OBJECTIVES: Reimbursement decisions are often unsystematic and lack transparency, especially for orphan drugs. The objective of this study was to demonstrate whether multi-criteria decision analysis (MCDA) can support rational and explicit reimbursement decision process for orphan drugs in the Netherlands. **METHODS:** An Analytic Hierarchy Process (AHP) framework was used in which Health Economics students were asked to weigh criteria used in drug reimbursement decisions through a web-based survey. Criteria were identified by a systematic literature review. Three different orphan drugs (alglucosidase alfa in infantile Pompe disease, canakinumab in cryopyrin-associated periodic syndromes and investigational product in rare disease) were also assessed by the students on their performance on these criteria. Criteria weights and performance scores were aggregated to an overall score for each orphan drug. Rank-ordering on overall scores prioritized the reimbursement of the three drugs. The students were also asked to assess the AHP survey on feasibility. **RESULTS:** Nine criteria were identified and categorized in four domains; disease (burden of illness without treatment, life-threatening nature of the disease), drug (availability of other treatments, effectiveness of the drug, side effects and safety of the drug), financial aspects (annual costs of the drug per patient, budget impact, cost-effectiveness) and quality of evidence. The criterion 'life-threatening nature of the disease' was given the highest importance weight and budget impact the least. Alglucosidase alfa for treatment of infantile Pompe disease ranked highest of the three orphan drugs examined, particularly due to its performance in the disease and drug domains. The AHP survey was perceived as difficult by the respondents, which was confirmed by poor values for consistency ratios. **CONCLUSIONS:** Performing MCDA can enable explicit, transparent and auditable reimbursement decision-making for orphan drugs. However, its feasibility and applicability needs further investigation.

PSY115

ORPHAN AND RARE DISEASES - THE PAYER PERSPECTIVE

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OBJECTIVES: To look at the affordability of orphan medications across Europe and whether payer attitudes to high-price medications are changing in the face of rising health care expenditure and tighter budgets. **METHODS:** We conducted an online semi-quantitative survey of 10 European markets and the USA to understand how payers views and attitudes are changing in response to new treatments coming to market for rare and ultra-rare conditions. The payers selected for the survey hold or have held senior positions within their respective market institutions. The USA was included to provide international context to the European results. **RESULTS:** 82% of payers surveyed believe that the current approach to orphan drug pricing is unsustainable in the future and all respondents predict a tougher approach from payers going forward. 73% of payers do not believe that patent expiry alone will free up the necessary space for innovative orphan and ultra-orphan products. 82% of the payers surveyed believed that less than half of all orphan and ultra-orphan drugs coming to market are supported by an adequate evidence base for reimbursement. Although payers view rare diseases as a relatively high priority to fund, they are still behind therapy areas such as oncology and cardiovascular disease. **CONCLUSIONS:** As the financial performance of European countries begins to diverge, so do attitudes towards the funding of orphan medicines. The increasing number of rare diseases is forcing payers to view orphan drugs in a new light and they are becoming increasingly sceptical about the prices charged in relation to the clinical benefit offered. There is space for innovation; and patent expiry is freeing up funds, but rare diseases are competing with other therapy areas for limited budget. The bottom-line is that as rare disease spending becomes a higher proportion of pharmaceutical budgets, payers will take action to curb this trend.

PSY117

SOURCES OF INFORMATION AND PHARMACISTS' KNOWLEDGE REGARDING RARE DISEASES AND ORPHAN DRUGS: CROSS-SECTIONAL STUDY IN SERBIA

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OBJECTIVES: The lack of information and scientific knowledge of rare diseases (RDs) and orphan drug (ODs) could affect the quality of health care delivered to patients suffering from rare diseases. The aim of this study was evaluation of the level of the general epidemiological knowledge among pharmacists regarding RDs and ODs as well as how that knowledge is influenced by information sources, education level and years of experience. **METHODS:** The research design was based on a descriptive cross-sectional study. A questionnaire previously used in a pilot KAP study in Serbiain2012 was applied. The respondents were 182 pharmacists from public pharmacies in seven of 29 districts in Serbia. Individual level of knowledge was assessed by total number of correct answers from a maximum of 9, and overall knowledge was an average of the individual level of knowledge. **RESULTS:** In total, 155 pharmacists were included in the full analysis set (response rate was 86.3%). Overall, the mean age was 43.4 years, and 94% were women. The average number of information sources regarding RD was 1.7%, and mostly one source out of five was used (56.1%). Pharmacists who were engaged in post-graduate programmes or completed such programmes tended to use more sources of information (69.2%) than those who were not involved in any such programme (41.9%). The mean value of correct answers about pharmacists' knowledge regarding RD and OD was 4 ± 1.77. Most pharmacists (n = 30, 19.35%) replied correctly to 6 questions. **CONCLUSIONS:** The results indicate that years of experience and age among pharmacists do not have influence to the overall knowledge about RD. The positive impact of education was evidently, and for the better pharmaceutical care of RD patients the training of pharmacists to proper use of professional sources of information should be usefully.

