The number of medicines being used by individual patients is rising inexorably. As more medicines are added, regimens become increasingly complex and the effort of coping with these presumably also rises. No work has explored the complexity of medicine regimens in England and no research has studied the relationship between medicines complexity and patient burden.

Methods

Patients presenting prescriptions at six community pharmacies were invited to complete the Living with Medicines Questionnaire (LMQ), which assesses burden of using medicines, and permission requested to review their medication record, to assess complexity. The Medicine Regimen Complexity Index (MRCI) was applied to prescription records; this gives higher weightings to dosage forms with complex administration modes, higher dosing frequency and more additional directions. NHS Ethics approval was obtained.

Results

In total 776 patients were invited to participate, and 582 agreed. Of these, 488 gave consent for researchers to review medication records and 160 of these also returned a fully completed LMQ. The number of medicines prescribed ranged from 1 to 30, with patients from pharmacies in more deprived areas using more medicines. The MRCI score was strongly correlated with number of medicines prescribed ($r=0.908$; $p<0.001$), but varied considerably for patients taking the same number of medicines.

Among patients also completing the LMQ, there were weaker but statistically significant relationships between overall medicines burden and MRCI score ($r=0.229$; $p=0.002$) and number of medicines ($r=0.228$; $p=0.002$). LMQ domains covering side effects, concerns and interference with daily life were most strongly associated with both number and complexity of medicines.

Conclusion

Both the number of medicines and regimen complexity may be a useful means of identifying patients overburdened by medicines, particularly those with side effects which may interfere with day-to-day living, who could benefit from medicine review. However other factors appear to contribute to overall medicines burden.

P14F.1

Shining some light on confidential arrangements: Relevance of discounts for pharmaceutical pricing in European countries

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Background

There are strong indications that official medicine list prices are impacted by discounts, rebates and similar arrangements that pharmaceutical industry offers to public payers. Given the confidential nature of such contracts, there is little evidence on this matter. The aim of this study was to survey the relevance and extent of discounts and similar arrangements in pharmaceutical pricing in European countries.

Methods

We did a primary data collection with competent authorities involved in the Pharmaceutical Pricing and Reimbursement Information (PPRI) network. After a pilot with one country (Austria) launched in August 2016, the survey ran from September till December 2016. Preliminary findings were discussed with the respondents during a face-to-face meeting in November 2016. Due to the sensitivity of this matter, respondents were offered anonymity if they wished so.

Results

18 European countries responded to the survey. All 18 countries reported that public payers were granted discounts and similar price reductions by pharmaceutical industry for some new medicines. Discount arrangements were particularly common in the indications of oncology, multiple sclerosis, hepatitis C, and TNF alpha inhibitors. Most frequently reported arrangements included 'simple' discounts on list prices of medicines as well as price-volume agreements; some countries also informed about performance-based agreements. The extent of the price reductions varied between countries and products; it was reported to be up to 50% for some medicines. In 14 of the 18 responding countries, the discount arrangements were subject to confidentiality.

Conclusion

The study confirmed that confidential discounts and similar arrangements play a major role in pharmaceutical pricing, in particular related to new high-priced medicines. As a result, published list prices do not necessarily reflect the actually paid prices. Policy-makers that set their medicine prices with reference to list prices of other countries, without accounting for possible discounts, risk over-paying.

P14F.2

The implementation of managed entry agreements in Central and Eastern Europe: Findings and implications for future policies

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Background: Managed entry agreements (MEAs) are a set of instruments designed to facilitate access to new high priced medicines which are widely used across Europe. However, there are concerns with the costs associated with their administration, the confidentiality surrounding them, and whether they achieve their aims in practice.

Methods: A comprehensive survey regarding the implementation of managed entry agreements among Central and Eastern European (CEE) countries between January-March 2017 among key personnel in each country. 16 CEE countries participated.

Results: Across the five countries with available data on the number of different MEA instruments implemented, the most common MEAs were confidential discounts (n=806, 81%), followed by price-volume agreements (n=37, 4%), free doses of medicines (n=25, 2%), bundle and other agreements (n=19, 2%), and payment by result (n=10, 1%). Most trade names associated with one or more MEA instruments belonged to the ATC-L group, antineoplastic and immunomodulating agents (n=201, 31%). The second most frequent therapeutic group for MEA implementation was ATC-A, alimentary tract and metabolism (n=87, 13%), followed by medicines for neurological conditions (n=83, 13%).

Conclusion: This is the first comprehensive comparative study on the implementation of MEAs in Central and Eastern Europe. Experience in implementing MEAs varied substantially across the region and there is considerable scope for sharing experiences and mutual learning. European citizens, authorities and pharmaceutical companies should also ask themselves whether within public health systems confidential discounts can still be tolerated, particularly when it is not clear which country and party they are really benefiting. Furthermore, if MEAs are to improve access to medicines, including new medicines, countries should establish clear objectives for their implementation and a monitoring framework to measure their performance as well as assess the overall burden of their implementation. Outcome based schemes also require comprehensive IT systems and recognised outcome measures for efficient administration.

P14F.3

How do average prices of high-cost medicines in Europe develop in the years following marketing authorisation?

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Background: The majority of EU countries benchmarks prices of other EU countries for their pricing of pharmaceuticals. There are indications for staggered market entry of high-priced medicines in the national markets of the EU Member States, with pharmaceutical industry tending to bring medicines first to markets in countries with high medicine prices. The aim of the study is to analyse price developments of medicines in the years after their authorisation based on the illustrative example of five medicines.

Methodology: We selected five pharmaceutical specialities that represented different indications and were centrally authorised by the European Medicines Agency between March 2011 and January 2014. Price data were collected 6, 12, 18, 36 and 60 months after the centralised marketing authorisation of these products. We calculated the average of unit prices for all 28 EU member states and compared the price developments.

Results: Six months after their centralised authorisation pharmaceutical specialities were available only in a small number of EU countries (5–7, usually with high per-capita income), but their availability increased (18–24 after 60 months). Five years after the central authorisation the average prices of the surveyed pharmaceutical specialities decreased between 10 and 16.5 per cent. At all observation points, the average price of the products was lower than at the previous timing. The largest decreases were observed between six and twelve months after authorisation (4%).

Conclusion: The results seem to confirm strategic launch behaviour of pharmaceutical manufacturers. If policy-makers use prices of a medicine in several countries in order to derive a benchmark or reference price for the purposes of setting the price of the product in their country, they should consider regularly re-evaluating pharmaceutical prices over time since the average prices decrease over time. The timing of re-evaluations has to be carefully selected (not too shortly after marketing authorisation).

P14F.4

Biologicals: Possibilities and limitations of efficiency gains through biosimilars. An analysis of the German market 2004–2016 using health care funds claims data

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Background:

Biologicals play an increasingly important role in drug therapy, opening innovative paths for treatment, while creating a substantial burden on social security systems due to high prices. Given a growing number of patent expiries, secondary manufacturers may legally offer copies. The specific production mechanisms for biologicals make it, however, virtually impossible to produce exact copies of their complex molecules, so that exchangeability of different products of the same chemical substance is the subject of debate. Also, production requires more specialised processes than for ordinary drugs, limiting the number of manufacturers with sufficient capabilities. Hence, efficiency gains through market forces observed for generics are not easily reproducible for biologicals, while payers are eager to find ways to combat high expenditure.

Methods:

German prescription data for 3 biologicals available as biosimilars for a longer period were analysed descriptively for the years 2004 to 2016. The effects of regulatory and contractual interventions were analysed with ARIMA-based models.

Results:

Erythropoietin has seen shifts of market shares and price erosion similar to that known from generically available substances, with several sharply defined declines of price. Somatropin, with similar shifts of market shares towards biosimilars, shows stable initiator prices and rising biosimilar prices, while for filgrastim prices have remained stable overall. Time series analysis suggests that competition for the erythropoietin market was reinforced through regulatory steps.

Conclusion:

The example of erythropoietin shows that efficiency gains from biosimilars can be achieved, similarly to developments known from the earlier phases of generics adoption. This can happen independently of concerns about switching patients between different biosimilar strains. Market forces alone, however, seem to be insufficient drivers for more efficiency. Without effective support through regulatory or contractual interventions, both shifts towards biosimilars and price pressure on originators will, at best, be substantially delayed.

P15F.1

Essential medicines list implementation dynamics: a case study using Brazilian federal medicines expenditures

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Background – The concept of Essential Medicines (EM) is internationally recognized as a health strategy to rationalize the use of medicines with beneficial clinical and managerial outcomes. We analyze the implementation dynamics of the Essential Medicines List (EML).

Methods - We use the government expenditures on medicines and Brazil as a case study. Drug purchases were considered as a proxy for utilization. The essential medicines (EMs) expenditures were followed over time by Brazilian National EMLs lifetime and defined by broad therapeutic categories and by specific medicines.

Results - Brazil increased the number of the EMs during the last four editions of your Brazilian National EMLs and the federal government expenditures on them. We identified a common set of 404 EMs present in all four editions of the Brazilian National EMLs. There was a proportional decrease in expenditures on Anti-infectives for systemic use, Blood and blood-forming organs and Alimentary tract and metabolism, and increase in expenditures on Antineoplastic and immunomodulating agents. The expenditures distribution per specific medicines revealed that a small set of EM was responsible for 50% or more of expenditures considering Brazilian National EML lifetime for all four periods. The increase in expenditures on EMs in Brazil was a consequence of the newer medicines incorporated over time in the Brazilian National EMLs.

Conclusion - The use of the medicines expenditures as a source of data and the definition of an EML lifetime permitted follow-up of the implementation dynamics of different versions of the Brazilian National EMLs. Our results have implications for policy-makers and stakeholders to gain a better understanding of the role EMLs play in health system sustainability and in the provision of the most beneficial health care.

P15F.2

Medications Prescribed, Stopped and Modified at Hospital Discharge and Filled Medications in the Community: Failure to Follow in-Hospital Medication Changes and Adverse Health Outcomes 30-days Post Hospital Discharge

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Background: Preventing drug related adverse events in complex patients with multimorbidity remains challenging. Thus, evaluating the impact of in-hospital medication changes and post-discharge adherence is of significant interest.

Methods: Study patients included those admitted at two urban, tertiary care academic hospitals in Montreal, Quebec, Canada between October 2014 and May 2016 with at least two chronic conditions. Failure to follow in hospital medication changes was measured by comparing patient discharge prescriptions (from the patient chart) to medications which were filled in community by patients 30-days post-discharge (via dispensing data) and included i) community medications that were stopped in-hospital and filled post-discharge, ii) community medications that were modified in-hospital but not filled according to the modified daily-dose, and iii) new medications which were not filled post-discharge. PRN & OTC medications not covered by the public payer were excluded. Cox Models were utilized to determine the association between the number of change failures post discharge and adverse health outcomes.

Result: Of the 885 included patients, mean age was 69 (SD 15) and 66% were male with an average of 5 chronic conditions (SD 2). 46% of patients did not have any changes failures post discharge, 45% had 1-3 failures and 9% had 4+. 266 (30%) patients were re-admitted to hospital or visited the ED. After adjustment, each additional failure post discharge was associated with a 10% increased risk of re-admission or ED visit in 30-days (adjusted HR: 1.10, 95% CI: 1.01-1.8) where those with 4+ failures were 2.3 times more likely to be re-admitted than those without any failures (aHR: 2.3, 95% CI: 1.10-3.25).

Conclusion: A number of patients did not follow all medication changes that were made during hospitalization in the 30-days post discharge and the extent to which this occurred impacted the risk of hospital re-admissions and emergency department visits.

P15F.3

Association between Stigma, Beliefs about Medicines and Adherence to Antiretroviral Therapy: A Cross Sectional Study in People Living with HIV (PLHIV) in Papua, Indonesia

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Background: In people living with HIV (PLHIV), taking antiretroviral treatment is lifesaving, but studies on medication adherence mainly covered urban cities. Little is known about this from Papua where the HIV prevalence is up to 24 times higher than the national rate in Indonesia.

Objective: To investigate the association between stigma, beliefs about medicines patient's characteristics and adherence to medication in people who live with HIV in Papua, Indonesia.

Methods: This was a cross-sectional study using validated questionnaires. We included participants who received antiretroviral treatment for more than six months, above 18 years old, and who gave signed informed consent. Patients completed the Medication Adherence Rating Scale (MARS), Beliefs about Medicines Questionnaire (BMQ) and HIV-stigma scale and questions on sociodemographic characteristics. Information about antiretroviral treatment was collected from medical records. The primary outcome was self-reported adherence as measured by MARS. MARS was dichotomized into adherence and non-adherence using an 80% cut off of the total score. Data were analyzed using multivariate logistic regression.

Results: Overall, 311 out of 363 participants completed the questionnaires. Mean age (33.3 ± 9.4) years, 38.4 % male, 67.1% were Papuan, 32.9% were non Papuans. A total of 65.9% of participants were adherent. Being Papuan decreased the likelihood of adherence (OR=0.52; 95% CI, [0.310-0.872]). Feeling more distant, a stigma type, also decreased the likelihood of adherence (OR= 0.93; 95% CI, [0.882-0.997]). PLHIV taking distance represents a way to avoid being asked by others to hide because of fear and anticipation of social rejection.

Conclusion: Self-reported adherence was relatively low in PLHIV in Papua, Indonesia. Ethnicity of being Papuan, and taking a distance were associated with non-adherence. Targeted interventions should be developed to improve adherence in this patient group.

Keywords: PLHIV, Adherence, Stigma, Beliefs, Papua

P15F.4

De-prescribing of antipsychotics in residential aged care

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Background:

De-prescribing should be considered when the risk of harm outweighs potential benefits. The limited benefits in terms of behaviour management and considerable harms associated with antipsychotic use among older individuals highlights the need for routine antipsychotic review and de-prescribing.

The aim of this study was to explore antipsychotic de-prescribing in a large cohort of nursing home residents.

Methods:

Design and setting: A retrospective cross sectional study nested within a longitudinal cohort of 2440 nursing home residents from 36 facilities was conducted.

Data source: Pharmacy supply data was used to identify medication use profiles for each resident.

Definitions: Cessation was considered stopping of an agent without initiation of an alternate agent within 7 days of swapping, switching was cessation of one antipsychotic and commencement of an alternate antipsychotic within a 7 day period and recommencement was cessation of and antipsychotic and commencement after more than 7 days of the same antipsychotic or an alternate antipsychotic

Main outcome measures: Antipsychotic cessation, switching and recommencement of any antipsychotic.

Results: 30% of cohort residents (n=732) used an antipsychotics during their nursing home admission. Antipsychotics were ceased for 284 residents. 5.5% (n=40) of antipsychotic users switched agents. Only 7 residents recommenced an antipsychotic following cessation. The average duration of use prior to antipsychotic cessation was 416 (0.40) days.

Conclusions: De-prescribing of antipsychotics appears to be occurring in nursing homes, however residents are using antipsychotic agents for extended periods of time. Given the limited potential benefits of antipsychotic medicine and the extensive harms associated with use of these medicines in older populations, strategies focussed on timely de-prescribing of these medicines are warranted.

P15F.5

Appropriate and non-medical use of methylphenidate by residence students at a South African tertiary institution

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Background

Reports from around the world indicate that students use methylphenidate in non-medical ways. Non-medical use can refer to either using methylphenidate without a prescription, or using excessive amounts of prescribed methylphenidate. The purpose was to determine to what degree residence students from a tertiary academic institution use methylphenidate in both non-medical and appropriate manners in the South African context. Reasons for use, doses consumed and side effects experienced were investigated.

Method

The study followed a quantitative cross-sectional design and used a structured questionnaire to gather data. University students from a tertiary academic institution were chosen as the target population. Appropriate users were defined as students who have only used methylphenidate as prescribed, whereas non-medical users were defined as those using methylphenidate without a prescription, or using prescribed methylphenidate in a non-medical manner (for example in excessive doses). Data were collected during May 2015.

Results

One in four residence students in the study population (N=328) have used methylphenidate at least once in their lives. Only 7.3% (n=24) were appropriate users, whereas 16.8% (n=55) were non-medical users. Half of the appropriate users have never been diagnosed with Attention Deficit/Hyperactivity Disorder (ADHD). All non-medical users used methylphenidate to study or concentrate; however, 4 participants used it for euphoria and 8 participants to party. The preferred product, especially by non-medical users, was extended release methylphenidate (72.7%). The most common side effects experienced were sleep difficulties (69.0%) and reduced appetite (67.1%).

Conclusion

There is evidence to suggest that methylphenidate is being used in non-medical ways by residence students in the study population and that these students may experience more adverse events. Non-medical stimulant use has been considered an indicator of problematic behaviours in students. This study also presented emerging evidence of off-label methylphenidate prescriptions; the safety of which has not been established.

P15F.6

Incidence and Determinants of Medication Errors among Paediatric In-Patients at a Rural Referral Hospital in Kenya

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Introduction: Medication errors in paediatric patients typically carry a much higher risk, with medication errors up to three times more common in children versus adults due to rapidly changing body surface area, height and weight. Objective was to determine prevalence, types and predictors of medication errors in paediatric in-patient wards at Kisii Hospital.

Methodology: Descriptive cohort study of children aged 0-5 years admitted to the general paediatric ward and newborn unit. Review of treatment files upon admission and prospectively for a period of up to one month thereafter. Retrieved data on prescription and medication use analyzed for prevalence, types, and predictors of medication errors.

Results: 405 treatment files, with 307 containing at least one medication error, yielding an overall medication error rate of 75.8%. The total number of medication errors was 1023, consisting of documentation errors (73.9%), dosing errors (8.8%), monitoring errors (8.6%) and timing errors (5.7%). Medication errors were more frequent in male children, children less than one year (45.9%) and those admitted to the general paediatric ward (48.4%). Logistic regression of dosing errors revealed that children receiving more than five medicines had over six times odds of experiencing dosing errors (OR 6.4; 95% CI: 2.7-15.1; P<0.001). Route of drug administration was a significant predictor of dosing errors (P <0.001).

Conclusions: Incidence of medication errors was high among pediatric in-patients, with documentation and dosing errors most common. Number of drugs and route of administration were found to be important predictors of dosing errors. Medication errors can be a major risk factor in sick children under 5 years who are already subject to significant morbidity and mortality. Some of these errors can be potentially fatal. Consequently, a need for hospitals to have strategies for detection and prevention of medication errors, focusing on healthcare providers at all levels of health care.

1-1

Personalised feedback of prescribing data to primary care teams to drive improvement in antibiotic use in primary care in Scotland

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Background

The Scottish Antimicrobial Prescribing Group (SAPG) has had success in reducing antibiotic use in Scotland but further reductions are believed possible. As a catalyst to further reduce unnecessary antibiotic use a programme to provide GP practices with information on their antibiotic prescribing plus action orientated goal setting text was developed by NHS National Services Scotland. This approach is based on studies which provided information on high risk medicines to GPs and antibiotics to dentists.

Method

The first phase involved 50% of practices in four NHS board areas (n=183), randomly selected using a stratified sampling frame, receiving antibiotic prescribing feedback reports. The reports were emailed to practices with a covering letter, signed by the Scottish Government Chief Medical Officer and the SAPG Chair, calling on practices to consider how they can make changes to improve prescribing and preserve antibiotics for the future.

Results

Practices in the feedback arm received quarterly reports containing their rates of antibiotic prescribing compared to benchmarks for their NHS board and Scotland. These benchmarks are the 25th percentile. The report also contained suggested improvement actions that practices could take and detailed available support resources. All reports contained information on total use of antibiotics. Additionally reports contained information on: antibiotic use in various age groups (April 2016); antibiotics for urinary tract infection (July 2016); broad-spectrum antibiotics (October 2016); and antibiotics for skin infection (January 2017). A time series analysis of changes in prescribing rate in the intervention practices compared to control practices in each health board is to be conducted in 2017 and will be available at the conference.

Conclusion

This automated feedback intervention is an attractive addition to our stewardship programme as this approach can be implemented nationally at relatively low cost, subject to evidence of impact.

1-2

Are pharmacist's good knowledge and awareness on antibiotics taken for granted? The situation in Albania and implications across countries

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Introduction: Irrational use of antibiotics is a major driver of antimicrobial resistance (AMR), exacerbated by dispensing of antibiotics without a prescription. Such dispensing is very common in Albania despite legislation forbidding this, similar to other countries including South Eastern Europe, Africa and Asia. Pharmacists play a key role to improve the appropriate use of medicines especially where an appreciable proportion of patients are not covered by health insurance; consequently, preferentially seek care from community pharmacists. Consequently, important to ascertain whether community pharmacists in Albania have the necessary skills and knowledge to appropriately dispense antibiotics where needed. Alternatively, recommend other forms of care particularly for viral infections. The findings will be of interest to other countries.

Method: Qualitative cross-sectional survey among 370 community pharmacists across Albania. Topics carefully selected and validated to determine knowledge of antibiotics and current legislation.

Results: There was variable knowledge among community pharmacists. 54% knew colds are caused by viruses and 93% knew that antibiotics are ineffective against influenza. However, 18% believed if a cold lasts for more than 4 days an antibiotic can bring a patient back to work and only 13% stated that antibiotics are ineffective against viruses. Encouragingly, 92.5% of pharmacists knew penicillins can cause anaphylactic shocks, 74% that antibiotics kill bacteria that cause infections and only 7% that antibiotic misuse cannot cause AMR. However, 13% of pharmacists stated that the main disadvantage of antibiotics is that they are ineffective against viruses and 93% admitted they had no treatment protocols to consult in their work to direct appropriate care.

Conclusion: There were encouraging signs regarding pharmacist knowledge of antibiotics to help improve future care. However, a number of concerns including lack of treatment guidelines. Instigating further education as well as greater enforcement of legislation should help reduce AMR rates in Albania in the future.

1-3

Compliance to the Primary Health Care Treatment Guidelines and the Essential Medicines List in the Management of Sexually Transmitted Infections in Correctional Centres in South Africa: Findings and Implications

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Introduction: Emergence of antimicrobial resistance (AMR) is a global concern and a growing health crisis. Evidence has shown that non-compliance to standard treatment guidelines (STGs), especially in the management of communicable diseases such as sexually transmitted infections (STIs), has the potential of increasing AMR rates. Data on the extent of these challenges in Primary Health Care (PHC) facilities in correctional centres in South Africa (SA) is limited. This study aimed to determine the level of compliance with the 2008 PHC STGs and Essential Medicines List (PHC STGs/EML) in the management of STIs in two correctional facilities, and to identify potential factors contributing to the compliance and non-compliance to guide future strategies.

Methods: An investigational and descriptive study was conducted. Prescriptions for the treatment of STIs were reviewed retrospectively to determine the level of compliance with the PHC STGs/EML. Interviews were conducted with 8 of 12 authorised prescribers at the facilities to identify factors that lead to non-compliance with guidelines.

Results: From 262 prescriptions reviewed, male urethritis syndrome (MUS) (47.6%), lower abdominal pain (LAP) (22.1%) and genital ulcer syndrome (GUS) (18.8%) were the most common STIs treated. Doxycycline, ciprofloxacin and metronidazole were prescribed for most of the STIs. Although prescribers indicated that they used the PHC STGs/EML when managing STIs, compliance was 75.9% for MUS, 14.8% for GUS and 11.4% for LAP. In 80.5% of the medicines prescribed, the dosage was compliant with the PHC STGs/EML. A barrier that negatively impacted on compliance with guidelines was non-availability of certain STI medicines.

Conclusion: Compliance with the PHC STGs/EML for treatment of STIs was variable, which could contribute towards increasing AMR rates. Recommended interventions include targeted training, antimicrobial stewardship programmes and monitoring of prescribing by PTCs to promote the rational use of antimicrobials in PHCs in SA. This will be followed up.

1-4

A situational analysis of current antimicrobial governance, regulation and utilisation in South Africa

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Introduction

The Global Action Plan (GAP) on antimicrobial resistance (AMR) calls for optimising the use of antimicrobial medicines in human and animal health, together with strengthening the knowledge and evidence base through surveillance and research. However there is a paucity of consumption data in South Africa (SA) and determining antimicrobial consumption data in low resource settings remains a challenge.

Methods:

Alternative mechanisms such as Intercontinental Marketing Services (IMS), and contract data arising from tenders (an open Request for Proposal, RFP) was used to quantify utilisation. Four quantitative indicators, the total number of antimicrobial units (QTY units), total sum of the quantity of units per ATC class, moving annual total (MAT) Units and compound annual growth rate (CAGR) was used to derive a comparable metric of antimicrobial consumption across time.

Results:

A decrease in overall utilisation of antibiotics was noted in the private sector, but with an increase in utilisation of all other antibacterials' (J1X9), comprising daptomycin, fusidic acid, linezolid and tigecycline for both sectors. Antiretroviral (ART) utilisation data indicated an increase in fixed dose combination (FDC) utilisation (both sectors) with a significant increase in protease inhibitor use (public sector). The utilisation of anti-tuberculosis (TB) medicines in the public sector was considerably higher than that of the private sector and may be because TB in SA is mainly treated in the public sector as part of the national Directly Observed Therapy, Short Course (DOTS) programme.

Conclusion:

Despite its limitations, this analysis serves as an indicator of antimicrobial exposure at population level and as an alternate method for ascertaining antimicrobial consumption in human health.

1-5

Antibiotic utilisation in the Republic of Srpska – initiatives, their influence and implications

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Background: Antimicrobial resistance (AMR) and irrational antimicrobial use are one of the biggest public health challenges threatening modern civilization. There have been a number of initiatives to improve antibiotic utilisation and reduce AMR in the Republic of Srpska, one of the two constituent entities of Bosnia and Herzegovina, in recent years. The aim is to analyse total antibiotic utilisation following these initiatives. Subsequently, compare utilisation with other similar countries to review potential additional measures that could be instigated to further improve antibiotic use.

Methods: Observational study of total outpatient antibiotic utilisation from 2010 to 2015, based on data obtained from the Public Health Institute of the Republic of Srpska involving all community pharmacists including self-purchasing. Data expressed in DIDs according to WHO guidelines. Quality of antibiotic prescribing assessed against ESAC and ECDC quality indicators.

Results: Antibiotic utilisation remained relatively stable at 15.6 DIDs to 18.4 DIDs, with decreasing utilisation in recent years. Penicillins were the most used antibiotics, accounting for approximately 50% of total antibiotic utilisation, with amoxicillin the most used penicillin (29 - 40% of total utilisation) versus low use of co-amoxiclav (7 - 11% of total utilisation). This is encouraging and compares favourably with other countries. The second most used antibiotics were the cephalosporins (14% of total utilisation on average), followed by macrolides (9 %) and quinolones (9 %). There was low use of third and fourth generation cephalosporins (0.6 – 1.9% of total use) versus first and second generation. However, rising utilisation of co-amoxiclav and azithromycin, as well as higher rates of quinolone utilisation in recent years, are noted and will be addressed

Conclusions: The study indicates that multiple interventions in the Republic of Srpska have helped enhance the appropriate use of antibiotics. However, current trends will be monitored as well as instigating further measures where concerns.

1-6

What is the impact of mortality predictors in ICU patients with sepsis in a real case scenario?

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Background: Sepsis is a worldwide health problem with high rates of mortality (64%). Some factors seem to contribute to complications and death in patients with sepsis, such as delayed initiation of antimicrobial therapy, cardiovascular failure, respiratory compromise and preexisting terminal illness. Therefore the objective of this study is to analyze predictive factors related to mortality in patients with sepsis and septic shock in the ICU in Brazil.

Methods: Multicentric case-control study conducted in hospitals located in São Paulo State, Brazil. The cases and controls were identified from medical records of patients admitted to the ICU from 2010 to 2013 who were diagnosed with sepsis or septic shock defined according to the Surviving Sepsis Campaign. Cases were defined as those who had died during hospitalization, and controls were defined as those who had survived. The following variables were investigated for the greatest chance of mortality: age, sex, comorbidities, complications, multidrug resistance, the presence of more than three bacteria and the use of more than three antibiotics. Odds Ratio (OR) was used as a measure of association, 95% CI and significance level of 5%.

Results: From the total of 201 patients that met the inclusion criteria, 118 (58,7%) had died. The average length of stay in ICU and hospital in days were 22,4±23,2 and 33,5±26,6 for the case group; 24,2±21,6 and 40,7±28,8 for the control group, respectively. APACHE II scores ≥ 25 was predominant in the case group (54,5%). Considering the analysis of predictive factors adjusted, acute kidney failure complications [OR 1,88 (1,04-3,40) p=0,037] and the presence of ESKAPE group bacteria [OR 1,98 (1,08-3,63) p=0,026] were found as predictors related to mortality.

Conclusion: This study showed an association between mortality in patients with sepsis or septic shock with acute kidney complications and the presence of ESKAPE group bacteria.

1-7

Initiatives to reduce non-prescription sales and dispensing of antibiotics in the Republic of Srpska; findings and implications

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Introduction: Irrational use of antimicrobials is a major driver of resistance, exacerbated by dispensing of antibiotics without a prescription. The previous study conducted in the Republic of Srpska suggested this was a problem despite legislation banning this. Since then, a number of activities have taken place to address this including extensive education of pharmacists and the launch of national guidelines with treatment protocols. This recognizes the important of community pharmacists as part of the healthcare system as they are often the first contact point for patients. Consequently, the study aim was to ascertain whether these multiple initiatives had reduced dispensing of antibiotics without a prescription in recent years.

Method: Pseudo patients visited all community pharmacies in the Republic from October 2014 to July 2015 presenting with symptoms typical of an acute, viral and mostly uncomplicated upper respiratory tract infection, with results compared to the previous study. If an antibiotic was suggested, the maximum allowance was Euro 3/ pack.

Results: Self-medication with antibiotics significantly decreased from 58% to 19.1% of pharmacies. In both studies, most patients were offered over-the-counter medication (72.3% in the current study). The most common reason for not dispensing an antibiotic was 'antibiotics can be dispensed with a prescription only'. The penicillins were the most dispensed if an antibiotic was dispensed (93%). Fewer patients in the second study were given instructions about antibiotic use in terms of dosage and other recommendations and no discussion on their side-effects.

Conclusion: Whilst encouraging that self-medication decreased significantly, 19.1% was disappointing given the extent of recent activities. Disappointing also to see patients given fewer instructions about their use than before, which is against good pharmacy practice. This suggests the need for even stronger enforcement of the laws as well as further training of pharmacy personnel to ensure future appropriate use of medicines.

1-8

Evaluation of Prescribing of Carbapenems and Piperacillin/Tazobactam in acute hospitals in NHS Scotland

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Background

Following a national trend of increased use of carbapenems and piperacillin-tazobactam (piptazo) use the Scottish Antimicrobial Prescribing Group (SAPG) to develop and implement guidance¹ to optimise the use of these antibiotics and encourage use of carbapenem-sparing antibiotics. A quality improvement approach programme was developed comprising:

- A self-reported survey of health board prescribing guidance for carbapenems and piptazo;
- A point prevalence survey (PPS) of carbapenem and piptazo;
- Interviews with clinicians in selected health boards in NHS Scotland to evaluate prescribing behaviours.

Methods

- An online survey sent to Antimicrobial Management Teams (AMTs) in the 15 health boards.
- A bespoke point prevalence survey (PPS) was carried out in all acute hospitals to determine the prevalence and patterns of use for carbapenems and piptazo.
- Interviews were conducted with 28 clinicians from different specialties and grades across 4 health boards.

Results

- The survey showed that meropenem is subject to prescribing restrictions in a larger number of Boards (87%) than piptazo (46%) and carbapenem-sparing antimicrobials are used to varying extents. Nationally there was low approval of carbapenem-sparing antibiotics.
- 478 prescriptions were analysed in the PPS. The results showed good compliance with prescribing guidance and documentation of indication for meropenem but this was variable for piptazo. Documentation of indication and review/stop date was low for both antimicrobials.
- Key findings from the clinician interviews were that clinicians rely on infection specialists for advice on initiation and continuation/de-escalation and there is a lack of awareness and confidence in using carbapenem-sparing antibiotics unless within local guidelines and/or microbiology reports.

Conclusion

This study demonstrates variation in practice across Scotland for restrictions on prescribing and compliance with local guidance for both meropenem and piptazo. Clinician interviews suggest more support from specialists is required to improve use of these important antibiotics.

1-9

Prevalence of antibiotic prescription in pediatric outpatients in Italy: the role of local health districts and primary care physicians in determining variation

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Background. Antibiotic resistance is a growing international threat. However, antibiotics are prescribed for conditions that do not benefit from antibiotic therapy. The objectives were to analyze geographic variation in antibiotic prescribing and to identify the priority axes for action to improve the rational use of antibiotics.

Methods. The study was conducted among pediatric outpatients of the Lazio Region, Italy, aged 13 years or less. Antibiotic prescription patterns were analyzed during a 1-year follow-up. Multilevel models were performed to analyze geographic variation. Variation was expressed as Median Odds Ratios (MORs). If the MOR is 1.00, there is no variation between clusters. If there is considerable between-cluster variation, the MOR will be large.

Results. We enrolled 636,911 children. Most of them were aged 6-13 years (57.3%). In 2015, the antibiotic prescription prevalence was 46% in the 0-13, 58% in the 0-5, and 37% in the 6-13 age group. Overall, penicillins were the most prescribed antibiotics, their consumption increased from 43% to 52% during the 2007-2015 period. In 2015, the antibiotic prescription prevalence ranged from 30% to 62% across local health districts (LHDs). Moreover, a significant ($p<0.001$) variation was also observed between physicians working in the same LHD: MORs were equal to 1.52 (1.48-1.56) and 1.46 (1.44-1.48) in the 0-5 and 6-13 age groups, respectively. The probability of prescribing antibiotics was significantly ($p<0.001$) lower for more-experienced physicians.

Conclusion. Pediatric antibiotic use in the Lazio region is still much higher than in other European countries. The intra-regional variability underlines the lack of therapeutic protocols shared at regional level and raises equity issues in access to optimal care. Both LHD managers and primary care physicians should be involved in interventions aimed to improve the rational use of antibiotics and mitigate the effect of contextual variables, such as the spatial-related socioeconomic status of the patient/parent binomial.

1-10

EVALUATION OF SELF MEDICATION WITH ANTIBIOTICS AMONG PATIENTS IN THE LOW AND MIDDLE INCOME COUNTRIES: A SYSTEMATIC REVIEW PROTOCOL

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Background:

Self medication and self purchase of antibiotics for confirmed or suspected bacterial infection is common in low and middle income countries, with rates up to 70% among community pharmacies in Kenya and up to 100% in some African countries. These high rates reflect community pharmacies and drug shops being easily accessible and usually the first point of care before patients seek treatment from physicians. Patients who find it expensive to seek care from physicians, as often cannot afford both, and those who wish to avoid hospital processes before they can secure treatment, prefer to purchase medicines straight from pharmacies. Weak regulatory systems also contribute to the rise in self medication with antibiotics across countries. The study aims to determine the extent and impact of self- medication on antimicrobial use and resistance development, and potential ways to address this in Kenya.

