knowledge of the FDA-approved indications of commonly prescribed drugs, and to assess whether physicians’ belief that an indication is FDA-approved increases with level of evidence supporting such use. METHODS: We conducted a national random sample mail survey of 399 primary care physicians and 680 psychiatrists conducted from August through August 2008. Physicians were presented with 36 drug indication pairs (e.g., gabapentin [Neurontin®] for diabetic neuropathy) that varied in their FDA-approval status and levels of supporting evidence. The main outcome measure was physicians’ knowledge of whether each drug was FDA-approved for the indication in question. RESULTS: The adjusted response rate was 47.4%, and the mean (median) number of drugs examined that were prescribed during the previous 12 months was 11 (12). The average respondent correctly identified the FDA-approval status of just over half of the drug-indication pairs queried (mean 55%; median 57%). The proportion increased modestly (mean 59%; median 61%) when limited to drugs the respondent reported having prescribed during the previous 12 months. There was a strong association between physicians’ belief that an indication was FDA-approved and greater evidence supporting that use ( Spearman’s r=0.74, p < 0.001). However, 41% of physicians believed at least one drug-indication pair uncertain or with no supporting evidence (e.g., quetiapine [Seroquel®] for dementia with agitation) was FDA approved. CONCLUSIONS: These findings highlight an important need for more effective methods to inform physicians about the evidence base, or lack thereof, for drugs they prescribe off label.

A800

THE IMPACT OF LEGISLATION AND PRICING ON GENERIC DRUG UTILIZATION: AN ANALYSIS OF 26 COUNTRIES
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OBJECTIVES: Across countries with varying political, socioeconomic and cultural environments, we sought to identify predictors of generic drug utilization. METHODS: Data were collected from national and international regulatory agencies, MEDLINE and internet searches for 37 countries classified as “advanced” or “emerging” economies by the International Monetary Fund: Argentina, Australia, Austria, Belgium, Brazil, Canada, China, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, India, Luxembourg, Malta, Mexico, Netherlands, New Zealand, Norway, Portugal, Russia, San Marino, Singapore, Slovenia, South Korea, Spain, Sweden, Switzerland, Taiwan, UK. We compared the presence of generic policies, first year of generic legislation, branded drug patent duration, proportion of generic drug utilization, and pricing for generics (government control, free market, or other), gross domestic product, and population across countries. Only independent variables with p < 0.20 in univariate regression were included in the multivariate model: population, year of generic legislation, patent life, and pricing for generics (market vs. government control). RESULTS: Of 37 countries, data was available for 26 (70%): Argentina, Australia, Austria, Brazil, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Japan, Mexico, Netherlands, New Zealand, Norway, Portugal, Russia, Singapore, Spain, Sweden, Switzerland, UK and United States. Most countries enacted generic drug legislation in the 1990s, 9 (33%) introduced legislation before 1990 and 3 (12%) after 2000’s. Brand drug patent duration was 15–20 years for 65% of countries. Among countries with generic drug laws, only free market-based generic pricing, compared to government-controlled pricing, was associated with a modest increase in generic drug utilization (B = 0.17, 95% CI: -0.01, 0.35). CONCLUSIONS: Countries with minimal or no generic pricing had minimally greater diffusion of generic drugs compared to countries with government pricing controls. Further investigation of other characteristics, namely the political and social climates that foster greater generic drug utilization is planned.