PSY118

BEHAVIOR THERAPY FOR OBESITY TREATMENT CONSIDERING APPROVED DRUG THERAPY – AN UPDATE

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OBJECTIVES: Many obesity-associated diseases require intensive medical treatment and are cause of a large proportion of health-related expenditures in Germany. Treatment of obesity includes nutritional, exercise and behavior therapy, usually in combination. The goal of behavior therapy for obesity is to bring about a long-term alteration in eating and exercise habits of overweight and obese individuals. Depending of the severity of obesity, drug treatment may be indicated. To evaluate the clinical and economic effectiveness of behaviour therapy for obesity considering approved drugs reducing weight, a Health Technology Assessment was carried out in the year 2008. This HTA was updated with publications up to 12/2013, along with new developments in behavior therapies and drugs. **METHODS:** A systematic review was carried out using relevant electronic literature databases Publications chosen according to predefined criteria were evaluated by approved methodological standards of evidence-based medicine and health economics systematically and qualitatively. **RESULTS:** Nine randomized controlled trials showed moderate but statistically significant reduction of weight in the intervention groups compared to control groups between 1.1 kg (at month 4) and 6.6 kg (at month 9). Studies with several examination time points resulted in statistically significant differences in the first evaluation time point (month 6) but not in the subsequent time points (month 12, 18, 24). The most frequent approach used for behavior therapy, was per phone or Email, two studies offered behavior therapy face-to-face. New behavior therapy approaches applied were techniques such as "Motivational Interviewing" and "Transtheoretical model". No study was identified examining behavior therapy in combination with approved drug therapy. Two identified studies evaluating cost-effectiveness of behavior therapy per Email or phone showed cost-effectiveness for this kind of intervention but the results are biased due to a high rate of drop-outs. **CONCLUSIONS:** Behavior therapy considering new approaches is an effective method to reduce weight.

PSY119

COMPARISON OF TREATMENT PATTERNS AND DISEASE SEVERITY AMONG PATIENTS WITH PSORIATIC ARTHRITIS (PSA) RECEIVING THEIR FIRST BIOLOGIC, TREATED BY RHEUMATOLOGISTS AND DERMATOLOGISTS IN EUROPE (EU)

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OBJECTIVES: To compare rheumatologists and dermatologists in terms of treatment patterns and disease severity among PsA patients receiving their first biologic in 5EU (UK/Germany/France/Italy/Spain). **METHODS:** A medical chart-review study of psoriasis and PsA patients was conducted among rheumatologists and dermatologists in hospitals and private practices to collect de-identified data on disease and treatment characteristics. Physicians were screened for duration of practice (3-30yrs) and patient volume (≥2 Psoriasis/PsA biologic patients/month) and recruited from a large panel to be geographically representative in each country. Physicians abstracted charts of the next 5 consecutive Psoriasis/PsA patients in their respective sites. Treatment patterns and disease severity among PsA patients on their first line of biologic therapy treated by rheumatologists and dermatologists respectively were compared using descriptive statistics. **RESULTS:** In Q42012, 337 rheumatologists abstracted 527 PsA patient-charts (mean-age: 47.4yrs, male: 51.4%) and 225 dermatologists abstracted charts of 109 psoriasis patients with PsA (mean-age: 49.0yrs, male: 56.0%; 55.1% were managed in conjunction with a rheumatologist; 67% were referred by GP/another dermatologist). Time to first biologic since diagnosis was 41.0mo/20.8mo for the rheumatologist/dermatologist-treated cohorts; disease severity at biologic initiation per physician judgment was (mild/moderate/severe): rheumatologist-treated-cohort: 2.7%/60.2%/37.2%, dermatologist-treated-cohort: 1.96%/46.08%/ 51.96%. In rheumatologist-treated-cohort: treatment naïve-12.9%, non-biological DMARDS-experienced: 74.0%; in dermatologist-treated cohort: treatment nainve-6.5%, 1-or-2 systemic-treatment-experienced prior to their first biologic-initiation: 69.5%. 38.7%/61.3% and 27.5%/72.5% had moderate-severe/remission-mild disease-status among rheumatologist- and dermatologist-treated cohort respectively. Average current PASI score was higher among rheumatologist-treated-cohort (18.7 vs. 10.3). **CONCLUSIONS:** Across the EU5, PsA treatment patterns and disease severity varied based on physician specialty (rheumatologist vs. dermatologist); at biologic initiation dermatologists reported a significantly higher proportion of moderate/severe PsA patients than rheumatologists, but once first biologic treatment was well established dermatologists reported a lower disease burden then rheumatologists. Factors influencing these observed variations, including optimal therapeutic approaches and care coordination between specialties to alleviate patient burden may warrant further scrutiny.

