of needed raw data, *r* can be computed from relative risks, odds ratios, *t* statistics, *F* statistics, chi square statistics, standard normal deviate *Z* statistics, and beta coefficients. In studies reporting p-values only, p-values can be converted to their associated one-tailed standard normal deviate *Z* values to allow the calculation of *r*. Before computed *r*'s can be combined, they must be transformed using the Fisher *Z* transformation in order to normalize their distribution. The weighted and unweighted Fisher *Z* transformed *r*'s are then converted back to *r*'s, and the weighted and unweighted mean *r*'s are calculated. Confidence intervals around these estimates show the degree to which they significantly differ from zero. For the unweighted mean *r*, the random effects confidence interval is usually preferred. Although such confidence interval tends to be wider, it allows generalization to studies other than those included in the sample. This methodology is demonstrated using a dataset from a systematic review of published scientific literature. The analysis shows how diversely-reported effects sizes can be converted and combined to produce a summary *r*, which explains the association between specific determinant and outcome variables. Despite the value of correlation *r* in meta-analysis, it continues to be underused in the synthesis of scientific evidence.

PRM47

DEVELOPMENT OF LOCALLY ADAPTABLE VALUE ARGUMENTS: HOW CAN BUCKETING OF COUNTRIES AT GLOBAL LEVEL HELP MANUFACTURERS?

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Data requirements from reimbursement authorities globally vary greatly due to variation in importance of HTA and levels of acceptable complexity in submitted economic evidence. Often market differences have been addressed by global pharmaceutical companies by developing value arguments that address the most developed reimbursement systems, which then have to be adapted locally, often resulting in the duplication of effort among local affiliates. Placing customer requirements and informal preferences as the starting point of the development of value arguments can increase efficiency and more specifically meet local HTA needs. Methodologies that will support development of locally adaptable value arguments – both value dossiers as well as health economic messages - requires first of all the understanding of local payer needs. Countries requiring submission of economic data can be classified on the basis of commonly required assessment methods – budget impact analysis, cost effectiveness analysis and cost minimisation analysis, as well as the complexity accepted in both submitted clinical and economic evidence. This complexity is in terms of level of complexity of data requirements for Health Economic analysis, technical modelling approach, CE outcome, local/international data preference, preference for comparator, preferred time horizon amongst others. This can be used to divide these countries into buckets with similar requirements. Globally developed value arguments can be developed and adapted to these buckets of countries and their needs. Basing value arguments that are developed globally as mentioned, and then sent to local affiliates to adapt to the specific needs of their HTA system, on the preferences of customers is expected to be crucial to ensure local success for reimbursement.

PRM48

DESIGN AND OPERATIONAL CONSIDERATIONS FOR PRAGMATIC CLINICAL TRIALS TO SUPPORT HEOR EVALUATIONS

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Unlike randomized controlled trials (RCTs), pragmatic clinical trials (PCTs) measure the relative benefits of competing treatments in actual practice, thus, are an important pharmacoeconomic data source. Depending on the design features, trials can vary in their degree of pragmatism. We undertook a brief review of the literature to highlight specific PCT design considerations that optimize their utility for health economic and outcomes research (HEOR) applications. A broad population and active control groups, typical in PCTs, can help achieve generally representative HEOR assessments and reduce reliance upon indirect comparisons. A minimally restrictive protocol is needed to preserve a naturalistic focus, and for reducing Hawthorne effects. Some control is required, however, to minimize study biases. Randomization to initial treatment choice remains essential to avoid selection bias and confounding, but little control should be exerted on regimen changes so that real-world prescribing patterns (switching, adding, and dropping) patterns and patient behaviors (non-compliance, non-adherence) can be evaluated. In the absence of blinding, ascertainment bias is also a risk; use of objectively measured outcomes that may even be identifiable from medical charts can help. Capturing clinical, resource utilization, safety, preference, and quality of life, outcomes can lead to richer economic models, and better understanding of usual-care treatment decisions. With a broad patient base, it is important to explore subgroup effects, and to prioritize predictive analyses to identify response variation. Beyond a thoughtful study design, key operational elements such as site selection, patient recruitment and retention and ongoing study support are critical to PCT success.