Methods: A systematic review will be undertaken. A PICO question which incorporates the population, intervention, comparator and outcomes will be formulated. A search strategy will be developed and entered into various databases including the Cochrane database of systematic reviews, CENTRAL, EMBASE, MEDLINE and Google scholar. Boolean terms like “AND” and “OR” will be used. All studies that evaluate the extent, impact of policies to reduce self- medication of antibiotics and the outcomes of self-medication will be included. Studies that evaluate self- medication of other drugs apart from antibiotics will be excluded, as well as those from developed countries. The studies obtained from the search will undergo title, abstract and full text screening for compliance with PICO. Evaluation of the quality of evidence will be done using the GRADE system.

Results: The study is on going and the preliminary results will be presented at the EURODURG conference to guide future strategies in Kenya, mindful of the population characteristics in Kenya.

2-1

Comparative effectiveness of non-vitamin K antagonist oral anticoagulants (NOACs) and warfarin in the Scottish atrial fibrillation population: the value of real world evidence

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Introduction: Different methods are available to correct for the absence of randomisation when estimating average treatment effects (ATE) using observational data. This study explores these methods, assessing whether RCT findings are generalizable to Scottish clinical practice.

Methods: Propensity score (PS) matching, Inverse Probability Weighting and PS regression were explored utilising linkage of the Prescribing Information System (PIS), Scottish Morbidity Records 01 and death records for newly anticoagulated patients, with a diagnosis of atrial fibrillation (AF) or atrial flutter. AF related outcomes were compared for four treatment groups: Warfarin (79.1%), Apixaban (9.7%), Dabigatran (1.3%), Rivaroxaban (9.9%). Patients were followed from first oral anticoagulant prescription to first clinical event or death. Censoring was applied for treatment switching and various follow-up times. Using a continuous treatment approach, hazard ratios were estimated, adjusting for age, sex and comorbidities.

Results: At 2 years follow-up PS matching showed no difference in risk of ischaemic stroke for Apixaban (HR: 0.94 (CI: 0.63-1.38)), Dabigatran (HR: 0.71 (CI: 0.34-1.47)), and Rivaroxaban (HR: 1.09 (CI: 0.82-1.45)) compared with Warfarin. A reduced risk of death was observed for Apixaban (HR: 0.44 (CI: 0.34-0.58)) and Rivaroxaban (HR: 0.65 (CI: 0.54-0.79)). Hazard ratios were consistent across methods for these two drugs. The risk of death for Dabigatran differed substantially depending on the method used.

Conclusion: For each NOAC the risk of ischaemic stroke was different from RCT findings. Results were generally consistent regardless of the method used. For small sample sizes, methods may yield different results and PS matching may not be appropriate.

2-2

Use of direct oral anticoagulants after market entry of edoxaban: A Danish nationwide drug utilization study

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Background

Edoxaban is the fourth direct oral anticoagulant (DOAC) to enter the market. In Europe, edoxaban is licensed for use in atrial fibrillation as well as treatment and prevention of deep vein thrombosis and pulmonary embolism. The role of edoxaban in a field with four highly similar drugs is not clear. The aim of this study was to describe the early uptake of edoxaban in the first six months after market entry in Denmark.

Methods

Using nationwide health registries, we identified new users of edoxaban (n=153) from June 6 (day of marketing) through December 2016. For comparison, we also identified new users of dabigatran (n=1,132), rivaroxaban (n=9,515), and apixaban (n=7,142). Users were compared according to the indication of use and described with regard to previous anticoagulant experience, comorbidity and comedication.

Results

The rate of edoxaban initiation increased to 1.0 per 100 000 person months in December, compared to 3.2, 32.3 and 25.7 for dabigatran, rivaroxaban, and apixaban, respectively. Atrial fibrillation was the most common registered indication for edoxaban (63%) as well as the other DOACs (38-51%). In a substantial proportion of DOACs users (34-47%), no registered indication could be identified. Overall, users of edoxaban were comparable to users of the other DOACs with regard to age, gender distribution and comorbidities. However, 97% of edoxaban users had previously received anticoagulant treatment compared to only 31-40% among users of other DOACs.

Conclusions

Use of edoxaban is still limited. Edoxaban is primarily used in atrial fibrillation, and edoxaban users are very often switchers from another oral anticoagulant. Continued monitoring of DOACs, including effectiveness and safety, is considered essential to the safe and rational use of these drugs. Lack of registered indications for DOAC use is a challenge in register-based studies and may be an important source of selection bias.

2-3

An investigation into the utilisation and prescribing patterns of the direct oral anticoagulants compared to warfarin in the community setting in England.

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Background: Direct oral anticoagulants (DOACs) – dabigatran, apixaban, rivaroxaban and edoxaban – are a novel alternative to the vitamin K antagonist warfarin for anticoagulation treatment. This study aimed to investigate the uptake of DOACs compared to warfarin in England from 2006-2015.

Methods: This repeated cross-sectional study collected anonymised dispensing data from the community setting in England from the Prescription Cost Analysis (PCA) annual database from 2006-2015. The utilisation of DOACs and warfarin was measured using annual number of items dispensed, defined daily dose (DDD) per 1000 inhabitants per day and the annual cost to the National Health Service (NHS) in England. The utilisation trends were analysed using descriptive statistics.

Results: From 2006-2015, warfarin items dispensed rose by 74.7% (n=4.94 million) from 6.61 million-11.55 million, while the DOACs increased by approximately 3000-fold (n=2.57 million) from 758 in 2009 to 2.57 million by 2015, accounting for 22.26% of total oral anticoagulants in 2016. The DDD per 1000 inhabitants per day of warfarin rose by 37.1% (n=2.21) from 5.97 to 8.18 from 2006-2015, while the DOACs increased by approximately 6000-fold (n=3.02) from 4.59×10^{-4} in 2009 to 3.02 in 2015. Despite the significant increase in warfarin utilisation, the cost of Warfarin rose only by 15.65% (n=3.12 million) from £19.97 million in 2006 to £23.09 million in 2015, while the DOAC cost increased significantly by 2000-fold (n=144.17 million) from £73,000 to £144.24 million from 2009-2015, accounting for 86.20% of total anticoagulant cost in 2015.

Conclusion: Warfarin was still the most utilised oral anticoagulant, but the DOACs utilisation had significantly increased in recent years. Although DOACs accounted only for a small proportion of the total warfarin/DOAC utilisation, they contributed to the majority of total cost. Further research is needed to investigate regional variations in DOAC utilisation, stratified by their clinical indications to evaluate their prescribing appropriateness.

2-4

Prescription patterns and adequacy of blood pressure control among adult hypertensive patients in Kenya; findings and implications

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Background: Hypertension is a major cause of morbidity and mortality across countries, with high prevalence rates in Africa including Kenya (up to 55% of the adult population). Consequently, imperative to understand current treatment approaches and their effectiveness. Currently, there is paucity of such data in Kenya which is a concern. The objective was to describe current prescribing patterns and adequacy of blood pressure (BP) control among adult hypertensive patients in Kenya to guide future practice.

Method: Descriptive cross-sectional study conducted in medical out-patient clinics between January and April 2015 using a mixed-method approach. Quantitative data of anti-hypertensive therapies and BP control collected via retrospective analysis of patients' medical records. Semi-structured interview guide used to collect qualitative data from prescribers. Quantitative data were analysed using STATA 10. Analysis of interviews was undertaken by grouping discerning patterns or themes.

Results: 247 hypertensive patients, predominantly female, with a mean age of 55.8 years, on antihypertensive therapy for 1-5 years were analyzed. Angiotensin converting enzyme inhibitors (ACEIs) and thiazide diuretics were the most commonly prescribed anti-hypertensive medicines, mainly as combination therapy. Treatment typically complied with current national Kenyan guidelines, mainly for stage 2 hypertension (75%). Control of BP was observed in 46% of the patients, with a significant reduction in mean systolic (155 to 144 mmHg) and diastolic (91 to 83 mmHg) BP ($P < 0.001$) from diagnosis to the last clinic visit. Multi- drug regimens predisposed patients to poor BP control. Prescribers had been trained on the guidelines enhancing compliance. Most common challenges were poor adherence to medications, cost of medications, and inadequate patient counseling.

Conclusion: Encouragingly, good compliance to current guidelines due to training. Poor BP control in the majority needs to be addressed. Additional training of prescribers and follow-up of measures to improve adherence and BP control will be introduced and followed up.

2-5

Variations in initiation with oral anticoagulants for atrial fibrillation in the region of Valencia: a multilevel analysis with real-world data.

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Background: Beyond clinical trials, clinical practice guidelines and administrative regulation, treatment decision-making can be influenced by individual and contextual factors. Our aim was to describe variations in the patterns of initiation of anticoagulation therapy in patients with atrial fibrillation by Health Areas (HA) in the region of Valencia and to quantify the influence of the HAs on variations in treatment choice.

Methods: Population-based retrospective cohort study of all atrial fibrillation patients who started treatment with oral anticoagulants between November 2011 and February 2014 in each of the region's 24 HAs. We described patient and utilisation characteristics per HA and initiation patterns over time, and we identified contextual and individual factors associated with differences in initiation patterns.

Results: 21.879 patients initiated treatment with an oral anticoagulant in the 24 HAs. Initiation with direct oral anticoagulants (DOAC) in the first year was 14,6%. In November 2013 the ratio was 25,4%, with HA ratios ranging from 3,8% to 57,1%. DOAC-initiating patients had less comorbidity but were more likely to present episodes of previous ischemic stroke, hemorrhagic stroke or TIA when compared with patients initiating with VKA treatment. Variability among HAs was statistically significant, with the majority of HAs ranking above or below the regional initiation average (ICC≈8%).

Conclusions: There was high variability in the percentage of DOAC initiation and in the choice of DOAC among HAs. Interventions aimed to improve DOAC initiation decision-making and to reduce variations should take into account the Health Area component.

2-6

Trends in the use of combinations of substances for cardiovascular therapy. A longitudinal survey using claims data from Germany.

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Background:

In cardiovascular therapy, like in several others, combinations of substances are in widespread use, in accordance with guidelines for treating conditions of varying severity. Recommendations whether to employ free combinations of mono preparations or fixed-dose combinations have changed over time. While pharmacologists praise free combinations for their potential for fine-grained tuning, practitioners may prefer fixed combinations, because they are seen as improving adherence especially for elderly, multi-morbid patients, who often receive several medications anyway.

Methods:

Prescription data for cardiovascular treatment (ATC groups C03, C07 to C09) from Germany were analysed for a 10-year period, describing prevalent and incident use of either free or fixed combinations and tracking changing prescription patterns over time for patients between 60 and 70 years of age.

Results:

For incident cases, the share of fixed combinations decreased substantially over time, most markedly for combinations containing beta-blockers. For combinations with AT II antagonists, the decrease was weakest, with ACE inhibitors in between. Still, fixed combinations of ACE inhibitors with diuretics are the most commonly used combination in absolute terms, while their free combinations are getting close, just as are fixed combinations of AT II antagonists with either diuretics or calcium antagonists. For patients with previous cardiovascular therapy, where a switch to combination therapy may be called for by a worsening condition, changes are less marked, and fixed combinations are used more often than for new recipients.

Conclusion:

Cardiovascular therapy is changing slowly towards a higher use of single substance therapy. Where two substances are employed, free combinations are increasingly used, but overall still on a low level. For patients with ongoing therapy, similar changes occur still more slowly.

2-7

Patterns of long-term use of cholesterol-lowering drugs in Tuscany

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Background

Reduction of levels of low-density lipoprotein cholesterol (LDL-C) in patients at risk of vascular events is associated with risk reduction. Long-term use of statins is recommended in patients with high LDL-C levels and other risk factors. High-potency statins and ezetimibe (HPEZE) are recommended in those not reaching the LDL-C target. Adherence to therapy after an acute event was observed to be suboptimal in real-world studies, but the pattern of long-term use of cholesterol-lowering drugs (CLD) is poorly investigated. We described the long-term use of CLD in Tuscany, an Italian region with 3.6 millions inhabitants where data on drug utilization has been collected since the early 2000s.

Methods

All the patients living in Tuscany on 31/12/2015 and who had started a CLD treatment since 2007 entered the study. Adherence to CLD treatment in 2016 was observed, stratified per period of treatment inception, and classified as: not treated (NT), undertreated (UT: at least one prescription but less than 270 tablets in 365 days), adherent. The prevalence of use of HPEZE was observed.

Results

352,258 persons started a CLD treatment between 2007 and 2015 and were living in Tuscany by the end of 2015 (9.8% of the population). 40.3% of them were NT in 2016: the earlier the therapy inception, the higher this percentage. Among the treated, 41.2% were UT, and this percentage increased from older to recent initiators (from 38.0% to 47.0%). 1,470 patients were treated with HPEZE in 2016 (0.7% of those treated), and 84.3% among them were adherent.

Conclusion

Adherence to CLD therapy was low, which may be due to an inappropriate prescription. Among those who were treated, two on five were undertreated: the increase per cohort of treatment may be due to depletion of undertreated patients. In patients on the strongest treatment non-adherence was lower.

2-8

Utilisation and dispensing patterns of warfarin and DOACs in Wales and Northern Ireland

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Background

Four direct oral anticoagulants (DOACs) were approved nationally in Wales and Northern Ireland (NI) in 2009. This study examined the utilization trend for warfarin and DOACs in both countries.

Methods

Prescription cost analysis (PCA) of Wales and NI from 2007-2015 was analyzed. Data was categorized into number of dispensed items, costs and number of DDD/1000 population/day for each anticoagulant. Descriptive statistics and linear regression analysis were done.

Results

In Wales, dispensing of warfarin and DOACs increased significantly, by 56.3% ($p < 0.05$) and 107,926-fold ($p = 0.03$) respectively from 2007-2015, with DOACs accounted for 2.2% of total anticoagulants dispensing. Among DOACs, rivaroxaban has the highest dispensed items (53.1%). Costs of warfarin and DOACs increased significantly, by 24.1% ($p = 0.03$) and 89,573-fold ($p = 0.03$) respectively, with DOACs represented 39.3% of total cost. Rivaroxaban has the highest cost (50%) among DOACs. Number of DDD/1000 population/day of warfarin and DOACs increased significantly, by 30.55% ($p \leq 0.05$) and 307,692-fold ($p = 0.03$) respectively.

In NI, dispensing of warfarin and DOACs increased significantly, by 34.02% ($p \leq 0.05$) and 5,956-fold ($p = 0.02$) respectively from 2007-2015, with DOACs accounted for 6.8% of total anticoagulants dispensing. Of DOACs, apixaban has the highest dispensed items (41.6%). Costs of warfarin and DOACs increased by 26.2% ($p = 0.06$) and 6,394-fold ($p = 0.02$) respectively, with DOACs represented 69.1% of total cost of anticoagulants. Apixaban has the highest cost (40.9%) among DOACs. Number of DDD/1000 population/day of warfarin and DOACs increased significantly, by 17.65% ($p = 0.002$) and 14,633-fold ($p = 0.02$) respectively.

Conclusion

Use of DOACs were increasing in Wales and Northern Ireland. Despite the upward trend in DOACs, warfarin remained as the most commonly dispensed anticoagulants in 2015. It appears that Wales and NI adopted different individual DOAC as their preferred choice. Further research is required to explore regional variations in the utilisation of DOACs across their various indications to assess their effective prescribing using patient level data.

2-9

Pharmacoepidemiology of arterial hypertension in Semey region: analysis of pharmacotherapy and patient compliance to treatment.

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We performed pharmacoepidemiological study on hypertension treatment in Kazakhstan to provide more insight into the epidemiology of arterial hypertension and into the extent of the population taking antihypertensive drugs. Pharmacoepidemiology is the scientific backbone of therapeutic risk management —the process of assessing a product's benefits and risks, and developing, implementing, and evaluating strategies to enhance the overall balance of such benefits and risks.

Methods: The study included 618 patients with hypertension of the I-III degree. The age of patients ranged from 38 to 77 years (mean age - $61,2 \pm 2,7$ years). Among the surveyed men was -353, women - 265.

Carried out an analysis of medical records and patient survey to determine the structure of antihypertensive therapy, compliance to it and the existing violations preparations reception mode.

Results: Was revealed prevalence in the appointment's structure the combinations of antihypertensive drugs (46.0%) and fixed combinations (29.0%). Monotherapy performed more frequently with beta-blockers and calcium channel antagonists.

It revealed the greatest compliance to the use of fixed combinations of drugs and most high clinical efficacy of antihypertensive therapy options.

Conclusion: According to the results of the study, both the low adherence of patients to treatment and the very low clinical efficacy were revealed. The data obtained are in substantial agreement with the results of other studies. So, very low adherence to antihypertensive therapy was demonstrated in the Belarusian study in patients with moderate and severe arterial hypertension. According to the Morisky-Green test, it was only 13.7% . Thus, increasing the effectiveness of antihypertensive pharmacotherapy in patients with arterial hypertension requires the use of modern approaches, in particular, the wider use of fixed combinations of antihypertensive drugs, individual work with patients, aimed at increasing adherence to treatment and eliminating violations of the order of taking prescribed medications.

2-10

Knowledge of hypertension and its management among hypertensive patients on chronic medicines at primary health care public sector facilities in South Africa; findings and implications

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Introduction: Prevalence rates of hypertension in South Africa (SA) are high, with hypertension ranked seventh amongst the major underlying causes of death. The government recently introduced the Central Chronic Medicines Dispensing and Distribution programme to improve care and access to medicines for chronic diseases. Consequently, a need to assess knowledge and management among hypertensive patients receiving chronic medication from primary health care (PHC) facilities in SA as a basis for improving future management.

Method: A descriptive, quantitative study was conducted amongst 253 conveniently selected chronic hypertensive patients collecting their medication from PHC facilities in the Vhembe District, Limpopo Province of SA. Patients were interviewed face-to-face by pharmacists using a structured questionnaire. Ethical clearance was granted and participants provided written informed consent.

Results: Half (53.7%) of the patients had uncontrolled blood pressure (BP) and 62.3% were on antihypertensive treatment >5 years. Less than half (46.9%) of patients knew what causes high BP, and less than a third knew what hypertension is (27.7%). Less knew what normal BP should be (19.9%) and the meaning of recorded BP numbers (4.5%). The difference between patients with- and those without education regarding knowledge concerning the causes of BP, the meaning of BP numbers, and what normal BP should be, was significant ($p < 0.001$). Less than half (46.9%) of the patients indicated that they can do something to lower their BP. Over half of the patients (56.0%) indicated receiving hypertension information from the clinics; however, only 15.6% of whom claimed to have received specific information about antihypertensive medicines.

Conclusions: The majority of patients lacked hypertension specific knowledge and only half had controlled BP. Interventions to improve the control of high BP should be targeted at closing knowledge gaps as part of the current chronic treatment initiatives to ensure the benefits of increased access to care are realised.

3-1

ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS RECEIVING LONG-TERM BIOLOGICAL AGENTS IN A REAL-LIFE SETTING

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BACKGROUND: Biological agents (abatacept, adalimumab, efalizumab, etanercept, infliximab, rituximab and tocilizumab) used for the treatment of psoriatic arthritis and rheumatoid arthritis are associated with serious adverse effects. In addition, these biological agents are expensive medicines and should be consider economic aspects as well. The safety of these drugs remains uncertain. The goal of this research is to determine the frequency and severity of adverse effect associated with use of biologic agents for psoriatic arthritis and rheumatoid arthritis, and possible risk factors for such events.

METHODS: Sources of information included dispensing pharmacy data and interviews with patients. Research staff conducted telephone interviews with patients suffering from psoriatic arthritis and rheumatoid arthritis who used biologic drug, inquiring about any apparently medication-related adverse drug reactions (ADRs) or serious adverse events (SAEs).

RESULTS: Of the 305 patients identified, 37 proved ineligible; we interviewed 268 patients. From this total, 10 (3.7%) were taking abatacept, 127 (47.4%) adalimumab, 9 (3.4%) efalizumab, 52 (19.4%) etanercept, 42 (15.7%) infliximab, 25 (9.3%) rituximab, and 3 (1.1%) tocilizumab. Of the 268 patients, 116 (43.3%) experienced one or more adverse events related with biological agents with 1.6 events per patient and of these 29 (25%) experienced one or more SAE. Neither risk of factor studied was associated with adverse drug events.

CONCLUSION: Biologic agents were associated with high rates of ADRs, withdrawals due to adverse events and SAEs. Patients who use biologic treatment should be aware of these risks. Our data suggests that in patients with comorbidity, warnings of possible adverse events and enhanced surveillance is necessary.

3-2

SWITCH FROM EPOETIN ORIGINATOR TO ALPHA BIOSIMILAR: CLINICAL EFFICACY OF BIOSIMILARS ON HEMOGLOBIN AND SAFETY IN A POPULATION OF PATIENTS ON STABLE HEMODIALYSIS

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Background: The aim of the study was to evaluate the clinical efficacy of switch from original ESAs to intravenous biosimilar epoetin alfa on hemoglobin, iron status and safety in hemodialysis patients. A cost analysis to assess the economic impact on healthcare saving was performed.

Methods: This was a 12-month observational study. Patients switched from different ESAs to epoetin biosimilar were monitored for six months before and six months after the switch. The primary end point was response to treatment in term of hemoglobin and iron parameters stability, incidence of fistulae thrombosis and cardiovascular disease. Secondary endpoint included the cost analysis related to the switch.

Results: We enrolled 87 patients (36 male, mean age 65.2 ± 16.1 yrs). No significant changes in hemoglobin, ferritin and transferrin saturation were observed ($p=0.29$; $p=0.41$; $p=0.05$ respectively) after the conversion. No changes in the incidence of FAV thrombosis and cardiovascular events were observed. The mean monthly epoetin consumption per patient changed from 52460 ± 36167 UI six months before the switch to 49517 ± 29154 UI six month after the switch ($p=0.29$). The average monthly expense per patient dropped off from 317.78 € to 155.91 €.

Conclusions: According to our experience in hemodialysis patients receiving intravenous epoetin, the conversion from different ESAs to biosimilar was safe and effective. Moreover, a cost analysis showed a strong impact on healthcare expenditure. Finally, in this paper we concluded that the main decision to shift a patient to biosimilar should be a clinician responsibility discussed in depth with the patient.

3-3

Real-world data about biosimilar and originator somatropin use in Italian clinical practice: a population-based multiple databases study during the years 2009-2014

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Background: Somatropin (rGH) is approved for conditions involving growth disturbances and growth hormone deficiency. Since 2006, biosimilar rGH is available in Italy. No population-based data about pattern of originator and biosimilar rGH use in Italian routine care are available. This study aimed at exploring the pattern of biosimilar and originator rGH use in six Italian centres, where different healthcare policy interventions promoted biosimilars use.

Methods: This retrospective, drug-utilization study was conducted in the years 2009-2014, using administrative databases of Tuscany, Lazio and Umbria Regions and Caserta, Treviso and Palermo Local Health Units. Characterization of naïve rGH users, prevalence of rGH users and discontinuation of therapy were assessed over time and across centers (anonymised).

Results: Overall, 6,785 patients were treated with rGH in the years 2009-2014. Naïve users were 4,493 (66.2%; males/females= 1.3; median age: 12 years). The prevalence of rGH use slightly increased from 2009 to 2010 (0.2-0.3 per 1,000 inhabitants), stabilized thereafter, but was heterogeneous across centers (in 2014, prevalence of use in centre n.2 doubled prevalence in centres n.4 and 1). The proportion of biosimilar rGH users was low (7.8% in 2014), and heterogeneous across centres and over years, with the greatest increase in centre n.3 (5.2-16.9%), and the greatest decrease in centre n.1 (11.6-2.1%).

During the observation period, therapy discontinuation was observed in more than half of rGH naïve users (54.0%), more frequently in females than males (58.1% vs. 50.9%). Within the first year of treatment, discontinuation was frequent (36.9%).

Conclusions: A relevant geographical variability in the prevalence of rGH use was observed, confirming previous concerns about potential inappropriate rGH use. The proportion of biosimilar rGH users was low and heterogeneous among centres, probably due to different loco-regional healthcare policies. Effective post-marketing monitoring may improve treatment appropriateness and guarantee greater savings than only promoting lowest cost rGH.

3-4

Changes in medication use in advanced cancer patients when death approaches. The international multicentre EPCCS study

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Background: Little is known how medication evolves in the last months of life of advanced cancer patients. Therefore, our aim is to describe the medication use in advanced cancer patients being admitted to a palliative care (PC) program at different time points before death.

Method: In this prospective study, advanced cancer patients were recruited in 30 oncology / PC units in 12 countries. From recruitment on, medical data and symptoms were registered every 3 to 5 weeks, using case report forms completed by patients and health care providers at each encounter. Medication was dichotomous; use: yes/no for 19 therapeutic groups. Data were analysed retrospectively using death as the index date. Only patients with a verified date of death with at least 1 case report were included here. We compared medication use at 1, 2, 3, 4 and 5 months before death by constructing 5 cross-sectional subsamples with medication use during that month.

Results: On average age was 67, 56% were males (n=720). The most prominent diagnoses were bowel (37%) and lung (21%) cancer. Chemotherapy decreased from 43.8 at 5 to 15.5% at 1 month before death. While the use of non-opioids declined from 59.5 at 5 to 56.4% at 1 month before death, significantly more opioids (61.8 to 80.5%) were prescribed. Comparing drug use between 5 (n=249) and 1 month (n=400) before death, a significant increase in the use of corticosteroids (43.9 to 70.6%), neuroleptics (9.6 to 19.6%), sedatives (35.1 to 46.0%), laxatives (56.5 to 65.5%), antibiotics (9.7 to 18.6%), diuretics (18.9 to 28.0%) and antithrombotics (27.1 to 38.3%) and a decrease in cardiovascular drugs (37.9 to 26.9%) were found.

Conclusion: When death approached, medication for symptom control increased, as well as most other medication groups. To appraise the decrease in cardiovascular drugs, more detailed medication data are needed.

3-5

Impact of a regulatory intervention on the use of targeted oncologic drugs in the Ecuadorian public and private healthcare sector

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Background

In April 2012, the Ecuadorian government launched a regulation aimed to speed up the selection and procurement of potentially useful medicines not included in the National Essential Medicines List. We performed an interrupted time series analysis (ITSA) aimed to measure the impact of this policy on the use of targeted oncologic drugs in both, the public and private sectors.

Methods

Individual dispensing data of oncologic drugs routinely collected over 5 years (2010-2014) from the six largest Ecuadorian cancer hospitals, 3 public/3 private (country's catchment area 60-70%), was analyzed. Targeted drugs were defined as monoclonal antibodies, proteinkinase inhibitors, vismodegib and vorinostat.

The monthly incidence rate of targeted drugs users (out of 1000 users of oncologic drugs) was obtained. An ITSA on incident users of targeted drugs was applied to measure changes in level and trend after intervention. The analysis was split on private/public hospitals.

Results

In the public sector, new users of targeted drugs dropped by 14.5/1000 users after the intervention ($p < 0.01$). There was a monthly increase trend of 0.18 new targeted drug users, it was not statistically significant. The incidence at the beginning of 2010 was 31.6.

In the private sector results were opposite, new users of targeted drugs increased by 2.3/1000 users after policy implementation. There was a slight monthly increase of 0.11 new targeted drug users. Both, level and trend were not significant. The incidence at the beginning of 2010 was 5.8.

Conclusions

The policy implemented produced an opposite adoption pattern of new targeted drugs according to the healthcare sector where it was applied; meanwhile new users of targeted drugs immediately dropped in the public sector, in the private it increases. In both sectors, raising trends were not modified after the intervention. Differences in policy response according to the healthcare sector must be studied in depth.

3-6

Oncoematologic utilization of Rituximab: linking administrative with hospital pharmacy data for studying real world utilization of infusive antineoplastics

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Infusive antineoplastics (IA) are administered in hospital settings where patient level information on drug utilization is usually not recorded or incomplete. This study aimed to explore the feasibility of linking the Regional Administrative Database of Tuscany (RAD) with the database of the Hospital Pharmacy of Siena (HPS) for studying the real world utilization of IA.

Methods

The utilization of rituximab was chosen as the study case. All patients aged 18+ with ≥ 1 rituximab administration between 2009 and 2016 received in the oncology or haematology units of the University Hospital of Siena were retrieved from HPS. The regional anonymized identification code was attributed to each patients and used for linking RAD information. The first rituximab administration recorded in HPS was the cohort entry. New users (no rituximab administration in RAD prior cohort entry) were followed up for 1 year. Rituximab utilization and hospitalizations for infectious diseases were described.

Results

Record linkage was possible for 557 out of 619 patients identified in HPS. New users were 539, of which 130 had <1 year of follow-up in RAD (one-year mortality was 10%). The remaining 409 new users were treated for non-Hodgkin lymphoma (NHL, n=333), chronic lymphocytic leukemia (CLL, n=58) or other indications (n=18). Overall, male/female ratio was 1/2 and mean age was 64. About 56% of patients received between 5 and 8 administrations. Mean dose for LLC varied from 700mg at first administration to 860mg for the following. Rituximab was the first-line treatment for over 90% of patients. Among all 539 new users, 17% had ≥ 1 hospitalization for infectious disease. Sepsis was the most frequent event (N=25).

Conclusions

This study demonstrates the feasibility of linking HPS with RAD. The two data sources provided complementary information on rituximab utilization. Combining HPS with RAD is an extremely promising approach to study IA utilization.

3-7

Immunosuppressive therapy in transplanted patients: a descriptive analysis of common practice in the Lazio Region, Italy.

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Background. Different drug therapies, formulations and availability of generics fuel the complexity of treatment choice in transplanted patients. This study aimed to evaluate maintenance immunosuppressive therapy in transplanted patients.

Methods. A cohort of transplanted patients, residents during 2006-2015 in the Lazio Region, was enrolled using a national transplant information system. Patient clinical history (previous prescriptions and hospitalizations) and immunosuppressive therapy (ATC L04) was identified through the Lazio health data warehouse. Temporal trends, regimens and switching patterns were analyzed for all settings. Determinants of immunosuppressive therapy were estimated by logistic regression.

Results. Overall, 1,787 newly transplanted patients were identified with median age of 52 years and higher prevalence of males (66.9%); the majority of transplants occurred in kidney and liver settings (57.5% and 37.2%, respectively), while only 6.7% concerned heart. Temporal trends showed a continuous increased use of tacrolimus over years and a relative decrease of cyclosporine for both kidney and liver settings. Heart transplanted patients mainly received cyclosporine (around 90%) which is constant over time. An in-depth analysis on kidney patients showed a more frequent tacrolimus based therapy (67.3%) than cyclosporine as a first treatment. Moreover, around 50% of incident tacrolimus and cyclosporine users added a second immunosuppressive (mycophenolate or mTOR). Switching pattern in a 1 year follow-up was 10% for cyclosporine users and negligible for tacrolimus (1%). However, a relevant switching pattern (26.9%) between tacrolimus formulations (twice daily versus once daily) was observed with a 8.4% of switch back. The number of co-administered drugs and severity of the patient influenced the prescription of the formulation.

Conclusion. Tacrolimus was the most frequent drug used as maintenance therapy in kidney and liver transplanted patients. Switching from cyclosporine to tacrolimus and between tacrolimus formulations is a common practice. Determinants of switching should be further analyzed.

3-8

TRASTUZUMAB FOR METASTATIC BREAST CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Breast Cancer (BC) is the most prevalent among women and in advanced stages is considered terminal. It is estimated that 25% to 30% of tumors overexpress type 2 human epidermal growth factor (HER-2), with a negative impact on prognosis. Trastuzumab, a monoclonal antibody that blocks HER-2, is used in various stages. The aim of this study was to evaluate the efficacy of trastuzumab in the first line of treatment or after progression in women with metastatic BC in relation to overall survival (OS) and progression-free survival (PFS).

Methods: A systematic review (RS) of randomized controlled trials (RCTs) was performed by two independent reviewers. The databases MEDLINE (Pubmed), LILACS, Cochrane Library and EMBASE (accessed November 2016) and manual search with the terms: BC and trastuzumab were used. Cochrane Collaboration tool was used for risk of bias assessment. The results OS and PFS were evaluated in reverse-variance meta-analysis with random effects model, presented as hazard ratio (HR) with 95% confidence intervals (CI), I^2 and p value for heterogeneity.

Results: A total of 2,238 publications were found. Six studies with 13 publications were included (1,283 women). Five of them were funded by pharmaceutical industry. The studies generally were classified as moderate methodological quality. The combined analysis revealed better result of OS (HR = 0.79, 95% CI 0.67 to 0.94, I^2 = 0%, p = 0.86) and PFS (HR = 0.56, 95% CI 0.48 to 0.64, I^2 = 0%, p = 0.53) in patients who used trastuzumab as the first line. The OS result for second line therapy were (HR = 0.80, 95% CI 0.64 to 1, I^2 = 7%, p = 0.30). There was no difference for PFS.

Conclusion: RS showed a discrete favorable result for first line trastuzumab. Until now evidence is too fragile to recommend continuation of trastuzumab after progression.

3-9

COST-EFFECTIVENESS OF THERAPY WITH TRASTUZUMAB FOR METASTATIC BREAST CANCER: HOW MUCH ARE WE PAYING FOR MORE FOR THE BENEFIT OF A NEW TECHNOLOGY?

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Background: Breast cancer (BC) is more common among women and its prevalence increases over the years. Human epidermal growth factor receptor 2 (HER-2) is observed in 25% to 30% of cases. Trastuzumab (T), a monoclonal antibody, is used in several stages of BC acting on the HER-2 blockade. O T a high impact on the budget in the Brazilian Unified Health System (SUS), about 11.125USD for maintenance treatment. A cost-effectiveness assessment of the addition of the T to the docetaxel (T + D) versus D alone in the first line of the metastatic BC was performed in a time horizon of four years from the SUS perspective.

Methods: A Markov model, using monthly cycles, was used to assess the incremental cost-effectiveness ratio (ICER) of two different strategies to treat HER-2 positive patients. The model consists of three health states: "stable metastatic disease," "disease progression," and "death." The model was based on the clinical trial population of Marty et al. (2005) and the costs attributed were extracted from the tables of SUS. The model was created using TreeAge® Pro 2014 software and calculated by the expected values method.

