tended to be protective of discontinuations due to adverse events relative to standard dose EFV. Use of arm-specific regression supplemented by endonodal trials led to tighter confidence intervals facilitating decision-making. Specifically, DTG was consequently superior to EFV with respect to CD4 cell counts and raltegravir was distinguishable from EFV when it was not otherwise. **CONCLUSIONS:** Making full use of available evidence is the focal strength of NMA methodology. Therefore, we recommend use of endonodal trials to further supplement evidence bases requiring arm-specific meta-regression.

PRM9

CRITICAL APPRAISAL OF REAL WORLD EVIDENCE – A REVIEW OF RECOMMENDED AND COMMONLY USED TOOLS

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OBJECTIVES: In an absence of randomized controlled trials (RCTs) and to verify RCT evidence, health technology assessment (HTA) agencies commonly rely on real-world (RW) studies to provide efficacy evidence for healthcare interventions. RW study designs can introduce considerable bias into a systematic review (SR) and several methodologies exist to evaluate the risk of bias in such studies. We conducted a series of reviews to identify which tools are commonly used and which are recommended by HTA bodies. **METHODS:** A targeted search of SRs including RW studies, conducted in MEDLINE and EMBASE (OVID SP), identified reviews published January 2013-June 2015. Studies identified were reviewed to determine which appraisal tool was used. Secondly, recommendations for the critical appraisal of RW studies by expert review groups (Cochrane, CRD) and HTA bodies (NICE, SMC, NCPE, AWMSG, IQWiG, PBAC, AMCP, AHRQ and CADTH) were reviewed. **RESULTS:** 1885 studies were identified and screened. Commonly used tools included Downs & Black, Chalmers, the Newcastle-Ottawa Scale, and the CriSTal checklist. Neither Cochrane nor CRD recommend a particular risk of bias instrument. The AHRQ developed the MORE checklist following a SR of existing critical appraisal tools. Of the other HTA bodies only CADTH recommend use of a specific critical appraisal tool; SIGN 50 (for cohort or case-control studies). The tools identified examine a variety of criteria including reporting, external validity, bias, confounding, and power. **CONCLUSIONS:** There is no consensus on a preferred instrument that allows for the assessment of all types of RW evidence and critical appraisal of RW evidence is often omitted from HTA submissions. There is thus a need for cross communication between groups to reach a consensus and develop a suitable tool. Until a suitable tool is developed, reviewers should select the most appropriate checklist for the design of the studies identified in a particular SR.

PRM10

DOES ATTRITION IN SUBJECT-BASED STUDIES OF DRUG SAFETY LEAD TO BIAS RELATED TO MORBIDITY?

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OBJECTIVES: Sample quality in prospective long-term drug safety studies can be impaired by selective lost-to-follow-up. Attrition will especially bias the sample, when patients with relevant risk factors selectively drop out. In this case, effects in endpoints cannot be related to study-relevant independent variables. The present contribution will demonstrate how careful follow-up procedures can prevent disease-related drop-out bias of the sample. **METHODS:** For a long-term prospective safety study of new Oral Contraceptive (OC) 25,213 women aged 20 to 40 years were enrolled from gynecological practices in Germany. The women filled-in a baseline questionnaire and were followed-up over two years with four follow-up questionnaires in total. Whenever safety-relevant signs were reported in the questionnaires, physicians validated the report. After two years 12,823 women were still in the sample and completed the fourth questionnaire. Disease differences between the "Retained" and the "Lost" group, which could indicate sample bias, were analysed using multivariate methods. **RESULTS:** The "retained" and the "lost-to-follow-up" group did not differ in initial disease status or in risk factor at study start: High blood pressure: 2.9% in "Retained Group"; 2.7% in "Lost Group" (phi=.006; n.s.), diabetes : 0.6% vs. 0.6% (phi=.001; n.s.), high cholesterol: 2.6% vs. 2.4% (phi=.007; n.s.),venous thrombosis : .8% vs. .8% (phi=.002; n.s.), smoker-rate : 34.9% vs. 42.3% (phi=.127), BMI>30: r=.004 (n.s.), age r=.048 (n.s.). The results show that drop-out of the initial sample is not related to study relevant morbidity and that sample bias cannot be concluded. **CONCLUSIONS:** Careful follow-up methods guarantee low lost-to-follow-up in longterm prospective studies of drug safety. Since drop-out cannot be attributed to study-relevant confounders, attrition does not lead to sample bias.