PRM49

TRANSLATION AND LINGUISTIC VALIDATION – METHODOLOGICAL IMPLICATIONS WHEN THE SOURCE MEASURE IS NOT ENGLISH

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The majority of new PRO measures are developed in English, with a small minority developed in other languages. This poses the question of how to translate and linguistically validate measures developed in languages other than English, when the resources are simply not available for translating from the source language (e.g. Hungarian) into the target language (e.g. Bengali). The URAM Scale assesses functional performance of the hand in patients with Dupuytren's Contracture. It was developed in French and initially translated and linguistically validated into UK English. The methodology employed for this translation was the reverse of a typical English to French translation, whereby the French in-country investigator acted as the project manager and an in-house project manager (qualified in French to English translation) acted as the in-country investigator. The translation into English required consultation with the developer and two issues needed to be resolved in order to develop the UK English version. One item required alternative wording as it mentioned wash mitts, which are very rarely used in the UK, and for another item, two verbs were required to convey the meaning of a single French verb. On completion of the translation, the UK English version was then used as a source version for the translation of the URAM Scale into several other European languages. During this process the translators were asked to work from the English version but to also consider the relevance of the original French wording for the two items that required a change in English. For example, in countries where wash mitts are used, this wording was retained instead of the new English wording which used 'flannel'. This experience highlights the importance of always considering the original development language when translating a measure using a generated English version as the source.

POSTER SESSION III: DISEASE-SPECIFIC STUDIES

Cancer – Clinical Outcomes Studies

PCN1

CHEMOTHERAPY INDUCED NAUSEA AND VOMITING EVENT RATE AMONG PATIENTS WITH CANCER TREATED WITH HIGHLY OR MODERATELY EMETOGENIC CHEMOTHERAPY AND INITIATED ON PALONOSETRON VERSUS OTHER 5-HT3-RECEPTOR ANTAGONIST ANTI-EMETIC PROPHYLAXIS IN A HOSPITAL OUTPATIENT SETTING

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OBJECTIVES: To assess the rate of chemotherapy induced nausea and vomiting (CINV) associated with palonosetron (a 5-hydroxy tryptamine$_3$-receptor antagonist [5-HT$_3$-RA]) initiation versus other 5-HT$_3$-RAs among patients with cancer on highly [HEC] or moderately emetogenic chemotherapy (CT) [MEC] treatment in a hospital outpatient setting. **METHODS:** Patients with a cancer diagnosis initiating HEC or MEC and anti-emetic prophylaxis with palonosetron (Group 1) or other 5-HT$_3$-RAs (Group 2) for the first time (index date) between 4/1/2007 – 3/31/2009 were identified from the Premier Perspective comparative database. Inclusion criteria were patients aged ≥ 18 years with no evidence of nausea and vomiting or use of HEC/MEC or anti-emetic medication in the 6-month pre-index date period, and with 36-consecutive months of hospital data. Follow-up time was first of eight CT cycles (a cycle was the unit of analysis) or six months post-index date. A negative binomial distribution generalized linear multivariate regression model estimating the CINV event rate on CT matched groups in the follow-up period was developed after controlling for demographic and clinical variables. **RESULTS:** Of 6418 identified patients, 1522 (23.7%) initiated palonosetron. Group 1 patients comprised of less African Americans (8.7% vs. 14.2%) and more Hispanics (5.7% vs. 4.5%); $p<0.0001$, more patients on HEC [50.5% vs. 41.5%; $p<0.0001$], and more non-colon gastrointestinal (10.3% vs. 6.3%) and breast cancer patients (19.5% vs. 16.8%); $p<0.0001$. In the follow-up period, the number of unadjusted CINV events between the matched groups was lower for Group 1 [6957 vs. 7784; $p=0.054$] patients. The regression model predicted a significant decrease (12.5%) in the CINV event rate per CT cycle for Group 1 patients versus Group 2 patients; $p=0.0044$. **CONCLUSIONS:** In this retrospective hospital outpatient study, patients with cancer treated with HEC/MEC and initiated on palonosetron were more likely to experience a significantly lower rate of CINV events versus those initiating other 5-HT3-RAs.