PSY120

VARIATIONS IN TREATMENT PATTERNS AND DISEASE SEVERITY AMONG PATIENTS WITH PSORIASIS RECEIVING THEIR FIRST BIOLOGIC THERAPY IN EUROPE (EU)

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OBJECTIVES: To assess treatment patterns and disease severity of psoriasis patients receiving their first biologic-therapy in EU. **METHODS:** A medical chart-review study of psoriasis patients was conducted in 4Q2013 in EU5 (UK/Germany/France/Italy/Spain) among dermatologists to collect de-identified data on disease/treatment characteristics. Physicians were screened for duration-of-practice (3-30yrs) and patient-volume (≥2psoriasis biologic patients/month) and recruited from a large panel to be geographically representative in each country. Physicians abstracted the charts of next 5 consecutive psoriasis patients in their center/practice. Results from patients on their first biologic treatment were analyzed and comparisons made to EU5-averages. **RESULTS:** 877 patient-charts were abstracted; 702 (80.0%) were on their first biologic (mean age: 47.3yrs, male: 64.1%). Prior to initiating biologic therapy, immunomodulators/phototherapy were more widely used in UK than in other countries (90.3%/43.1% vs. 76.6%/30.4% overall, respectively); in Germany, fumarates/

corticosteroids were more widely used (46.5%/26.8% vs. 12.3%/11.0%) and retinoids were less commonly used (5.1% vs. 18.0%). UK physicians were less likely to prescribe a biologic-treatment before trying >=1 other systemic-treatment (1.8% vs. 8.5%), and to wait longer after diagnosis to initiate biologic-therapy (25.8movs. 20.1mo); in Germany, patients were more likely to have tried 3-5 other systemic-treatments before initiating biologic-treatment (28.0% vs. 14.2%); patients in France were the most likely to initiate a biologic without trying another systemic-treatment first (11.2% vs. 8.5%). Patients in Germany were started on biologics later on average (25.8mo after diagnosis vs. 14.0mo). The average flares in past-year was highest in Germany (1.4 vs. 0.9). Average current PASI-score (26.4 vs. 16.0) and BSA-score (22.8 vs. 19.5) were highest in Germany. In France, 41.2% of patients had not had a PASI score done past year (vs. 23.3%). In Germany, 56.0% of patients had severe/terminal disease severity at biologic-therapy-initiation (vs. 47.8%). **CONCLUSIONS:** Among psoriasis patients receiving their first biologic-therapy, treatment patterns and disease severity varied across the EU5. Factors influencing the observed variations in treatment patterns and outcomes warrant further scrutiny to decrease patient disease burden.

