

outcomes and costs was not conducted because the time horizon of the analysis did not exceed 1 year. Bivariate sensitivity analysis (SA) was performed. **RESULTS:** The cost of the 1st year therapy of compared drugs was: 28,822, 20,810, 57,449 and 54,332 rubles for piribedil CR, pramipexole ER, ropinirole ER and rasagiline respectively. Total therapy cost was estimated by summarizing the cost of therapy and ADR costs. Total costs for comparator drugs constituted: 28,930, 21,009, 57,576 and 54,381 rubles for piribedil CR, pramipexole ER, ropinirole ER and rasagiline respectively. Utility effect of the comparison drugs was: -6.1, -8.2, -0.3, -2.7 for piribedil CR, pramipexole ER, ropinirole ER and rasagiline respectively. In the analysis was found that pramipexole ER has the lowest cost-utility ratio (CUR) - 2,562 rubles for 1 point reduction of daytime activity disruption and severity of motor impairment as indicated by UPDRS scale. **CONCLUSIONS:** Pramipexole ER has the lowest CUR. SA confirmed these results. Pramipexole ER was the dominant strategy for PD treatment demonstrating higher utility rate at lower costs.

PND60

COST-EFFECTIVENESS OF INCOBOTULINUMTOXIN-A WITH FLEXIBLE TREATMENT INTERVALS COMPARED TO ONABOTULINUMTOXIN-A IN THE MANAGEMENT OF BLEPHAROSPASM AND CERVICAL DYSTONIA

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OBJECTIVES: Incobotulinumtoxin-A is a formulation of botulinum neurotoxin type A (BoNT/A) that is free of complexing proteins. The advantages of incobotulinumtoxin-A include flexible treatment intervals determined by clinical need. The objective of this study was to assess the cost-effectiveness of incobotulinumtoxin-A administered with flexible treatment intervals compared to onabotulinumtoxin-A in blepharospasm (BLEPH) and cervical dystonia (CD) from the Australian healthcare providers' perspective. **METHODS:** A Markov state transition model was developed to perform a cost-utility analysis (CUA) comparing the cost and health benefits of incobotulinumtoxin-A with onabotulinumtoxin-A. The CUA compared incobotulinumtoxin-A treatment, given at minimum intervals of 6 weeks and maximum intervals of 20 weeks, with onabotulinumtoxin-A treatment given at fixed 12 week intervals. The Markov model consisted of three health states and followed patients in weekly cycles for one year. Only direct healthcare costs associated with the acquisition and administration of BoNT/A's were included. Utility values were derived from a prospective, open-labelled cohort study. The primary outcome measure was the incremental cost per quality-adjusted life year (QALY). Univariate and probabilistic sensitivity analyses were conducted. **RESULTS:** Incobotulinumtoxin-A dominated onabotulinumtoxin-A in both BLEPH and CD. The option to administer incobotulinumtoxin-A according to patient needs resulted in patients experiencing fewer number of weeks with symptoms compared to onabotulinumtoxin-A administered at fixed 12 week intervals. Incobotulinumtoxin-A provided cost savings to the Australian healthcare system. Results held under sensitivity analyses. **CONCLUSIONS:** Incobotulinumtoxin-A administered at flexible treatment intervals, determined by patient needs, represents a more cost-effective treatment option when compared with onabotulinumtoxin-A in the Australian healthcare system.

PND61

COST-UTILITY OF FINGOLIMOD COMPARED WITH DIMETHYL FUMARATE (DMF) IN HIGHLY ACTIVE RELAPSING REMITTING MULTIPLE SCLEROSIS (RRMS) IN ENGLAND: COMPARISON OF A MARKOV AND DISCRETE EVENT SIMULATION MODEL