PCN2

SAFETY AND TREATMENT PATTERNS OF ANGIOGENESIS INHIBITORS IN PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (MRCC) IN THE UNITED KINGDOM: PRELIMINARY RESULTS OF AN ONGOING CHARTS REVIEW STUDY

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OBJECTIVES: This study evaluated the rates of and reasons for treatment modifications and occurrence of adverse events (AEs) among patients treated with anti-angiogenic agents in UK clinical practice. **METHODS:** Data from medical records were retrospectively reviewed at 3 large UK oncology centers for mRCC patients who were ≥18 years and received sunitinib (N=90) as first-line treatment from January 1, 2005 to October 15, 2010. Proportions of patients with treatment modifications (i.e.: discontinuation, interruption, or dose change) and reasons for modifications were determined. Time to treatment discontinuation and proportion of patients with all grade and grade 3/4 AEs were also determined. Data on clinician assessed response rates was collected. **RESULTS:** Ten percent of patients were cytokine-pretreated. Average daily dose over initial cycle was 31.98 mg; 77.8% of patients started treatment with recommended dosing of 50 mg QD 4/2. Among the 62 patients with available tumor response assessments, 35.5% had an objective response (OR; complete or partial response). A total of 84.4% of patients experienced AEs; 24.4% experienced grade 3/4 AEs. The most commonly reported all grade AEs were diarrhea (35.6%), mucositis/stomatitis (34.4%), and fatigue (26.7%);

43.3% of patients had a dose reduction. Adverse events led to treatment modifications in 60.0% of patients. Among patients who discontinued treatment, 27.3% discontinued within 18 weeks (9.1% in 0-6 weeks, 6.1% in 7-12 weeks, and 12.1% in 13-18 weeks). Among those who discontinued, 30.3% discontinued due to AEs. **CONCLUSIONS:** Objective response rate (35.5%) was higher than that observed in expanded access trial (17%) but lower than that observed in randomized clinical trial. A large proportion (60%) of patients experienced treatment modifications due to AEs. About 15.2% of treatment discontinuations occurred within the first two cycles. This real-world clinical practice study suggests that tolerability with sunitinib is a challenge for physicians in the clinical care of mRCC patients in the UK.

PCN3

CARDIOVASCULAR COMORBIDITIES AMONG PATIENTS WITH METASTATIC COLORECTAL CANCER

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OBJECTIVES: To determine the rate of comorbid cardiovascular diseases in patients with metastatic colorectal cancer (mCRC), as comorbidities may impact treatment decisions, prognoses, and quality of care. **METHODS:** From the PHARMO Record Linkage System (RLS), including among other things, drug dispensing and hospitalisation records of approximately 3.2 million residents in The Netherlands, all patients with a primary or secondary hospital discharge code for CRC and distant metastasis between 2000 and 2008 were selected and defined as patients with mCRC. The first discharge diagnosis defining metastases served as the index date. Prevalent cardiovascular comorbidities were assessed during the 12 months prior to the index date and patients were required to be registered in the PHARMO RLS in this period to be included in the study cohort. Cardiovascular comorbidities were captured using information on drugs dispensed for the treatment of cardiovascular diseases in the outpatient setting, which include antihypertensive agents, antithrombotic agents, agents acting on the renin-angiotensin system, and cardiac therapy. Results were summarised descriptively by the number and proportion of patients receiving these agents. **RESULTS:** A total of 2,964 patients with mCRC were included in the analysis. Mean (± standard deviation) age at diagnosis was 68 (± 12) years and 53% were male. Overall, cardiovascular comorbidities were observed in 50% of the patients, with 27% having diseases requiring antithrombotic treatment (such as arterial thromboembolism, strokes, and deep vein thrombosis) and 11% having cardiac therapy. **CONCLUSIONS:** Cardiovascular comorbidities are commonly seen in patients with mCRC, which might be explained by the high mean age at diagnosis. Consideration of these conditions should be an integral part of the treatment strategy in individual patients with mCRC.