PRM11

ESTIMATION OF THE PROGRESSION OF COLON CANCER BY JAPANESE LARGE-SCALE INSURANCE BENEFITS DATA ANALYSIS

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OBJECTIVES: Accurate determination of the progression degree in colon cancer is of paramount importance for the decision making in treatment policy. However, it had been difficult to extract the exacerbation status from the real-world data. The objective of the study was to develop the model to determinate the progression degree using the insurance benefits data in Japan. **METHODS:** We conducted analyses using claims data provided by Medical Data Vision Co., Ltd. We extracted target patients by the criteria those who meets all of the following conditions; at least one colon cancer diagnosis (ICD-10 code C18~20), tractable from the first diagnosis to death, and have at least 365 days of observation. We set the progression degree as a scale from 0% to 100%. The degree of 100% indicates the patient death. For the first diagnosis, the scale was adjusted based on the patient's condition. We have developed a linear regression model by using the medication frequency of ATC codes as independent variables and the logit of progression degree as a dependent variable. **RESULTS:** 1,436 target patients were extracted from the database. When the actual progression degree is over 80%, the estimated progression degree rises with the actual degree, however, at the lower progression degrees, the estimated degree was excessively overestimated. **CONCLUSIONS:** We have developed a model to estimate the progression degree in colon cancer. The model estimates the progression degree well only for the last phase patients. The model should further be improved to minimize the bias at the lower degree.

PRM12

BEYOND THE MIDDLE: EVALUATING SURROGACY OF CLINICAL TRIAL ENDPOINTS ACROSS TRIAL DURATIONS

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OBJECTIVES: Overall survival (OS) remains the gold standard measure of clinical efficacy for oncology clinical trials due to its objective nature and consistency between diseases and treatments. However, given recent advances in treatments, and prolonged survival, OS benefits are becoming more challenging to establish, requiring more extensive follow-up. A number of methods to test this rationale have been developed but these often lack adequate data, relying solely on mean or median survival. Recognising these limitations, we developed an alternative methodology whereby surrogacy is established over time, to ensure that a surrogate is not only valid at the mean, but also throughout treatment duration. **METHODS:** A number of different survival points were derived from selected oncology trials by digitizing available survival curves. PlotDigitizer 2.6.4 software was used to establish time points for 10%, 25%, 50%, 75%, and 90% OS and progression-free survival (PFS). Correlation and regression analysis were evaluated at these percentiles based on survival times. Patient populations between the clinical trials were comparable to one another. Statistical analysis was conducted in STATA 12. **RESULTS:** Correlation analysis found the strongest association between PFS and OS between 75% and 25% survival (0.865 to 0.953; $p<0.01$), with a weak association at 90% survival (0.61; $p=0.096$). Regression analysis also found that PFS had the largest influence on OS between 75% and 25% survival ($R2>0.75$). **CONCLUSIONS:** Given the varying nature of how patients progress across and within types of therapies, it is essential to ensure the surrogacy of the endpoint across the full trial duration. For example, patients may progress early on in a disease and surrogacy may not be consistent across different time points. Additionally, in evaluating older studies, using this approach of scanning survival data will provide a richer picture of the disease area that may no longer be available from authors or research institutions.

PRM13

NETWORK META-ANALYSIS OF MULTIPLE OUTCOMES INCORPORATING DOSE-RELATED CONSTRAINTS: APPLICATION TO OVERACTIVE BLADDER SYNDROME