Results: The total cost with D alone was 178.066USD with an associated effectiveness of 0.9 Year of Life Adjusted for Quality (AVAQ). For T + D the cost was 365.341USD with an effectiveness of 1.25 AVAQ. The ICER was 539.884USD/AVAQ. Tornado analysis, a 20% variation, showed that the utility used had a greater impact on the value.

Conclusion: We paid monthly 5352USD (20 months of OS x 5352USD = 107.040USD) in the SUS with D alone and with T + D, with the possible incorporation of the T by the Brazilian for Technology Assessment Agency, we would pay 16.475USD (Marty et al. 2005 - 23 months of OS X 16475USD =378.925USD).

4-1

Formulary management activities of public sector Pharmacy and Therapeutics Committees in the Gauteng Province of South Africa: An analysis of observations of Pharmacy and Therapeutics Committee meetings

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Introduction: The World Health Organisation (WHO) identified Pharmacy and Therapeutics Committees (PTCs) at district and hospital levels as one of the pivotal models to promote rational medicine use. Formulary development and management is one of the functions of PTCs as per WHO guidelines. This study aimed to describe the formulary management activities among PTCs in public hospitals in the Gauteng Province of South Africa (SA).

Methods: A quantitative, non-participatory, observational method was employed, whereby 26 PTC meetings were observed between June 2011 and October 2013. Where permission was granted, meetings were recorded and transcribed verbatim. In instances where permission to record meetings was not granted, detailed notes of the meeting were taken and later compared to the minutes of the meeting from the PTC secretariat. Data were coded, categorised and themes identified using NVivo9™ qualitative data analysis software.

Results: More than half of the observed PTCs reviewed their formulary lists. There was variation in the review process amongst institutions providing different levels of care. Various aspects were considered for formulary management, including cost considerations, which focused mainly on acquisition costs, evidence-based evaluation of clinical trials, patient safety, clinical experience and changes in the National Essential Medicines List. Lack of expertise on the application of pharmacoeconomic analysis and evidence-based decision-making in formulary management were identified as some of the challenges at all PTC levels.

Conclusion: No previous studies from the Gauteng Province, SA, have reported on how decisions are taken to include or exclude medicines onto formularies at public sector hospitals providing different levels of care. Different approaches are adopted at different levels of care when adding to- or removing medicines from the formulary lists. Future programmes should strengthen PTCs in specialised aspects of formulary management. Training on the principles of pharmacoeconomics and evidence-based medicine is required to enhance formulary management.

4-2

Use of Scottish Therapeutics Utility EFIPPS searches in NHS Lothian to improve patient safety

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Aim

NHS Lothian aimed to improve patient safety within prescribing by reviewing patients targeted by six patient safety searches within the Scottish Therapeutics Utility (STU). The goal was to achieve a 20% sustained reduction in patients triggering the measure. The project focused on one GP practice, following a Quality Improvement methodology.

The six EFIPPS measures are a robust list of high risk prescribing searches (Guthrie et al, 2012). STU is a computer programme that interrogates general practice clinical systems.

Methods

The patients identified within STU were reviewed in a holistic manner by a Pharmacist, following NHS Scotland Polypharmacy guidance. The review was initially notes based, with either a telephone call or face to face review for follow up if required. All medication changes were communicated to the GPs.

The pharmacist regularly reviewed STU in order to determine the number of patients identified by the searches. The first Plan-Do-Study-Act (PDSA) cycle involved two-weekly clinics and data collection. Following review, the data collection processes were amended and the clinical capacity increased to a weekly session.

In order to target an appropriate practice, data from the national Prescribing Information System (PIS) was reviewed.

Results

The reduction in patients identified by the searches over the full project period was 26% (21 patients).

During the second cycle, the pharmacist conducted 30 reviews, and identified a total of 80 pharmaceutical care issues. A total of 64 of these issues were actioned, a rate of 80%. The pharmacist spent a total of 38 hours working on this project.

The targeted 20% reduction in patients identified by the searches was achieved within 14 weeks of work commencing, during the second cycle period.

STU runs in real time from the local clinical system (rather than prescriptions paid), and also has an advantage in identifying irregular ordering patterns.

4-3

Assessing the impact of changes in national antibiotic use in Scotland on Gram-negative resistance using the NHS Scotland Infection Intelligence Platform

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Background

Associations between antibiotic use and antimicrobial resistance (AMR) are well documented, but there are few studies investigating the effect on AMR of reductions in antibiotic use. Since 2008 use of broad-spectrum antibiotics associated with increased risk of *Clostridium difficile* infection (CDI) has reduced across Scotland. This study investigated associations between use of these specific antibiotics and AMR among Gram negative bacteraemia over time.

Methods

Using the NHS Scotland Infection Intelligence Platform (IIP), national data on antibiotic use for (2009-14) were extracted from the Hospital Medicines Utilisation Database and Prescribing Information System (primary care medicines use). Combined defined daily doses (DDD) per 1000 population per month were calculated for co-amoxiclav, fluoroquinolones and 3rd generation cephalosporins. Data on *E.coli* and *Klebsiella* bacteraemias with drug susceptibility were extracted from the dataset "Electronic Communication of Surveillance in Scotland". Binomial general linear regression models incorporating time, NHS region and antibiotic use, with proportion resistant bacteraemia as the outcome, quantified associations between use and resistance for each bacteria/antibiotic combination.

Results

Use of fluoroquinolones and co-amoxiclav was 35% lower, and cephalosporins 41% lower, in 2014 compared to 2009, with significant trends over time. Resistance to cephalosporins and fluoroquinolones decreased among *E.coli* (relative reductions of 24% and 17% respectively), but not to co-amoxiclav. There were no changes in *Klebsiella* resistance. There were significant associations between antibiotic use and *E.coli* resistance for cephalosporins OR 1.07 (95% CI 1.02–1.13); interpreted as 7% (2-13%) increase in resistance with each additional DDD/1000 pop, fluoroquinolones (OR 1.02 (1.01–1.03)) and co-amoxiclav (OR 1.01 (1.01–1.01)). There were no significant associations between use of these antimicrobials and *Klebsiella* resistance.

Conclusions

Reductions in use of antibiotics with high CDI risk has been associated with reduced resistance among *E.coli* but not *Klebsiella* bacteraemia. The Infection Intelligence Platform enabled this analysis across the Scottish population.

4-4

Aspects of medicines regulation in four Latin-American countries: a DURG LA cross-national study

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Background: Although Latin-America has not been a usual contributor to comprehensive cross-national studies, important regulatory issues may be discussed through this study design, explored by examining basic regulatory aspects of market approval and prescribing in Brazil, Guatemala, Cuba and Colombia.

Methods: Researchers jointly drafted a straightforward descriptive study protocol on market approval and prescribing regulations for 20 medicines, during a DURG LA Technical Meeting in Rio de Janeiro, in November 2015. Medicines were chosen considering more than five years in the market and broad utilization in countries, and pre-categorized according to prescribing and dispensing characteristics. Data were collected from legislation and public databases. Results were compiled in a template for analysis.

Results: Regulations on market approval dates and legislation on prescribing and dispensing were collected for acetylsalicylic acid, amoxicillin, clindamycin, clonazepam, clonidine, clozapine, codeine, enalapril, fluoxetine, haloperidol, imatinib mesylate, isotretinoin, loratadine, losartan, metamizole sodium, metformin, methylphenidate, metoclopramide, montelukast, norethisterone, norfloxacin, omeprazole, oseltamivir, paracetamol, promethazine, ranitidine, rituximab, sibutramine, sildenafil, thalidomide, tramadol, zidovudine. An inconsistency of market approval data was found for 5 medicines in Brazil and 4 in Cuba, possibly due to problems in registries. Guatemala and Colombia presented market approval data for all 32. While the scientific literature points to mandatory prescriptions presentation for dispensing of 19 of the 32 medicines, country regulations differ considerably. Guatemala does not demand prescriptions for dispensing of anti-infectives or for nervous system drugs, and only two are under mandatory prescribing: clonazepam and methylphenidate. All nervous system drugs warrant prescriptions in Brazil, Colombia and Cuba. Only Brazil and Cuba compel generic prescribing in the public sector.

Conclusion: An empirical study with the collaboration of several researchers in four Latin-American countries presented some difficulties in data retrieval, possibly due to problems in access to relevant information. Discrepancies in prescribing and dispensing requirements were observed among countries.

4-6

Protocols for the introduction and follow-up of new medicines in Sweden

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Background

In order to achieve an equal, cost effective and appropriate use of new medicines in Sweden, all county councils, several governmental agencies and the pharmaceutical industry, collaborate in a process for the introduction of new medicines. The collaboration started in 2015 and includes different steps, e.g. horizon scanning, price negotiations, recommendations for clinical use and protocols for introduction and follow-up. For medicines at the highest level of collaboration, an introduction and follow-up protocol is produced. The protocol, accompanied with a recommendation for use from the New Therapies council (NT-council) at the Swedish Association of Local Authorities and Regions, helps the clinicians to put the new medicines in the right context. A health economic evaluation from the Dental and Pharmaceutical Benefits Agency complements the NT-councils decision-making and the budget prioritizations in central economical functions within the local health organizations.

Methods

Commissioned by the NT-council, a working group with representatives from the four largest county councils in Sweden, manages the production of the protocol on behalf of and benefit for all the county councils.

Managing the production of a protocol, includes involving eligible clinical experts within the therapeutic area and corresponding with governmental agencies.

Results

To date, protocols for approximately 25 medicines have been produced, including several updates due to new or changed indications, e.g. PD-1-inhibitors and hepatitis C-medicines.

Discussion

The follow-up is important to achieve an equal use of new medicines as well as learning more about safety and effectiveness of a new treatment. However, the possibility to monitor the use of the medicines in the different county councils varies depending on existing quality databases, if the medicines are on prescription or requisition, as well as therapy traditions and incentives perceived by prescribing doctors on the concerned medical units.

4-7

Severing selection decisions from the concept of essential medicines: expenditures with fibrates in the Brazilian Essential Medicines List

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Background: The concept of essential medicines is internationally recognized as a health strategy to rationalize the use of medicines. Brazil has had an Essential Medicines Lists (EML) since 1964. In 2012, the number of items in the Brazilian EML (BN-EML) increased 54,4%. In that year ciprofibrate was included, although fibrates were already covered. The aim of this study was to analyze the trends in Brazilian Federal Government expenditures with ciprofibrate and fenofibrate between 2008 and 2013.

Method: Data were extracted from the Brazilian Federal Government procurement database and the four last editions of the BN-EML. The analysis considered all medicines purchased by the federal government from January 2008 to December 2013. To measure expenditures, the total value of each purchase was calculated by multiplying the unit price by the volume and this value was adjusted for inflation using the Extended National Consumer Price Index (IPCA). Cost was presented in Reais (R\$); 3 Reais = 1 Canadian dollars (CAD) (March 2016).

Results: The expenditures with both medicines increased over time. The Brazilian Federal Government expenditures with ciprofibrate from 2008 to 2014 amounted to 240 thousand Reais. In the same period, the expenditures with fenofibrate were 110 thousand Reais. The increase between 2011 and 2012 was higher for ciprofibrate than for fenofibrate. The government spent 27.392,11 Reais with ciprofibrate in 2011 and 75.879,27 Reais in 2012 (increase of approximately of 177,0%), while the expenditures with fenofibrate increased 12,2% from 2011 to 2012 (from 19.004,00 to 21.317,00).

Conclusions: The Brazilian Federal Government spent more with ciprofibrate than with fenofibrate, although the evidence of therapeutic benefits for the first one is lower and inconclusive. The inclusion of ciprofibrate on the NB-EML greatly increased the expenditures of the Federal Government with this class of medicine.

5-1

Anticholinergic exposure in primary care and in long-term care: differences in medications involved and intensity?

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Background: Older adults are more vulnerable to the effects of medications with anticholinergic properties. The objective of this study was to identify and compare the anticholinergic exposure in a cohort of community-dwelling older adults (aged 80, and over) and a cohort of newly-admitted nursing home residents in Belgium.

Methods: Chronic medications were coded to the Anatomical Therapeutic Chemical (ATC) classification. Using the MARANTE scale, anticholinergic exposure was quantified taking anticholinergic potency and dosages into account. Baseline data of the Belfrail-Med cohort of primary care patients (n=503) and the Ageing@NH cohort of newly-admitted nursing home residents (n=741) was used. Survival analysis until death was performed at 18 months after baseline, using Kaplan-Meier curves and Cox regression models to adjust for covariates.

Results: Mean age was 84 (80 – 102) and 84 years (65 – 105), and mean number of medications was 5 (0 – 16) and 9 (1 – 25) for primary care and nursing home patients, respectively.

Prevalence of anticholinergic use was 31.8% and 63.8% in primary care and nursing home patients respectively. The mean MARANTE scores were 0.7 (0 – 7) and 1.6 (0 – 9.5) respectively. For primary care, out of n=217 anticholinergics, ranitidine (14.7%), trazodone (7.4%) and escitalopram (4.6%) were most prescribed. For nursing home residents, out of n=514 anticholinergics, trazodone (10.7%), quetiapine (9.9%) and escitalopram (8.6%) were most prescribed.

The mortality rates were 8.9% and 35.3% respectively. After adjusting for the number of medications, significant associations with mortality were found in primary care for those with high anticholinergic exposure (MARANTE ≥ 2 , HR 2.3, 95%CI 1.07 – 4.78), but not in nursing home residents.

Conclusion: The anticholinergic exposure is higher in nursing home residents, possibly due to more antipsychotics and antidepressants. Associations with mortality were only significant in primary care patients with a high anticholinergic exposure.

5-2

How can health care pathways explain polypharmacy in France? A Longitudinal analysis between 2011 and 2014

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BACKGROUND: Polypharmacy particularly affects the elderly and exposes to various health risks. Little is known about factors leading to polypharmacy. This article intends to analyse how different health care “events” – GPs visits, inpatient stays... affect polypharmacy.

METHODS: Data were extracted from a French Public Health Insurance database and are representative of the French population. Every people who were at least 50 years old and had at least one drug reimbursement in 2011 were selected (187.783 persons). Information concerning their drug consumptions over a four year period (from January 2011 to December 2014) was recovered in order to calculate a monthly indicator of polypharmacy as well as information concerning their care pathways: GPs and specialists visits, hospital outpatient visits, inpatient stays and visits to hospital emergency services. A typology allows us to identify people with similar profiles of health care use. In a second step, we use a fixed-effect model in order to estimate the effect of each event on the pattern of drug consumption, among people with the same health care profile.

RESULTS: First results show that three months before a patient’s admission as an inpatient, the number of drugs prescribed progressively increases and reaches a peak at the time of admission before decreasing in the subsequent three months. The number of drugs prescribed increases at a higher pace for care pathways with several events than pathways with only one event. Being exclusively hospitalized does not increase the number of drugs prescribed while being hospitalized and consulting a specialist increases the number of drugs prescribed.

CONCLUSION: this study will help to identify which event of the healthcare pathway is associated with a higher level of polypharmacy and hence guide public policy.

5-3

Defining optimal therapy for an older individual with multimorbidity proves challenging: results of a survey among pharmacists and geriatricians

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Background: Clinical practice guidelines are useful to suggest optimal therapies for the treatment of single chronic diseases. However, there is few guidance for multimorbidity. The objective of this study was to describe what pharmacists and geriatricians consider to be an optimal therapy of an elderly individual (65–75 years old) with diabetes (T2D), chronic obstructive pulmonary disease (COPD) and heart failure (HF).

Methods: We performed an online survey among pharmacists and geriatricians in the Canadian province of Quebec. Participants were invited to choose, from a list of 32 medications or classes, the optimal therapy for an individual aged 65–75 years with three chronic conditions (T2D, COPD, HF). We used descriptive statistics to calculate the median number of medications chosen and the proportions of participants who chose each medication, according to the participant's specialty.

Results: Among the 162 participants, 92 (56.8%) were community pharmacists, 43 (26.5%) were hospital pharmacists (including 12 specialized in geriatrics), and 17 (10.5%) were geriatricians. There was little consensus on the optimal therapy, but five medications were chosen by at least 70% of the participants: metformin, long-acting anticholinergic agents, ACE inhibitors/ARA, beta-blockers, and short-acting beta-agonists. The median number of medications considered to be part of an optimal therapy was 10 (interquartile range [IQR]: 6–13). For geriatricians only, the median number of medications was 7 (IQR: 5–10).

Conclusions: At least half of the participants considered polypharmacy (≥ 10 medications) inevitable for an optimal treatment of T2D, COPD and HF. However, our results indicate that it is difficult to reach consensus on optimal therapy when treating multimorbid individuals. This raises issues when considering quality indicators in population-based studies.

5-4

The chronicity of polypharmacy: duration of polypharmacy in a nationwide cohort of older adults

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Background

The prevalence of polypharmacy (i.e. the concurrent use of ≥ 5 drugs) is reported to be high among older adults in cross-sectional studies. However, few longitudinal studies have investigated how “chronic” the exposure to polypharmacy is. We aimed to investigate the duration of polypharmacy over three years.

Methods

We created a longitudinal register-based cohort including all persons aged ≥ 65 years residing in Sweden at baseline (1 November 2010) surviving until the end of the study (20 December 2013), with either polypharmacy at baseline or incident polypharmacy during the first 12 months of follow-up ($n=738,694$). Drug use was assessed from the Swedish Prescribed Drug Register. Monthly exposure to polypharmacy was calculated based on the date of drug dispensing, the total amount dispensed, and the prescribed daily dose. The ‘duration’ of the first episode of polypharmacy was calculated for individuals free of polypharmacy at baseline (incident users). The ‘maintenance’ of polypharmacy was calculated for individuals exposed to polypharmacy prior to baseline (prevalent users).

Results

For incident polypharmacy users, the median duration of polypharmacy was 2 months (inter quartile range, IQR: 1-4). The duration was slightly higher (≈ 3 -4 months) for individuals aged ≥ 85 years, living in institution, with multimorbidity, and multi-dose dispensing scheme. Among prevalent polypharmacy users, the median length of maintenance was 22 months for men compared to 28 months for women. The maintenance increased with age, and after 85 years more than 50% of the prevalent polypharmacy users spent the complete follow-up with polypharmacy. The proportion of individuals spending $\geq 80\%$ of the follow-up with polypharmacy was 9% among the incident users and 75% among the prevalent users.

Conclusion

This longitudinal study of the duration of polypharmacy suggests that polypharmacy is relatively chronic for individuals with a history of polypharmacy, whereas it is a more transient state for incident users of polypharmacy.

5-5

Criteria for adequate and inadequate drug prescribing in older adults near the end of life: European expert consensus

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Background

A growing body of evidence suggests inadequate drug prescribing in older adults with limited life expectancy. Clinical guidance is needed to continue or discontinue drug treatments near the end of life. We aimed to develop a set of explicit criteria for potentially adequate and inadequate medications in older people at the end of life.

Methods

A total of 58 European experts in geriatrics, clinical pharmacology and palliative medicine were invited to participate in a Delphi consensus panel, representing 10 different countries. Participants (n=40) were asked to characterize drug classes as “often adequate”, “questionable” or “often inadequate” for use in older adults aged ≥75 years with an estimated life expectancy of 3 months or less. They completed two consecutive rounds of web-based assessment between June and December 2016. Consensus was considered to be achieved for a given drug or drug class if the level of agreement was at least 75%.

Results

Regarding the continuation of previously prescribed medications, the panel reached consensus on a set of 14 drug classes deemed “often adequate”, 32 drug classes deemed “questionable”, and 10 drug classes deemed “often inadequate”. The latter category included – among others – lipid-lowering drugs, bisphosphonates, anti-dementia medications, vitamin D, and calcium supplements. Regarding the initiation of new drug treatments, the panel reached consensus on a set of 11 drug classes deemed “often adequate”, 26 drug classes deemed “questionable”, and 24 drug classes deemed “often inadequate”. Consensus remained unachieved for very commonly prescribed drug treatments such as proton-pump inhibitors, furosemide, NSAIDs, zopiclone, zolpidem, and SSRIs.

Discussion

In the absence of robust evidence from randomized clinical trials, our criteria provide guidance to support prescribers in their effort to reduce the burden of medications of unfavorable risk-benefit ratio or inadequate time-until-benefit in older adults near the end of life.

5-6

The impact of the number of medications on unplanned hospitalization and mortality in Swedish community-dwelling elderly

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Background: High drug consumption and associated adverse outcomes are common in older adults. This study investigates the association of the number of medications with unplanned hospitalizations and mortality among all community-dwelling older people (aged 65 and over) in Stockholm, Sweden.

Method: An observational study using administrative data for the 2.3 million inhabitants from the catchment area of greater Stockholm, Sweden (VAL database). VAL contains demographic information on patient demography, migration, death, diagnoses, and individual based drug dispensing data from ambulatory care. Patients eligible for inclusion were ≥ 65 years old, living in the Stockholm region on 31.12.2014. A medication was recorded if the active substance was dispensed at least two times in the period of 1 year (from January 1 to December 31, 2015).

Results: Patients' ($n=315.121$) mean age was 74.3 years (range 65–114), and 54.7% were female. The mean number of different medications was 7.1 (range 2-72, 6.5 for men, and 7.6 for women, $p<.001$). The mean Charlson score was 1.9 (range 0-16, 2.19 for men and 1.70 for women, $p<.001$). The unplanned hospitalization and mortality rate were 15.0%, and 2.8% respectively. Multivariate linear model adjusted for age, gender and Charlson score, showed 5% increased unplanned hospitalization rate (OR 1.045, 95% CI 1.043–1.047) and 2% increased mortality rate (OR 1.019, 95% CI 1.015–1.023), for every additional medication taken.

Conclusion: In the Swedish community-dwelling older population, a high number of different medications was associated with unplanned hospitalization and mortality. Whether that is related to inappropriate polypharmacy or a mere consequence of residual confounding due to higher morbidity, needs to be further investigated.

5-7

Measuring drug use in the last months of life of older adults through large administrative databases: results from a feasibility study in France

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Background

Near the end of life, the goals of care for older adults with life-limiting conditions often shift from disease-targeted therapies to a more palliative approach. However, the evidence suggests a potential overuse of healthcare resources, including prescription drugs. In this study, we aim to assess the feasibility of measuring the burden of medications through large administrative databases.

Methods

Retrospective cohort study including older adults aged ≥ 65 years who died in France in 2014 and who were included in the Echantillon Généraliste des Bénéficiaires (a 1/97th representative sample of the French population). Using all diagnoses reported during the last 2 years of life, we created three cohorts typical of the three illness trajectories previously described by Murray et al. (2005): 1) dementia, 2) heart failure and 3) colorectal cancer. Healthcare utilization (including drugs) was calculated on a monthly basis.

Results

A total of 2149 deceased individuals were included (1082 with dementia, 219 with colorectal cancer, and 1242 with heart failure). History of drug utilization during the final 3 months of life could be retrieved for 1701 (79%) decedents, including 72% among older adults with dementia, 82% among patients with colorectal cancer and 85% in the 'heart failure' cohort. Individuals with missing drug history ($n=448$) were older than average, had less chronic comorbidities, and died less often in hospitals ($p<0.001$). Among the individuals for whom drug history was available, the average number of reimbursed medication during the final 3 months of life was 20.7 (SD=12.3). In addition, 31.4% of decedents were hospitalized twice or more, 6% spent at least half of their remaining life expectancy hospitalized, 70% had ≥ 3 GP visits and 77% had biological tests.

Conclusion

Our study confirms the feasibility of using large administrative databases to measure healthcare and drug consumption among older adults near the end of life.

5-8

Advanced care planning and associated changes in medication use in newly admitted nursing home residents

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Background: Little is known about advanced care planning (ACP) in nursing home residents. We aim to explore the prevalence and evolution of ACP and the associated changes in medication use in these residents.

Method: Baseline and 2nd follow-up data (year2) were used from Ageing@NH; a prospective, observational cohort study on the general health of nursing home residents in Flanders, Belgium. Data were collected using a structured questionnaire and validated measuring tools. Medications were coded by the Anatomic Therapeutic Chemical classification.

Results: Data were available on 741 newly admitted residents at baseline (mean age 84, 66% female, 35% highly care dependent, 31% dementia) and on 342 in year2 (40% highly care dependent, 46% dementia). Between baseline and year 2, the prevalence of ACP increased from 21% to 56%. Residents with delayed ACP initiation (> 3 months after admission) had a worse mental condition than those without ACP and those with ACP from admission on. Residents with delayed ACP initiation also showed a larger increase in number of medications (8-10), analgesics (29%-44%), and drugs for acid-related disorders (32%-44%) compared to the 2 other groups, controlled for care dependency and dementia. A significant decrease in lipid modifying agents was only found in those with delayed ACP initiation, and diuretics remained stable. No associations were found between ACP and antidementia drugs.

Conclusion: ACP increased from baseline to year 2, which shows that ACP is negotiable in our nursing homes. In general, medication use increased, and associations were found between ACP and an increasing use of analgesics and drugs for acid-related disorders, a decreasing use of lipid modifying agents and a stable use of diuretics, which might indicate a shift from disease to symptom control, and a more palliative care oriented mindset.

5-9

Potentially inappropriate medication use among elderly, hospitalized patients

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Background

Presence of polypharmacy and use of potentially inappropriate medications (PIM) are common among elderly patients and may increase drug-related problems such as geriatric falls. Resulting from falls patients may suffer hip fracture, reduced quality of life and earlier death.

The aim of the study was to evaluate the medication of elderly, hospitalized patients with hip fracture, regarding the PIM medications and to assessing the prevalence of polypharmacy (taking 5 or more chronic medications concomitantly).

Methods

Patients (65 years or older) admitted to the Trauma Department between January 2011 and December 2012 and operated with osteoporotic hip fracture were included in the study. Data were recorded from the patient documentation and a retrospective analysis was performed.

Results

604 patients met the inclusion criteria (143 male, 461 female). The mean age was 81.8 ± 7.5 years. The mean number of chronic medications was 7.1 ± 3.8 . The prevalence of polypharmacy was 74.0% and 158 patients (26.2%) were taking 10 or more chronic medications concomitantly. 76.8% of patients were taking at least one PIM and 69.75% of the patients were taking at least one PIM with fall risk. 53 patients died within 3 months after the hospital admission and 81.8% of the deceased patients were above 80 years. The 3 month mortality rate was significantly higher among male patients (15.4% vs 6.7%; $p=0.002^*$). Prevalence of polypharmacy was 81.1% of the deceased patients and 69.9% of the surviving patients.

Conclusion

Medication use of elderly demands a special attention, many risk factor have to be take into consideration. Considerable risk factors are age, male gender, PIM meds and polypharmacy. With careful attention these risk factors may be partly reduced.

6-1

Reasons for (non)adherence of co-prescribing laxatives with opioids

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Background

Constipation is a well-known side-effect of opioid use, which can have major consequences such as bowel obstruction and hospital admission. To prevent opioid-induced constipation, guidelines recommend to prophylactically prescribe laxatives to patients who start with an opioid, unless there is a good reason not to. However, general practitioners (GPs) do not always follow this recommendation. As part of the Medication Safety study requested by the Dutch Ministry of Health and Welfare, the aim of this study was 1) to determine the proportion of opioid starters that are concomitantly prescribed a laxative; 2) to explore reasons for not co-prescribing laxatives with opioids.

Methods

Electronic patient records were used from 185 general practices participating in the NIVEL Primary Care Database. Per practice, the proportion of opioid starters that concomitantly received a laxative was calculated. Questionnaires were sent to participating general practices about possible reasons for not prescribing laxative co-medication to opioid users. GPs were asked for their three most common reasons. Moreover, five potential explanatory factors were addressed: registration quality, collaboration with the pharmacy, familiarity with and acceptance of the recommendation and use of a decision-support system. Multilevel logistic regression analysis was performed to assess the association between guideline adherence and these factors.

Results

Almost all GPs (99%) were familiar with the recommendation, and 89% thought it is useful. Laxatives were co-prescribed to opioid starters to 18 to 88% of patients per practice. None of the studied explanatory factors were related to following the recommendation. GPs mentioned a variety of reasons for not prescribing a laxative with an opioid, which were mainly patient-related (“patient still has laxative”, “patient does not want laxative”).

Conclusion

The large practice variation in co-prescribing laxatives with opioids suggests room for improvement to follow this recommendation. Reasons mentioned by GPs suggest that GP-patient communication should be improved.

6-2

Use of tramadol among long-term opioid users in Denmark

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Background: Opioids are highly addictive pain-relieving drugs. Use of opioids is higher in Denmark compared to other Nordic countries. This analysis examines long-term use (> 6 months) of tramadol and other opioids amongst patients without cancer.

Methods: : Danish Register of Medicinal Product Statistics (DRMPS) covers redeemed prescriptions to all persons living in Denmark and was used to identify the yearly number of opioid users in Denmark from 2010-2015. Opioids (excl codeine and acetylsalicylic acid), codeine and methadone were included in the analysis. The Danish Cancer Register was used to exclude users with a cancer diagnosis. A long-term user is considered having multiple purchases within 4 months and a duration of minimum 6 months between the first and last purchase.

Results: The total number of opioid users in Denmark, who redeemed at least one prescription increased from 479.173 in 2010 to 483.893 in 2015. The number of long-term users without cancer increased from 162.797 users in 2010 to 168.334 users in 2015. In 2015, 49.033 long-term users had only redeemed prescriptions on tramadol. Of these tramadol users, 27.988 (57 %) redeemed prescription on conventional tablets, 12.355 (25 %) on sustained-release tablet and 8626 (18%) on a combination of sustained-release tablets and conventional tablets. Less than 1 % preferred other formulations or combinations.

Conclusion: The number of long-term opioid users without cancer in Denmark has slowly increased since 2010. Long-term users in 2015 accounted for 34 percent of all users in 2015. Tramadol was the most commonly used opioid and conventional tablets was the most used dosage form among long-term users. As opioids are associated with potentially serious harms, including opioid-related adverse effects, it is of great importance to minimize this risk. One way to minimize this risk is by using a sustained-release formulation in long-term treatment.

6-3

Long-acting injectable antipsychotics: determinants of prescription and continuity of treatment in a Northern Italy area

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Background. The use of Long-Acting Injectable AntiPsychotics (LAI-AP) is steadily increasing with controversial opinions on their benefit-risk profile in clinical practice. We aimed to characterize LAI-AP utilization in the Community Mental Health Centres (CMHCs) of Bologna area (2010-2015).

Methods. Patients receiving new LAI-AP treatment cycles were selected. A new cycle was defined when no LAI-AP prescriptions were received in the preceding 6 months. The first LAI-AP prescription date represented the cohort entry-date; demographic and clinical information available at that time were collected. Length of treatment and hospitalization for psychiatric diagnosis (proxy of recurrences) were evaluated during a six-month follow-up. Factors influencing treatment continuity were assessed by multivariate analysis. A Kaplan-Meier model was used to identify differences in psychiatric admissions by continuity of LAI-APs.

Results. The LAI-AP annual incidence rate was stable throughout years (about 2% out of AP users). Out of 1.070 patients of the cohort, 54% suffered of schizophrenic-like disorders; 37% of subjects never used oral APs in the past six months. During follow-up, 21% of patients continued LAI-AP treatment, whereas 48% underwent therapy for a shorter cycle and 31% were intermittent users (with gaps longer than 30% of standard dose duration). Continuous uses were more frequent in patients receiving first generation agents (OR: 1.71; 95%CI: 1.18-2.49) and with previous psychiatric hospitalizations (2.00; 1.47-2.74). Overall, recurrences strongly decreased during follow-up (from 43% to 20%), without statistically-significant difference between continuous and non-continuous patients.

Conclusions. LAI-AP use remained stable and limited in the 6-years period; continuity of treatment was associated with use of first generation agents and previous psychiatric hospitalizations, which probably characterized more severe cases. Continuity of LAI-AP in the 6-month follow-up did not yield differences in hospitalization, suggesting that discontinued LAI-APs were replaced by other effective therapeutic strategies.

6-4

Patient factors associated with SSRI dose for depression treatment in general practice: a primary care cross sectional study

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Background: Antidepressant prescribing continues to increase. Partly due greater selective serotonin re-uptake inhibitor (SSRI) use and the use of higher SSRI doses. However, evidence does not support the use of higher SSRI doses for depression, and factors associated with their use are unknown. This study aims to investigate patient factors associated with SSRI doses for depression treatment in general practice.

Methods: A stratified sample of low to high prescribing practices were selected. Routine individual patient-level data were extracted one practice at a time: September 2009 to January 2011. Inclusion: patients ≥ 18 years, and prescribed an SSRI for depression. Logistic regression analysis was undertaken to assess individual predictor variables on SSRI daily dose; standard therapeutic dose versus higher dose. Predictor variables included: age, gender, deprivation, co-morbidity, smoking status, being prescribed the same SSRI for ≥ 2 years, and patients' general practice. Subgroup analysis included long-term benzodiazepine and/or z-hypnotic (B&Z) as a variable.

Results: Inter-practice SSRI prescribing varied significantly; practice point prevalence ranged from 2.5% to 11.9%. Overall 5.8% (3066/52575) were prescribed an SSRI for depression of whom 84.7% (2596/3066) had data for regression analysis. Higher SSRI doses were significantly associated with, in descending order of magnitude, individual practice attended, being prescribed the same SSRI for ≥ 2 years (Odds Ratio (OR) 1.80, 95% CI 1.49 to 2.17) and living in a more deprived area (OR 1.55, 95% CI 1.11 to 2.16). For the B&Z subgroup higher doses were associated with individual practice attended, being prescribed long-term B&Zs (OR 2.05 95% CI 1.47 to 2.86) and the same SSRI for ≥ 2 years (OR 1.94, 95% CI 1.53 to 2.47).

Conclusion: Higher SSRI doses for depression were associated with practice attended and being prescribed the same antidepressant for ≥ 2 years. As long-term use increases, the use of higher doses may further contribute to prescribing growth.

6-5

Prescribing trends of antipsychotic medications in Ireland primary care from 2005-2015

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Background: The indications for antipsychotic medication in children and adolescents (<18 years of age) have increased immensely for a wide range of disorders. This study aimed to: (1) evaluate the prescribing patterns of anti-psychotic medication in Ireland between 2005-2015 in children (0-11 years), adolescents (12-15 years) and young adults (16-24 years) and (2) to examine the concomitant use of other associated medications.

Methods: Data was obtained from the Irish Health Service Executive Primary Care Reimbursement Services (HSE-PCRS) pharmacy claims database. All authorised anti-psychotic medicines (N05A) were identified as well as concomitant psychotropic medications including: anxiolytics [N05B], hypnotics and sedatives [N05C], antidepressants [N06A] and psychostimulants [N05BA].