PCN4

BODY MASS INDEX AND STAGE OF DIAGNOSIS OF OVARIAN CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: The majority of ovarian cancer cases are not diagnosed until late stages, which carry dramatically greater risk of death. Obese women experience higher rates of ovarian cancer, and are at higher risk of ovarian cancer mortality. Delayed diagnosis of ovarian cancer in obese women may explain this relationship. **METHODS:** A MEDLINE search was performed to systematically identify articles that present stage of diagnosis of ovarian cancer by BMI. We included 7 of 252 articles identified in the search, and conducted a meta-analysis of 3,275 cases of ovarian cancer in these 7 studies to determine if there was an association between stage at diagnosis and BMI. **RESULTS:** 74% of cases were diagnosed at a late stage; 15% had a BMI of at least 30 kg/m^2. The data showed a significant downward trend in proportion of late-stage cases by BMI. Patients who were underweight were most likely to be diagnosed at a late stage (81%). Women with higher BMIs were less likely to be diagnosed at a late stage, with 72% of overweight women and 71% of obese women having stage III/IV ovarian cancer (p=0.009). The odds of late-stage disease were lower in high-BMI women compared to the odds of late-stage disease in women with a normal BMI (OR=0.783; 95%CI: 0.623-0.987). **CONCLUSIONS:** These findings suggest a modest inverse association between BMI and stage at diagnosis. This is contrary to the hypothesized relationship, and could be explained by diagnostic differences, increased symptoms of ovarian cancer in the obese, tumor characteristics, or cancer-related weight loss. Future studies should investigate why obese women have higher mortality rates despite earlier diagnosis of ovarian cancer.

PCN5

USING HEALTH CLAIMS DATA TO STUDY PATTERNS OF CERVICAL CANCER SCREENING AND DIAGNOSIS IN A STATE MEDICAID FEE-FOR-SERVICE POPULATION (FUNDING: AHRQ – P20-HS15930)

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OBJECTIVES: Cervical cancer (CC) is the 11th most common cancer among American women. In West Virginia (WV), it is second most common cancer and also second leading cause of cancer-related mortality in 25-44 years aged women. The study objective was to use claims data for surveillance of CC and precancerous cervical intraepithelial lesions (PCL) among women enrolled in the state Medicaid Fee-For-Service program. **METHODS:** Enrollment, demographic, and claims data for continuously enrolled female recipients aged 18-64 years for the period 2003 to 2008 were analyzed for this study. All medical claims were aggregated to reflect each recipient's medical utilization. **RESULTS:** Pap smear testing prevalence declined between 2003 (238.9/1,000) and 2008 (158.8/1,000). During the study period, approximately 58% women had at least 1 Pap smear test. While prevalence of CC diagnosis declined from 139 to 113 during the study period, the prevalence of cervical intraepithelial neoplasia-1 (CIN1) and CIN2 increased to 85 and 207 from 2003 to 2008, respectively. Approximately 73% of the women received Pap testing during the 365 day period prior to their index date of CC or PCL diagnosis. Poisson regression model found age, race, location, contraceptive use, access to provider and co-morbidity status as significant (p<.05) predictors of persistence with Pap testing. Ordinal logistic regression model predicted Pap screening persistence as a significant factor that was associated with the likelihood of an initial diagnosis of CC, high grade PCL, or low grade PCL. Only 10% of the women received appropriate follow-up care following a diagnosis of low grade PCL; for high grade PCL diagnosis 32% of the women received appropriate follow-up care. **CONCLUSIONS:** The study found declining screening rates for CC during the study period in fee-for-service Medicaid population. Disparities in appropriate follow-up care following a diagnosis of high grade or low grade PCL were also identified.