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BACKGROUND: Overactive bladder(OAB) is characterized by symptoms of urgency, incontinence, frequency and nocturia. With the syndromic nature of the condition, clinical trials often solely report the most effective outcome i.e. the symptom with the largest improvement. As a result different interventions are evaluated for different outcomes, which can have severe implications for network meta-analyses, and consequently, decision-making. **OBJECTIVES:** To evaluate the use of multivariate network meta-analysis(MVNMA) to identify the most effective intervention for treating OAB syndrome. **METHODS:** Using Bayesian Markov Chain Monte Carlo methods, we developed MVNMA accounting for the correlation between multiple outcomes to predict treatment effects for missing data. We extended this model to incorporate the exchangeability between treatment effects of the same intervention with different methods of administration (e.g. immediate release, extended release, intravesical etc.) and incorporated dose-response constraints on increasing doses. The outcomes of interest were mean change from baseline in incontinence, and urgency episodes. **RESULTS:** Independently, the datasets included 109 and 56 trials, evaluating 93 and 51 interventions, for incontinence and urgency episodes respectively. Sacral nerve stimulation appeared to be the most effective intervention for reducing incontinence with an estimated mean reduction of -8.9(95%CrI:-10.9,-7) episodes per 24hours relative to placebo. For urgency, sacral nerve stimulation was disconnected from the network and thus could not be not evaluated. Borrowing information between outcomes, the dataset for multivariate analyses included 117 trials evaluating all 95 treatments for OAB. Sacral nerve stimulation appeared to be the most effective intervention for both incontinence and urgency episodes with an estimated mean reduction of -8.3(95%CrI:-10.1,-6.9) and -9.1(95%CrI:-10.5,-7.3) episodes, respectively. **CONCLUSIONS:** Sacral nerve stimulation appeared to be the most effective intervention for treating OAB symptoms. MVNMA allowed us to evaluate all interventions across all outcomes, and in this case also increased precision in treatment effect estimates. Further work includes adjustment for baseline severity.

PRM14

THE VALUE OF PROGRESSION-FREE SURVIVAL (PFS) AS AN ENDPOINT IN ONCOLOGY TRIALS

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OBJECTIVES: The clinical endpoints selected for oncology trials have to meet the needs of diverse stakeholders: patients, clinicians, regulators, and HTA agencies, each with a different perspective. PFS is becoming a more widely accepted measure of treatment efficacy, but there is tension between regulators and payors regarding its acceptability. This study investigated PFS as a valid and credible endpoint from the perspectives of relevant decision-makers. **METHODS:** Published and gray literature (2005–2015) were searched for regulatory and HTA guidance on PFS as an endpoint. We identified examples of decisions by regulators and HTA agencies in which PFS

was the primary endpoint, and compared the assessments. **RESULTS:** Guidance from regulatory and HTA agencies indicates the suitability of PFS as an endpoint depends on the cancer type and stage, seen in assessments of afatinib and erlotinib in non-small cell lung cancer and bevacizumab in ovarian cancer: FDA and EMA approvals were based on PFS data. However, the TC in France awarded ASMR IV for erlotinib and bevacizumab and ASMR V for afatinib. NICE in the UK approved afatinib and erlotinib based on additional interim OS data and a patient access scheme; bevacizumab was not approved because of uncertainty in translating PFS gain to OS. **CONCLUSIONS:** PFS is a valid and credible endpoint in many oncology trials. However, differences in stakeholder perspectives and evidentiary requirements may mean that products approved on the basis of PFS data face delays in HTA or protracted pricing negotiations, or are rejected for reimbursement. PFS as an endpoint allows shorter trials , efficiency is improved, and fewer patients are exposed to an investigational drug. The limitations associated with PFS as an endpoint are largely manageable. Thus, the value and relevance of PFS needs to be recognized consistently across HTA agencies, and approaches harmonized between HTA agencies and regulators.

PRM15

STAKEHOLDER VIEWS ON THE ACCEPTABILITY OF REAL-WORLD EVIDENCE FOR INFORMING TRIAL DESIGN AND ASSESSMENT OF RELATIVE EFFECTIVENESS OF NEW MEDICINES