The prescribing rates per 1000 eligible population and 95% confidence intervals (CIs) were calculated and negative binomial regression models were used to determine significance of trends over time. The likelihood of any concomitant medication was examined using multivariate logistic regression.

Results: The overall rate of antipsychotic use did not significantly change over time and was 3.94 per 1000 eligible population in 2005 and 3.97 in 2015. There was significant decline over time for males aged 16-24 years only ($p < 0.001$). For females there was a significant decline in the rate of prescribing for those aged 5-11 years ($p < 0.001$), 12-15 years ($p = 0.006$) and 16-24 years ($p = 0.016$).

Males and the oldest age group (16-24 years) were twice as likely to initiate a concomitant psychotropic medicine, and the likelihood of concomitant medicine increased significantly over time from 2010 onwards compared to the base year of 2005.

Conclusion: There was no overall change in the rate of antipsychotic prescribing in children from 2005-2015, but significant changes in the older age groups, particularly for females. There were significant increases in co-prescribed psychotropic medicines in males, particularly those aged 16-24 years and from 2010 onwards.

6-6

Trends in opioid prescribing in Dutch general practices

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Background

There is more and more evidence that there is an increase in the prescription of opioids in Western countries. This is especially true for the opioid prescriptions for non-cancer related pain conditions even though there is no evidence of its effectiveness in long-term pain management while there is substantial evidence of the risks. This study aimed to describe the trend of the prescription of opioids in Dutch general practices with a specific focus on diagnoses for which the opioids are prescribed.

Methods

Data were derived from routine electronic health records of general practices participating in NIVEL Primary Care Database. Opioid prescriptions were selected on ATC-code N02A, with the exception of codeine because this is mostly prescribed for coughing and not for pain management. Diagnoses were recorded using ICPC-classification.

Results

Between 2005 and 2015, the number of patients with an opioid prescription doubled, with a sixfold increase for strong opioids. The highest increase in prescription was found for oxycodone and buprenorphine. Most opioids were prescribed for non-cancer related pain, in particular for musculoskeletal conditions (69%). The increase in opioid prescriptions was stronger among patients with non-cancer pain in comparison with patients suffering from cancer pain. The majority of patients with non-cancer pain, received a weak opioid like tramadol before oxycodone. Patients with cancer were mostly prescribed strong opioids.

Conclusion

We observed an increase in strong opioid prescribing, particularly for non-cancer related pain. An explanation for this increase could possibly be the development of aging of the population and the prevalence of certain diseases.

6-7

Trends in psychostimulant drug use among adults in the Netherlands

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Background:

Use of psychostimulants among children and adolescents receives a lot of attention. However, less is known about the use of these drugs among adults. The aim of our study was to describe trends in the use of psychostimulants among adults over time.

Methods:

Data on adults (≥ 18 years), receiving two or more prescriptions for a psychostimulant drug (ATC-code N06BA; excluding modafanil) within 12 months, were selected from the IADB, a Dutch database of filled prescriptions (59 public pharmacies, about 600.000 patients). We calculated both the number of new users as well as the total number of users of psychostimulants in 2004-2014. Furthermore, we determined the most commonly prescribed psychostimulant drug and whether the psychostimulant was initiated by GP or medical specialist.

Results:

The proportion of psychostimulants users (methylphenidate, dexamphetamine and amphetamine) increased from 1,5 per 1000 adults in 2004 to 7,8 per 1000 adults in 2014. Users were mainly male (63,0%) and methylphenidate predominated (85,7%). The proportion of new users of these drugs increased from 0,5 to 1,5 per 1000 adults. The largest increase was observed among young adults (< 30 year). Since 2012, the increase in new users seems to stabilize. Around 40% of new treatments were initiated by GPs.

Conclusion:

The large increase in use of psychostimulants seems mainly due to an increase in the proportion of new users, especially among young adults. As psychostimulants are only approved for the treatment of ADHD among children (>6 years) and adolescents, short and long term effects and side effects of these drugs need to be assessed in the adult population.

7-1

Dose adjustment of metformin in elderly patients with diabetes and impaired renal function

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Background

According to the European Medicines Agency (EMA), metformin can be prescribed to patients with moderately impaired renal function (estimated glomerular filtration rate eGFR=30–59 ml/min). Still, metformin doses should be reduced depending on renal function. Our aim was to analyze the extent to which metformin doses are adjusted to the renal function in elderly patients with diabetes.

Methods

We performed a register-based cohort study with data extracted from the SCREAM database. SCREAM contains information on renal function, drug purchases and chronic diseases in elderly patients in Stockholm, Sweden. eGFR was calculated with Lund-Malmö-formula based on the first outpatient creatinine measurement during January 1, 2010 to December 31, 2011. Drug purchase was assessed during the year following creatinine measurement. Drug dose was estimated as follows: „number of packades dispensed during 12 months multiplied with packages' DDD, divided by 365 days“. We used Charlson comorbidity index to describe morbidity. We calculated frequencies and percentages as well as Pearson correlation.

Results

We identified 27 350 elderly patients with diabetes and at least one creatinine measurement. They had a mean age of 75.7 (SD 7.4), 48% were female, and had a Charlson index of 2.9 (SD 1.9). One third (n=7 799, 28%) had eGFR 30-59, and 4% < 30. More than half of diabetes patients (n=13 906, 51%) had dispensed metformin at least once, whereof 79% (n=11 082) had eGFR>60 and 20% (n=2 734) eGFR between 30-59. Less than 1% (n=90) had eGFR<30. Renal function and metformin dosing were positively correlated (regression coefficient 0.13).

Conclusion

In agreement with EMAs recommendations, physicians reduce metformin doses in their elderly patients with diabetes and moderately impaired renal function. However, even 90 patients with eGFR<30 were treated with metformin which is contraindicated at this stage of renal impairment.

7-2

QUALITY OF LIFE OF PATIENTS IN TYPE 1 DIABETES IN USE OF INSULIN GLARGINE VERSUS NPH: SYSTEMATIC REVIEW

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Background: Studies report an improvement in quality of life (QoL) with the use of insulin glargine (GLA), since it would reduce hypoglycemia by glycemic control in type 1 diabetes (T1D). However, systematic reviews (SR) point to a lack of clinical benefit, especially in the control of glycated hemoglobin, in addition to the high price of the technology compared to neutral protamine hagedorn (NPH). This study aims to evaluate the QoL of T1D patients in use of GLA versus NPH, through a SR of cohort studies and randomized clinical trials (RCT).

Methods: A SR of observational studies and RCT was performed by two independent reviewers, with registration in the international database PROSPERO: CRD42016046875. We used MEDLINE (Pubmed), Latin American and Caribbean Literature in Health Sciences (LILACS), Cochrane Library and EMBASE (accessed January 2017) databases, including manual search and gray literature, with the terms: T1D, GLA, NPH and QoL. Methodological quality assessment was performed using Newcastle scale for observational studies and RCT's risk of bias from Cochrane Collaboration.

Results: A total of 634 publications were found. After a careful reading, eight studies remained, with ten publications. These included two retrospective cohorts, two prospective cohorts and four RCT. Follow-up time ranged from 6 to 24 months. Three studies did not report conflicts of interest and five reported conflict with funding from pharmaceutical industry. Studies evaluated 1855 individuals and 14 QoL instruments (2 generic and 12 specific) were used. Cohort studies obtained moderate methodological quality in general and RCT showed poor methodological quality.

Conclusion: The SR did not evidence a substantial improvement in QoL in patients with T1D; the permanence of GLA in the list of drugs for this disease should be reviewed.

7-3

SOCIODEMOGRAPHIC CHARACTERISTICS OF TYPE 1 DIABETES' PATIENTS USING INSULIN GLARGINE IN A STATE IN BRAZIL: ARE THERE BARRIERS IN ACCESS?

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Background: About 5% to 10% of people with Diabetes Mellitus (DM) in the world have the type 1 of the disease (T1DM). The incidence and prevalence of T1DM can range from 0.5 to 60 cases per 100,000 inhabitants. After the diagnosis of T1DM, treatment with insulin is started. Among available insulins, glargine (GLA) has been used since its incorporation into the list of medicines of the Unified Health System (SUS) of the Brazilian state of Minas Gerais (MG), in 2009. GLA has as a possible benefit a better control of glycemia and decreases in hypoglycaemia's episodes. We aimed to evaluate sociodemographic characteristics related to access to GLA in SUS.

Methods: A cross-sectional study was performed in patients, SUS users, with T1DM in the state of MG. It was approved by Ethics and Research Committee of the Federal University of Minas Gerais (Presentation Certificate for Ethical Appreciation no. 55876816.0.0000.519 and seems favorable no. 1,572,257). Data collection was carried out during March, 2017, with a convenience sample by a callcenter company. A structured sociodemographic questionnaire with internal validation was used with a sample of 30 patients. Variables were described in the form of relative and absolute frequencies.

Results: 401 diabetics patients were studied. Of these, 50.4% were male, with a mean age of 40.1 years (SD ± 16,831, range 18-83), 53.4% had no partner, 57.6% obtained about ≤ 9 years of study, 63.9% were black, 93.3% lived with other people in the same house, 81.3% owned their own home, 34.9% said they earned between 298.52 USD and 597.04 USD. About social classes, 49.6% belonged to class A (stratification by standard of consumption of goods and services).

Conclusion: Access to GLA by higher economic classes was substantially superior in comparison to other social classes for access to the technology.

7-5

Pregabalin prescribing patterns in a private healthcare sector setting in South Africa

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Background: Pregabalin, registered in South Africa for post-herpetic neuralgia and painful diabetic neuropathy, is increasingly prescribed for neuropathic pain, generalised anxiety disorder and epilepsy, but many patients discontinue treatment. Pregabalin is relatively expensive in South Africa and since limited information on the prescribing patterns of pregabalin is available, the primary aim was to analyse the prescribing of the newer antiepileptics in South Africa, with the focus on pregabalin.

Methods: A retrospective drug utilisation study was conducted on a South African medical insurance administrator database for 2016. The database contained 3 567 170 records for medicine, medical devices and procedures. All products in ATC subgroup N03AX were extracted and analysed.

Results: A total of 4 649 “other antiepileptics” (ATC group N03AX) were prescribed to 949 patients in 2016. Five different active ingredients were prescribed, namely lamotrigine (38.20%), pregabalin (32.78%), topiramate (12.71%), gabapentin (10.11%) and levetiracetam (6.19%). No prescriptions for vigabatrin were dispensed. In a previous South African study on 2013 data, pregabalin accounted for only 21.60% of prescriptions in this ATC group, while in this study it increased to 32.78%. The 1 524 prescriptions for pregabalin was dispensed to 525 patients (no gender preference), with an average of 2.90 (SD=4.25) prescriptions over the year, which is lower than the average of 4.90 (SD=6.06) for all five active ingredients. Half of the patients (50.86%) received only one pregabalin prescription during the year. Pregabalin is available in three dosage strengths. The 75 mg dosage strength was the most popular (59.45% of prescriptions for pregabalin), followed by 25 mg (23.88%) and 150 mg (16.67%). The ages of patients ranged from 12 to 93 years, with the average age 53.59 years (females: 56.06 years; males 50.42 years).

Conclusion: The results are comparable to those of international studies. Follow-up studies should include diagnoses and dosages.

7-6

Evaluation of HbA1c in relation to prescription costs for oral diabetes medicine in the treatment of type 2 diabetes patients in the county of Östergötland, Sweden

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Background: The total prevalence of type 2 diabetes in Sweden is nearly 5 %, which means about 20 000 patients in the county of Östergötland. These patients are mainly treated in primary health care. Optimized treatment of the primary disease, including reducing HbA1c and blood pressure, will decrease the risk of secondary diseases. However, treatment goals for HbA1c-values and blood pressure are rarely reached, as described in a report from the Swedish board of Health and Welfare.

The aim of this study is to evaluate the correlation between HbA1c in type 2 diabetes patients in relation to prescription costs for oral diabetes medicines and the number of prescribed defined daily doses (DDD) of metformin in primary health care centers of the county of Östergötland.

Methods: Data on prescription costs and number of prescribed DDD of oral diabetes medicines from regional prescription statistics were combined with quality data from the Swedish National Diabetes Register. The analysis did not take into account the number of type 2 diabetes patients registered in the diabetes register per medical unit.

Results: Data shows a large variation among the primary health care centers. The difference between the highest and lowest value is twofold regarding both proportion of patients reaching target HbA1c-values and number of prescribed DDD of metformin per 1000 patients, while the cost of prescription varies fourfold. There is no correlation between target values and prescription cost or number of prescribed DDD.

Conclusion: Results indicate that HbA1c target values can be achieved at a relatively low cost. However, variation shows there is a need for further optimization of the treatment of diabetes type 2 diabetes patients in Östergötland.

7-7

Pharmacist-led self-management interventions to improve diabetes outcomes. A systematic literature review and meta-analysis.

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Introduction: Diabetes has a complex disease management. Treatment includes a combination of lifestyle adaptations and medication therapy. Due to the complexity of the disease diabetes patients need to develop and maintain self-management skills. The aim of this review is to examine the effectiveness of pharmacist-led interventions to support self-management in order to improve diabetes outcomes.

Methods: The PRISMA statement for reporting systematic reviews has been followed. An extended literature search strategy was used with the keywords “pharmacist”, “diabetes” and “self-management”. Seven electronic databases have been searched in December 2016. Only randomized controlled trials (RCTs) were eligible for inclusion. A meta-analysis was performed for results of HbA1c with a random effects model in Review Manager 5.3. The included studies were assessed for methodological quality with the Cochrane Risk of Bias tool.

Results: In total 5.591 unique references were assessed and 22 RCTs were included. The included studies represented a total of 3,259 participants and the follow-up time ranged from three to 24 months. Topics addressed in the intervention varied. The most addressed topics were medication, lifestyle and self-management skills. Overall, pharmacist-led interventions had a significant effect on the improvement of HbA1c values (-0.71% [-0.94; -0.48]). Moreover, the interventions had a significant positive effect on both the systolic blood pressure (-4.79 mm Hg [-7.58; -2.00] and diastolic blood pressure (-3.50 mm Hg [-6.74; -0.25]), BMI (-0.37 kg/m² [-0.61; -0.14]) and self-management skills development.

Conclusion: This review demonstrates the added value of pharmacists in self-management support interventions for diabetes patients. Overall, pharmacist-led interventions had a significant and clinically relevant effect on HbA1c values which could be associated with risk reduction of microvascular complications.

7-8

MEASURING THE QUALITY AND THE FINANCIAL IMPACT OF ANTIDIABETIC DRUG USE TRENDS IN EUROPE: A CROSS-COUNTRY COMPARISON IN 2015.

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Background: Considering the importance of measuring the quality of prescription across different countries in Europe, this study aims to develop a cross-country comparison of Glucose Lowering Drugs (GLD) consumption trends and evaluate the potential cost-savings incurred by applying different consumption patterns.

Methods: A retrospective cross-national GLD (WHO ATD/DDD classification drug class A10) 2015's use trend was performed using a two-step approach analysis:

- Quality consumption evaluation, measured in defined daily dose (DDD) per 1000 inhabitants per day (DID), for Portugal, Denmark, England and Wales, Finland, the Netherlands, Norway and Sweden.
- Cost-saving analysis, ie, a scenario of a potential savings in the Portuguese overall expenditure by simulating other European Countries' consumption patterns.

Portuguese sales data were retrieved from hmR Pharmacy Sales Information System, and data from other countries were obtained from public open-access databases.

Results: Regarding the insulin consumption, the cross-country analysis showed that Portugal is still the country with the lowest consumption ratio (19.7%) and the second highest consumption of Long-acting insulins (37.2%) in the total GLD market.

Regarding oral antidiabetic drugs consumption trends, Portugal revealed the highest consumption of fixed-dose combinations with the highest cost/DDD (34 times more than England), simultaneously with the lowest consumption of metformin alone (33.3%; 0.14€/DDD).

When applying consumption patterns from others countries (% in DDD), cost-saving analysis showed that Portugal would have saved up to €134.1 million euros (65.3%) in GLD excluding insulins and up to 7.6 M€ in insulins.

Conclusions: The results presented emphasize the importance of optimize prescribing patterns of GLDs in Portugal. Developing collaborative and multidisciplinary interventions may help to improve clinical and economic outcomes and to achieve a more rational and sustainable use of GLDs.

7-9

Pattern of use of incretin-based medicines in a large sample of the Italian general population

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Background

Since 2008, incretin-based medicines, glucagon-like peptide-1analogues (GLP1a) and dipeptidyl peptidase-4 inhibitors (DPP4i), have been reimbursed by the Italian Healthcare Service as second/third line treatment for type 2 diabetes. The aim of this study was to describe the real world patterns of utilization of incretins in a large sample of the Italian general population.

Methods

Administrative data collected between 2008 to 2014 from three Italian areas, Tuscany, Umbria and Caserta, were analyzed. Subjects aged ≥ 18 with ≥ 365 days of look-back were selected. Patients with ≥ 1 reimbursed dispensing of GLP1a or DPP4i were identified. New users (NU) were patients without any dispensing of interest in the past. NU were classified according to the specific active substance they started with. Use of antidiabetics during 1 year before and after the first incretin dispensing was described. Trend of annual incidence of use was observed. One-year persistence to incretin-based therapy was estimated (i.e. no treatment gap ≥ 90 days).

Results

A total of 7,357 NU of GLP1a and 41,907 of DPP4i were identified. The incidence of use increased between 2008 (0.2‰ for both GLP1a and DPP4i) and 2011 (GLP1a=0.6‰; DPP4i=2.5‰), decreasing thereafter (2014:GLP1a=0.3‰; DPP4i=1.4‰). Since 2009, 50% of new DPP4i users received fixed-dose combinations with metformin. Between 2010 and 2013, NU of liraglutide increased from 38.5% to 87% of new GLP1a users. Overall, around 12% of NU did not receive any antidiabetic before starting an incretin. One-year persistence was over 60%.

Conclusions

A rapid uptake of incretin-based medicines was observed in the first four years of utilization. DPP4i soon became the most widely used incretin based-medicines. Formulations/substances with a higher convenience of use were increasingly prescribed in NU. One-year persistence to incretin therapy was satisfactory. The disagreement between the observed use of incretins as first line pharmacotherapy and national reimbursement criteria deserve further investigations.

8-1

Introducing Academic Detailing in primary care in Norway

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Background – Academic Detailing combines interactive educational outreach with the best evidence for a specific therapeutic topic, delivered by specifically trained personnel who meet clinicians one-to-one in their practices during office hours.

We received a small grant from the Norwegian Health authorities to do two pilot projects on Academic Detailing in Norway in the spring of 2015 and the winter of 2015/2016.

Method – We trained pharmacists and medical doctors employed at The Department for Clinical Pharmacology and the Regional Medicines Information and Pharmacovigilance Center (RELIS) to do the visits.

The first campaign was on Wiser use of NSAIDs, with focus on reducing the widespread use of diclofenac in Norway, due to the high risk of cardiovascular disease associated with diclofenac. 213 general practitioners received a 20-minute one-to-one visit with a brochure developed for the campaign.

The second campaign, Wiser use of Antibiotics was developed in cooperation with The Antibiotic Centre for Primary Care, The Norwegian Institute of Public Health and The Norwegian Surveillance System for Antibiotic Resistance. 455 general practitioners was visited.

The pilots was evaluated through electronic questionnaires to all participating doctors, in-depth-interview with a group of participating doctors and data from The Norwegian Prescription Database (NorPD) to evaluate changes in prescribing.

Results – The general practitioners gave a very high rating, with most doctors welcoming a new visit with another campaign. The prescribing of diclofenac and broad-spectrum antibiotics was reduced in the intervention areas compared to other areas in Norway.

Conclusion – Academic Detailing is an effective method to deliver updated knowledge for specific therapeutic topics to general practitioners. During 2016 and 2017, we have implemented our antibiotics campaign in large parts of Norway, and are working to establish Academic Detailing as a national service for all general practitioners in Norway.

8-2

Development of an interactive data visualization comparing medicines use within the National Health Service in Scotland to support identification of unwarranted variation and improve effectiveness and efficiency.

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Background: An aging population and new medicinal technologies are placing unprecedented demands on healthcare resources. It is therefore imperative that medicines are used to maximum effectiveness with maximal efficiency. This involves identifying and addressing unwarranted variation but this can be challenging to identify. The National Health Service in Scotland is developing readily accessible data visualization tools built around comprehensive national medicines data sets.

Method: Data, aggregated by British National Formulary based therapeutic classification, was extracted from the national pharmacy claims database and developed as an interactive Tableau® visualization. Measures calculated were costs and defined daily doses per 1000 weighted population and per treated patient. Data were presented by administrative health board and at general practitioner (GP) practice level to allow comparison and identification of variation.

Results: The visualization was well received by health board staff and seen as an accessible and useful tool for comparing practice and performance with their peers. Cost per treated patient measures were seen as particularly valuable as they minimized the effects of differences in disease prevalence that could skew more general population based measures.

Discussion: Data visualizations make information readily available to those with neither the appropriate skills nor time to analyze often complex data sets. This enables the rapid identification of themes and issues and, in turn, the formulation of better questions for more detailed analysis.

8-4

Prescribing patterns of physicians working in both the direct and indirect treatment sectors in Iran; findings and implications

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Background: The implementation of regulations is one of the main methods to improve the rational prescribing of medicines among physicians across sectors. However, there continues to be concern with appropriate prescribing. There can also be concerns with issues of equity and appropriateness if physicians change their prescribing habits depending which sector they are currently practicing in. This issue has been rarely reported to date. Consequently, the aim of this study is to evaluate the effect of Social Security Organisation (SSO) rules and regulations on prescribing patterns of physicians working simultaneously in both the Direct and Indirect treatment sector of SSO in Iran. Subsequently, use the findings to suggest initiatives to improve prescribing in either sector if needed.

Methods: A retrospective cross sectional study on claims data. All prescriptions written by general practitioners, internists, gynecologists and pediatricians that had at least 100 claims and working in both direct and indirect treatment sector of the SSO were collected. Non-parametric tests were undertaken to compare prescribing patterns among the sectors.

Results: 455549 prescriptions were analyzed. The average medicine items per prescription was 4 in the direct treatment setting compared to 2 in indirect treatment setting, while the proportion of prescriptions including at least one antibiotic, injectable, corticosteroid and injectable corticosteroid medicine item. were 31.5%, 16.1%, 8.7% and 3% respectively in the indirect treatment setting compared to 28.7 %,13.7%, 7.7% and 3.2% in the direct treatment setting. Except for antibiotics prescribing, all other differences were significant.

Conclusions: Our study highlighted a number of areas of concern including the high use of antibiotics, potential inappropriate polypharmacy in the direct sector, and the potential overuse of injections especially in the Indirect sector, increasing costs and potential patient harm. These will be the subject of future research projects to improve future care.

8-5

Ongoing initiatives in Scotland to improve the quality and efficiency of prescribing in ambulatory care

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Introduction:

Need to assess initiatives across Scotland to enhance quality and efficiency of prescribing given increasing pressures.

Methodology:

Descriptive review of strategies for oral diabetes and lipid lowering therapies, PPIs, SSRIs and inhaled respiratory preparations. National Administrative Prescription Dataset used covering all ambulatory care prescribing in Scotland. Utilisation measured as items dispensed and costs in GB£s.

Results:

(i) Lipid lowering therapies: multiple initiatives including patient identification, encouraging preferential prescribing of generics with high INN prescribing (up to 99.7% with 92% to 97% price reductions) and encouraging higher dose statins (especially following generic atorvastatin) resulted in statin expenditure falling by 56% in 2015 vs. 2001 despite 4.03 fold increase in utilisation. Influence of higher strength statins on adherence studied separately. Initiatives to reduce ezetimibe prescribing as little evidence of benefit led to 60k items dispensed in 2015 vs. 219.5k in 2010; (ii) PPIs: similar initiatives resulted in 68% reduction in expenditure between 2001 and 2015 despite 2.91 fold increase in utilisation; (iii) SSRIs: similar initiatives and encouraging prescribing of citalopram vs. escitalopram resulted in expenditure falling by 60.1% between 2001 and 2015 despite 2.12 fold increase in utilisation; (iv) Oral antidiabetics: metformin dominated prescribing at over 1.14million items dispensed in 2015. Expenditure mirrored utilisation increase with 94% generic. This compares with appreciably lower use of glinides and gliptins; however, their increasing use appreciably increased expenditure in recent years, and subject to scrutiny; (v) Respiratory medicines: inhaled medicines (tiotropium and combined salmeterol and fluticasone) among highest expenditure items with relatively high unit costs that have remained stable for decades. New inhalers and copies of originators may help to reduce costs.

Conclusion: Scotland has used a range of policy levers to improve efficiency of prescribing, more important than ever, providing exemplars to others. Inhalers and new oral diabetes medicines subject of ongoing scrutiny.

8-6

Use of prescribing quality indicators for patients with type 2 diabetes in primary care audit and feedback: a pilot study

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Background: We developed and validated a set of prescribing quality indicators (PQIs) for primary type 2 diabetes (T2D) care. The aim of this pilot study was to evaluate the use of these PQIs in a primary care audit and feedback program in The Netherlands.

Methods: In February 2017, audit and feedback sessions were conducted in three Dutch pharmacotherapy counseling groups, including general practitioners (GPs) and pharmacists. The program included feedback on seven PQIs, of which six action PQIs assessed timely start and intensification of glucose-lowering drugs (GLDs), statins and antihypertensives. One PQI assessed potential overtreatment with GLDs in elderly patients. Feedback was based on routinely collected prescribing and clinical data from the prior year. During the sessions, the GPs received individual and group feedback in the form of number and percentage scores on each of the PQIs. The groups subsequently identified priority areas for improvement. After the sessions, the participants completed a survey to assess the usefulness of these PQIs.

Results: The GPs scored low on intensification with insulin (overall score 43%) and start with statins (44%), while the other scores on start and intensification were acceptable (>55%). Overtreatment with GLDs occurred in about 17% of the elderly T2D patients. The groups identified one of these three PQIs as priority area for improvement. The main comment of the GPs on the usefulness referred to the complexity of the PQIs and the low numbers of patients included per PQI. Furthermore, participants missed general measures to assess quality of care in all T2D patients.

Conclusion: Priority areas for improvement of pharmacotherapy in T2D patients were identified, including intensification with insulin, starting with statins and overtreatment with GLDs in elderly. However, several limitations regarding the usefulness of the PQIs for practice were also identified. This information is used to improve the feedback program.

8-7

Prescribing practices in primary care from a physician perspective: A descriptive pilot study

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Background

Despite the focus in healthcare and academia on safe and rational use of medicines, little is known regarding the quality of drug treatment from a physician perspective, as well as the performance of medication reviews in clinical practice. The aim of this study was to assess the quality of drug treatment in primary care, from a physician perspective, and to describe prescribing practices by attending physicians, with focus on medication reviews.

Methods

Descriptive pilot study of patients, ≥ 65 years of age, attending a primary health care centre in the Region Västra Götaland, Sweden, for non-urgent physician consultation in January 2016 (n=123). The drug treatment was assessed from a physician perspective, as either appropriate or suboptimal, taking the patient's condition into account. Suboptimal drug treatment was further categorized regarding priority: immediate change suggested or an action suggested in the longer term. Screening tools were used to identify Potentially Inappropriate Medications (PIMs) and Potential Prescribing Omissions (PPOs). Medication reviews, documented by a procedure code, were identified.

Results

When individual factors like morbidity, life expectancy, and concurrent drug treatment were taken into account, 45 (37%) patients had suboptimal drug treatment. Immediate handling was suggested in 13 (11%) patients, most often concerning withdrawals of propiomazine or hydroxyzine. Handling in the longer term was suggested in 32 (26%) patients, most often concerning overuse of proton pump inhibitors. The screening tools identified PIMs/PPOs in 117 (95%) patients. In all, 65 (53%) patients had a procedure code 'medication review' recorded over the last year, explicitly stating that a medication review had been performed.

Conclusions

When individual factors are considered and a physician perspective applied, the prevalence of suboptimal drug treatment is considerably lower compared to that identified with general screening tools. Most quality problems concerning drug treatment may be considered low priority in complex clinical situations.

8-8

Medicines Reconciliation at the Community Mental Health Team and General Practice Interface

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Background: Drug related harms contribute to avoidable morbidity, mortality and extra costs. Medicines reconciliation (MR) at healthcare interfaces can help minimise drug related risks to patients. However, previous MR work has focused on acute sector interfaces. This study aims to determine the prevalence of psychotropic drug discrepancies between Community Mental Health Teams (CMHTs) and general practice in primary care and the proportion of patients with discrepancies.

Methods: Routine psychotropic prescribing information was collected from patients' most recent CMHT review letter and compared with their general practice prescription records. Phase 1: Three CMHT centres participated. 30 patients' prescriptions per centre were assessed. Data collected: December 2012 to October 2013. All discrepancies were assessed and graded for potential patient harm, as outlined in a previous study. Phase 2: Three CMHTs with 10 patients psychotropic prescriptions per centre per audit cycle were assessed. Quality improvement methodologies were used to reduce the proportion of patients with psychotropic prescription discrepancies by January 2017.

Results: Data for 90 and 360 patients' respectively for phase 1 and 2 were collected. Two patients were lost to follow up in phase 1. Phase 1, 42% (37/88) patients had ≥ 1 psychotropic medicines discrepancy; mean 1.4 (range 1 to 4) discrepancies per patient; 23% (51/219) of all psychotropics prescribed. 33% (17/51) of discrepancies were assessed as serious with 45% (23/51) being associated with long-term (≥ 8 weeks) benzodiazepine and/or z-hypnotic prescribing ($p < 0.001$). Phase 2, a consistent reduction in the proportion of patients with psychotropic prescribing discrepancies was not achieved, however improvements in practice were observed.

Conclusion: Psychotropic medicines discrepancies rates for primary care CMHTs were similar to those observed in acute sector studies. A reduction in the proportion of patients with discrepancies was not achieved.

8-9

Quality Improvement tools to improve the safe use of high risk medicines – a theory based evaluation

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Background

The Scottish Patient Safety Programme - Pharmacy in Primary Care (SPSP-PPC) collaborative is a Quality Improvement (QI) initiative striving to improve patient safety within community pharmacy. One element of the collaborative has involved implementation of High Risk Medicine (HRM) Care Bundles (CBs) which focused on non-steroidal anti-inflammatories and warfarin. These were implemented in 27 pharmacies across four National Health Service (NHS) regions by applying the Institute of Healthcare Improvements' "Breakthrough Series Collaborative Model". This study reports on (1) implementation of the HRM CBs and (2) application of the collaborative model.

Methods

Mixed-method evaluation involved questionnaires, semi-structured interviews, case studies, process mapping and documentary evidence. Informed consent was obtained throughout. Analysis was informed by two theoretical frameworks: the Kirkpatrick Model to investigate impact of training delivered; and Proctor's Taxonomy of Implementation Outcomes to understand the factors influencing implementation.

Results

The evaluation involved approximately 187 participants. The collaborative model was rated positively, provided networking opportunities and motivation to engage, yet further consideration of learning needs and how best to deliver the QI approach at scale requires attention. The CBs were considered acceptable, appropriate, feasible and compatible within community pharmacy practice. Adoption of QI methods was variable and risks to sustainability included lack of whole-team involvement in CB delivery. Significant variation of the CBs between NHS regions existed; posing challenges for further implementation, such as equality of patient care.

Conclusion

The findings demonstrate capacity for community pharmacy to deliver safety-focused initiatives within a collaborative. Application of frameworks helped develop key recommendations informing strategic decision-making. Key issues are being taken forward through consolidation and further testing of the CBs, and resource development to facilitate whole-team engagement.

8-10

Improving the communication skills of pharmacy technicians in the outpatient pharmacy using an online feedback intervention: the COM-MA project

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Background: Pharmacy technicians have an excellent position to prevent, detect and discuss medication-related problems. However, the communication at the counter is not yet optimal, sometimes leaving opportunities to discuss medication use with the patient unused. The aim of this study is to improve the communication skills of pharmacy technicians in the outpatient pharmacy using an online intervention based on video-recordings, self-reflection and personal feedback (COM-MA).

Methods: COM-MA uses video-recordings of patient-pharmacy technician conversations at the counter. After making these available online through the secure COM-MA webportal, pharmacy technicians complete a self-reflection task for two conversations. Using a protocol, all conversations are scored on instrumental and affective communication aspects by the trainer. Based on these scores and the self-reflection online personal feedback is given. Finally, pharmacy technicians reflect on the feedback and have the opportunity to ask the trainer questions.

Results: COM-MA was tested in three outpatient pharmacies in the Netherlands. In total, 141 eligible conversations of 32 pharmacy technicians were video-recorded. They each received personal feedback on two conversations, consisting of their communication strengths (the 'tops') and suggestions for improvement ('tips'). The most frequently given tops were: 1) being friendly and calm, 2) explaining clearly what the medication is for and how to use it in case of first prescriptions, 3) giving patients room for posing questions or other remarks, 4) being patient-centred in starting and ending the conversation. The most frequently given tips were: 1) listen more attentively, 2) provide information better tailored to the patients' needs, 3) better detect possible (implicit) concerns, 4) further exploring possible uncertainties of patients, 5) explicitly mention interactions are checked when multiple medications are used.

Conclusion: COM-MA provides pharmacy technicians with more insight in their patient-centred communication at the counter. These insights can be used to further improve their communication skills.

9-1

Therapeutic ratios predict asthma control in the ASTROLAB cohort

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Background: Inhaled corticosteroids (ICS) are the cornerstone of asthma therapy. The ICS-to-total-asthma-medication ratios (ICS therapeutic ratios) indicate suboptimal disease management in asthma.

Aim: To verify whether therapeutic ratios predict asthma control in the ASTROLAB cohort.

Method: ASTROLAB included UK and French persistent asthma patients (6-40 years) prescribed $\geq 6/12$ months of asthma therapy. Patients were prospectively followed for ≥ 12 months, with 4-monthly asthma control assessments. Adults were administered the ACQ (score ranges 0-6, uncontrolled asthma cut-off score >0.75). Parents of children completed the RCP3Q (score range 0-9, cut-off score ≥ 1). Medication data from French claims (SNIIRAM) or UK prescribing (THIN) databases were used to calculate therapeutic ratios over 12 months before each control assessment. We compared the occurrence of uncontrolled asthma in patients with ICS therapeutic ratios $<50\%$ vs. $\geq 50\%$, using Generalized Linear Mixed (GLM) models, for the overall cohort and in three specific subgroups with adequate sample sizes (UK and French adults, and French children).