PSY121

APOPTOSIS AND OXIDATIVE STRESS INDUCED BY EXPOSURE OF MICROWAVE RADIATION IN RAT THYMUS: MODULATORY EFFECT OF MELATONIN

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OBJECTIVES: Exposition to microwave radiation (MW), from mobile phones, satellite communications, radio relays, radars and microwave devices in medicine induce disturbances in thymus. The pineal secretory product, melatonin (Mel), exerts a veriety of effects on the immune system. The aim of the present study was to evaluate the effect of melatonin on apoptosis and oxidative stress parametars in thymus tissue of rats after 40 days long exposure to MWs. **METHODS:** Wister rats were divided in 4 experimental groups: I (control), II (Mel group) - rats treated with Mel every day (2 mg/kg b.w., i.p), III (MW group) - rats exposed to MW (4 h/day), IV (MW+Mel) - rats treated with Mel every day (2 mg/kg b.w., i.p) and exposed to MW radiation (4 h/day). Ten animals from 4 group were successively sacrificed after 40 days of the experiment. MW was produced by a mobile test phone (SAR = 0.043-0.135 W/kg). **RESULTS:** The current study results demonstrate that MW significantly increased thymocyte apoptosis, detected using the Annexin V-FITC/PI detection kit ($p<0.001$). DNA fragmentation in thymocytes injury of MW is probably triggered by the increase activation of alkaline-DNase I (caspase 3-activated) and acid-DNase II ($p<0.05$). A significant increase in the thymus malondialdehyde (MDA) and carbonyl group concentration ($p<0.001$), and decreased activity of catalase ($p<0.001$) was registered during exposure. Melatonin was found to be effective on rat thymocyte: (1) decreased apoptotic rate of thymocytes ($p<0.001$), (2) effect on terminal apoptotic reaction, because of the decrease DNase I and DNase II activity ($p<0.01$), (3) decreased MDA and carbonyl group levels ($p<0.01$), (4) increase activity of catalase ($p<0.05$), comparated with MW group. **CONCLUSIONS:** Having in the mind obtained results we can conclude that melatonine exerts protective effects on rat thymocyte by preventing apoptosis and oxidative stress disturbances in rats' thymus under exposure of MW.

RESEARCH POSTER PRESENTATIONS - SESSION IV

RESEARCH ON METHODS STUDIES
RESEARCH ON METHODS – Clinical Outcomes Methods

PRM1

SYMTOMATIC FACTORS IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER (MDD): RESULTS FROM AN OBSERVATIONAL STUDY

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OBJECTIVES: To explore the existence and clinical implications of symptomatic factors in patients with major depressive episodes. **METHODS:** Data are from a 6-month prospective, non-interventional, observational study that included 1,549 MDD patients without sexual dysfunction in twelve countries. Depression severity was measured using the Clinical Global Impression (CGI) and the 16-item Quick Inventory of Depressive Symptomatology Self-Report ($QIDS\text{-}SR_{16}$). Pain and quality of life were measured using the pain related items of the Somatic Symptom Inventory (SSI) and the EuroQoL-5D, respectively. The $QIDS\text{-}SR_{16}$and the SSI items were jointly included in a factor analysis. Exploratory factor analysis (EFA) was conducted in a randomly selected half of the sample and confirmatory factor analysis (CFA) in the remaining half. **RESULTS:** The EFA showed that a four factor model explained the data apropriately (RMSEA 0.041, 90%CI 0.034- 0.048; CFI 0.979). The four factors were mood (feeling sad, concentration/decision making, self criticism, suicidal thoughts, interest in people or activities, energy/fatigability, psychomotor retardation and agitation); sleep (initial, middle insomnia, early awakening and sleeping too much); appetite and weight, and pain (muscle soreness, cramps in abdomen, pain in lower back, pain in heart or chest, pain in joints, neck pain, headache). The CFA showed good fit indexes for this four-factor model (RMSA 0.054, 90% CI 0.049-0.059; CFI 0.954). There was a highly statistical significant correlation (Spearman) between each of the four factors and CGI severity score and quality of life at each of the visits, with higher scores in the factors (higher severity) associated with higher CGI and lower quality of life ($p<0.001$, all comparisons). **CONCLUSIONS:** Considering the results presented, the data reasonably support that pain symptoms be included in the evaluation of patients with major depression. More severe pain symptoms are associated to higher severity of depression and lower quality of life.

PRM2

PREDICTORS OF FUNCTIONAL DISABILITY IN PATIENTS WITH CHRONIC LUMBOSACRAL RADICULAR PAIN

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OBJECTIVES: Chronic lumbosacral radicular pain has significant morbidity and burden to the society. The objective of this study was to assess the functional disability and factors affecting it in patients with chronic lumbosacral radicular pain. **METHODS:** We performed an observational cross sectional study in a public tertiary care hospital in north India. Adult patients (18 and 75 years), with >12 weeks of low back pain, without any co-morbidities were included in this study. Data regarding socio-demographics, duration of low back pain, prescribing pattern and depression collected at baseline. Pain assessed using visual analogue scale (VAS), functional disability using modified oswesrty disability questionnaire (MODQ). Patients also asked for health care utilization at the end of study. Predictors of high disability were analysed using multivariate regression analysis. **RESULTS:** A total of 246 patients (51% males and 49% females) with mean age of 44.9 (12.25) years were included for final analysis. Mean VAS and MODQ scores at baseline are 72.3+12.5 and 48.3+11.2 respectively. Based on disability scores, 62% of patients found to be crippled whereas 62% and 24% of patients fall in severe and moderate disability category respectively. VAS and MODQ scores were positively correlated ($r=0.84$, $p<0.05$). Multi factorial analysis reveals that severe pain (higher VAS scores), high duration of pain, older age, over-weight, patients from urban region and depression were significantly associated with high disability. **CONCLUSIONS:** Our study results suggest that chronic lumbosacral radicular pain patients suffer with sever disability. Severity of pain was significantly correlated with levels of disability.