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OBJECTIVES: To elicit a comprehensive stakeholder view on the acceptability of using real-world evidence (RWE) for informing trial design and establishing relative effectiveness (RE) of new medicines in regulatory and HTA assessments. **METHODS:** IMI GetReal (www.imi-getreal.eu) is facilitating stakeholder dialogue on the role of RWE through case studies which focus on RE issues in several disease areas. In a series of pilot workshops, stakeholders considered challenges in establishing the RE of multiple sclerosis (MS) medicines. Alternative solutions were proposed for using RWE to mitigate these challenges: participants provided views on the usefulness and acceptability of solutions and the potential impact on regulatory and reimbursement decision making. **RESULTS:** Three approaches were proposed: 1) supplementing trial results with RWE in network meta-analysis (NMA) to generate RE estimates; 2) incorporating RWE in NMA to support simulations informing trial designs; 3) using risk equations derived from RWE to inform risk stratified trial designs. Stakeholders cautiously welcomed the proposals as additional options for reducing decision-making uncertainty, raising the key issue of potential biases that could be introduced by including RWE in these ways. The inclusion of RWE would most likely be considered as supportive of or adding context to regulatory submissions, but could be more central in HTA decision making and early medicine development if appropriate quality control measures are put in place to mitigate biases commonly associated with non-interventional data. **CONCLUSIONS:** For the use of RWE to become more acceptable by decision makers, standard methods for data synthesis should be developed, as well as guidelines to ensure transparency in selection of data sources and data synthesis. The GetReal consortium provides a 'safe harbour' for stakeholders to discuss the potential use of RWE for decision making, and further work is ongoing to develop methods for the 'early' use of RWE and to foster dialogue between stakeholders.

PRM16

KNOWLEDGE AND AWARENESS OF BREAST CANCER AMONG YOUNG WOMEN LIVING IN SOUTH INDIA

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OBJECTIVES: Objective of this study was to provide a baseline against which to monitor trends in breast cancer awareness and the effect of interventions to promote breast cancer awareness. **METHODS:** A cross sectional house hold survey was conducted on 365 young women between the age group of 18-40 in urban and rural areas of South India using a validated questionnaire. **RESULTS:** A total of 99% respondents knew that breast cancer is the leading cancer with a mean knowledge of 73.7±15.1% for urban and 47.2±13.9% for rural women. Sources of information for their knowledge were mainly health professionals/workers (98.2%), friends/neighbors (83.5%), TV/Radio (76.0%) and printed materials (60.2%). Rural women had significantly less awareness compared to urban women. Majority of the respondents knew the risk factors of breast cancer aging (69%), nulliparity (56.4%), delivery at more than 30 years old (46%), shorter duration of breast feeding (72.0%), contraceptive pills (46.0%), obesity (80.0%), big breast (81%), hormone replacement therapy (HRT) (54.4%), menopause after the age of 50 (20%) and menarche before age 11(34.8%). most of the respondents agreed that the following are risk factors smoking (85.2%), alcohol intake (86.8%) and exposure to radiation (67.2%).the rural respondents strongly believed that breast cancer with wearing of underwire bra (34.3%) but most of the urban respondents not believed (65.6%). Regarding awareness of the screening methods, 66% and 49% were aware about BSE and CBE respectively, 78% were aware about mammography. **CONCLUSIONS:** The study showed awareness of breast cancer and practice of screening procedures increases with higher education and urban living. Therefore, there is an urgent need to conduct breast cancer awareness camps in rural areas for an intensive breast cancer awareness campaign and availability of screening centers prioritized in rural areas.

PRM17

ANALYSIS OF EVIDENCE DATA ABOUT ADDING SUCCINIC ACID TO THE VARIOUS MEDICINES

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OBJECTIVES: Succinic acid as endogenous metabolite, has a wide range of applications in medical care. We conduct research on the development of new medicines based on succinic acid, ascorbic acid and rutin for the prevention and treatment of influenza. A systematic review was carried out to perform a qualitative assessment of succinic acid adding in the various medicines and to determine of their pharmacological action. **METHODS:** MEDLINE®, EMBASE®, Scopus, Cochrane Library databases and clinical trials registers between 1966 and Jun 2015 were performed. To analyze the RCT were selected and Review on the Study of the pharmacological action of drugs, which include succinic acid. Quality of evidence was assessed and each article was rated of quality. **RESULTS:** Our study included 29 articles (23 RCT and 6 Review). The evidence varied in terms of: scope and years of research, type of treatment, study duration, sample size (<100 to> 500 patients). Generally, the mean age of included patients was middle. For pharmacological properties and by relevance RCT are grouped as follows: antigypoxic action were 7 RCT (2003-2013 years), improve iron absorption in the gastrointestinal tract - 6 RCT (1966-1974), hepatoprotective - 4 RCT (2013-2014 years). One RCT proves the efficiency of succinic acid used in gastroenterology (a combination with omeprazole, 2012), depression (2013), in transplantation (1993) at menopause (2008), renal failure (2013), to improve body temperature during surgery (2007). Analysis of Review opens the new prospects for the use of succinic acid in cancer, diabetes and hepatitis C treatment. **CONCLUSIONS:** A comprehencive overview of these studies estimated the evidence of succinic acid addition of the drugs. Succinic acid as endogenous metabolite, is a part of drugs of different pharmacological actions. These clinical trial results have been retrieved and give the possibility to develop of new drugs with succinic acid also in Ukraine.