PCN6

BREAST, PROSTATE AND COLORECTAL CANCER SCREENING BEHAVIOR AND INCIDENCE OF LATE STAGE CANCER DIAGNOSIS IN ELDERLY WEST VIRGINIANS

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OBJECTIVES: Age-adjusted all-site cancer incidence and overall cancer mortality rates are higher in West Virginia (WV) compared to the US. Population-based screening is an effective tool that helps in early detection\treatment of cancer. However, incidence of late-stage diagnosis remains frequent among screening-amenable cancers in WV. The objective of this study is to identify: (1) breast, prostate and colorectal cancer screening-behavior and (2) factors associated with late-stage breast, prostate and colorectal cancer diagnosis among elderly West Virginians. **METHODS:** Cancer stage and demographic information for individuals with incidence of breast, prostate or colorectal cancer during years 2002-2005 were extracted from the WV Cancer Registry (WVCR) database. Data on cancer screening behavior were obtained from Behavioral Risk Factor Surveillance System (BRFSS) survey for 2002-2005. **RESULTS:** Age-adjusted late-stage colorectal cancer incidence rates were significantly higher in WV compared to the US population during 2002-2005. Invasive incidence rates (per 100,000) were higher among both men (WV: 67.0; US: 56.4) and women (WV: 44.2; US: 41.9). Nearly half of all colorectal cancers were diagnosed at regional or distant stage. WV rates for late-stage breast and prostate cancer incidence were lower compared to US. Screening rates for all 3 cancers in WV were lower compared to US; Colorectal Cancer (46.3% vs. 53.8%), Breast Cancer (72.5% vs. 74.6%), Prostate Cancer (59.7% vs. 61.6%). **CONCLUSIONS:** Unlike CDC report [MMWR-2010;59(No.SS-9)], West Virginians in this study had lower incidence of late-stage Breast and Prostate Cancer compared to US. However, colorectal cancer late- stage incidence rates remained higher in WV vs. the US. This difference in late-stage cancer incidence rates might be explained partially by differences in screening use, which also remained lower for all three cancers in WV compared to US. Patient, provider and health care system related factors may account for variation in the proportion of populations that get screened.

PCN7

COMPARATIVE EFFECTIVENESS ASSESSMENT OF ERLOTINIB VERSUS GEFITINIB IN FIRST-LINE EGFR ACTIVATING MUTATION POSITIVE NON-SMALL CELL LUNG CANCER

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OBJECTIVES: A biological and genetical variation of lung cancer is non-small cell lung cancer (NSCLC) bearing activating mutations in the tyrosine kinase domain of the epidermal growth factor receptor (EGFR m+). In this population the EGFR tyrosine kinase inhibitors (TKIs) erlotinib and gefitinib have shown significant increase in progression-free survival (PFS) compared to chemotherapy. Erlotinib is not yet licensed for this indication; however, an EMA marketing authorization submission is currently ongoing. Therefore both therapies will be competing to be primary choice in treatment naïve patients with EGFR m+ NSCLC; hence, in the absence of direct head-to-head comparison, there is a need for indirect treatment comparison (ITC) assessment. **METHODS:** Published phase-III evidence was used as the basis for the ITC. The Bucher et al. ITC methodology was applied to the PFS hazard ratios (HRs) obtained by comparing the TKIs versus chemotherapy. Erlotinib obtained a HR of 0.16 (95%CI: 0.10-0.26, p<0.0001) based on the OPTIMAL trial; gefitinib obtained the following PFS HRs vs. chemotherapy: IPASS trial: 0.48 (95%CI: 0.36-0.64, p<0.001); WJTOG trial: 0.33 (95%CI: 0.20-0.54, p<0.0001) and NEJGSG trial: 0.30 (95%CI: 0.22-0.41, p<0.001). Besides comparing the erlotinib PFS HR with each single gefitinib trial, erlotinib was compared to the pooled gefitinib evidence. **RESULTS:** Comparing the PFS HRs of erlotinib versus gefitinib based on the OPTIMAL trial and the IPASS trial resulted in a statistically significant PFS difference (ITC HR: 0.33; 95%CI: 0.19-0.58; p=0.0001). This statistically significant PFS difference was also observed when comparing OPTIMAL versus WJTOG (ITC HR: 0.48; 95%CI: 0.24-0.97, p=0.0395) and versus NEJGSG (ITC HR: 0.53; 95%CI: 0.30-0.9, p=0.0307). Comparing erlotinib vs. the pooled gefitinib phase-III evidence confirmed these findings. **CONCLUSIONS:** According to the underlying indirect comparison of published phase-III evidence, erlotinib is the most efficacious EGFR TKI in first-line EGFR m+ NSCLC.