PRM3

HIERARCHICAL NETWORK META-ANALYSIS INCORPORATING ORDERING CONSTRAINTS ON INCREASING DOSES OF INTERVENTIONS - APPLICATION TO OVERACTIVE BLADDER SYNDROME

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BACKGROUND: For the conservative treatment of Overactive Bladder (OAB) symptoms, the National Institute for Health and Care Excellence (NICE) in the UK currently recommends a course of supervised pelvic floor muscle training, behavioural therapy, anticholinergic medication, sacral nerve stimulation, and more recently, botulinum toxin type A (BoNTA) and Mirabegron. Given the large number of interventions and relatively few primary trials, network meta-analyses (NMAs) produce considerable uncertainty in the estimated treatment effects and consequently, there is little evidence of the most clinically effective intervention. **OBJECTIVES:** To evaluate the use of hierarchical NMAs incorporating ordering constraints on increasing doses in order to identify the most effective intervention for the treatment of OAB symptoms. **METHODS:** Using Bayesian Markov Chain Monte Carlo methods, we apply a 3-level hierarchical NMA that accounts for both the correlation between treatments within the same class, as well as the residual between-study heterogeneity. We further extend this model to incorporate ordering constraints on increasing doses of the same intervention. We apply the methods to a dataset obtained from a systematic literature review of randomised controlled trials evaluating interventions for OAB syndrome. The primary outcomes of interest were mean change from baseline for voiding, urgency, and incontinence episodes. **RESULTS:** The dataset includes 78 trials comparing 39 interventions that can be further categorised into 10 classes of interventions, including placebo. For voiding, and urgency episodes, BoNTA 200u was the most effective intervention with estimated mean reduction of -2.24 (95% CrI: -2.95, -1.48), and -2.6 (95% CrI: -3.46, -1.7) episodes relative to placebo, respectively. BoNTA 300u was the most effective intervention for reducing incontinence episodes with an estimated mean reduction of -1.81 (95% CrI: -2.39, -1.33) episodes relative to placebo. **CONCLUSIONS:** Use of hierarchical NMAs, incorporating ordering constraints, increases the precision in the effect estimates but maintains the interpretability of individual interventions. BoNTA was found to be the most effective intervention for reducing symptoms of OAB.

PRM4

TREATMENT EFFECT HETEROGENEITY IN CLINICAL TRIALS: AN EVALUATION OF 13 LARGE CLINICAL TRIALS USING INDIVIDUAL PATIENT DATA

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OBJECTIVES: Using randomized clinical trials (RCTs) for clinical decision-making necessitates making decisions for individuals based on average treatment effects. While many assume important patient variation in treatment effects, identifying patients most likely to benefit is problematic. Stratifying patients by their risk of the primary outcome was proposed as a method to identify high versus low benefit patients. **METHODS:** From publically available sources, we identified 13 large RCTs with greater than ~1000 enrollees and overall statistically significant results. We derived Cox or logistic regression models using established risk factors blinded to treatment assignment and stratified the patient population into quartiles of risk for the outcome. Treatment effect within each risk quartile was estimated on relative and absolute scales. Heterogeneity of treatment effect (HTE) was evaluated statistically by testing for an interaction between treatment and the linear predictor of risk, and by comparing hazard (or odds) ratios and absolute risk reduction in the extreme risk quartiles. **RESULTS:** Among 19 unique treatment comparisons analyzed, there was no apparent relationship between baseline risk and the hazard (or odds) ratios across trials; only 1 of 19 analyses had a significant interaction between treatment and baseline risk on the proportional scale. The difference in the log hazard ratio between the extreme risk quartiles ranged from -0.89 to 0.60 (median=0.03; inter-quartile range (IQR) =-0.4-