Results: Among 773 patients (mean age = 22.2 years, 48.6% women) with 2,622 measurements, the risk of having uncontrolled asthma was significantly higher for patients with ratio $<50\%$ (OR=1.86, 95%CI=[1.45-2.38]) compared to patients with ratio $\geq 50\%$. This was the case for the 3 subgroups: UK adults (OR=2.80, 95%IC=[1.36-5.81]), French adults (OR=1.71, 95%IC=[1.24-2.36]) and French children (OR=1.96, 95%IC=[1.20-3.20]).

Conclusion: In this study, low ICS therapeutic ratios reflected insufficient prescribing of ICS relative to all asthma therapy, which facilitated deterioration of asthma control. Acknowledgment: FP-7 Project funded by the EC (GA 282593)

9-2

How often do asthma patients claim prescribed therapy?

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Background: Adherence is a pivotal issue in asthma, and differences between prescriptions and dispensations have been little explored.

Objectives: To identify a potential gap between prescriptions issued by General Practitioners' (GPs) and dispensations recorded in French national claims data, among patients with allergic rhinitis (AA) and asthma.

Methods: Using Electronic medical Records (EMRs) from IMS Disease Analyzer, we identified a cohort of French patients with AA and asthma, based on GPs' diagnoses and prescribing data. For each patient, the EMR was linked to claims data with individual medical resource utilization. Percentages of dispensed prescriptions were assessed from July 2012 to July 2013 (study period), using information recorded in both data sources. Sub-groups analyses were performed according to the level of asthma control assessed in the 12 months before the study period.

Results: 3,654 patients were included: 49.0%, 32.3% and 18.7% of patients had well controlled, not well controlled, and poorly controlled asthma, respectively. Altogether, 87.2% of asthma prescriptions were dispensed to patients. Regarding specific therapy, 85.8% of short acting beta agonists (SABAs), 87.0% of long acting beta agonists (LABAs), 90.6% of montelukast, 84.9% of inhaled corticosteroids (ICs), and 87.6% of fixed dose combinations (FDCs) of ICs+LABAs were dispensed. Percentages of dispensed prescriptions varied according to asthma control: SABAs prescriptions were more often filled when asthma was poorly controlled while this was the opposite for ICs and FDCs of ICs+LABAs.

Conclusions: In primary care, asthma patients did not refill all prescriptions; unfilled prescriptions varied with specific asthma therapy and level of asthma control.

9-3

Adherence to long-acting bronchodilators after discharge for COPD: how much of the geographic variation is attributable to the hospital of discharge and how much to the primary care providers? A cross-classified multilevel design

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Background. In moderate-severe COPD, long-acting bronchodilators (LBs) are recommended to improve quality of life. Observational studies reported poor adherence to LBs. From current evidence, it is not possible to quantify how much of the “gap from guidelines” is attributable to patients, hospitals or primary care providers, i.e. Local Health Districts (LHDs) and General Practitioners (GPs). The objectives were: to measure adherence to LBs after hospital discharge for COPD; to compare amounts of variation attributable to hospitals and primary care providers; to identify determinants of adherence.

Methods. This cohort study was based on the population of the Lazio region, Italy. Patients discharged from hospital in 2007-2011 for COPD were included. The two-year follow-up started immediately after discharge. Adherence was defined as “MPR>80%”. Cross-classified models were performed to analyze variation. Variation was expressed as Median Odds Ratio (MOR). A MOR of 1.00 stands for no variation between clusters, a large MOR indicates considerable variation.

Results. We enrolled 13,178 patients. About 29% of patients were adherent to LBs. Adherence was higher for patients discharged from pneumology wards and for patients with GPs working in group practice. A relevant variation between LHDs (MOR=1.21, p=0.001) and GPs working in the same district (MOR=1.28, p=0.035) was detected. When introducing the hospital in the analysis, the MOR related to LHDs decreased to 1.05 (p=0.345), the MOR related to GPs dropped to 1.22 (p=0.086), whereas the MOR associated with hospitals was 1.38 (p<0.001).

Conclusion. Only 29% of patients were adherent to LBs in the two years after discharge. A relevant geographic variation was observed between LHDs. This heterogeneity raises equity concerns in access to optimal care. The reduction of the variability among LHDs and GPs after entering the hospital level proved that differences we observe in primary care partially “reflect” the clinical approach of hospitals of discharge.

9-4

Assessing LABA safety in routine asthma care from the ASTROLAB cohort: the need to look at detailed patterns of use

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Background: Recent randomized trials suggest that Long-Acting β -Agonists (LABAs) are safe when used together with Inhaled Corticosteroids (ICS) in fixed-dose combinations (FDCs), but safety of non-combined LABAs is still debated.

Aim: The ASTROLAB FP7 European project investigated LABA safety in routine medical practice, in patients using LABA in FDCs or in distinct inhalers (free combination with ICS or monotherapy).

Method: ASTROLAB included in France and the United Kingdom persistent asthma patients (6-40 years) prescribed ≥ 6 months of one of 4 treatment patterns: ICS without LABA, LABA without ICS, LABA and ICS in distinct inhalers (LABA+ICS), and LABA/ICS in FDCs. Patients were prospectively enrolled, with patient-reported data on LABA use and asthma exacerbations (AEx: new courses of oral corticosteroids). Generalized linear mixed models assessed the risk of AEx during follow-up in LABA users versus non-users, measured as time-varying use of single LABA and LABA/ICS FDCs in the last 7 days, after adjusting for age, gender, country, baseline severity and concomitant asthma therapy.

Results: Among 908 patients (mean age = 21.8, 46.6% women, 56% adults), followed on average for 15.2 (7.8) months, those under ICS without LABA, LABA without ICS, LABA and ICS in distinct inhalers, and FDCs were 28.9%, 3.0%, 9.1% and 59.0% at inclusion, respectively. Altogether, 29.2% of the patients experienced ≥ 1 AEx. After adjustment, the risk of AEx observed under regular use of single LABA and LABA/ICS FDCs were OR=1.22, 95%CI=[0.73-2.03] and OR=1.02, 95%CI=[0.78-1.33], respectively.

Conclusion: A small increased risk, albeit non-significant, was observed when patients used LABA in a distinct inhaler daily for ≥ 1 week, while the risk was not increased when patients used LABA in FDCs. The safety of single LABA should be verified on larger patient samples.

Acknowledgment: Project funded by the EC (GA 282593).

9-5

Determinants for healthcare professionals to take action on Direct Healthcare Professional Communications (DHPCs)

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Background

Direct Healthcare Professional Communications (DHPCs) are letters that are distributed by pharmaceutical companies to inform healthcare professionals (HCPs) about new safety information. HCPs do not always act on such information. This study aimed to assess whether HCP characteristics and their perceptions towards safety information are associated with the extent of action taking in response to DHPCs in Europe.

Methods

In the context of the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action, general practitioners (GPs), cardiologists and pharmacists from nine European countries (Denmark, Spain, Croatia, Ireland, Italy, the Netherlands, Norway, Sweden, and the UK) completed a web-based survey. HCPs were asked how often they take action in response to DHPCs (VAS 0%-100%). This outcome measure was dichotomized on the median per country. Associations between HCP characteristics (gender, profession, years of accreditation) and their perceptions (regarding usefulness of DHPCs, pharmaceutical companies as source, preference for letter as channel) and the outcome measure were tested using logistic regression analysis on the total population and per country.

Results

In general, the 2,645 included HCPs (52% GP, 61% female) reported high levels of action taking (median VAS 83%, range 62% in the Netherlands to 90% in Italy). HCP characteristics were not associated with taking action in analyses of the total population. However, in Ireland pharmacists reported more action taking than GPs (OR 2.21; 95% CI 1.33-3.66). Some associations were observed between HCPs' perceptions and action taking. A positive view on the usefulness of DHPCs (OR: 3.43; 95% CI 2.58-4.55), on pharmaceutical companies (OR 1.85; 95% CI 1.56-2.20), and preference for letter (OR 1.71; 95% CI 1.43-2.04) were associated with more action taking. These associations were similar among the countries, except for Denmark and Sweden.

Conclusion

Other channels and senders may be needed to further improve the impact of DHPCs.

9-6

A real world evaluation of the clinical effectiveness, safety and direct medical expenditure of high intensity statin therapy in high risk patients: A study protocol

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Background

Based on recent evidence from clinical trials, the new British guidelines have recommended high-intensity, high-dose statins as first choice for secondary prevention of cardiovascular diseases (CVDs). However, there are concerns around their safety, potentially increasing the incidence of statin-related side effects (myopathy, hepatotoxicity, diabetes) which in turn might impede patients' adherence/persistence and hence compromise obtaining statin's clinical benefits. This is a concern as persistence with statin therapy is already poor without dose increasing. This is important in real world settings given the limitations associated with the generalisability of clinical trials' findings, and the high prevalence of CVD in Scotland. This study aims to evaluate the clinical/economic impact of using high-intensity statin therapy compared to moderate and low-intensity therapy to provide future guidance

Methods

This retrospective cohort study will use data from the Scottish Prescribing Information System (PIS) from April-2010 to March-2016 to identify new statin users. PIS contain information about dispensing medications in primary care. Patients will be categorised into high, moderate and low-intensity groups based on the NICE classification. The study outcome measures will include adherence/persistence (using Proportion of Days Covered), clinical outcomes (lipid levels, any hospitalisation, overall mortality, cardiovascular mortality and morbidity), incidence of statin-related side effects (myopathy, hepatotoxicity, diabetes, cancer, renal dysfunction), and healthcare resource utilisation. Data on the study outcomes will be extracted by linking PIS records to hospitalisation data (SMR01), out-patient data (SMR00), cancer registry (SMR06), lab data (SCI Store), and the death registry. The association between the exposure groups and study outcomes will be examined using survival analysis, Cox regression and logistic regression as appropriate.

Results/Implications

The results of this comprehensive study will be available by November 2017. Understanding the safety/effectiveness of high intensity statins will assist in evaluating the appropriateness of these recommendations. If pertinent, initiate a modification/revision as necessary and re-research.

9-7

Awareness among European healthcare professionals of four recent drug safety issues

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Background

Knowledge of healthcare professionals' (HCPs) awareness of specific drug safety issues and factors that are associated with awareness can help to improve safety communication strategies. This study aimed to assess European HCPs' awareness of specific safety issues, sources through which HCPs had become aware, and which HCP characteristics are associated with awareness.

Methods

In the context of the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action, a web-based survey was distributed among HCPs from nine European countries (i.e. Denmark, Spain, Croatia, Ireland, Italy, the Netherlands, Norway, Sweden, and the UK). HCPs were asked about awareness of the recent safety issues of combined hormonal contraceptives, diclofenac, valproate, and ivabradine. HCPs aware of a specific safety issue were additionally asked to indicate the source through which they had become aware. Associations between HCP characteristics (gender, profession, years of accreditation) and awareness of each of the safety issues were assessed using a penalized maximum likelihood logistic regression analysis per country.

Results

In total, 3,620 HCPs were included ranging from 68 from Denmark to 1,075 from Spain. Awareness was highest for the diclofenac safety issue (91%). Variation across the countries was largest for the ivabradine safety issue (range 24% in Sweden to 87% in Italy). Direct Healthcare Professional Communications were the main source of awareness followed by information on a website or in a newsletter but this differed across the countries. Of the assessed HCP characteristics, profession was mostly associated with awareness. Cardiologists were less aware than general practitioners, except for the ivabradine issue where cardiologists in the Netherlands were more aware than general practitioners (OR 8.79; 95% CI 2.64-29.22).

Conclusion

In several countries, additional strategies are needed to improve awareness of safety issues. DHPCs may not be sufficient to reach cardiologists when communicating safety issues of drugs outside their field.

9-8

Communication on safety of medicines in Europe: Current practices and general practitioners' awareness and preferences

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Background

National competent authorities for medicines (NCAs) coordinate the communication on safety of medicines in Europe. The effectiveness of current communication practices has been questioned, particularly with regards to reaching general practitioners (GPs). This study aimed to assess current European NCA safety communication practices, and to investigate European GPs' awareness of and preferences for such communications.

Methods

Web-based surveys were distributed among European NCAs and healthcare professionals (HCPs). The survey among regulators was emailed to a representative of the 27 European countries participating in the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) joint action. HCPs from nine European countries (i.e. Denmark, Spain, Croatia, Ireland, Italy, the Netherlands, Norway, Sweden, and the UK) were asked about their preferences through a link to the survey on websites, in newsletters and/or in a direct email. Data from GPs were used for this study. Descriptive analyses were conducted.

Results

Current practices were reported for 26 countries. In 23 countries (88%), NCAs published direct healthcare professional communications (DHPCs) on their website in addition to distribution to HCPs. Educational materials were available on the NCA's website in 10 countries (40%). Twenty-one NCAs (81%) indicated to have their own newsletter.

More than 90% of the 1766 GPs who completed the survey, were aware of DHPCs. Preferred senders of safety information were mostly NCAs and professional bodies. Preferred channels for safety information were medicines reference books and clinical guidelines. GPs found repetition of safety issues useful (range 80% in the UK to 97% in Italy). Preference for an electronic rather than a hardcopy format varied per country (36% in Sweden to 72% in Spain).

Conclusion

NCAs use similar methods for medicines safety communications. Most GPs were aware of urgent communications and preferred similar senders of safety communications. However, their preferences towards the format differed per country.

9-9

An analysis of patient reports of adverse drug reactions (ADRs) via the UK Yellow Card scheme

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Background

Patients have been reporting suspected ADRs to the Medicines and Healthcare products Regulatory agency (MHRA) via the Yellow Card (YC) scheme since October 2005. An evaluation of the first 5180 patient reports submitted found that 63% involved females, 16% contained more than one suspected drug and 58% were considered serious by the MHRA. This study compared recent reporting to early reporting.

Methods

Anonymised YC patient reports covering July to December 2015 were provided by the MHRA, following approval from the Independent Scientific Advisory Committee. 2284 reports (excluding vaccines) were analysed for the number and type of drugs reported classified using the British National Formulary, age and gender of the sufferer, and seriousness of ADR as classified by the MHRA.

Results

1524 (66.7%) of reports concerned females. Age was missing for 130, but 122 reports concerned under 19s and 441 those over 64. The mean age of males experiencing an ADR (51.8 ± 21.1 years) was significantly higher than females (44.6 ± 18.0).

Most reporters (94.4%; 2155) cited one drug, 93 (4.1%) two, 20 (0.9%) three and 16 four or more, maximum six. Males cited two or more drugs more often (59; 7.8%) than females (70; 4.6%). Age did not affect the number of drugs reported. The most frequent therapeutic category reported was central nervous system; SSRIs the most frequently cited drug group, followed by antiepileptics.

1621 (71.0%) reactions were categorised as serious. Females were significantly more likely to experience serious ADRs (1115; 73.2%) than males (506; 66.6%). Seriousness was not related to the number of drugs cited, or to age.

Discussion

While the proportion of reports concerning females was similar to early reports, the proportion involving only one drug was much higher, as was the proportion of serious reports, suggesting the potential value of reports may have improved.

9-10

Impact of a pharmacist-driven pharmacovigilance system in a secondary hospital in the Gauteng Province of South Africa

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Introduction: Spontaneous reporting of adverse drug reactions (ADRs) for hospital inpatients is limited with many obstacles identified. This is a concern as reporting of ADRs improves future clinical practice. Evidence of a functional pharmacovigilance (PV) system is a requirement in South African (SA) hospitals; hence, the need to evaluate this.

Methods: Descriptive, operational intervention study of a structured pharmacist-driven PV system for ADR reporting at Sebokeng Hospital, Gauteng, SA, including targeted training at different forums, implemented and monitored over 18 months. Knowledge, attitudes and practices of health care professionals (HCPs) were assessed pre- and post-intervention using structured questionnaires and compared along with numbers of ADRs reported.

Results: At baseline, only 5.3% of HCPs had received previous training on ADR reporting, while 89.4% indicated the need for training. Post-intervention, 32.5% of HCPs indicated receiving training and 96.6% will support the system, with 84.8% understanding the need to report ADRs helped by posters (52.3% noticed these) and training. Statistically significant ($p < 0.001$) improvements pre- and post-intervention included: necessity to report ADRs (46.2% vs. 98.0%); previously reported an ADR (12.1% vs. 33.8%); awareness of an ADR reporting system (18.9% vs. 70.2%); know an ADR form is available (15.2% vs. 68.9%) and to whom to submit to (18.9% vs. 72.8%). Reasons for non-reporting decreased significantly, e.g. Not knowing 'how, where and when to report' ($p = 0.0027$); 'Concern that report may be wrong' (34.1% vs. 18.7%; $p = 0.0041$). Numbers of ADR reports submitted increased more than 10-fold from 6 reports for the 18-month pre-intervention period to 69 reports during the intervention period.

Conclusion: A pharmacist-driven PV system contributed to better knowledge and attitudes of HCPs and increased ADR reporting. For future interventions, hospital management and policy makers should consider the leadership role that pharmacists can play in improving rational and safe use of medicines in the inpatient setting.

11-1

Investigating Orthopaedic Surgical Prophylaxis Changes and Post-op Acute Kidney Injury in NHS Grampian – using NHS Scotland Infection Intelligence Platform

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Background

To support reduction of Clostridium difficile infection (CDI) the Scottish Antimicrobial Prescribing Group (SAPG) recommended that NHS boards in Scotland restrict antibiotics associated with a high risk of CDI. In June 2010 NHS Grampian changed its policy for antibiotic prophylaxis in orthopaedic surgery to include flucloxacillin and gentamicin. Recent studies found increased post-operative acute kidney injury (AKI) following similar changes. This study used individual level linked data to examine rates of both post-operative AKI and post-operative CDI before and after antibiotic surgical prophylaxis policy change in NHS Grampian.

Methods

Patients who underwent an orthopaedic surgical procedure, with prophylaxis recommended, from 01/06/2008 to 31/05/2012 were selected. Cases were linked to local creatinine data and to national patient level hospital activity, national infection data, community prescribing and Scottish Renal Registry data. Segmented regression analyses of interrupted time series were used to evaluate changes in level and trend of AKI rates associated with the intervention and estimate effect sizes. Incident rate ratios were used to examine changes in post-operative CDI rates.

Results

There was a significant increase in AKI rate trend following policy change ($\beta=0.28$; 95%CI, 0.03 to 0.53; $p=0.028$) in trauma patients, equating to an increase of 0.28 cases of AKI/100 procedures/month and a relative intervention effect at 24 months of 150% (95% CI 25% to 250%). There was no significant change in AKI rate among elective patients. A significant reduction in post-operative CDI rates were identified in trauma patients (IRR 0.36; 95% CI 0.18-0.74).

Conclusion

We found that a change in orthopaedic antibiotic prophylaxis policy in NHS Grampian was associated with an increase in post-operative AKI. This is consistent with observations in other health boards and supported a subsequent change in SAPG policy in 2012 to avoid this adverse event based on the accumulative evidence generated.

11-2

Development of Clinical Decision Support (CDS) Mobile App for Antimicrobial Prescribing

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Introduction

Development of clinical decision support (CDS) is a priority for Scottish Government to give clinicians easy access to decision support tools and relevant guidance at the point of care. Antimicrobial prescribing was identified as a 'quick win' to demonstrate CDS due to national evidence-based guidance and treatment algorithms and a robust clinical network.

Method

The Scottish Antimicrobial Prescribing Group (SAPG) and NHS Education for Scotland (NES) developed a proposal for a national app targeting antimicrobial safety issues across community and acute care settings. Funding was secured from Scottish Government, an app developer was appointed and a Clinical Reference group was established.

Results

The app was launched on 1st August 2016, available to download free from iTunes and Google Play app stores for use on any mobile device.

The app includes:

- Dosage calculators for gentamicin and vancomycin (registered as medical devices with the Medicines and Healthcare products Regulatory Agency)
- Antibiotic prescribing guidance for primary care and hospitals which can be customised by each health board.
- A decision aid to support management of urinary tract infections in older people.
- An audit tool to support data gathering for local and Scottish Government targets.

Conclusion

This bespoke national app provides customised board-level guidance and CDS tools to enable clinicians to use antibiotics more safely and effectively. The unique audit component will support improved practice through timely audit and feedback of key prescribing measures. An evaluation of its impact is planned using the outcomes chain model and contribution analysis. Plans for further development include translation of other national guidance currently presented as algorithms into decision support format and creation of CDS tools utilising risk-based modelling of individual patient data for management of urinary tract infection and sepsis.

11-3

Evaluating initial antimicrobial use in an adult medical intensive care unit at an academic teaching hospital in Pretoria, South Africa

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Introduction: Antimicrobial resistance is increasing globally enhanced by irrational use of antibiotics. It is estimated that in hospitals 50% of antimicrobial usage is either unnecessary or inappropriate. However, there is limited knowledge regarding antibiotic use in many countries including South Africa. This includes Intensive Care Units. This study aimed to explore factors surrounding initially prescribed antibiotics and direct medicine-related costs in the adult medical intensive care unit (MICU) at Steve Biko Academic Hospital (SBAH). A clinically trained pharmacist was included as part of the multi-disciplinary team and evaluated patients' prescription charts daily against established criteria including indication, dose and blood cultures.

Methods: Operational study with a descriptive and observational design, conducted through daily ward rounds over a seven month period. Antibiotics that were prescribed after a patient was admitted to the MICU were included in the study and considered as the "initial course of antibiotics". Antimicrobial agents that the patient was admitted on were documented and are referred to as "antibiotics prior to review".

Results: Less than half of the patients, 23 (44.2%; n = 52) were initiated on antibiotics on the first day of admission to the MICU. More than half (60.5%) of the antibiotics were prescribed appropriately during the study period. The total cost of initial antibiotic use for the treatment period during the study was R209 140.40, with an average cost of R31 240.77 per day for all initial antibiotics.

Conclusion: A coordinated effort from the infectious diseases specialist, and the clinical pharmacist within the multi-disciplinary team, assisted in the appropriate prescribing of antibiotics to patients admitted to the MICU. However, room for improvement. The presence of a clinical pharmacist and infectious diseases specialist, with the addition of an antibiotic policy and training, may further enhance rational antibiotic use in the future. This will be explored further.

11-4

An Observational Study of Antibiotic Therapy in Women Diagnosed with Peripartum Sepsis

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Background: Sepsis is the leading cause of maternal death in 11-15% of women worldwide. The association of some physiological changes with the obstetric population increases the challenge of detecting infection. The administration of intravenous broad-spectrum antibiotics to women with suspected or confirmed sepsis is recommended. Our aim was to observe the antibiotic therapy prescribed to sepsis patients admitted to maternity wards and to describe the therapeutic journey of these women from suspicion of sepsis to discharge.

Patients and method: In a prospective observational study in one single Scottish health board, data were collected on women diagnosed with suspected or confirmed sepsis in their peripartum period.

Result: Incidence of sepsis was 331 in every 10,000 maternities, with a median hospital stay of four days. Co-amoxiclav was prescribed to 57.5% of all women receiving antibiotic therapy. Group B Streptococcus was associated with 20.8% of maternal sepsis, while in 60% of the samples no causative pathogen was identified. Appropriate switching from intravenous to oral therapy was observed in 92.3% of cases. A difference was found in C-reactive protein values between caesarean section and other modes of delivery ($p < 0.001$).

Conclusion: Pyrexia in labour is a concern for practitioners in maternity wards and a trigger to treat for sepsis. While there was good adherence to the local antibiotic guidelines for the empiric treatment of maternal sepsis, the negative results contained in microbiology reports blocked de-escalation to narrow-spectrum antibiotics.

11-5

Antibiotic consumption in Serbia

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Background: Monitoring antimicrobials consumption is important to reduce future antimicrobial resistance. The Medicines and Medical Devices Agency as regulatory institution which helps ensure the quality, efficacy and safety of medicinal products in Serbia. As a mandatory duty according to Medicines and Medical Devices Law, the Agency collects and estimates total medicines consumption including reimbursed and self-pay medicines.

Methods: Total antimicrobial consumption data were processed using Anatomical Therapeutic Chemical (ATC)/Defined Daily Doses (DDD) methodology and consumption expressed in the number of DDDs per 1000 inhabitants per day (DID). ESAC quality indicators were used to assess the quality of prescribing.

Results: Consumption antibiotics has an increasing trend from 2011 to 2015. In 2015, total antibacterial use (ATC J01) was 37 DID, with reimbursed antibiotic use at 15 DID. Proportional consumption of ATC subgroups (3th level) antibacterials for systemic use (J01) expressed as percentage of the total consumption: tetracyclines [J01A - 6.09%], penicillins[J01C - 45.69%], cephalosporins[J01D - 14.13%], sulfonamides and trimethoprim [J01E - 2.95%], macrolides, lincosamides and streptogramins [J01F - 15.76%] and quinolones [J01M - 10.33%]. Proportional consumption of ATC subgroups (4th level) a expressed as percentage of the total consumption for the class: beta-lactamase sensitive penicillins [J01CE - 0.35%], combinations of penicillins [J01CR - 12.4%], 3rd and 4th generation of cephalosporins [J01DD+DE - 3.5%], and fluoroquinolones [J01MA - 7.87%]. With respect to oral antibacterials, amoxicillin was mainly used, followed by co-amoxiclav, cefalexin, azithromycin and doxycyclin. With parenteral forms, gentamicin was mainly used (33%), followed by ceftriaxone, benzilpenicillin and metronidazole.

Conclusion: This results suggests good antibiotic prescribing practise (e.g. high use of amoxicillin) but also opportunities for quality improvement, i.e. initiatives to reduce total use of antibiotics, reduce use of co-amoxiclav, macrolides and quinolones. These data provide a basis for establishing antimicrobial quality targets in Serbia.

Keywords: Antibiotics, ATC/DDD methodology

Category: Antibiotic usage

11-6

Polypharmacy partnership: patient, general practitioner & prescribing advisor

Successful delivery of polypharmacy reviews for at-risk patients in a Scottish Deep End Practice

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Background

A Glasgow Deep End Practice received funding in July 2016 through the primary care investment fund for a prescribing advisor (PA) to work with the practice team for three days per week. A targeted approach was designed for joint working between the prescribing advisor and practice prescribers to deliver patient centred polypharmacy reviews for those most at risk of hospital admission or use of unscheduled care.

Methods

All patients > 65 years with a hospital admission in the previous 12 months were identified. The PA completed a polypharmacy notes review and recorded evidence based recommendations in the GP prescribing system. The patients had a face-to-face medication review with their GP to discuss the prescribing advisors recommendations.

Results

From 24th August 2016 until 31st January 2017, 130 patients had received a face-to-face medication review with their GP, based on PA recommendations. A wide range of medication related issues were identified and 473 interventions were recorded (3.6 interventions per patient). One intervention led to patient harm. Significant cost savings were achieved with £9,853 saved during the five month period (£75.80 per patient). GP's and the PA advisor report that the current approach is working very well. Feedback from patients has also been positive, most being very receptive to suggested changes, knowing that the review has been done by an appropriate "specialist" and suggested changes are evidence based.

Conclusions

This patient centred model of care utilises the strengths and skills of all multidisciplinary team members, provides a unique opportunity for shared learning between practice prescribers and prescribing advisor whilst ensuring continuity of care for a group of deprived patients most at risk of hospital admissions. The patient centred approach allows shared decision-making and responsibility and increases the quality and range of services provided by the practice to improve health and narrow inequalities.

11-7

Building a national Infection Intelligence Platform to improve antimicrobial stewardship and drive better patient outcomes – the Scottish Experience.

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Background

The better use of new and emerging data streams to understand the epidemiology of infectious disease and to inform and evaluate antimicrobial stewardship improvement programmes is paramount in the global fight against antimicrobial resistance (AMR). The development of a national informatics platform that synergises the wealth of disjointed, infection-related health data, builds intelligence capability and allows rapid enquiry, generation of new knowledge and feedback to clinicians and policy makers is a key component of the NHS Scotland strategy to understand AMR and support national and local stewardship programmes.

Methods

A multi-stakeholder community, led by the Scottish Antimicrobial Prescribing Group, secured government funding to deliver a national program of work centred on three key aspects: technical platform development with record linkage capability across multiple datasets; a proportionate governance approach to enhance responsiveness; and, generation of new evidence to inform policy and guide clinical practice.

Results

The NHS Scotland Infection Intelligence Platform (IIP) is now hosted within the national health data repository of NHS National Services Scotland to assure ongoing resilience and sustainability. The IIP includes technical solutions providing simplified “data views” of complex, linked datasets and embedded statistical programmes to enhance analysis capability. These developments have enabled better responsiveness, flexibility and robustness in conducting national population-based studies including a focus on intended and unintended effects of antimicrobial stewardship interventions and quantification of infection risk factors and clinical outcomes.

Conclusion

We have completed the build and test phase of IIP, overcoming the technical and governance challenges and produced new capability in infection informatics to generate new evidence for improved clinical practice. IIP provides the foundation and framework for informatics expansion and the opportunity for global collaborations.

11-8

Point prevalence survey of antimicrobial utilisation in an academic hospital in the Gauteng province, South Africa

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INTRODUCTION: Antimicrobial resistance (AMR) is a serious health concern and direct threat to patient safety. There is a paucity of data pertaining to antimicrobial utilisation and consumption in the world and similar in South Africa. This study aimed to determine antimicrobial consumption using a point prevalence survey (PPS) in order to document current antimicrobial use.

METHODS: A PPS was conducted in Dr George Mukhari academic hospital using a paper based data collection instruments previously used in Botswana. Data were collected by trained data collectors over a period of three weeks. The sample comprised of all inpatients at 08h00 on the day of the survey. All inpatient files of the 39 wards were completely surveyed in a single day. The total number of patients in the respective ward served as the denominator, and the number of patients on antimicrobials the numerator.

RESULTS: Preliminary results analysed from 220 files, from 15 of the 39 wards (paediatric and adult medicine) indicated that females predominated (59.1%). Just less than half (104; 47.3%) of the patients were on antimicrobials, of whom 37.5% were previously hospitalised and 29.8% used antimicrobials in the last 90 days. A total of 155 antimicrobials were prescribed, of which 48.4% were prescribed before requesting a culture sensitivity test. Meropenem and amikacin were the most used antibiotics in the paediatric wards and ceftriaxone was the most prescribed antibiotic in the adult medical wards.

CONCLUSION: Determining antimicrobial consumption data in low resource settings remains a challenge. The PPS method offers a standardized tool to identify targets for quality improvement. South Africa is well placed to contribute to the growing knowledge based on antibiotic use and create a platform, to increase collaboration and initiate regular documentation and measurement of robust data of antimicrobial consumption.

11-9

Cross national comparison of paediatric antibiotic use

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Background: According to the European Surveillance of Antibiotic consumption (ESAC-net) network data for 2014, Norwegian and Hungarian antibiotic use was very similar (~16 DDD per 1000 inhabitant days), while Portuguese ambulatory antibiotic use was a higher (20 DDD per 1000 inhabitant-days). The aim of this work was to explore whether differences may exist or not in the paediatric antibiotic use of Hungary, Norway and Portugal.

Methods: A cross national cross sectional analysis was conducted. Ambulatory care systemic antibiotic use (ATC: J01) stratified by age-groups were retrieved from national databases. Analysis was focused on children aged 0-19 years. Antibiotic use was expressed as number of packages or was standardized in different measures: number of packages per children inhabitant per year and DDD per 1000 children inhabitants per day (ATC/DDD index, 2016). Population data were derived from Eurostat.

Results: In Hungary the population rate of children is 19.9%, in Portugal 19.5%, in Norway 24.6%, while the rate of antibacterial packages consumed by this age group shared 32.2 %, 20.0 %, and 15.0% from total ambulatory care antibiotic use, respectively. The annual number of antibacterial packages per one children inhabitant was 0.3 in Norway, 0.76 in Portugal and 1.18 in Hungary. Antibiotic use expressed as DDD per 1000 inhabitants per day (DDD) a different ranking was obtained: it was 7.3 DDD in Norway, 15.6 in Hungary and 17.7 DDD in Portugal.

Conclusion: Paediatric ambulatory antibiotic use differed largely between the three countries. The different ranking determined by the two standardized measures may be due differences of antibiotic utilisation by age-groups. Compared with Norwegian use of antibiotics in children, the Portuguese and Hungarian consumption are higher. The reasons for these differences should be investigated.

12-1

Utilisation and prescribing patterns of direct acting oral anticoagulants (DOACs) in the Scottish primary care setting

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Background

Four direct acting oral anticoagulants (DOACs) have been licensed by the Scottish Medicines Consortium (SMC) as alternatives to traditional OAC warfarin, but without providing any specific guidance for preferable uptake/implementation to local health boards. This study aims to evaluate the prescribing patterns/uptake of DOACs in Scotland's primary care setting.

Methods

A descriptive cross-sectional study was carried out between 2006 and 2016 using the Scottish primary care prescribing data. Three metrics were used to quantify utilisation: number of dispensed items, cost and defined daily dose (DDD)/1000 population per day.

Results

There was a 2,000-fold increase ($p=0.01$) in the number of dispensed DOAC items between 2010 and 2016. This was supported by a 3,500-fold increase ($p=0.01$) in the DOAC DDD within this time period. DOACs only accounted for 18.6% of total OAC prescribing in 2016, but this equated to 88.6% of total OAC expenditure in 2016. Rivaroxaban dispensing increased by over 1000-fold ($p=0.007$) between 2010 and 2016, making it the most favoured DOAC by 2016. Apixaban dispensing increased by over 3,000-fold ($p=0.08$) between 2013 and 2016, but there were 30.4% ($n=33,490$) less apixaban items dispensed in 2016 compared to rivaroxaban.

Discussion

Warfarin was still the most dispensed OAC. The sharp increase in DOAC dispensing was correlated with a decline in warfarin dispensing between 2015 and 2016, which may indicate that DOACs were beginning to be favoured. Rivaroxaban was shown to be the favoured DOAC, likely due to its longer licensing time and once daily dosing. Apixaban use was likely popular due to its lower bleeding risk. This study provides a baseline understanding of prescribing patterns of DOACs collectively as well as individual DOACs. Further research is needed to explore any regional and national variations in relation to their various indications, including a cost-effective analysis.

12-2

PERSISTENCE OF STATINS THERAPY IN BRAZIL AND SCOTLAND

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Background

Long-term utilization of prescription drugs for chronic conditions such as hypercholesterolemia is a reality for millions of individuals worldwide. Recent evidence has suggested that the effectiveness of statins in real-world settings can be inferior to that seen in clinical trials, which may be due to issues of dosing and sub-optimal persistence. Measurement of persistence is important not only for general drug-utilization studies, but also for the accurate quantification of drug exposure in a population over time. This study aims to assess the persistence of statin therapy in Brazil and Scotland, with universal access to healthcare in both countries.