PRM18

OBJECTIVE DATA IN PARKINSON'S DISEASE THERAPY MANAGEMENT – A RETROSPECTIVE ANALYSIS OF THE PARKINSON'S KINETIGRAPH (PKG) DATABASE

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BACKGROUND: The Parkinson's Kinetigraph (PKG) is the first device that objectively measures treatable Parkinson's Disease (PD) symptoms in daily living. Collected symptom scores – Bradykinesia [BKS], Dyskinesia [DKS], and Fluctuation [FDS] – have been validated and correlate with PD reference standard instruments (UPDRS, AIMS, Patient Diaries). The PKG is used globally – in Europe, Asia-Pacific, and the USA. There is a de-identified central repository of all PKG reports. **OBJECTIVES:** Using the central repository, to assess whether patients who received a PKG analysis in routine care featured improved PD symptom scores over time. **METHODS:** PD patients who had 2+ PKGs within a 6-month time frame were eligible for analysis. A total of 591 patients were included and split into "controlled" and "uncontrolled" at baseline (first PKG), based on pre-defined cut-off scores for BKS (23) or DKS (5); for FDS, a normal range was defined, above and below which patients were considered uncontrolled. The Mann-Whitey U test was used for analysis. **RESULTS:** For those patients featuring scores considered "uncontrolled" (BKS high, DKS high, FDS low or high) at baseline, a statistically and clinically significant improvement, on average, was recorded for that score in their second PKG in all 4 subgroups ($p<0.01$). For those patients with uncontrolled FDS at baseline, 43% (FDS low) and 34% (FDS high) had scores considered controlled in their second PKG; regarding high DKS, 69% showed some improvement. All improved scores were sustained or somewhat augmented on average in those patients having more than 2 PKGs. **CONCLUSIONS:** The analysis suggests that adding a PKG to a PD patient's therapy management may significantly improve, and subsequently sustain, patient PD scores over time. This is important as, due to natural PD progression, one would expect PKG symptom scores to deteriorate over time. Other potential PKG benefits were not part of this analysis.

PRM19

MACHINE LEARNING FOR IDENTIFYING POTENTIALLY UNDIAGNOSED POST-STROKE SPASTICITY PATIENTS IN UNITED KINGDOM

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OBJECTIVES: Spasticity is one of the well-recognized complications of stroke which may give rise to pain and limit patients' ability to perform daily activities. The predisposing factors and direct effects of post-stroke spasticity (PSS) also involve high management costs in terms of healthcare resources and case-control designs are required for establishing such differences. In 'The Health Improvement Network' (THIN) database, such a study was difficult to provide reliable estimates since the prevalence of post-stroke spasticity was found to be substantially below the most conservative previously reported estimates. The objective of this study was to use predictive analysis techniques to determine if there were a substantial number of potentially under-recorded patients with PSS. **METHODS:** This study used retrospective data from adult patients with a diagnostic code for stroke between 2007 and 2011 registered in THIN. Two algorithm approaches were developed: 1) a statistically validated data-trained algorithm using machine techniques and 82 potential predictors; and 2) a clinician-trained algorithm based on the review of 200 stroke cases by two expert neurologists. The algorithm with the better performance was used to identify PSS cases. **RESULTS:** In THIN data, 45,613 stroke events were identified, with 660 having a diagnosis PSS. A data-trained algorithm using Random Forest showed better prediction performance than the clinician-trained algorithm, with higher sensitivity and only marginally lower specificity. Overall accuracy was 84% and 72%, respectively. The data-trained algorithm predicted an additional 3,912 records consistent with patients developing spasticity in the 12 months following a stroke. **CONCLUSIONS:** Using machine learning techniques, additional unrecorded post-stroke spasticity patients were identified, increasing the condition's prevalence