A801

ANALYSIS OF ITEMS DISPENSED IN WALES
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OBJECTIVES: Prescription charges were abolished in Wales in April 2007. We hypothesised that as a result, the demand for prescription medicines might increase, and compared the rates of dispensing of the 15 medicines that most frequently incurred a prescription charge, versus a region with similar socioeconomic characteristics that continues to charge patients (NE England). METHODS: HBOC Monthly data from January 2002 to October 2008 (one year post abolition) on the quantities of dispensed medicines were obtained from Health Solutions Wales and the Prescription Pricing Authority. Descriptive comparative analyses of unadjusted dispensing rates (per 1000 list size) were conducted for each of the 15 medicines. The combined dispensing rates for all 15 medicines increased significantly in both regions, but the change in Wales was higher than that in England (Wales increase = 57.67, p < 0.0001, 95% CI: 55.09 to 60.28; NE England change = 30.18, p < 0.0001, 95% CI: 27.32 to 33.03). The difference between regions was statistically significant (p 0.001) for those who reached generic coverage (27.51, p < 0.0001, 95% CI: 23.66 to 31.35). Whilst an expected widening of the difference between regions was apparent for some medicines, factors beside the abolition of prescription charges are likely to account for the observed differences in others. For atenol, a reduction in overall dispensing is observed to coincide with trial evidence that cast doubts for its suitability as a first-line drug for hypertension. The dispensing of co-codamol has risen dramatically in Wales, but not NE England, possibly related to different recommendations following the withdrawal of co-proxanol. CONCLUSIONS: The abolition of prescription charges is associated with changes in dispensing rates in Wales for some evaluated medicines. However, the data require to be interpreted in the context of the low proportion of prescriptions that were previously charged, and changes in clinical practice.

A802

CHARACTERISTICS OF MEDICARE PART-D ENROLLEES WITH AND WITHOUT PRESCRIPTION DRUG COVERAGE GAP
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OBJECTIVES: To compare socioeconomic and behavioral characteristics of Medicare Part-D enrollees with coverage gaps to those who did not (no-gap), in 2007. The study is unique because it examined characteristics of Medicare Part-D enrollees that are typically not available in administrative claims databases. METHODS: A survey based on the Seniors’ Prescription Coverage, Use and Surveying and the Brief Medication Questionnaire was developed and distributed to elderly persons seeking care at the pharmacies within the University of Arkansas for Medical Sciences College of Pharmacy Advanced Community Practice Network. Patients recruited were 65 years or older, enrolled in Medicare Part D in 2007, and taking medications for any of the following conditions: hypertension, hyperlipidemia, diabetes, asthma/COPD, or depression. RESULTS: In this 2007 third phase, 69 patients were enrolled and 24 (34.8%) reported reaching the coverage gap in 2007. Among in-gap patients, 95% were aged 65–83 years and 58% were female, compared to 73% and 64% respectively for the no-gap subjects. Compared with the no-gap subjects, more in-gap subjects attended college (78% vs. 46%), had a monthly income of $2000 or more (70.8% vs. 56%), and spent more than $300 per month on medications (42% vs. 24%). Compared with no-gap patients, in-gap patients were less likely (54% vs. 69%) to report overall satisfaction with Part D programs. Finally, 87.5% of the in-gap patients reached the gap in September 2007 or later. CONCLUSIONS: One-third of the subjects reached the coverage gap and most of them reached the gap within the last quarter of 2007, mitigating the impact of coverage gap to some extent. The in-gap group belonged to higher socioeconomic status, which was expected since the no-gap group appeared not to be at the risk of coverage gap because of low-income subsidies. Experiencing coverage gap negatively impacted patients’ satisfaction with Part-D plans.