Methods

This retrospective cohort study will use data from the Scottish Prescribing Information System (PIS) and from the Brazilian Unified Health System (SUS) from April-2010 to Dec-2015. Scottish data will be extracted by linking PIS records to hospitalisation data, out-patient data, lab data and the death registry. In Brazil, a national population-based cohort focus on the patient is being constructed by the linkage of the SUS administrative systems (hospitalization, outpatient and mortality). Statin users will be identified according to the ICD-10 codes E780, E781, E782, E783, E784, E785, E786 and E788 reported as the indication for prescribing one of the following drugs of interest: simvastatin (only for Scotland), atorvastatin, fluvastatin, lovastatin and pravastatin. Persistence will be measured through the hybrid model (refill-sequence and proportion of days covered), in two periods: one year and two years after cohort entry. The association between the exposure groups and cardiovascular events or death will be examined using survival analysis and Cox regression as appropriate.

Results/Implications

The results of this study will be available by November 2017. Understanding the duration and intensity of statins persistence will assist in evaluating the quality of medicines use and impact on clinical outcomes in routine clinical practice across countries.

12-4

Safety and clinical effectiveness of direct oral anticoagulants in patients with atrial fibrillation in Scotland

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Background: Direct oral anticoagulants (DOACs), used long-term in patients with atrial fibrillation (AF), have proven safe and efficacious in clinical trials. However, information regarding their safety and clinical effectiveness in the real world is still limited.

Methods: Retrospective cohort study using linked routinely collected administrative data. Patients had a diagnosis of AF and received a first prescription for a DOAC between September 2011 and December 2015. Treatment outcomes, stratified by drug, will be analysed using time dependent Cox proportional hazard models; drug exposure will be defined as days' supply. Clinical endpoints will include stroke, systemic embolism, and death due to cardiovascular reasons; the main safety indicator will be major bleeds.

Preliminary results: A total of 14,721 patients initiated DOAC treatment during the study period; 6,231 with apixaban, 1,123 with dabigatran, and 7,367 with rivaroxaban. The majority of DOAC treatments were initiated in 2014 (32.2%) and 2015 (47.3%). Median time of follow-up was 346 [IQR 167 – 597] days, ranging from 260 [IQR 122.5 – 435] days for apixaban to 864 [IQR 536.5 – 1170] days for dabigatran. Mean age at time of first prescription was 74.1 [SD11.3] years (range 71.1 [SD 12.0] – 74.8 [SD 11.0] years), and 45.5% were female (range 37.3 – 46.5%). Polypharmacy was observed in 87.6% of all patients (range 82.9 – 88.6%), and mean CHA₂DS₂-VASc score was 2.9 [SD 1.7] (range 2.5 [SD1.7] – 3.0 [SD 1.7]).

During the study period, 385 patients had a stroke (apixaban 120, dabigatran 48, rivaroxaban 217); gastrointestinal bleeds occurred in 314 patients (88, 36, and 190, respectively), and 976 patients died due to cardiovascular reasons (282, 97, and 597, respectively).

Conclusion: To prevent strokes, AF patients in Scotland increasingly receive DOACs instead of warfarin. Findings from this study will inform patient care and enable improvement of treatment outcomes.

12-6

Adherence to chronic antihypertensive medication by patients managed at primary health care facilities in a rural district of Limpopo Province, South Africa

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Introduction: One of the cornerstones of blood pressure (BP) control in hypertensive patients is adherence to both pharmacological and non-pharmacological management. This study aimed to determine the level of adherence to antihypertensive treatment and possible associations between adherence and factors affecting adherence in ambulatory care. This is important in South Africa (SA) with its high prevalence rates for cardiovascular disease and current initiatives to improve care and access to medicines for patients with chronic diseases.

Method: Descriptive, quantitative study design at primary health care (PHC) clinics in the Vhembe District, Limpopo Province, SA. Trained pharmacists interviewed 251 conveniently selected chronic hypertensive patients collecting their medication. Adherence was assessed using a self-reported rating scale with six pre-defined categorised responses. Patients were categorised as adherent (excellent) or sub-optimally adherent (very good, good, fair, poor, very poor) according to ratings. Associations between adherence and patient characteristics were determined using Chi-square test.

Results: All patients were treated with one/more antihypertensive drugs, listed in the SA PHC Essential Medicines List, of whom 54.6% were categorised as adherent. Less than half had controlled BP, of whom 59.8% were adherent. Two thirds (62.2%) of educated patients (n=111) were adherent, compared to 48.9% of patients without education (n=139) (p=0.036). Only 31.0% of 29 smokers were adherent, compared to 57.7% of 222 non-smokers (p=0.006). With borderline significance (p=0.054), 61.9% of 118 patients with co-morbidities reported adherence compared to 49.6% of 127 patients without any co-morbidity.

Conclusion: Both adherence and BP control were sub-optimal in this study population. Only half of the patients rated themselves as adherent to antihypertensive medication and only half of the patients' BP was controlled. Improving adherence in this hypertensive patient population can improve BP control, with further research needed to identify factors contributing to non-adherence and to inform relevant strategies to improve adherence and care.

12-7

Amiodarone monitoring in primary care: Pilot study

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Background: Amiodarone is an effective antiarrhythmic associated with significant adverse effects: thyroid toxicity, hepatotoxicity and pulmonary toxicity; estimated number needed to harm of 11. Since 2007, Scottish Intercollegiate Guidelines Network (SIGN) have provided clear guidance on use and monitoring, however national and local near patient testing guidance does not. It is unknown if patients are monitored in line with current guidance.

Methods: Retrospective audit of routine general practice data: August 2007 to April 2014, with data collected from 4 urban general practices, May 2014. Practices gave Cauldicott guardian approval for use of anonymised data. Patient data collected: age; gender; amiodarone dose and duration; baseline and ongoing monitoring in line with SIGN-94.

Results: 46 patients received amiodarone during the 7 year period with 10 of 35,243 registered patients currently received treatment. Patients were 71 ± 10 years old (Range 36 to 91 years), 65% male. Cardiology initiated 94% (43/46) of patients: 26% (13) post-operation atrial fibrillation; 41% (19) AF; 15% (7) paroxysmal atrial fibrillation and 18% (8) other arrhythmias. Baseline pulmonary function tests (PFTs), liver function tests (LFTs) and thyroid function tests (TFTs) were recorded for 13%, 52% and 43% of patients respectively with 6.5% receiving all tests. Six monthly LFT and TFT monitoring occurred in 33% and 24% of patients with 21% of patient receiving both tests. Of the 10 patients currently receiving amiodarone one received inappropriately for 12 months for post-operative atrial fibrillation and one patient had possible early signs of interstitial lung disease.

Conclusion: National guidance is poorly adhered to. Amiodarone's inclusion in local near patient testing guidance may help to improve patient safety.

12-8

Utilisation and impact of community-based antiplatelet therapy on outcomes in patients following Acute Coronary Syndrome in Scotland during 2012-2014

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Introduction

Acute Coronary Syndrome (ACS) is a life threatening condition that occurs when blood flow to the heart is reduced due to a partial or complete blockage of a coronary artery. The clinical presentations are classified as non ST-segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI) or Unstable Angina (UA). Adherence to antiplatelet therapy following ACS is important for the secondary prevention of atherothrombotic events. The aim is to assess the utilisation of traditional and novel antiplatelets following ACS and investigate the impact of community-based treatment on effectiveness and safety outcomes.

Methods

Secondary care hospital diagnoses from the Scottish Morbidity Records were used to identify a retrospective ACS cohort during 2012 to 2014 and were also used to retrieve prior and prospective healthcare events. Record linkage using a common patient-identifier was used to obtain community dispensed drug therapies from the Prescribing Information System. Information related to the dosage, unit and frequency of therapy was extracted from free-text dosage instructions.

Results

There were 17,186 patients (73.8% clopidogrel; 25.3% ticagrelor; 0.9% prasugrel) initiated to community-based therapy following discharge from hospital after an ACS. The mean age of patients initiated on clopidogrel was older (Mean=65.9 years; SD=13.5) than ticagrelor (Mean=62.7 years; SD=12.7) and prasugrel (Mean=58.9 years; SD=10.7). A greater proportion of males were initiated to therapy than females which was observed across all treatment groups (65.2% clopidogrel; 67.3% ticagrelor; 72.6% prasugrel). Prospective clinically relevant effectiveness and safety outcomes of these patients will be presented with comparisons between treatment groups, adjusted for any disparities in multimorbidities, adherence and persistence to therapy.

Conclusion

These findings will provide real-world evidence on the utilisation and clinical impact of different antiplatelet regimens in Scotland, considering the varying constraints of individuals with multimorbidity, adherence and persistence to this therapy.

12-9

STATINS USE IN PRIMARY CARE OF THE UNIFIED HEALTH SYSTEM (SUS) - BRAZIL

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Background: Several literature reviews have highlighted the benefits of using statins to prevent cardiac events in high risk patients as well as for secondary prevention, promoting their use on a global scale. Knowledge of the profile of medicines use in the real world is essential for improving health care and public policies. This study aims to characterize the use of statins in primary health care of the Unified Health System (SUS) in Brazil and evaluate associated patients factors.

Methods: This cross-sectional study is part of the Brazilian Research of Access, Use and Promotion of Rational Use of Drugs (PNAUM). Interviews were conducted with a representative national sample of patients in primary health care services in 2015. Defined variables were described with absolute and relative frequencies, using complex sample analysis. The Pearson chi-square test was used for group comparison. Association between statins use and sociodemographic and health condition variables was assessed by logistic regression. The quality of model was checked by the Hosmer-Lemeshow test.

Results: There were interviewed 6.511 medicines users. The prevalence of statins use was 9.4% (603). The average number of medicines used was 4.1 ± 3.1 per person. The most used statins were simvastatin (90.3% CI 95% 84.2-94.2), atorvastatin (4.7% CI 95% 1.7-12.4) and rosuvastatin (1.9% CI 95% 0.9-3.9). Noteworthy, rosuvastatin is not included in the national list of essential medicines. Statins use was significantly associated with age 45-64 (OR 2.49), white race (OR 1.40), metabolic disorders (OR 9.67), circulatory system diseases (OR 1.47) and polypharmacy - five or more drugs used (OR 9.35).

Conclusion: The average of medicines used per person and the association between polypharmacy and statins may be related to inappropriate use of drugs. This needs further evaluation as well as comparisons with other countries.

12-10

The effect of health care professional-led interventions to modify lifestyle in people with hypertension – a systematic review

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Background. About 0.9 billion people in the world have hypertension. The annual death rate due to hypertension increased by 51% from 1990 to 2015. The challenge is to provide an effective intervention, both pharmacological and nonpharmacological. Modifications of lifestyle are essential in decreasing blood pressure and lowering risk of cardiovascular disease.

AIM: To determine if health care professional-led interventions/recommendations on life style change are effective in lowering blood pressure in patients with hypertension.

Methods. A systematic literature review following PRISMA guidelines was carried out. We searched in PubMed and EMBASE. We included randomized controlled trials of life style interventions carried out by health care professionals (physician, nurse, pharmacist etc.). Papers were independently reviewed by two reviewers and were analyzed using Cochrane software Revman 5.2. Outcomes for the meta-analysis were systolic blood pressure (SBP), diastolic blood pressure (DBP) and number of patients under blood pressure (BP) control.

Results. A total of 27 randomized controlled trials and 5 cluster randomized trials with the recommendation on life style change like diet, smoking cessation, physical activity etc. were included. In the included studies total of 22,226 patients were randomized (age M=58,2), 49% of them were woman, 69,7% were already using antihypertensive medications. SBP decreased by 4.42 [95% CI -5.56, -3.28] comparing intervention group vs usual care group, DBP by 1.63 [95% CI -2.44, -0.83]. Overall, 56% of patients achieved BP control in intervention group vs 44% in usual care group, OR=1.87 [95% CI 1.51, 2.31]. In subgroup analysis, there were no differences on SBP between the studies with different intervention management or lengths.

Conclusion. Overall, interventions were effective and achieved almost 5 mmHg decrease of SBP. This may have a huge impact on preventing morbidity and mortality in hypertensive patients. Health care professionals should use more interventions to address life style modification.

13-1

Evaluation of health direct costs associated with the use of biosimilar and originator erythropoiesis stimulating agents (ESAs): An Italian, multi-Regional, population based study

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Background

Chronic kidney disease (CKD) is a growing public health issue worldwide. In Italy, the prevalence of CKD is 7.5% in men and 6.5% in women. The annual direct costs of management of patient on dialysis were estimated to be around € 30,000 for peritoneal dialysis and € 44,000 for haemodialysis. Erythropoiesis stimulating agents (ESA) biosimilars can allow around 30.0% saving of ESA purchase costs in CKD patients.

Methods

A population-based, retrospective, multicentre study was conducted during the years 2009–2014, using administrative databases of five regional centres of Italy. CKD incident ESA users with at least one year of treatment were identified and characterized. Annual mean direct costs related to ESA drugs, other concomitant drugs, hospitalizations, diagnostic tests and dialysis per incident CKD patient stratified by severity of CKD, type of ESA and year of treatment were calculated.

Results

The highest total costs were observed for dialysed patients, with crude estimates ranging from €20,715 in ESA biosimilar users to €35,176 in users of other ESAs still covered by patent. The cost for yearly ESA treatment represented 16.3% (€4,524) of total yearly direct costs of CKD management in stage 1-3. Such a proportion decreased to 11.9% (€3,842) in CKD 4-5 stage and to 6.7% (€5,913) of total costs in dialyzed patients. As compared to ESA reference product and other ESAs still covered by patent, using biosimilar guaranteed yearly economic saving for ESA treatment specifically equal to €906 and €604 in CKD 1-3 stage, €335 and €755 in CKD 4-5 stage, and €838 and € 616 in dialysed patients, respectively.

Conclusions

The management of CKD patients requires high costs especially in dialyzed patients. Using ESA biosimilars may save economic resources which are proportionally more significant in the early stages of the diseases.

13-2

FEDERAL PURCHASES OF THE INFLIXIMABE IN BRAZIL: AN ANALYSIS OF THE PERIOD 2007-2015

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In 2002, infliximab was included in the program of pharmaceutical assistance for treatment of rheumatoid arthritis in Brazilian Unified Health System (SUS). Subsequently, its indications were expanded for psoriatic arthritis, ankylosing spondylitis and Crohn's disease. Purchases of infliximab for use in the SUS were centralized by the Brazilian Ministry of Health (MoH) in 2010, but are also carried out by other federal agencies. In April/2015, CT-P13, the biosimilar of infliximab, was the first biological product approved in Brazil based on comparability to a reference product. The potential cost savings will play an important role in its introduction into the market. This study analyzed the purchasing profile of infliximab by Brazilian federal institutions considering quantities purchased, expenditures and pricing patterns. Methods: This exploratory study examined the federal purchases of infliximab (100mg-vials) from January/2007 to December/2015. Purchasing data was retrieved from the government procurement system (SIASG). We analyzed quantity, unit price, date of purchase, type of acquisition and purchase (regular procurement or health litigation), and purchasing agent. We calculate the weighted average unit price (WAUP) for each year. All prices were adjusted by the IPCA (Brazilian Pricing Index) to December/2015 to allow comparison. Results: There were 151 purchases in the period, corresponding to 1.099.046 units and overall spending of R\$1,597,322,702.00. The volume of purchases was small until 2010 but has increased significantly since then. The MoH was the main purchasing agent (99.1% of units). 97% of the units were purchased out-of-bid, 80.1% due to sole source and only 1.0% due to health litigation. The WAUP decreased progressively through the years (-46.2% from 2010), but prices are still high. Conclusions: High federal expenditures and the high unit price of infliximab point to the possibility of resource savings with the introduction of the biosimilar product in the Brazilian market.

13-3

Antineoplastic agents of greater impact on medicine expenditures in Brazil's National Cancer Institute

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Background: High drug prices for antineoplastic medicines are an obstacle for access to appropriate cancer care in many countries. This study examined the antineoplastic agents with greater impact on drug expenditures in Brazil's National Cancer Institute (INCA). **Methods:** Medicines' purchase data from January/2007 to December/2014, were extracted from the federal government procurement system (SIASG). Unit prices were deflated to December/2014 using the National Consumer Price Index and values were converted to US dollars according to purchasing power parity for 2014 as reported by the World Bank. A trend analysis of prices was performed. A 50% cut-off point of contracted annual spending identified antineoplastic agents with greater financial impact.

Results: During the period INCA spent 545,665,500 USD on medicines. Sixteen antineoplastic agents produced greater financial impact. Trastuzumab (L01XC03) (440mg vial) presented the major among total expenditures: 71 million USD (13%). Imatinib mesylate (L01XE01) (100 mg and 400 mg dosage forms) featured first in purchases during 2007 and 2008, reaching 8.8% of total expenditures. Docetaxel (L01CD02) (80 mg vial) appeared as third (3.4%), followed by rituximab (L01XC02) (in 500 mg vials) with 3.2% of total expenditures. These four items totaled 153 million USD in tender purchases and were procured directly from the patent holder during most of the period. Although there was a tendency towards reduction of purchase prices over time, discounts were observed only prior to the expiration of the patent or after price negotiation by the Ministry of Health in order to include drugs in therapeutic protocols.

Conclusions: Antineoplastic agents causing major financial impact on medicines expenditures should be the focus for price negotiations and price reduction strategies. Results have important consequences for public cancer medicines expenditures in Brazil, given the nationwide scope of the reference institution.

13-4

Comparing utilisation of subcutaneous biologics delivered through homecare services in a cohort of patients with rheumatic diseases

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Background

Patients with rheumatic diseases such as ankylosing spondylitis (AS), psoriatic arthritis (PsA) and rheumatoid arthritis (RA) unresponsive to conventional treatment can receive biologics. In the UK subcutaneous biologics are delivered to patients' homes by external healthcare providers commissioned by the National Health Service (NHS). This is the first study in a Scottish NHS Board comparing utilisation of these medicines.

Methods

A retrospective study was conducted using records from patients with AS, PsA and RA receiving subcutaneous biologics in the NHS Greater Glasgow and Clyde Health Board between 2012- 2015. These were linked to their primary care prescriptions, hospital admissions and death records. Discontinuation, persistence, Medication Refill Adherence (MRA) and Compliance Rate (CR) were evaluated.

Results

A total of 105 AS, 227 PsA and 419 patients with RA received subcutaneous biologics, with a median follow up of: 494(285-838) days AS; 544(280-831) PsA; and 529(284-867) RA. Discontinuation occurred in < 46% of patients in the three groups, of which 40-53% terminated. In patients reinitiating therapy (47-60%) 26% AS, 18% PsA and <4% with RA switched to another biologic.

Overall persistence slightly decreased from 88% at 6 months to 77% at 24 months.

Adherence was evaluated in 671 patients receiving their first biologic. AS patients had a median MRA 84% (55-95) and median CR 96.55% (87-104), whilst PsA and RA patients had MRAs 85%(51-98) and 82%(47-96) respectively, and both CRs of 97%(86-103).

Conclusion

Patients with three rheumatic diseases receiving subcutaneous biologics in a Scottish NHS Board had similar discontinuation rates. Persistence decreased over time and adherence to their first biologic was good.

Future research on evidence of infections in this cohort will give a better insight into the factors influencing drug utilisation.

13-5

Defining a population of castrate resistant prostate cancer (CRPC) patients using record linkage of routine healthcare datasets within Greater Glasgow & Clyde (NHS GGC)

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Background

The Cancer Medicines Outcome Programme (CMOP) aims to determine clinical and patient reported outcomes for patients receiving cancer medicines in the 'real world'. Abiraterone and enzalutamide are two systemic anti-cancer therapies licensed for men with metastatic castration resistant prostate cancer (MCRPC). There are challenges describing the prevalence of MCRPC accurately. The objective of this study within CMOP is to define our CRPC population who may be eligible for treatment.

Methods

Two methods will be deployed to ascertain the patient cohort: firstly, retrieval of prostate cancer figures through the local Cancer Audit Facilitator; secondly, electronic record linkage of routinely captured health datasets (Cancer Registry (SMR06), Prescribing Information Systems (PIS and Chemocare®), Operation/Procedure/Intervention (SMR01), death records from National Records for Scotland (NRS) and Scottish Clinical Information (SCI) store). This data will be compared for the period January 2012 to December 2015 via a secure local Safe Haven infrastructure to establish a complete patient cohort for subsequent investigation of treatment use and outcome.

Results

The results to be presented will include the number of patients diagnosed with prostate cancer and the number of patients who present with metastatic disease; generated through two methods. The patients prescribed abiraterone and enzalutamide identified via Chemocare® will also be assessed to identify if they are recorded in each methodology.

The number of patients with chemical castration (on Luteinising-Hormone Releasing Hormone analogues) and surgical castration (that have had an orchidectomy) who also have a rising prostate specific antigen (PSA) level will be captured via electronic linkage to estimate the CRPC population. This can be further compared to the total number of deaths recorded from prostate cancer.

Conclusions

Although the CRPC patient population is not routinely captured the use of electronic record linkage gives the opportunity to provide a best estimate of our population.

13-6

Comparing clinical trial populations to real world patients in the West of Scotland – experience in treatments for advanced (unresectable or metastatic) melanoma

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Background

Information about new medicines comes from clinical trials which can have strict entry criteria that may not be fully representative of the population who will use the medicine in clinical practice. Anecdotal experience in the Beatson West of Scotland Cancer Centre suggests that this can lead to different outcomes for patients utilising medication in the real world. The Cancer Medicines Outcomes Programme (CMOP) aims to evaluate the effectiveness of cancer medicines used in the real world to provide further information for clinicians and patients to use when making treatment decisions. A first step is to compare the demographics of patients participating in the pivotal trials with the local population utilising the medicine in a real world setting.

Method

Patients who commenced treatment, between January 2011 and December 2016, for advanced (unresectable or metastatic) melanoma with new immunotherapies such as ipilimumab, nivolumab or pembrolizumab or tyrosine-kinase inhibitors such as vemurafenib, dabrafenib or trametinib will be identified via the electronic prescribing system Chemocare®. Demographic data including gender, age and tumour stage at diagnosis will be recorded by searching patient records and electronic datasets. This will be compared with published demographic data from pivotal clinical trials and any differences identified.

Results

The results of approximately 350 treatment episodes are expected to be presented including details of any differences between the clinical trial patient cohorts and the population receiving treatment in the real world. Examination of data routinely captured electronically versus manual case note review will also be presented.

Conclusion

This comparison of baseline demographics is the initial step in identifying differences between how patients in the real world respond to medicines compared to those participating in clinical trials.

13-7

Utilization of biological drugs for the treatment of rheumatoid arthritis in Tuscany, Italy

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Background

Rheumatoid arthritis (RA) is a chronic progressive autoimmune disease that causes severe joint damage and functional impairment. Several biological drugs are currently available for treating RA.

Objectives

To describe the utilization of biological drugs for RA treatment of in Tuscany region.

Methods

Information recorded between 2012 and 2015 into the administrative database of Tuscany were used. Prevalent users (i.e. ≥ 1 dispensing) of certolizumab, golimumab, infliximab, etanercept, adalimumab, tocilizumab, anakinra, abatacept or rituximab were identified. Those without AR diagnosis (ICD9CM code "714" in hospital discharge or exemption from copayment records) preceding or concomitant the first dispensing of interest were excluded. All users with ≥ 1 year of look-back or ≤ 1 year of age were considered. New users were those without any dispensing of the drug of interest during the available look-back period. Incidence and prevalence of use among patients with RA were observed. Persistence (i.e. no treatment gap ≥ 90 days) was also observed at 1st, 2nd and 3rd year of treatment.

Results

Between 2012 and 2015, a total of 2,117 biological drug users with an RA diagnosis were identified. Among RA patients, prevalence of use of biologic drugs increased from 9.0% in 2012 to 10.1% in 2015. Adalimumab showed the highest prevalence of use, ranging from 3.7% in 2012 to 3.3% in 2015. Incidence of use increased from 1.0% to 1.2% during the study period. In 2015, the highest incidence of use was observed for abatacept (7.2‰). Tocilizumab, infliximab and abatacept showed the highest persistence that ranged between 49% (abatacept) to 56% (tocilizumab) among patients at 3rd year of treatment.

Conclusions

During the study period, an increasing proportion of patients with RA started a treatment with a biologic drug. Adalimumab, which can be self-injected subcutaneously, had the highest prevalence of use. However, infusion drugs showed the highest level of persistence.

13-8

Validation of the use of administrative data sources for the study of pharmacoutilization of cancer therapies

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Background

Infusive antineoplastics (IA) are administered in hospital settings: patient-level information on drug utilization is only partially captured by administrative healthcare databases. Moreover, administrative databases do not record indication of use. The evidence currently available about the use of rituximab (RIT) in real clinical practice is limited, particularly for oncoematologic indications. This study aimed to validate the quality of administrative data of the Tuscany region in Italy as a source for conducting drug utilization studies on cancer drugs, using RIT as a case study, and data collected by hospital pharmacy as a reference standard.

Methods

All patients 18+ with ≥ 1 RIT administration between 2011 and 2015 in the oncology or haematology units of the University Hospital of Siena were identified in the database of the hospital pharmacy (UHS). For each patient, information contained in UHS and the Regional Administrative Database of Tuscany (RAD) both contained the regional anonymized identification code, which allowed deterministic record linkage. The first administration of RIT recorded in UHS was the cohort entry date. We counted how many patients in UHS could also be found in RAD. The percentage of the dispensings recorded in UHS during the first 365 days after entry date that could be also found in RAD was also calculated.

Results

307 patients were found in UHS with a valid regional anonymized identification code. Among those, RAD identified at least one dispensation of RIT for 299 (97%). During the first year, 1758 dispensations were recorded in UHS for those patients, and 1249 among them could also be found in RAD (78.8%).

Conclusions

RAD is very reliable to identify patients treated with RIT, and almost 4 dispensations out of 5 can be found in RAD. More research is warranted to explore the determinants of discrepancies and validate proxies for indication.

14-1

First case of disinvestment using real-world evidence in Brazil; implications for the future

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Introduction: Beta-interferons are used as first-line therapy for relapsing-remitting multiple sclerosis in Brazil. In order to evaluate the possible inferiority of one of the beta-interferons available versus the others and support guideline update, we conducted an eleven-year (01/2000 to 12/2010) nationwide real-world performance assessment of the various beta-interferons available in Brazil using the Unified Health System (SUS) databases.

Methods: We assessed whether patients using subcutaneous beta-interferon switched treatment, relapsed or died (composite event) earlier than patients using intramuscular beta-interferons. Patients without dispensing registry longer than three months were censored. We used the Kaplan-Meier method to estimate the cumulative probability of persistence on initial treatment, and compared groups with Log-rank test. The influence of the different beta-interferons on outcomes was assessed with Cox proportional hazards analysis.

Results: 12,154 patients were included, the majority started treatment with subcutaneous beta-interferon-1a (45.7%), followed by subcutaneous beta-interferon-1b (27.7%) and by intramuscular beta-interferon (26.6%). 73.1% were women and the mean age was 38.93±11.34 years old. The group of patients who used intramuscular beta-interferon switched treatment, relapsed or died earlier (median 47 months; 95%CI 44-52) than patients using the subcutaneous beta-interferons (69 (95%CI 64-76) months for beta-interferon 1a and 73 (95%CI 66-84) months for beta-interferon 1b) ($p<0.0001$ for both comparisons). Accordingly, intramuscular beta-interferons were associated with a higher probability of an event (Hazard ratio - HR 1.38; 95%CI 1.29-1.48), while the use of the other beta-interferons had a protective effect (1a: HR 0.86; 95%CI 0.81-0.92; 1b: HR 0.89; 95%CI 0.83-0.95).

Conclusions: The inferiority of intramuscular beta-interferon found in the real-world corroborates findings from head-to-head studies and systematic reviews conducted by Cochrane and the National Commission for Technology Incorporation in SUS (CONITEC/Brazil). This result led to disinvestment in intramuscular beta-interferon in Brazil. This was the first case of a clinical guideline update using real-world evidence in Brazil.

14-3

Access to medicines in State of Minas Gerais - Brazil: analysis from different dimensions

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Background: To guarantee access to medicines considering its complexity, it is necessary to intervene in all its dimensions. In order to increase the access to medicines, was developed a plan in 2008 in a Brazil's State that created an Economic Incentive for the installation of public pharmacies. To evaluate the results of this intervention in access to medicines, in all its dimensions, in a comparative way between cities that has received State's Economic Incentive (SsEI) and cities that hasn't received.

Methods: A cross-sectional, exploratory, evaluative study, composed of information's survey in a representative sample of municipalities in the Brazil's State. Data were collected from July 2014 to May 2015. The values obtained with indicators for each dimension were multiplied by the weights calculated by the preferences and satisfaction of the users, in each dimension.

Results: A total of 1,080 users from 104 different municipalities were interviewed, of which 43 has received the SsEI. With a significant statistically difference, the users of the municipalities that has received the SsEI reported better conditions than the users of the other municipalities in four dimensions of access to medicines: availability (77.1% versus 61.4%), accommodation (93.7% versus 83.3%), economic accessibility (98.1% versus 97.0%) and acceptability (90.9% versus 81.5%). Only the geographic accessibility dimension was better evaluated by the users of the municipalities that hasn't received the SsEI when compared to the other municipalities (76.9% versus 73.0%). When applying the results of each dimension in the calculation of the single access's indicator to medicines, a total access of 86.2% was found for the users of municipalities that has received the SsEI and 79.6% for the other municipalities.

Conclusion: The results indicate greater access to medicines from the perspective of users in the municipalities that received the SsEI, even when the cities had low Human Development Index.

14-4

Description of Medicines Prices Websites in Five South American Countries

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Background: In order to facilitate the implementation of pharmaceutical pricing policies and research, a description of 6 web-based sources of information on medicines prices in 5 South American countries was conducted.

Methods: Information regarding characteristics of web sites, general features of information, and quality of price data was collected from the selected sites. Data sources described are the Brazilian Health Price Bank (BPS), the Brazilian Medicines Market Regulation Chamber (CMED), the Argentinean K@yros® website, the Peruvian Pharmaceutical Products Observatory (OPFP), the National Public Procurement Service of Ecuador (SERCOP) and the Drug Price Information System of Colombia (SISMED).

Results: Two websites published prices corresponding to the retail channel: K@yros® (Argentina) and OPFP (Peru). BPS (Brazil) and SISMED (Colombia) presented index prices. The Brazilian BPS weighted average price corresponds to the institutional channel, the corresponding Colombian presented the quarterly weighted average price of all national trades on pharmaceutical products. Three websites published the minimum or maximum prices as a reference for medicines public procurement. CMED (Brazil) gives both, maximum price for public procurement and maximum price for retail channel. These lists are updated monthly and are calculated from prices reported by the manufacturers. The Peruvian OPFP publishes a minimum price for public sector procurements without discriminating trademarks; it is calculated out of data from retail pharmacies. SERCOP (Ecuador) published unit prices for medicines that were offered in former procurement processes performed in the public sector.

Conclusions:

Web-based sources of information on medicines prices in South American countries are publicly available, hence encouraging transparency in the pharmaceutical sector. Data quality aspects and the source of price data are well described. If compared, prices should be adapted according to the corresponding setting.

14-5

Has Brazil abandoned the EM concept? Developments of the Brazilian National Essential Medicines List, lessons learnt and perspectives

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Background: The Brazilian National Essential Medicines List (EML) has been in process since 1964. From 2000 to 2012, six consecutive evidence-based editions were produced. In 2012, the government changed course to establish a new paradigm, substituting the essential medicines concept for medicines incorporation. Our objective is to report efforts to develop Brazil's national EML, policy changes over time, discussing results, challenges and perspectives.

Methods: Brazilian EML history and development process were collected from legislation, minutes, reports and legal ordinances, from 2000 to 2014. The number of medicines in the issues of the Brazilian EML and the WHO Model lists were analyzed. The Anatomical Therapeutic Chemical (ATC) system was used to classify listed medicines. Medicines were cross-referenced between Rename and the WHO Model List. Overlap between lists was verified and linear trends were plotted and compared.

Results: Type of membership, inclusion criteria, procedures, flow and the final list, as a product, varied greatly between work of the selection committees acting before 2012 and the country's new incorporation committee (Conitec). Three main characteristics were observed after the change: decision-making with a greater weight given to political and administrative stakeholders, the increasing trends in number of medicines over the years, and the decrease in use of WHO Model List as a reference, and the substitution of an essential medicines list review and update process by an incorporation decision process.

Conclusion: Although substantial efforts were made to produce and update the list, continuity of these efforts was abruptly severed by paradigm-changing legislation that turned the essential medicines concept upside down. Many challenges remain, first of which is adherence to the list by prescribers. The resolution of problems that influence list composition, such as health litigation, regulatory and market issues must be dealt with in the future.

14-6

Description of medicines public procurement websites for some Latin America countries

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Background: This study aims to describe the sources of information on medicines public procurement available in some Latin American countries, in order to facilitate the development of comparative studies and implementation of policies such as pharmaceutical pricing policies.

Methods: Description of the data sources regarding web sites features, general characteristics of information, and quality of medicines public procurement data.

Results: The sources of information described are Brazil's Health Price Bank (BPS/SIASG), the Chilecompra Public Procurement Website, the Procurement Website of the Mexican Social Security Institute (IMSS), the Panamacompra Public Procurement website, and the National Public Procurement Service of Ecuador (SERCOP). Whole five data sources belong to governmental entities such as ministries, public purchasing centers, or drug regulatory agencies. BPS from Brazil provide broad advantages regarding the three descriptive dimensions included in the study, each public institution complies its function of social control and surveillance of the public management, also benefit other sectors of society, which use the data for various queries and studies. Procurement data from open access websites brings accurately information for country expenditure and volume pharmaceutical estimations, comparing with other private sources.

Conclusions: The description carried out increases the transparency of information on medicines public procurement as input to contribute to the policy decision-making of Latin American governments regarding regional and country pharmaceutical procurement and negotiation process, recently reference price policies adopted, and other adjustments to pharmaceutical prices already regulated; the consumption of this information is valuable for the development of drug utilization research. Cross national studies implies further data validity efforts in order to guarantee accurately comparisons between Latin America countries, and to obtain regional expenditure and volume pharmaceutical estimations.

14-7

Electronic Prescription Data to Improve Primary Care Prescribing (EPIPP)

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Background

Scottish General Practitioners (GPs) have been provided feedback by National Health Service Health Boards on their prescribing cost and volume since the 1950s. Responding to feedback often required GPs to manually search patient records and complete audits. Since 2014, Health Boards have used patient-level prescription data to measure and feedback on Potentially Inappropriate Prescribing (PIP). The aim of this study was to evaluate the impact of feedback to practices of patient-level PIP data.