A803

A COMPARISON OF POLICIES ON PAEDIATRIC DOSING GUIDELINES AND INDICATIONS BETWEEN THE UNITED STATES AND EUROPE
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OBJECTIVES: To compare legislation on paediatric dosing guidelines and indications between the US and Europe and to examine whether the introduction of new regulations and financial incentives has resulted in more pharmaceutical companies providing paediatric data. METHODS: Information was extracted from published policies and reports on paediatric therapeutics as published by the US Food and Drug Administration and the European Medicines Agency. RESULTS: In the US, the Food and Drug Administration Modernisation Act (FDAMA; 1997) offered six months of marketing exclusivity to manufacturers voluntarily conducting paediatric studies. Current legislation in the US consists of the Best Pharmaceuticals for Children Act (BPCA; 2002), and the Paediatric Research Equity Act (PREA; 2003). Manufacturers are also encouraged to obtain orphan drug designation for drugs or biological products for use in a paediatric population. In January 2008, the FDA has sent written requests for paediatric studies to sponsors of 301 drugs. There have been 157 incidents of labeling changes under the BPCA and 76 labeling changes or submissions of supporting information under the PREA. Legislation on paediatric therapeutics was issued in the EU in January 2007 (Regulation EC No 1901/2006 as amended). Since this time, the EMEA has adopted decisions on 99 applications for paediatric investigational plans (PIPs) and waivers; 57 positive opinions on PIPs; 3 proposed modifications to PIPs; and 39 waivers in all age groups for all conditions. Additionally, most European Health Technology Assessment agencies do not make special allowances for the assessment of paediatric drugs. RESULTS: Legislation on in the US has been successful in encouraging research into the use of therapeutics in paediatric patients. In the EU, although many applications of PIPs and waivers have been reviewed, the situation should be monitored over the coming years to determine if the legislation leads to changes.

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THE IMPACT OF NON-REFERRAL OUTPATIENT CO-PAYMENT ON MEDICAL CARE UTILIZATION AND EXPENDITURE IN TAIWAN
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OBJECTIVES: Taiwan’s National Health Insurance’s (NHI) generous coverage and patients’ freedom to access different tiers of medical facilities has resulted in accelerating outpatient care utilisation. To deter non-referral, during the initial contact in primary care, a differential co-payment was introduced on July 15, 2005. Under this, patients pay more for outpatient consultations at higher medical facilities, particularly if accessed without referral. This study aimed to explore the impacts of medical activities and expenditure, different payment groups and tiers of medical facilities. METHODS: A segmented time-series analysis on regional weekly outpatient medical claims (January 2004 to July 2006). Outcome variables (number of visits, number of outpatients, total cost of outpatient care) and variables for cost structure were stratified by tiers of medical facilities and

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co-payment groups. Analysis used the auto-regressive integrated moving-average model in STATA 9.0. RESULTS: The overall number of outpatient visits significantly decreased after policy implementation due to a reduction in the number of patients using outpatient facilities, but total costs of care remained unchanged. The policy had its greatest impact on the number of visits to regional and local community health centers (secondary), but had no influence on those the medical centers (tertiary). Medical utilisation in physician clinics (primary) decreased due to an audit of reimbursement declarations. Overall, the policy failed to encourage referrals from primary care to higher tiers. CONCLUSIONS: Further research needs to explore how patients’ out-of-pocket payment affects medical utilisation and which forces (not susceptible to co-payment) act in tertiary facilities. It also needs to investigate, whether the reduction in outpatient numbers was due to an affordability barrier to accessing essential care, with a potentially negative impact on the region's health.

HOW NON-REFERRAL OUTPATIENT CO-PAYMENT IN TAIWAN IMPACTS ON UTILIZATION AND COST & CHOICE OF PRESCRIPTION PATTERNS Chan LC1, Schafftude E2, Noyce P1, Won YH1, Wu J1

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OBJECTIVES: To deter non-essential visits and encourage initial contact in primary care, Taiwan’s National Health Insurance’s (NHI) implemented a differential co-payment policy on July 15, 2005. A previous study has examined the impact of this policy on medical utilization and total cost to NHI using a regional reimbursement dataset. This study aimed to explore the impact of this policy on outpatient co-payment groups. Analysis used the auto-regressive integrated moving-average model in SIAIA 9.0. RESULTS: Despite the decrease in outpatient visits, the overall co-payment to patients increased by 1.2% after policy implementation and also increased in most medical facilities (4.8% to 17.9%). Number of general prescriptions decreased across different medical facilities; the average cost and duration per general prescription decreased in medical centers and regional hospitals. The number of continuous prescriptions did not change, except for non-significant decreases in medical centers and regional hospitals. There was an increase in the number of continuous prescriptions as compared to single prescriptions (7.3%). CONCLUSIONS: The police significantly increased patients’ out-of-pocket payment for outpatient visits. In response to the policy, physicians might prescribe more expensive drugs and extend prescription duration to help patients get the most benefit from the co-payment, and physician in medical centers are more likely to prescribe continuous prescriptions for patients with stable chronic diseases. Further research needs to identify vulnerable subgroups in obtaining necessary treatment, and to explore the impacts of cost-saving strategies on patients’ quality of medical care.