Method

Pragmatic, two-arm cluster randomised trial of feedback of patient-level PIP. All 235 general practices in one Health Board received the intervention. Practices were randomised to different PIP topics; either 'inappropriate asthma prescribing' (measured by prescription to a patient of (a) more than 12 short-acting bronchodilator inhalers per year and (b) long-acting bronchodilator inhalers without inhaled steroids) or 'potentially inappropriate use of urinary antimicrobials' (measured by prescription to a patient of more than 6 specified antimicrobial courses per year). Practices were sent feedback on three occasions in 2015-2016. Each feedback report contained background information on the topic and suggested actions, details of patients identified with PIP and summary prescribing data for each patient. For each arm the mean number of patients with PIP relating to that report at the time of the first feedback (July 2015) and 6 months after the last feedback (January 2017) will be compared with the practices in the other arm who have received feedback on the other PIP topic. Analysis will account for clustering of patients within GP practices.

Results

All GP practices were sent their allocated reports. Two practices in each group were lost to follow up. Statistical analysis is ongoing and will be completed by August 2017 (n=117 bronchodilator report and n=114 UTI antibiotic report).

Conclusions

This study will identify whether patient-level feedback of potentially inappropriate prescribing improves prescribing.

15-1

Economic evaluation of a physician-implemented, structured medication review screening tool in older hospitalised patients in Ireland

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Background: A recent, single-blind, cluster randomised controlled trial (RCT) conducted in an Irish hospital evaluating the screening tool of older person's prescriptions (STOPP) and screening tool to alert right treatment (START) criteria demonstrated positive outcomes in terms of reduction of adverse drug reactions (ADRs). The aim of this study was to examine the cost-effectiveness of physicians applying the STOPP/START criteria to unselected older hospitalised patients compared to usual hospital pharmaceutical care over a 13-month period.

Methods: Cost-effectiveness analysis alongside conventional outcome analysis in a cluster RCT. The trial was conducted in a tertiary referral hospital in the south of Ireland. The screening tool was applied to the medicines of intervention arm patients (n= 360). Control arm patients (n= 372) received usual care from the hospital medical team. Incremental cost-effectiveness was examined in terms of costs to the healthcare system and an outcome measure of ADRs during an inpatient hospital stay in 2011 and 2012. Uncertainty in the analysis was explored using a cost-effectiveness acceptability curve (CEAC).

Results: On average, the intervention arm was more costly but was also more effective. The associated incremental cost-effectiveness ratio (ICER) per ADR averted was €5,358 (95% Confidence intervals (CI) -€15,484, €26,018). The probability of the intervention being cost-effective at threshold values of €0, €1,000, €10,000 and €20,000 was 0.272, 0.319, 0.687 and 0.920 respectively.

Conclusion: Although physician-led implementation of the STOPP/START screening tool is more costly, it also proves more effective in reducing ADRs in older hospitalised patients. Such ADR reductions may potentially lead to significant savings and improved patient outcomes. Decision makers should consider the adoption of the STOPP/START criteria in routine hospital care.

15-2

The epidemiology of polypharmacy in older adults: a nationwide, longitudinal study of 1.7 million people over 3 years

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Background

The concurrent utilization of multiple drugs ('polypharmacy') has been extensively described in cross-sectional studies. However, evidence from prospective, longitudinal studies is scarce. We aimed to measure the prevalence of polypharmacy in older adults and its incidence over time.

Methods

We conducted a country-wide, longitudinal cohort study based on register data with national coverage in Sweden. All individuals aged ≥ 65 years and living in Sweden at baseline (1 November 2010) were included in the study population and followed-up until either death or the end of the study (20 December 2013). Monthly drug exposure was calculated based on the date of drug dispensing, the total amount dispensed to the patient, and the prescribed daily dose.

Results

A total of 1 742 336 individuals were included, accounting for 99.1% of the total number of older adults in Sweden. At baseline, the prevalence of polypharmacy (≥ 5 drugs) and excessive polypharmacy (≥ 10 drugs) was 44.6% and 11.9%, respectively. Among the 812 824 (46.6%) older adults who were free of polypharmacy at baseline, the incidence rate of polypharmacy was 19.9 per 100 person-years, ranging from 16.8% for individuals aged 65-74 years to 33.2% for those aged ≥ 95 years (adjusted HR= 1.49, 95%CI 1.42–1.56). The incidence rate for excessive polypharmacy (n=1 438 437) was 8.0 per 100 person-years. Older adults living in institution were more likely to be exposed to ≥ 10 drugs than those living in the community (adjusted OR= 1.12, 95%CI 1.09–1.14). However, institutionalization was found to be protective against developing both incident polypharmacy and incident excessive polypharmacy (HR= 0.79 and HR=0.86, $p<.001$, respectively).

Conclusion

Cross-sectional studies can only offer a truncated vision of polypharmacy at a single point in time. In a longitudinal approach, we show that incidence of polypharmacy is higher than previously reported, and continues to increase with age.

15-3

Quality assessment of pharmacotherapy in outpatients with chronic kidney disease in the Netherlands: a pilot study

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Background: In the Netherlands, an indicator set to assess prescribing quality in patients with chronic kidney disease (CKD) was lacking. Therefore, we recently developed and validated a set of prescribing quality indicators (PQI) for primary and secondary CKD care with the help of an expert panel (1). The aim of this pilot study was to apply these PQIs to assess the quality of pharmacotherapy in CKD patients in Dutch outpatient clinics and identify areas for improvement.

Methods: Between March 2015 and May 2016 data were collected over 12 consecutive months from patients with Stage 3-5 CKD seen at two academic nephrology departments, one in the north (n=566) and one in the west (n=901) of the Netherlands. Physical, laboratory and prescription data were extracted from the medical records. The PQIs used in the study assessed prescribing of antihypertensives, albuminuria lowering drugs, statins and phosphate binders and prescribing of potentially inappropriate drugs. For each PQI, the percentage receiving the appropriate or inappropriate pharmacotherapy was calculated.

Results: Both departments scored high on prescribing of antihypertensives in patients with high blood pressure (>81%). Two PQIs on prescribing of albuminuria lowering drugs and one on statins scored relatively low in both the departments (North: 61%, 49% and 49%; West: 52%, 39% and 41%). For potentially inappropriate drugs, both departments scored relatively high on prescribing of active vitamin D in patients with elevated calcium levels (17 and 29%, respectively).

Conclusion: We identified priority areas for improvement of pharmacotherapy in CKD outpatients, including underprescribing of albuminuria lowering drugs and statins and overprescribing of active vitamin D. This information is used in feedback to improve the treatment of these CKD patients.

1. Smits KP, et al. Development and initial validation of prescribing quality indicators for patients with chronic kidney disease. *Nephrol Dial Transplant*. 2016;31(11):1876-86.

15-4

Drug-drug interactions among old people with dementia

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Background

The prevalence of drug-related problems increases with age. One important cause is drug-drug interactions, which contribute to hospital admissions among elderly. Old people with dementia are particularly vulnerable. The aim of the present study was to assess the occurrence and characteristics of drug-drug interactions and to investigate associating factors among old people with dementia.

Methods

Medical records of people aged ≥65 years, with dementia or cognitive impairment that were admitted to two hospitals in Northern Sweden were reviewed. Information on medication use at the time of admission was collected. Drug-drug interactions judged as clinically relevant and requiring either dose adjustments or avoidance of concomitant use, were identified using the Janusmed interactions database. Interactions were further classified according to Stockleys interaction system.

Results

458 persons were included and a total of 401 drug-drug interactions were identified. 43.2% of the persons had at least one interaction. In 95.8% interactions were judged clinically relevant and to require dose adjustment, while in 4.2% of cases it was considered that the drug combination should be avoided. Pharmacodynamic interactions were the most frequently observed. The majority of interactions were classified as additive or synergistic. The following interactions were most frequently observed; furosemide – citalopram (n=35), acetylsalicylic acid – citalopram (n=32) and warfarin – acetaminophen (n=26). An association was found between the number of medications prescribed in the individual patient and the risk of one or more drug-drug interaction.

Conclusion

Clinically relevant drug-drug interactions are prevalent among old people with dementia living in Northern Sweden. To avoid drug-related problems, the risk of drug-drug interactions should be noticed, especially in present population. This is particularly important with increasing numbers of medications prescribed.

15-5

Electronic assessment of the anticholinergic exposure using the MARANTE scale

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Background: Anticholinergic medications are known to cause adverse effects in older adults. Methods exist to quantify the anticholinergic exposure, but seldom incorporate potency and the dosage spectrum. Our aim was to construct a new electronical method for quantifying the anticholinergic exposure based on the potency and dosages of medications, suitable for automated analysis of medication records.

Methods: From a systematic review (Duran's list, n=100), 41 medications with anticholinergic properties (currently used in Belgium by the oldest old) were matched with potency values and the dosage spectrum. Potency was divided no, low and high potency. For dosages, three reference values were selected (minimal, maintenance and maximal effective dosage), delimiting four dosage ranges in the dosage spectrum. We named this approach the Muscarinic Acetylcholinergic Receptor ANTagonist Exposure (MARANTE) scale, developed to be validated as a robust method for the estimation of the anticholinergic exposure.

Results: Potency and dosage information was collected for 41 active substances (69, including other routes of administration, enantiomers, or combinations). All reference values were based on information from authoritative sources, and then reviewed and completed by an expert panel. The MARANTE scale was tested in existing cohorts of older adults and made available on an interactive platform at <https://secureramit.ugent.be/marante>. Clinicians can enter medication data (dosages, and product name) from an individual medication chart to obtain the total anticholinergic exposure in patients. For researchers, the website could serve as a discussion platform.

Conclusion: Automated analyses of medication charts for the estimation of the anticholinergic exposure (based on identification of anticholinergics, their potency and their dosages) is feasible. Further completion of anticholinergics, and reviewing of current dosages and potency values are still required to ensure transferability to other medication markets. Future applications could indicate potential alternatives to anticholinergic medications.

15-6

LIMITATIONS IN RECORDING POLYPHARMACY AMONG OLDER PEOPLE IN GREECE

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Background

Polypharmacy among older people has not been studied in Greece, mainly because of restrictions in availability of medical records. The aim of this study was to explore medication use and polypharmacy among older people in Greece, using the new Electronic Health Records that have been applied in pharmacy stores during the last years.

Methods

The sample was collected using data of the new Electronic Health Records in a pharmacy store of western Thessaloniki. All prescriptions concerning patients older than 65 years and dispensed during November 2016 were used. Medications sold without prescription were not included in the study.

Results

101 patients were older than 65 years and met the criteria of the study. 30 of them were older than 80 years. Polypharmacy (≥ 5 medications) was observed in 28% of patients older than 65 years and in 30% of patients older than 80 years. The most commonly used medicines by patients older than 65 years were antihypertensive, antidiabetic, anticoagulant / antiplatelet, hypolipidemic and antiulcer medicines. The most commonly used medicines by patients older than 80 years were antihypertensive, anticoagulant / antiplatelet, hypolipidemic and antiulcer medicines. Excessive polypharmacy (≥ 10 medications) was observed only in 3 patients. Pain killers (like aspirin, paracetamol and ibuprofen) and vitamins were not included in prescriptions, as they are not reimbursed by the National Health System (NHS). Even medicines reimbursed by the NHS were not included in prescriptions, either because they are cheap and can be bought without prescription or because patients can't afford going to doctor, due to the financial crisis.

Conclusion

Polypharmacy among older people in Greece is not so common as in other European countries. This finding may be attributed to limitations in the Electronic Health Records kept by the NHS, and to restrictions in reimbursement due to the financial crisis in Greece.

15-7

Sustainable Implementation of Polypharmacy reviews as part of integrated care at Scale

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Medication is the commonest form of intervention to prevent disease or slow disease progression. There remains the mismatch between prescribing guidelines for specific medical conditions and the range of clinical complexity found in individual adults with multiple morbidities. The resulting polypharmacy (use of multiple medicines) can be both appropriate and inappropriate.

NHS Scotland developed, designed and implemented national policy to consider the patient pathway and the flow of work needed to be undertaken in clinical practice to address appropriate management of Polypharmacy. Implementation across all 14 health boards serving a population of 5.5 million people in Scotland utilised Kotter's 8 steps for implementation of change supported by clinical and policy leadership, economic data and clinical outcome data.

NHS Scotland has provided leadership for a European work plan. SIMPATHY has benchmarked European strategies to address polypharmacy and through in-depth case studies in 10 EU countries, is developing strategies and tools to support innovation in polypharmacy and adherence management across Europe.

Synthesis of the findings from application of change management tools such as Kotter, PESTEL and SWOT, together with the case studies serve to inform further innovation. Work undertaken in the Scottish programme has been used to develop an economic tool that may be used by other countries to explore the economic benefits of a national polypharmacy management programme.

Key principles of Kotter influenced the successful implementation of national policy for management of polypharmacy in Scotland. It was identified that policy and clinical leadership were essential drivers along with a policy change that supported implementation in the service.

Lessons learned from national policy implementation in Scotland and from local programmes in other EU countries, including facilitators and barriers, together with key features of an economic tool will inform innovation of integrated care at a policy level.

16-1

Signs of deprescribing in nursing home residents evolving towards worse physical and mental health

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Background: Medication use is high among nursing home (NH) residents, but there is a lack of longitudinal studies, exploring the medication use associated to the evolution of the physical and mental health, over time. The aim of this study is to describe the medication use two years after entering a NH in relation with the evolution of the physical and mental health.

Methods: Data from the observational prospective Ageing@NH study, based on a inception cohort of newly admitted residents at NHs (65+) was used, selecting those consenting and with medication chart available. Information about socio-demographic, functional and mental characteristics, as well as medication use, was collected at baseline, year1 and year2.

Results: Medication chart was available for n=741 at baseline (mean age 83.8, 66% female), and for n=342 residents in year2. The mean number of total medications increased from 8.9 to 10.1 ($p < 0.001$). Polypharmacy (≥ 5 medications) was high, with an increase in extreme polypharmacy (≥ 10 medications) from 23% to 32%. The functional dependency ($ADL \geq 17$), increased from baseline to year2 (from 29% to 40%, $p < 0.001$), and the same trend was observed for dementia (from 26% to 46%, $p < 0.001$). In year2, cardiovascular medication use was 89% in those with stable low dependency, 79% in those evolving from low to high dependency ($p = .053$), and 77% in those with stable high dependency ($p = .012$). Mean number of total medications in year2, was 10 in those with stable no dementia, and lower in those evolving from no to dementia (7.4, $p < 0.001$) and in those with stable dementia (6.9, $p < 0.001$). This was particularly observed in pain and sleeping medications.

Conclusion: Although medication use was high, signs of deprescribing were noted when physical and mental health of the residents declined.

16-2

Opioid maintenance therapy in France: high-dosage buprenorphine still predominant despite a high increase in methadone use: results from the 2009-2015 UTOPIA study

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Background: Methadone (MTD) and high-dosage buprenorphine (HDB) have been approved in France as opioid maintenance treatments (OMT) for twenty years. Since then, new formulations have appeared, and changes occurred in prescription and delivery conditions. We sought to describe the changes in OMT prevalent use since 2009.

Methods: Yearly repeated cross-sectional study (2009-2015) on quasi-exhaustive data from the French National Health Insurance database. For each year considered, all affiliates to the general scheme were included; an affiliate with ≥ 1 OMT reimbursement in the year was considered an OMT prevalent user.

Results: OMT prevalent users constantly represented 0.3% of affiliates whichever the year, corresponding to around 150,000 of the general scheme affiliates (49 to 53M). Sex ratio was stable (77% of men); median age increased from 35 to 39 years old. Main OMT in patients was HDB whatever the year, despite its use decreased from 2009 to 2015 (77.6% to 67.7% of patients). Among HDB users, 3,921 (3.5%) used HDB/naloxone in 2012 (year of marketing), and 7,248 (6.8%) in 2015. MTD use conversely increased from 2009 to 2015 (25.4% vs. 34.2% of OMT users); the deep decrease of MTD syrup use (88.7% to 49.8%) was counterbalanced by a high increase of capsule use made available since 2008 (27.7% to 63.8%). Median average daily doses rose from 6.8 to 7.7 mg/d for HDB and decreased from 46.6 to 44.4 mg/d for MTD. Patients proportion with severe chronic diseases increased from 52.3 to 61.7% and from 40.9 to 46.7% for MTD and HDB users, respectively. Interestingly, prevalence of HIV, hepatitis B or C, and depression decreased in the population over the study period.

Conclusion: Although HDB keeps being the main used OMT, MTD use increased markedly. The increase in OMT users with severe comorbidities could indicate marginal populations have been better reached for treatment.

16-3

Follow-up of patients who start with a benzodiazepine in general practice: prevalence and reasons for guideline non-adherence

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Background

The use of benzodiazepines should be limited to short courses for acutely distressed patients. In the Netherlands, guidelines recommend that, in case a patient receives a first prescription for benzodiazepines, the general practitioner (GP) contacts the patient within two weeks. As part of the Medication Safety study requested by the Dutch Ministry of Health and Welfare, the aim of this study was: 1) to determine the proportion starters who, after a first benzodiazepine prescription, had a follow-up consultation within two weeks; 2) to explore reasons for not following the recommendation.

Methods

Electronic patient records were used from 185 general practices from NIVEL Primary Care Database. Per practice, the proportion of first-time users of benzodiazepines with a follow up within two weeks was calculated as a : 1) proportion of all starters and 2) proportion of starters who also received a second prescription. Questionnaires were sent to participating general practices to capture possible reasons for not following the recommendations.

Results

Three quarters of the GPs (74%) knew the recommendation. The median percentage of patients per practice for whom this recommendation is followed, is 30% for all starters. However, only 15% of all patients receives a second prescription; the median percentage of patients per practice for whom this recommendation is followed then is 70%. Large variation between practices exists (43%-82%). Not prescribing follow-up prescriptions is also the most frequently mentioned reason not to follow the recommendation (74% of GPs), followed by “the patient previously used benzodiazepines” (31%), patient is seen by a medical specialist (20%) or the nurse practitioner (20%).

Conclusion

GPs are reluctant to prescribe a second prescription for benzodiazepines. When prescribing a second prescription, the recommendation to have a follow-up with the patients is followed in the majority of patients. Still, the large practice variation suggests room for improvement.

16-4

BURDEN OF DISEASE, HEALTHCARE PATHWAYS AND COSTS OF MULTIPLE SCLEROSIS THROUGH ITALIAN REAL-WORLD DATA ON 10 MILLION INHABITANTS

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Objectives: To estimate the prevalence of multiple sclerosis (MS) in Italy and to describe the drug choices in the real clinical practice and related costs for National Health Service.

Methods: A descriptive analysis of real-world data collected in the ARNO Observatory database, covering >10 million Italian inhabitants was performed. A cohort of patients affected by MS were selected through the presence in the 2013 of: the specific exemption code, or at least one hospitalization for MS, or at least one prescription of Disease-Modifying-Drugs. The prevalence of disease was estimated in the accrual year and patients were grouped according to the therapeutic choice into: “no-treatment”, “1st-line-treatment” and “2nd-line-treatment”. Each subject was followed in the subsequent year and the following outcomes were measured: therapeutic switches, healthcare utilization and average cost per patient.

Results: A cohort of 14,971 patients affected by MS, with a prevalence of 144 per 100,000 inhabitants, was selected (69.2% women, mean age 47 years old). Out of these, 9,522 patients (63.8%) had “no-treatment”, 4,783 (32.1%) were in “1st-line-treatment” and 612 (4.1%) in “2nd-line-treatment”.

During the follow-up, 7.3% of patients in “no-treatment” started a therapy, and 2.9% of patients in “1st-line-treatment” switched to “2nd-line-treatment”: among these, 97% switched to fingolimod and 3% to natalizumab. Through the follow-up, 29.3% of “no-treatment”, 22.5% of “1st-line treatment” and 40.7% of “2nd-line treatment” were hospital admitted.

In the 1-year costs analysis, pharmaceutical expenditure was the main item (64.3% of total expenditure), followed by hospitalization (21.4%) and ambulatory visits (12.6%). The average total cost per patient was 16,676€ for subjects in “2nd-line-treatment”, 8,883€ for those in “1st-line-treatment and 2,786€ for those in “no-treatment”.

Conclusions: This study provided real-world data of MS in Italy. Our findings, in line with epidemiological studies, depict the actual burden of MS in Italy with related healthcare utilization and costs.

16-5

Changing patterns of meprobamate-containing combination analgesic prescribing in South Africa

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Background: Meprobamate is an ingredient of several combination (or polycomponent) analgesics in South Africa, although meprobamate is no longer available in many other countries. Stricter controls for meprobamate-containing analgesics were considered in South Africa, but were not implemented. The primary aim of the study was to evaluate the prescribing patterns of products in ATC group N02B using electronic medication databases to determine the extent of usage of these combination analgesics.

Methods: Retrospective, cross-sectional drug utilisation studies were conducted on 2011 and 2015 South African dispensing databases. Records for “Other analgesics and antipyretics” (ATC group N02B) were analysed. Diagnoses codes were not complete and no clinical information was available.

Results: A total of 70 145 products in ATC group N02B were prescribed in 2011, of which 62.10% were analgesic combinations, and 20 326 products (28.98%) meprobamate-containing analgesics. In a further study, 2 292 522 products in ATC group N02B were prescribed in 2015, with anilides (N02BE) also the most often prescribed class. Paracetamol combinations (excluding psycholeptics) contributed to 77.50% of all products, and meprobamate-containing analgesics to 11.73% of products prescribed in ATC group N02B. The percentage of meprobamate-containing analgesics was therefore lower than in 2011. Fewer different trade names of meprobamate-containing combination analgesics were prescribed in 2015. In 2011, 22 different trade names were prescribed compared to only 13 in 2015. No new generic equivalents containing meprobamate have been introduced onto the South African market since the 2011 study. Tablet formulations remained the most often prescribed dosage form in both studies (86.35% in 2011 versus 85.06% in 2015).

Conclusion: Combination analgesics containing meprobamate are widely prescribed in South Africa and is effective, despite their potential for misuse and abuse. It seems that the prescribing of meprobamate-containing analgesics in South Africa is on the decline, but further studies are recommended.

16-6

Opioid prescribing patterns in South Africa: A database study

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Background: Tramadol was the most often prescribed opioid in a South African study conducted on 2011 data of a medical insurance scheme database. The primary aim of this study was to analyse the prescribing patterns of opioids dispensed by community pharmacies to determine if opioid prescribing patterns were similar if different prescriber and dispensing databases were used.

Methods: A retrospective, cross-sectional drug utilisation study was conducted on a 2013 pharmacy dispensing database in South Africa. All records for ATC subgroup N02A were analysed.

Results: A total of 212 527 opioids were dispensed to 105 118 patients at a total cost of R30 227 819.83 (average cost of R142.23 per product). Twelve different active ingredients or active ingredient combinations were prescribed. Tramadol, an atypical opioid, in combination with paracetamol accounted for 71.90% of products, followed by tramadol alone (22.74% of products). These two products therefore accounted for 94.64% of all the products dispensed in ATC subgroup N02A. The originator product of the combination of tramadol and paracetamol accounted for 90.08% of products dispensed, with only 2.00% generic prescribing. Oxycodone (N02AA05, 1.99%) and fentanyl (N02AB03, 1.10%) were the only other opioids dispensed that accounted for more than 1% of the total number of opioids dispensed. In the 2013 study, all the prescriptions were dispensed by community pharmacies. In the 2011 study on a medical insurance scheme database, most prescriptions for opioids were issued by private hospitals (62.89%), followed by pharmacies (24.42%) and general medical practices (12.16%). If only pharmacies are considered, 94.54% of prescriptions were for tramadol or the combination of tramadol and paracetamol (67.59% for tramadol in combination with paracetamol, and 26.95% for tramadol alone).

Conclusions: The dispensing patterns of opioids by community pharmacies were nearly identical in the community pharmacy and medical insurance scheme studies, with tramadol dominating opioid prescribing.

16-7

Consumption of anxiolytics and antidepressants in Serbia

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Background: The consumption of medicines has an impact on the medical, social and economic outcomes of treatment and includes marketing, distribution, prescription and use of drugs in the community. Medicines and Medical Devices Agency of Serbia (ALIMS) collects data on trade and consumption of medicines, in accordance with regulations, which regulate the field of medicines in the Republic of Serbia.

Method: Data on total sales in 2015, obtained from the holders of the marketing authorization are process using the ATC/DDD methodology recommended by the World Health Organization (WHO). The number of defined daily doses per 1000 inhabitants per day (DID) was used as indicator.

Results: In 2015 medicines that act on the nervous system are in third place in relation to the total consumption of drugs, with about 185,36DID, which represents 11.52% of the total consumption of drugs. In the reporting period, the group of drugs that act on the nervous system emphasizes the consumption of anxiolytics (107,78DID) and antidepressants (26,131DID). In the consumption of anxiolytics a leading position were bromazepam (40,36DID), diazepam (27,33DID) and lorazepam (22,40DID). The consumption of antidepressants most notable were medicines belonging to the group of selective serotonin reuptake inhibitors (SSRIs): sertraline (8,20DID), escitalopram (4,388DID), paroxetine (4,08DID), fluoxetine (2,30DID).

Conclusion: At the global level, in the context of mental disorders the highest prevalence of morbidity of depression and anxiety. Representation of anxiolytics and antidepressants in the consumption of medicines that act on the nervous system in Serbia also indicates that. Further qualitative research which should included the necessary parameters for the analysis of rational use of these medicines, will allow to identify the factors that affect the excessive use of these medicines as well as the evaluation of pharmacotherapeutic attitudes and prescription habits in practice.

Keywords: consumption anxiolytics, antidepressants, Daily Defined Doses, ATC/DDD

16-8

Change in medicine utilisation patterns for methylphenidate and atomoxetine in the South African private health sector from 2005 to 2013

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Background:

There is a marked paucity of data on the geographical ADHD treatment patterns in children. The aim of this study was to determine and describe the prescribing trends of methylphenidate and atomoxetine in children under the age of 18 years residing in the Western Cape Province of South Africa.

Methods:

This study followed a longitudinal design. A retrospective, descriptive, drug utilisation review was conducted by analysing medicine claims data for 1 January 2005 to 31 December 2013. The total number of patients, and total and average number of yearly prescriptions per patient was used as the drug utilisation metrics. Changes in the annual number of methylphenidate and atomoxetine prescriptions per patient per year were modelled over time by fitting a repeated measures Poisson regression model using the generalised estimating equations procedure in SPSS (IBM Corp., 2013). Pairwise comparisons were adjusted for multiple comparisons using the Bonferroni correction. The results were considered statistically significantly if $p \leq 0.05$.

Results:

A total of 2516 patients (male:female ratio 3.5:1) received ADHD treatment over the study period, with a 0.29% increase from 2005 to 2013. Children ≤ 6 years increased by 6% from 2005 to 2013. Prescriptions for ADHD treatment increased by 0.46% overall from 2005 to 2013 ($p < 0.001$), with that for methylphenidate and atomoxetine increasing by 0.36% and 3.15%, respectively. The average number of yearly methylphenidate prescriptions per patient increased from 3.96 ± 2.92 (95% CI, 3.69-4.23) in 2005 to 4.38 ± 2.85 (95% CI, 4.14-4.61) in 2013 (Cohen's $d=0.14$), and that for atomoxetine from 2.58 ± 1.86 (95% CI, 1.80-3.37) in 2005 to 4.85 ± 3.66 (95% CI, 3.84-5.86) in 2013 (Cohen's $d=0.62$).

Conclusion:

This preliminary study can lead to future studies on the influence of geographical area on the prescribing patterns of methylphenidate and atomoxetine.

17-1

Patient adherence to treatment for acute coronary syndrome in Vietnam: A prospective observational study.

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BACKGROUND

Long-term benefits of secondary prevention medications in acute coronary syndrome are proven. We aimed to determine the extent of patient adherence to treatment for acute coronary syndrome in the first six months after discharge from hospital and to identify factors associated with adherence.

METHODS

We conducted a prospective observational study on patients with a discharge diagnosis of acute coronary syndrome in two public hospitals in Vietnam. Adherence was measured using the Eight-item Morisky Medication Adherence Scale-8 (MMAS-8) at one, three, and six months after discharge. We defined adherence as returning for their scheduled outpatient appointments, using the most recent prescribed medications and having MMAS-8 scores of >5 at the follow-ups. Patient characteristics, illness perception (Brief Illness Perception Questionnaire, BIPQ), and medicine beliefs (Beliefs about Medicines Questionnaire, BMQ) were measured during hospitalization. Logistic regression was used to identify factors associated with six-month adherence.

RESULTS

Overall, 95 patients were included, median (interquartile range) age 64 (58; 79) years, and 56.8% males. Patient adherence at one, three, and six months after discharge were 83.2%, 80.0%, and 76.8%, respectively (Cochran Q test $p=0.354$). Factors associated with adherence were BIPQ 1 - Patient perception of consequences of the illness (OR 1.23, 95% CI 1.01-1.50), BIPQ 3 - Patient perception of personal control of the illness (OR 0.72, 95% CI 0.54-0.96), BMQ Specific Necessity - Patient beliefs about the necessity of prescribed medicines (OR 1.21, 95% CI 1.04-1.40), BMQ General Overuse - Patient beliefs about physicians' overuse of medicines as a whole (OR 0.76, 95% CI 0.63-0.93), and patient adherence at one-month (OR 7.50, 95% CI 1.69-33.35) and three-month (OR 11.56, 95% CI 2.98-44.77) follow-ups.

CONCLUSIONS

Adherence to treatment among patients with acute coronary syndrome in Vietnam was relatively high and stable over time, but there is still room for improvement with appropriate interventions.

17-2

The proportion of patients covered (PPC) method

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Background

Survival analyses are often used to study drug persistence. However, by only considering the first treatment episode, they underestimate the population in treatment at a given time. The proportion of patients covered (PPC) measures the proportion of initiating patients covered by treatment on a given day given their survival. However, one limitation is that it does not differentiate between old and new treatment episodes. In this study, we demonstrate how the PCC method is complementary to drug survival analyses when studying drug persistence.

Methods

Using prescription data, we identified new users of hormone replacement therapy (HRT), statins, selective serotonin reuptake inhibitors (SSRIs), and ibuprofen during 2010-2012. Each individual was followed up for three years. We applied the PPC and survival analysis for each drug class, allowing treatment gaps varying from 60 to 180 days (grace period).

Results

For statins, the PPC method estimated 60% of patients alive were covered by treatment after three years, while the survival analysis estimated 40% of patients were still in continuous treatment after three years, showing that 20% of statin users stopped initial treatment, but reinitiated subsequently. The survival estimates were dependent on the grace period applied (estimates varied from 30% to 55%) and approached the PPC estimates as the grace period increased. The difference in estimates was more pronounced for HRT and statins and less pronounced for SSRIs and ibuprofen.

Conclusion

While the PPC method estimates the proportion of patients alive covered by treatment on a given day, the drug survival analysis estimates the proportion of patients who did not yet experience a treatment break. In a complementary manner, the two methods provide information on the population in treatment at a given time, which may be useful in studies of drug persistence.

17-4

Lower risk of cardiovascular disease with higher refill adherence to lipid-lowering therapy in patients with type 2 diabetes

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Background

Lipid-lowering therapy (LLT) has shown to reduce the risk of cardiovascular disease (CVD) in patients with type 2 diabetes (T2D). The aim of this study was to analyze the risk of CVD in relation to refill adherence level in patients with T2D initiating LLT as primary or secondary prevention.

Methods

Patients ≥ 18 years, registered with T2D in the Swedish National Diabetes Register, who initiated LLT between 1 Jan 2007 and 31 Dec 2010 were identified using data from the Swedish Prescribed Drug Register. Patients with CVD prior to inclusion were defined as receiving LLT as secondary prevention; otherwise patients received primary prevention. Refill adherence was estimated by the medication possession ratio (MPR) during an 18-month exposure period following inclusion. MPR represent the proportion of days with LLT at hand and was divided into five levels; 0-20%, 21-40%, 41-60%, 61-80% and 81-100%. Risk of CVD was analyzed by MPR level from the day after the exposure period until migration, CVD, death, or 31 Dec 2013 using Cox proportional hazard regression adjusting for concurrent medicines, socioeconomic and clinical factors.

Results

In total, 86568 patients were included, 80% were born in Sweden and 57% were men. Mean age was 63 years and average diabetes duration 5 years. Mean HbA1c was 54 mmol/mol and average BMI was 30. Mean MPR was 77% in primary prevention (n=74909) and 83% in secondary prevention (n=11659). Compared to patients with MPR 81-100%, hazard ratios for CVD increased with lower MPR level, from 1.33 to 2.36 ($p < 0.001$) for primary prevention, and from 1.19 to 1.58 ($p < 0.001$) for secondary prevention.

Conclusion

The risk of CVD increased with lower refill adherence to LLT in primary and secondary prevention patients with T2D. This indicates that a high level of adherence to LLT is important to optimize the cardiovascular prevention in T2D

17-5

Relationship of Inhaler Adherence to Clinical Outcomes in Chronic Obstructive Pulmonary Disease

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Background

Adherence to maintenance inhaled therapy in Chronic Obstructive Pulmonary Disease (COPD) is known to be suboptimal. We examined the relationship between inhaler adherence and clinical outcomes in a cohort of COPD patients using a novel Inhaler Compliance Assessment Device (INCATM).

Methods

Two hundred and twenty-seven COPD patients hospitalised with an acute exacerbation of COPD and prescribed Salmeterol/Fluticasone maintenance therapy were recruited. Patients were provided with an INCA-enabled inhaler on discharge for three months of use. INCATM is an audio recording device that is attached to a Dry Powder Diskus Inhaler (DPI) and provides an objective assessment of both the pattern and timing of inhaler use (Attempted Adherence), and of errors in inhaler technique. Baseline demographic, medical and social data was collected. Patients also completed cognitive assessment. Any adverse clinical outcome (hospitalisation or Death) in the subsequent 12 months was recorded. The relationship between adherence and clinical outcomes was examined using regression analysis.

Results

Adherence data was available for 195 patients. The mean Attempted Adherence over the study period was 50.2(31.6)%. More than 50% of recordings contained errors in inhaler technique. Two-thirds had an adverse clinical event at 12 months. In all, the cohort experienced 300 admissions accounting for more than 3000 hospital bed days, one-fifth died.