COST-RELATED UNDERUSE OF MEDICINE DUE TO MEDICAID PHARMACY COST-CONTAINMENT POLICY ACTIONS

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OBJECTIVES: We sought to evaluate the impact of pharmacy cost-containment policy actions by state Medicaid programs on cost-related underuse of medicine, controlling for differences in pharmacy cost-containment policy actions and socio-demographic and temporal differences among states. METHODS: We used the data from the 2003 Community Tracking Study (CTS) household survey, and linked them with the census demographic data and the cost containment policy actions based upon 50 States Surveys on state Medicaid spending growth and cost containment policy actions by the Kaiser Family Foundation in 2003. A cross-sectional study was performed to evaluate the impact of policy actions, by comparing Medicaid beneficiaries to non-Medicaid-pharmacy-cost-containment-eligible residents. The outcome measures included: patients who do not receive needed medical care, patients cannot afford needed prescriptions, patients postpone needed medical care, and patients worry about the medical care cost. The outcomes were analyzed using logit model, with prior authorization, generic drugs required, copayment method, step therapy of fail-first requirement, limit on number of prescriptions and number of refills per month, preferred drug list, over the counter coverage, and prescription drug payment practices (payment by purchase/purchasing policies) as predictors. Additionally, non-pharmacy cost-containment policy actions, patients demographics and states’ socio-environmental variables were controlled. RESULTS: On average, each state has implemented 6.5% pharmacy cost containment policy actions in 2003. Only the worrying about costs was statistically significantly associated with individual pharmacy cost-containment policy action; however, such significance disappeared after other concurrent pharmacy cost-containment policy actions were controlled for. When the total number of pharmacy cost-containment policy actions was controlled for in the regression instead of individual policy action, each policy action was associated with 14% increase in odds ratio for unmet medical needs (p = 0.003), and 5% increase in odds ratio for postponing medical needs (p = 0.02). CONCLUSIONS: There was variable impact of pharmacy cost-containment policy actions when assessed concurrently, and collectively.

HAVE YOUR CAKE OR EAT IT: DO DECISIONS BASED ON COST-EFFECTIVENESS UNDERMINE INCENTIVES FOR RESEARCH AND DEVELOPMENT?

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OBJECTIVES: Although cost-effectiveness analysis allows efficient decisions about the use of existing technologies (static efficacy) it has been argued that it will disincentivise the development of innovative technologies (dynamic efficacy). These concerns have also been raised about the report by the UK Office of Fair Trading which recommended that the price of pharmaceuticals should be based on their cost-effectiveness. We aim to establish whether decisions based on cost-effectiveness necessarily undermine incentives for the development of pharmaceuticals. METHODS: The argument put forward as to why cost-effectiveness decisions might undermine incentives for innovation are examined and are used to consider the implications of the type of value-based pricing which has been proposed in the UK. RESULTS: The argument depends on whether the purpose of health care is to improve population health or to maximise welfare (consumer and producer surplus). If it is the former, then achieving static and dynamic efficiency requires a clear and predictable signal of value (cost-effectiveness). The public sector can then choose to invest in developments which it believes will be cost-effective and provide a satisfactory return on investment. Manufacturers should be allowed to appropriate some share of the surplus (monopoly rent) to incentivise investment in R&D. However, they should not take it all. The public sector subsidises research and development in many ways. Therefore, even if society was unconcerned about who benefits from innovation it would not be efficient to allow complete appropriation. In other words, the innovation co-payment groups that was targeted of medical facilities. METHODS: A segmented time-series analysis on regional weekly outpatient medical claims (January 2004 to July 2006). Outcome variables for co-payment and prescription patterns were stratified by tiers of medical facilities and co-payment groups. Analysis used the auto-regressive integrated moving-average model in SIAIA 9.0. RESULTS: Despite the decrease in outpatient visits, the overall co-payment to patients increased by 1.2% after policy implementation and also increased in most medical facilities (4.8% to 17.9%). Number of general prescriptions decreased across different medical facilities; the average cost and duration per general prescription decreased in medical centers and regional hospitals. The number of continuous prescriptions did not change, except for non-significant decreases in medical centers and regional hospitals. There was an increase in the number of continuous prescriptions as compared to single prescriptions (7.3%). CONCLUSIONS: The police significantly increased patients’ out-of-pocket payment for outpatient visits. In response to the policy, physicians might prescribe more expensive drugs and extend prescription duration to help patients get the most benefit from the co-payment, and physician in medical centers are more likely to prescribe continuous prescriptions for patients with stable chronic diseases. Further research needs to identify vulnerable subgroups in obtaining necessary treatment, and to explore the impacts of cost-saving strategies on patients’ quality of medical care.

ASSESSMENT OF ORPHAN DRUGS DEVELOPED AND DRUG UTILIZATION UNDER THE ORPHAN DRUG ACT: A DESCRIPTIVE EMPIRICAL STUDY

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OBJECTIVES: The Orphan Drug Act (ODA) was developed in 1983 to stimulate new drug development to treat rare diseases. The purpose of this analysis was to review new drug development with orphan designation drugs in the Medicaid program. METHODS: A literature review about orphan drug approvals was conducted through search engine like PubMed, as well as government and industry Internet websites. Nationwide Medicaid pharmacy data extracted from the Center for Medicare & Medicaid Services were analyzed from 1991 to 2007 regarding quarterly prescriptions, reimbursements, and cost per prescription for selected orphan drugs. Based on utilization patterns, two categories of orphan drugs were studied, including traditional ones with little use (like antizole, fabamaze, respigam, myozyme, and panhematin) and non-traditional ones with wide usages (like pacitaxel, epoetin alfa, and imatinib mesylate). RESULTS: Since 1983, over 1,700 drugs have been designated as having orphan status and 325 drugs have marketing approval to treat orphan diseases, focusing on oncology, metabolic and endocrine disorders, and hematology. From Medicaid pharmacy data, there was very little use for antizole, myozyme, and other traditional orphan drugs, such as fabame- zyme from 1983 to the peak of 375 in 2006. By contrast, non-traditional orphan drug like epoetin alfa prescriptions increased from 17,282 in 1991 to the peak of 824,485 in 2005, and imatinib mesylate prescriptions increased from 3,877 in 2001 to the peak of 26,325 in 2005. Fabamez drug cost per prescription started with $22,367 in 2003 and decreased to $5,538 in 2006. Other expensive orphan drugs included myozyme, panhematin, imatinib mesylate, and rizumixah ranging from $3,000 to $10,000 per prescription. CONCLUSIONS: ODA has made a significant impact on drug development for rare diseases. Non-traditional orphan drugs with dramatic increased utilization and spending were observed, which might require safety surveillance and appropriate utilization review.

MARKET DISCONTINUATION OF PHARMACEUTICALS IN THE UNITED STATES: ANALYSIS OF DRUGS APPROVED BY THE FDA FROM 1939 TO 2008

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OBJECTIVES: The pharmaceutical industry serves societal needs by bringing innova¬tive products and therapies to market. However, innovation does not guarantee market longevity. Consequently, some products will be evaluated and considered for market discontinuation. The purpose of this study was to identify drug market discontinuations, provide reasons for discontinuation, and characterize discontinued products by application type. METHODS: Data were derived from the FDA database of “Approved Drug Products” and the “Approved Drug Products with Therapeutic Equivalence Evaluations,” Federal Register, and Medline. Market discontinuations were classified by approval types (New Drug Application -NDA and Abbreviated New Drug Application-ANDA) and by reasons for discontinuation (safety, efficacy and