On multivariate analysis, adjusting for disease severity, co-morbidity, cognition and previous exacerbation history, those with high Attempted Adherence, $\geq 60\%$, were significantly less likely to have an adverse clinical event, $p=0.03$, and had lower bed occupancy, $p=0.02$, at one year. The probability of an adverse event was reduced by one-third in this cohort when compared to those with poor adherence, Hazard Ratio 0.63 (0.41 - 0.95), $p=0.03$.

Conclusion

Poor adherence to maintenance inhaled therapy results in increased adverse clinical outcomes and higher healthcare use amongst patients with COPD.

17-6

Comparison of one-year non-persistence rates with dabigatran or rivaroxaban versus vitamin K antagonists in newly treated atrial fibrillation patients aged 75 and over: results from the French nationwide healthcare databases.

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Background: As a more convenient alternative to vitamin K antagonists (VKAs), Direct Oral Anticoagulants (DOACs) are expected to improve the OAC underuse observed with VKA in nonvalvular atrial fibrillation (nv-AF).

Objectives: To compare one-year non-persistence rates with dabigatran or rivaroxaban versus VKA in newly treated nv-AF patients aged 75 and over.

Methods: Using data from the French National Healthcare databases (Régime Général, around 50 million beneficiaries), we conducted a cohort study comprising nv-AF patients initiating dabigatran (N=6,010), rivaroxaban (N=5,998) or VKA (N=8,163). Treatment discontinuation was defined as a switch between OAC classes or a 60-day gap with no medication coverage, with the additional criterion of no reimbursement for INR monitoring during this gap for VKA patients. Considering death as a competing risk (CR) then death and switch from index OAC class to another OAC class as CRs of treatment discontinuation, differences between one-year discontinuation rates were used to compare each DOAC versus VKA. 95% confidence intervals (CIs) were estimated via bootstrapping. Baseline patient characteristics (demographics, comorbidities, comedications) were adjusted using inverse probability of treatment weighting using the propensity score.

Results: Considering death as a CR, adjusted one-year discontinuation rates were higher for dabigatran than for VKA new users (21.7% vs 17.4%; difference, 4.3% [95% CI, 3.2 to 5.5]) and for rivaroxaban versus VKA new users (21.8% vs 17.5%; 4.3% [3.1 to 5.5]). Comparable results were observed when considering both death and switch between OAC classes as CRs: dabigatran vs VKA: 36.8% vs 26.2%; difference, 10.6% [95% CI, 9.2 to 11.9]; rivaroxaban vs VKA: 32.9% vs 26.3%; difference, 6.6% [95% CI, 5.2 to 8.0].

Conclusions: Results from this nationwide cohort study using a competing risk analysis show high non-persistence levels with all OACs and suggest better persistence with VKAs versus DOACs in nv-AF patients aged 75 and over.

18-1

Utilization patterns of gonadotropins among women in the Lazio Region, Italy.

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Background.

The gonadotropins play a major role in the assisted reproductive techniques. Follitropin (FSH) is indicated to stimulate ovulation and is reimbursed by Italian NHS in women up to 45 years. The availability of different types of FSH (recombinant or extractive), the introduction of biosimilar and the fixed combination of FSH with lutropin (LH), fuel the complexity of treatment choices despite evidence suggest similar efficacy and safety between different formulations. This study aimed to evaluate the utilization patterns of gonadotropins in current practice.

Methods.

Gonadotropins prescriptions (ATC G03GA) referred to women between 20 and 45 years, were selected from pharmacy claims data (2008-2015) of the Lazio region. Temporal trend, consumption for age classes and costs were described.

Result.

A cohort of 220,327 gonadotropins' prescriptions corresponding to 32,643 women was selected. The majority of prescriptions (45.4%) were recombinant FSH (rFSH), followed by menotropin (hMG) and recombinant LH (rLH), 20.8% and 11.2%, respectively. Prescription of extractive FSH (eFSH) was residual (6.1%). Temporal trends of prescription for FSH and hMG were stable over time, while eFSH was decreasing. An increased constant trend of rLH was observed over years (CAGR=14%), arriving to 17.3% in 2015. In 2015, a mean of 2.3 prescriptions per women corresponding to a mean of 48.4 DDDs was observed. Women aged over 35 had a higher use of gonadotropins compared to younger classes. Expenditure trend increased over years passing from 6,4 to 8,6 million euros, with rFSH representing the 70% of the gonadotropins expenditure (eFSH accounted to 4%).

Conclusion.

Despite available evidence documented similar efficacy and safety between different FSH formulations, the routine practice showed that rFSH was the most prescribed gonadotropin in the Lazio region, while eFSH appeared to be under-prescribed. Determinants of prescription need to be investigated in order to further evaluate the appropriateness.

18-2

Pediatric drug use of melatonin - a register linkage study in Sweden

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Background: The prescription of melatonin to children and adolescent has increased in recent years in Sweden. In 2013, 1% of all children between 5 and 19 years of age had a prescription of melatonin. There are a few registry studies investigating prescription patters of among children and no register link prescriptions and diagnoses on Swedish data.

The aim of the study was to assess prescribing patterns, sociodemographic characteristics, diagnoses and concomitant use of psychotropics in children and adolescents receiving melatonin.

Method: Patients initiating melatonin treatment in Sweden from 2005-2016 were identified using the Swedish prescribed drug register and were linked to diagnostic data from the Swedish patient register.

Results: Preliminary data suggest that prescription of melatonin among children and adolescent has increased since 2005 and especially in the most recent years. An increase is seen among all children over the age of five years old. The increase is most prominent among children and adolescent 10-19 years of age. Many children receive both melatonin and other psychotropic drugs.

Conclusion: It is important to further follow melatonin prescription and the appropriateness of the prescription of melatonin among children and adolescents in Sweden. There are concerns about long-term use of melatonin in children and adolescents because the safety of recurrent melatonin use still is uncertain.

18-3

An audit of aminoglycosides use in the paediatric wards of a tertiary hospital in Kenya

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Background: Aminoglycosides are high risk medicines. Gentamicin and amikacin are the most commonly used aminoglycosides at Kenyatta National Hospital (KNH). The use aminoglycosides normally requires monitoring, but to date, no clinical audit has been undertaken to assess compliance to guidelines. This needs to be addressed especially paediatric wards with KNH currently lacking a protocol on therapeutic drug monitoring (TDM) of these medicines.

Method: Audit in the general pediatric ward and the new born unit of KNH via a prospective cohort study between October 2016 and March 2017 using a mixed method approach. Quantitative data collected by review of patient files. Semi-structured interviews used to collect data from healthcare workers on their current knowledge, attitudes and barriers towards effective implementation of TDM of aminoglycosides.

Preliminary Results: A total of 194 paediatric patients, predominantly aged one month and below were recruited. Overall prevalence of aminoglycoside use was 8.3% with the new born unit having the highest prevalence (16.2%). The majority of children had neonatal sepsis as the main indication for aminoglycosides. Prescribed gentamicin dose per body weight for the neonates <7 days old weighing <2kg was significantly higher than the recommended 3mg/kg dose ($p = 0.0064$). Prescribed amikacin dose per body weight was not significantly different from 15mg/kg ($p = 0.5516$) recommendations. Adverse drug reactions were suspected in 65 patients (33.9%) with fever being the most common. There was one case each of nephrotoxicity and rash. Baseline creatinine levels were documented in the majority of the cases but there was no evidence of TDM for the aminoglycosides. Further data analysis is still on-going including qualitative aspects.

Preliminary Conclusions. To date, almost 20% of neonates were exposed to aminoglycosides with doses for the most vulnerable not conforming to national Pediatric Protocols. Inadequate monitoring of paediatric patients on aminoglycosides is a matter of concern that requires attention.

18-4

Polypharmacy in preterm neonates: prevalence and predictors.

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Background. The use of drugs in combination among preterm neonates is still insufficiently explored, although usually justified to prevent or treat specific diseases (1). The present study aimed at describing the pattern of use of drugs, especially those in combination with potential nephrotoxicity, in a neonatal setting and to identify factors related to such exposures.

Methods. This 3-year retrospective study was conducted in the tertiary-level Neonatal Intensive Care Unit (NICU) of the “S. Orsola-Malpighi” Hospital in Bologna (Northern Italy, pr. n. 34/2015/U/Oss). All newborns born prematurely (<37 weeks gestational age), weighing less than 1,500 g at birth and who survived at least 48h, were included. Co-administrations of drugs were calculated on the basis of daily therapy of each neonate; nephrotoxic agents were identified through an evidence-based approach (2). Statistical analyses were performed by using R software.

Results. Of 157 neonates included in the study, 66 of them weighted $\leq 1,000$ g at birth (Extremely Low Birth Infants, ELBW), and 91 weighted $>1,000$ g and $\leq 1,500$ g at birth (Very Low Birth Infants, VLBW). ELBW infants were more likely to be exposed to combination of nephrotoxic drugs, compared to VLBW (95% of ELBW, 45% of VLBW, $p<.0001$). In particular, they mainly received associations of two antibacterials (especially ampicillin and amikacin, 97% of ELBW and 64% of VLBW), and one antibacterial with furosemide (especially amikacin and furosemide, 28% and 17% respectively). Lower birth weight (VLBW vs ELBW: OR=0.04, 95%CI=0.01-0.18, $p<.001$) and patent ductus arteriosus (PDA; OR=2.58, 95%CI=1.08-6.37, $p=.04$) were identified as predictors for such exposures.

Conclusions. Preterm neonates with ELBW and PDA are at higher risk to be exposed to combination of nephrotoxic drugs compared to other preterm neonates. The safety of such exposures, for instance amikacin and furosemide, should be further investigated.

(1)

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003750.pdf

(2) Girardi A, et al. Drug Saf. 2015 Jun;38(6):535-51

18-5

Antidepressant use during pregnancy: a nationwide population-based study

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¹Univ. Bordeaux, Inserm, Bordeaux Population Health Research Center, Team Pharmacoepidemiology, Umr 1219, Bordeaux, France, ²Centre Hospitalier Charles Perrens, Bordeaux, France, ³Pharmacologie médicale, U 1171 CHU Lille, Univ. Lille, Lille, France, ⁴Pharmacologie Médicale, UMR INSERM 1027, CIC INSERM 1436, Faculté de Médecine de l'Université Toulouse III, CHU, Toulouse, France, ⁵CHU Bordeaux, Service de Pharmacologie Médicale, Bordeaux, France

Background:

To estimate antidepressant (AD) prevalence and incidence of use during pregnancy. This study was part of the DRUGS-SAFE programme, funded by the French Medicine Agency (ANSM).

Methods:

A cohort of women aged 12-55 years who started a pregnancy in 2014 was identified using data from the French reimbursement healthcare system (covering 90% of the population). AD prevalent use during pregnancy was defined as at least one reimbursement during pregnancy or one before conception but overlapping it. If AD reimbursement was identified during pregnancy but not in the prior year, use was considered as incident. Finally, AD use stopped before pregnancy was also evaluated (at least one reimbursement in the year preceding pregnancy start and no ongoing treatment at conception).

Results:

The cohort included 766,508 pregnancies (755,519 women). AD prevalent use declined from 58.1‰ [IC95%: 57.6-58.6‰] before pregnancy to 25.7‰ [25.3-26.0‰] during pregnancy; this corresponded to a 56% decrease for the 1st trimester compared to the year before pregnancy. Prevalent use decreased over pregnancy (23.9‰, 10.4‰ and 8.4‰ in 1st, 2nd and 3rd trimester, respectively); 70% of AD use was discontinued in 1st trimester. In 20% of pregnancies, AD use occurred during each trimester. Of exposed pregnancies, 89% were exposed to a single drug; 70% were exposed to serotonin reuptake inhibitors (SRIs, escitalopram being the most frequent), 17% to serotonin-norepinephrine reuptake inhibitors, and 14% to tricyclics. AD incident use was of 3.9‰ [3.7-4.0‰]; it decreased during pregnancy (2.7‰, 1.0‰ and 0.5‰ in 1st, 2nd and 3rd trimester, respectively). At treatment initiation, the most prescribed class was SRIs, while the most prescribed drug in 2nd and 3rd trimester was amitriptyline, a tricyclic.

Conclusion:

These results indicate a sharp decrease in prescription renewal after conception. Whether this relates to planned or early stopped treatment because of the pregnancy would require field studies.

18-6

Prescribing trends of ADHD medications in Ireland primary care from 2005-2015

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Background: Attention deficit and hyperactivity disorder (ADHD) is the most common childhood neurodevelopmental disorder. ADHD is also associated with comorbid psychiatric conditions including conduct disorders, anxiety disorders and mood disorders. Use of pharmacotherapy for ADHD has increased over the last 20 years in many countries. This study aimed to 1) evaluate the prescribing patterns of medications authorised for ADHD in Ireland between 2005-2015 in children (0-11 years), adolescents (12-15 years) and young adults (16-24 years) and 2) review the concomitant use of psychotropic medication.

Methods: Data was obtained from the the HSE-PCRS pharmacy claims database. Authorised medications used to treat ADHD during the study period (methylphenidate [N06BA04], dexamfetamine [N06BA02], lisdexamfetamine dimesylate [N06BA12] and atomoxetine [N06BA09]) were extracted from the database. Dispensing of concomitant psychotropic medications prescriptions was also extracted including antipsychotics [N05A], (anxiolytics [N05B], hypnotics/sedatives [N05C]) and antidepressants [N06A]. The prescribing rates per 1000 eligible population and associated 95% confidence intervals were calculated and negative regression models were used to determine significance of trends over time.

Results: Negative binomial regression showed significant changes over time for ADHD prescribing rate in males ($p < 0.001$), with significantly higher rates across the different age groups; the highest rate amongst the 12–15 years, followed by the 5-11 and 16-24 years ($p < 0.001$). For females significant changes were also found over time, with the rates significantly varying by age similar to males ($p < 0.001$). The rates overall were 3-5 times higher in males than females. The percentage of patients on concomitant antidepressants increased from approximately 2-3% in 2005 to 7-8% in 2015. The percentage of patients on antipsychotics also increased from 5-6% to 8-9%.

Discussion/Conclusion: Similar to other studies, there were significantly higher rates of ADHD prescribing in children/ adolescents over time and significant increase in the co-prescribing of anti-depressants and anti-psychotics over the study period.

18-7

SafeStart - an intervention study to promote healthier pregnancies

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Introduction: Common pregnancy-related ailments may have a profound impact on pregnant women's quality of life, but is often being neglected by health care personnel. This may explain the high rates of sick leave in pregnancy, especially seen in Norway. Our recent study showed that 42% of all women in two Norwegian maternity wards (n=212) had experienced at least one drug-related problem (DRP). Notably, 71% of all DRP (n=105) were solved by providing confidence or by giving information. These DRP could probably have been prevented by providing pharmaceutical care to women as part of antenatal care.

Aim: The aim of this study is, therefore, to investigate whether a pharmacist's intervention in early pregnancy can reduce sick leave, and improve the quality of life among pregnant women.

Design and participants: This is an intervention study where participants will be recruited in early gestation and followed up until the post-partum period. All Norwegian-speaking pregnant women over the age of 18 are eligible for inclusion. We aim to recruit 1000 women, mainly by online advertisement. All women will follow standard antenatal care. Women randomized to the intervention group (n=500) will, in addition, receive the intervention in ten community pharmacies.

Intervention: "A planned, structured and individualized conversation with the purpose to relieve pregnant women for any concern and answer questions she may have regarding self-care ailments during pregnancy".

Measurements: Data will be collected through four electronic questionnaires. Primary outcome measure is sick leave in pregnancy, but we will also collect data on socio-demography and lifestyle, health and medication use and, quality of life by using validated instruments.

Analysis: Appropriate regression analysis will be used to analyze the association between the intervention and the outcomes controlling for possible confounding factors. An economic cost-benefit calculation will also be performed.

Anticipated date of commencement and completion: 09.2017–09.2019.

18-8

PREVALENCE AND CHARACTERISTICS OF MEDICINE USE AMONG PREGNANT WOMEN IN A KENYAN HOSPITAL

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Introduction: Exposure to certain prescription and herbal drugs and over the counter (OTC) medicines in pregnancy have been linked to neonatal and maternal complications. Several studies have demonstrated widespread use of medications during pregnancy whose safety and effects on the developing fetus is unknown. The extent and the characteristics of drug use during pregnancy in Kenya has not been widely reported. The objective was to address this.

Method: Hospital based cross-sectional study to determine prevalence and characteristics of medicine use among pregnant women at a Sub County Hospital in Kenya. 385 pregnant women were recruited and data collected through questionnaire-guided interviews, review of patient files and registers. Descriptive and exploratory data analysis using STATA version 10.

Results: Prevalence of herbal, OTC and prescription medicines was 11.4%, 65% and 41% respectively. Ginger was the most frequently used herbal medicine while paracetamol the most used OTC and prescription medicine. Drug allergy and alcohol consumption positively associated with herbal medicine use, while co-morbidity was the only independent predictor variable for prescription medicine use. Urban residence significantly decreased odds of using OTC medicines. The most frequently used US-FDA pregnancy risk category medicine was C at 50%, while categories D and X accounted for 10% and 1.1% respectively. Medicines with known fetal risks without prior risk-benefit assessment also used.

Conclusion: Significant use of herbal medicines in pregnancy without any documentation, with self-medication prevalent. Drug allergy, alcohol use, urban residence and co-morbidity predictors of medicines use in pregnancy. In this population, the use of medicines requires caution and thorough understanding of possible outcomes particularly on the fetus. There is need for guidelines for risk-benefit analysis among physicians to ensure safe use of medications in pregnancy. Programs geared to the creation of awareness of the dangers of self-medication in pregnancy should also be instigated among community pharmacists.

18-9

Pregnancy use of prescription medication in Denmark -online available statistics 2000 to 2016

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Background: Medicine treatment in the pregnant woman is complex taking into account both the benefit for the mother and the health of the child. There is a lack of information regarding medicine use during pregnancy in general and whether the use has changed over time. We therefore aimed to make a publicly available statistics on medicines use in pregnancy on the national level.

Methods: We linked women in the national Medical Birth Register during 2000-2016 to data on prescription medicines use from the National Register of Medicinal Products Statistics using the unique civil registration number. The pregnancy period is defined by the birth date and information of the duration of pregnancy from the Medical Birth Register. We included women living in Denmark during the total pregnancy period and calculated number of pregnant women and number of women per 1,000 pregnancies using medications. Medications are presented at substance level (ATC level 5) as well as higher levels. The statistics demonstrates medicine use during trimesters, age groups. We also show medicine use before the pregnancy compared to use during the pregnancy.

Results: The statistics is free available online, includes 55,000 to 66,000 pregnancies per year and will be updated yearly. The statistics includes dispensed prescriptions, which is not exactly the same as actually taken medicines.

Conclusions: Due to national registers on prescription medicines and births, the Danish Health Data Authority is able to present this new online available statistics on prescription medicines use during all pregnancies in Denmark for the latest 17 years. The statistics will be of importance to health authorities, health care professionals, researchers and the public.

19-1

Prevalence of rheumatoid arthritis and associated chronic disease list conditions in the private health sector of South Africa

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Background

Rheumatoid arthritis (RA) is a debilitating autoimmune disease that causes progressive and chronic joint inflammation, resulting in the development of miscellaneous multisystem comorbid conditions. Little is known about the burden of RA in South Africa. The aim of this study was to establish the prevalence of RA and associated chronic disease list conditions (CDL) in the private health sector of South Africa.

Methods

A retrospective, cross-sectional analysis was performed on medicine claims data for 838 618 patients, for the period of 1 January to 31 December 2014 obtained from a Pharmaceutical Benefit Management (PBM) Company. The population was divided into first- (patients receiving only non-steroidal anti-inflammatories) and second-line (patients receiving corticosteroids, disease modifying antirheumatic drugs (DMARDs) and biologics) treatment, and then subdivided into those with RA only and those with RA and CDL conditions using the standard International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes.

Results

Overall, 4352 patients, mean age 60.32 ± 14.29 years (95% CI: 59.90-60.75), 74.8% female, had RA. In total 12.8% (n=556) received first-line and 87.2% (n=3796) second-line treatment. Of the patients on first-line treatment, 441 (79.3%) had one or more CDL conditions compared to 2250 (67.2%) on second-line treatment. Patients with RA and other CDL conditions were older than those patients with RA alone ($p < 0.0001$; Cohen's $d = 0.7$). Gender had no influence on presence of CDL conditions in RA patients ($p = 0.675$). CDL conditions present included hypertension (47.5%), hyperlipidemia (25.9%), cardiac failure (3.8%), dysrhythmias (2.2%), hypothyroidism (19.7%), type 2 diabetes mellitus (11.4%), epilepsy (2.1%), asthma (7.8%), and chronic obstructive pulmonary disease (0.9%).

Conclusion

This study may contribute to the body of evidence about the burden of RA and associated chronic conditions in South Africa.

19-2

Trajectories Of Long-term Exposure To Anticholinergic And Sedative Drugs: A Latent Class Growth Analysis

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Background: A variety of drugs, which are frequently prescribed to older people, have anticholinergic and sedative effects whereby they may impair cognitive and physical function. Although substantial inter-individual variation in anticholinergic and sedative exposure has been documented, little is known about subpopulations with distinct trajectories of exposure.

Methods: Data from the Longitudinal Aging Study Amsterdam (LASA), an ongoing Dutch population-based cohort study, collected over 20 years (1992-2012) at seven occasions, were analyzed. On each occasion, cumulative anticholinergic and sedative exposure was quantified with the Drug Burden Index, a linear additive pharmacological dose-response model. The most likely number of trajectories were empirically derived with Latent Class Growth Analysis using 'Goodness of fit' statistics. Trajectories were then compared on physical and cognitive function.

Results: A total of 763 participants completed all follow-ups (61% women; mean age 83, ± 6). 'Goodness of fit' statistics (Bayesian Information Criterion = 22916, Bootstrapped Likelihood Ratio Test of 3 vs. 2 classes = 514.12 $p < 0.01$, Entropy = 0.87) indicated the presence of 3 distinct trajectories: "Gradual Increase" (67%), "Stable High" (8%), and "Steep Increase" (25%). Linear mixed models adjusted for co-morbidities and other covariates demonstrated poorer physical function but not poorer cognitive function for "Stable High" and "Steep Increase" trajectories compared to the "Gradual Increase" trajectory.

Conclusion: Three trajectories of long-term anticholinergic and sedative exposure were identified. The present findings need corroboration by examining whether more adverse trajectories are associated with poorer outcomes on other measures of physical and cognitive function.

19-3

Self-medication in various professional groups

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Background: Self-medication (SM), defined as the selection and use of medicines by individuals to treat self-recognized illnesses or symptoms (WHO), can positively influence self-management and patient-responsibility and avoid health care consumption for minor problems. However, SM carries risks such as misdiagnosis, delay in treatment, incorrect medicines use, abuse, interactions and adverse reactions. Therefore, we aimed to examine prevalence and the nature of SM. The study focused on nine professional groups, as health problems can be related to profession, and it facilitates targeted interventions if needed.

Methods: In a cross-sectional survey design (March 2017) a convenience sample of professionally active respondents (9 professions) was questioned on personal and professional characteristics, lifestyle, the handling of medicines and the SM use (products, health problems, frequency, dose). All products perceived by the respondents as medicinal products were considered, including officially registered medicines, yet, also alternative and complementary products.

Results: A total of 3 244 respondents participated: 694 nurses, 216 midwives, 664 teachers, 675 administrative assistants, 179 construction workers, 203 factory workers, 231 hospitality and catering workers, 205 police officers and 177 military personnel. In the last month, 54% of the respondents used SM, with a mean of 2.1 (SD 1.9) different products per person. Of all products 80% were officially registered medicines. Based on ATC coding, registered medicines addressing the nervous (46%, 43% analgesics), the muscular-skeletal (23%, propionic acid derivatives 19%), the respiratory (16%) and the gastro-intestinal system (12%) were most commonly used. SM was significantly more prevalent in teachers and women and correlated negatively with age, working hours/week and work experience. While health did significantly influence SM, lifestyle characteristics did not.

Conclusion: SM is a common practice. Most products are registered medicines, and predominantly analgesics and anti-inflammatory medicines. However, a broad range of products with various risks were used.

19-4

Trends in prescribing proton pump inhibitors in the Netherlands between 2001 and 2015

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Background

There is increasing concern about the widespread use of proton pump inhibitors (PPIs). They are highly effective to treat upper gastrointestinal tract disorders and short term side effects are limited, but long term use may be associated with serious side-effects. The aim of our study was to investigate the prevalence, incidence and duration of use of proton pump inhibitors over time.

Methods

Retrospective data from IADB.nl, a Dutch database of filled prescriptions (59 public pharmacies, about 600,000 patients), were examined to identify all patients receiving a PPI between 2001 and 2015. We calculated the incidence and prevalence of PPI use and the duration of treatment. Data were stratified for age and gender.

Results

We identified 299,134 patients using PPIs during the study period. Most frequently prescribed PPIs in the Netherlands in 2015 were omeprazole (77%) followed by pantoprazole (14%). The prevalence of PPI use increased from 5.6% in 2001 to 15.0% in 2015. The incidence more than doubled from 2.2% in 2001 to 5.2% in 2011. Between 2012 and 2015, the incidence remained relatively stable around 4.5%. Both incidence and prevalence of PPI use was higher among female patients and showed age dependency. The median duration of PPI use during the study period was 1 month. Out of all patients, 15% used PPIs for at least 12 months. In the group of older patients (>60 years) more than 50% used PPIs for more than 12 months.

Conclusion

The use of PPIs increased largely over the last 15 years, especially among older patients. Most of these vulnerable patients use PPIs for more than one year increasing the risk for serious side effects. The decrease in new users of PPIs may be due to PPIs no longer being reimbursed for short time use since 2012.

19-5

Analysis and in-house development of an automated system for the management of pharmaceutical preparations in the Hospital

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Background:

In the past couple of years, the demand of galenic compounds has risen sharply.

In order to plan the activity, our team designed and set up a database which stores all the necessary information related to drugs and ingredients. This allows our internal Galenic Laboratory to better manage the pharmaceutical prescriptions for the hospital and the outpatients, optimizing the use and replacement of raw materials.

Methods:

The application is based on the interconnection of various prescription-related aspects such as patients' and prescriber's details and the prescription information. The prescription name is linked to the list of substances, which allows to monitor the stock levels interfacing with a centralized data store. Inserting the daily dosage of a drug into the system, our personnel can easily calculate the monthly supply of the medicine needed. Each prescription contains specific warnings on printable labels. A printed sheet, inclusive of label and checks on the final preparation, is produced for each prescription.

Results :

After a testing phase, during which its potential and improvements have been evaluated, the application gradually replaced our traditional process of pharmaceutical activity management, allowing for a more accurate scheduling of the medicine requests. The worksheet and its specific label are automatically generated after each data insert, together with a unique identifier. Then a prediction scheme is generated for the ordinary programmable galenic activity.

Conclusions:

The project successfully achieved the following goals:

- 1) Automate the information flow related to the pharmaceutical preparations;
- 2) Improve the response time of the Laboratory;
- 3) Minimize the number of emergencies.

Since it has been developed by means of resources already available within the Hospital, and given its great level of modularity, the application can be customized and/or implemented according to different internal requirements, in a timely fashion and without additional costs.

19-6

POWER CONSIDERATIONS FOR INTERRUPTED TIME-SERIES ANALYSIS: A SIMULATION STUDY

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Background

There is a scarcity of guidance on power calculations using Interrupted time-series (ITS) analysis. We aimed to assess statistical power to detect either a (1) slope or (2) step change under various conditions relating to number of time points, magnitude of impact and location of intervention.

Methods

Simulations were used to create aggregated datasets of outcome rates over time. Parameters were informed from an ITS regression model we recently published. We here estimated statistical power to detect a significant ($p=0.05$) post-intervention change in (i) trend or (ii) level of outcome, assuming no significant autocorrelation and approximately 20 outcome events per time point. We generated 1,000 datasets per scenario, varying the number of time points (16, 20, 24, 28, 30, 40 and 50), average relative reduction post-intervention (-15%, -34%, -50% and -75%) and location of intervention in the time-series (0.2, 0.4, 0.5, 0.7 and 0.8). Study funded by NIHR CS-2013-13-012.

Results

Given a mid-time-series intervention, to have 80% power to detect a slope change yielding an average relative reduction of -15%, -34%, -50% or -75%, a total of >50, 30, 28 and 28 time points were required, respectively. For a step change these numbers were >50, >50, 24 and 24, respectively. When the intervention occurred very early or late in the time-series there was insufficient power to detect any of the slope reductions when using a total of 50 time points, except when the slope change was -75%. This was similar for detecting step changes, except that power was generally sufficient for -50% and -75% reductions when using a total of 50 time points.

Conclusions

We provide guidance on power calculation for ITS analyses in different scenarios. Smaller changes in outcome and early or late interventions (in the time-series) required higher number of time points to ensure 80% power.

19-7

Drug utilization in patients with liver cirrhosis

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Background: Little is known about drug utilization in patients with liver cirrhosis although they are very susceptible to experience adverse drug reactions because of alterations in pharmacokinetics and pharmacodynamics. In this study, we aim to determine which drugs are most frequently used by patients with liver cirrhosis and whether drugs are used with known safety risks.

Methods: This was a descriptive, cross-sectional study based on data of drug dispensings from community pharmacies linked with hospitalization data (PHARMO Database Network). Patients with a diagnosis of liver cirrhosis (ICD-9 code 571.2 or 571.5) between January 1998 and December 2015 were included. The index date was the first date a patient was hospitalized with the diagnosis of liver cirrhosis. Dispensing data were analyzed one year after the index date. Safety of drug use was evaluated based on a new guideline on safe prescribing in patients with liver cirrhosis.

Results: In total 7,160 patients with liver cirrhosis were included. Of these, 4,302 (60.1%) were males and the mean age was 60.6 years (SD 13.9). The most frequently dispensed drugs were spironolactone (n=2,742; 38.3%), furosemide (n=2,370; 33.1%) and pantoprazole (n=1,584; 22.1%). Temazepam (n=1,025; 14.3%), oxazepam (n=886; 12.4%) and metformin (n=776; 10.7%) were most frequently dispensed for non-liver related comorbidities. General practitioners prescribed 77% of drugs, specialists 22% and there was no or an unknown prescriber in 1% of drugs. Of the 15 most frequently dispensed drugs, one (pantoprazole) was classified as unsafe in patients with liver cirrhosis and three (i.e. omeprazole, metoprolol and acetylsalicylic acid) were unsafe in certain situations (e.g. when a patient has severe liver cirrhosis).

Conclusion: Patients with liver cirrhosis frequently use drugs including medication with known safety risks. Implementation of the new guideline on safe prescribing in this patient group seems urgently needed.

19-8

Pattern of Use of Intravitreal Drugs with Antiangiogenic Properties for Age-related Macular Degeneration and Other Vascular Retinopathies

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Background

Intravitreal injections (IVI) of anti-vascular endothelial growth factor agents have played an important role in the treatment of neovascular eye diseases, particularly in age-related macular degeneration (AMD). For both aflibercept and ranibizumab, 3 monthly IVIs are recommended as loading dose. The use of bevacizumab for ophtalmic indications is not licensed. Observational evidence suggests that AMD patients may need more injections to maintain visual acuity gain. We described the pattern of use of anti-VEGF drugs in clinical practice in Tuscany, Italy.

Methods

All subjects registered in the Tuscan administrative database between January 1, 2011 and December 31, 2014, with ≥ 1 IVI record and ≥ 1 year of observation time were recruited. Number of contacts with ophtalmology services and number of IVI (nIVI) in the 1st year were observed, and interval between injections (IBI) was calculated in those with ≥ 3 IVI and ≥ 5 contacts. A subgroup analysis was performed in AMD patients.

Results

We identified 3,790 new users. In 87.2%, 72.1% and 40.4% of aflibercept, ranibizumab, and bevacizumab users ≥ 3 IVI were given. A large majority of users had ≥ 5 contacts. In those with ≥ 3 IVI and ≥ 5 contacts the mean nIVI/IBI values were 4.1/56.9 days for aflibercept, 4.0/52.9 days for ranibizumab and 3.7/61.7 days for bevacizumab. Proxy of AMD was found in 81.4%, 62.4%, and 52.9% of aflibercept, ranibizumab, and bevacizumab users. In this subpopulation, the mean nIVI/IBI values were 4.1/57.8 days for aflibercept, 4.0/52.8 days for ranibizumab and 3.7/61.8 days for bevacizumab.

Conclusion

A relevant proportion of new users did not complete the loading dose, especially bevacizumab users. Among those with ≥ 3 IVI, the nIVI of aflibercept and ranibizumab were similar, but aflibercept users had slightly longer IBI. AMD was more frequent among aflibercept users. The pattern of use of AMD patients was similar to the pattern of all users.

19-9

Translation and validation of a Danish version of the Medication-Related Quality of Life (D-MRQoL) Scale

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Background: Generic and disease specific health-related quality of life scales have not been found to be responsive to changes in medications in polypharmacy patients. The aim of this study was to translate and validate the Medication-Related Quality of Life (MRQoL) Scale, originally developed and validated by Tseng et al.* in Taiwan, in a Danish population.

Methods: The Taiwanese MRQoL included 14 items aimed at measuring medication-related quality of life for patients taking five or more medications simultaneously. It was forward-translated into Danish and backward-translated into Chinese according to a set protocol. The Danish translation (D-MRQoL) was pre-tested in eight patients, adjusted, and administered to 120 polypharmacy patients. The factor structure was examined using Exploratory Factor Analysis (EFA). Internal consistency reliability was evaluated using Cronbach's alpha. Two measures were used to establish construct validity, the Beliefs about Medicines Questionnaire (BMQ), for convergent validity, and the Medication Adherence Report Scale (MARS), for discriminant validity. Statistical analyses were carried out in SPSS version 23.

Results: Cronbach's alpha for D-MRQoL was 0.96. Scores on D-MRQoL correlated statistically significantly and negatively with those on the BMQ subscale concerns ($r=-0.455$; $p=0.000$), but not significantly with BMQ subscale necessity ($r=-0.029$; $p=0.754$). The correlation with DMARS-4 was positive and significant ($r=0.338$; $p=0.000$), indicating that the MRQoL is, contrary to hypothesis, related to medication adherence. The Danish version showed a two-factor structure if eigenvalue was set at 1.0, but seemed clearly differentiated in terms of underlying concepts. This diverges from the original Taiwanese scale which showed a three-factor structure.

Conclusion: The 14-item scale in Danish showed a high reliability and a two-factor structure which has face validity. Although convergent validity was somewhat established, the construct validity, known-group validity, and responsiveness of D-MRQoL needs to be examined further in future studies.

*Tseng HM et al. Qual Life Res 2016 May;25(5):1295-302.