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OBJECTIVES: A cohort Markov model based on disability scores was originally constructed. Due to constraints of a Markov structure and to test structural uncertainty, a discrete event simulation (DES), based on time to event, was subsequently developed. **METHODS:** The same inputs were used in both models, except that in the DES a cohort of individual patients that reflected the patients from the main fingolimod trials was used and risks of some events were linked to baseline characteristics. For both models, published post hoc clinical data in the HA RRMS subgroup were taken from the pivotal trials for fingolimod and DMF vs placebo. Utility data for each health state and for relapses were used in line with previous similar models. Published costs were inflated to NHS cost year 2013-14 and UK list prices used for both drugs. Possible Patient Access Scheme (PAS) discount scenarios were investigated. **RESULTS:** In the base case, using list prices, the average probabilistic incremental cost-effectiveness ratio (ICER) for fingolimod vs DMF was found to be £14,076 per QALY using the Markov model (incremental cost: £10,358, QALYs: 0.74) and £11,449 per QALY using the DES (incremental cost: £8,694, QALYs: 0.76), with a 73% and 72% chance of fingolimod being cost-effective at a willingness-to-pay threshold of £30,000/QALY, respectively. Both models were most sensitive to treatment effect on disability progression, but robust to other changes including incorporation of a wide range of PAS estimates. **CONCLUSIONS:** The Markov and DES models produced similar results, both concluding that fingolimod remains cost-effective in HA RRMS following the introduction of DMF to the UK market. This validates the use of a DES in this situation. DES has greater potential than the Markov model to be easily adapted in the future to deal with changing assumptions on long-term efficacy, treatment sequences and chronic adverse events.

PND62

DIFFERENCES IN WORK PRODUCTIVITY ACTIVITY IMPARMENT IN RRMS PATIENTS INITIATED ON ORAL DMF OR PLATFORM THERAPIES IN EUROPE AND US

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BACKGROUND: Multiple sclerosis (MS) is a chronic and debilitating disease of the central nervous system that affects approximately 570,000 persons in the United States and 2.3 million worldwide. As most individuals experience initial symptoms between the ages of 20 and 40 years, MS can have a significant impact on healthcare consumption, productivity and employment. **OBJECTIVES:** To compare the work productivity impairment in patients initiated on delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF) and prior approved interferon β -1a/b or glatiramer acetate (ABCRE) therapies. **METHODS:** Data were identified from the Adelphi MS Disease Specific Programme, a cross-sectional study of MS patients in five EU countries and US. Relapsing Remitting MS (RRMS) patients were identified, receiving DMF or ABCRE therapies with treatment duration greater than 12 months. Inverse-probability-weighted regression-adjustment estimated average treatment effects (ATEs) across DMF and ABCRE cohorts, utilizing a propensity score generated from age, gender, EDSS score at current treatment initiation, BMI, duration of current treatment, line of therapy, time since MS diagnosis, and number of comorbid conditions. Work productivity and daily activity impairment due to MS, as measured by the Work Productivity and Activity Impairment (WPAI:MS) questionnaire, were compared across treatment arms. **RESULTS:** Work productivity and activity impairment data was available for 160 and 243 patients, respectively. Overall work impairment due to MS was significantly lower in the DMF cohort (ATE=-13.92%, p<0.001, vs. 20.92%). Similarly, impairment while working (presenteeism) due to MS was significantly lower in the DMF cohort (ATE=-12.97%, p<0.001, vs. 19.45%). No percent of work missed (absenteeism) was observed in the DMF cohort (ATE=-2.06%, p=0.012, vs. 2.06%). Daily activity impairment was significantly lower in the DMF cohort (ATE=-17.26%, p<0.001, vs. 25.31%). **CONCLUSIONS:** Compared with ABCRE patients, patients on DMF had a significantly lower work productivity loss as measured by WPAI-MS.

PND63

THE IMPACT OF INCREASING MULTIPLE SCLEROSIS (MS) SEVERITY LEVEL ON EMPLOYMENT AND CAREGIVER BURDEN

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OBJECTIVES: MS is a chronic disease associated with substantial clinical and socioeconomic burden. MS patients experience increasing levels of disability as their disease progresses. This study investigates the association between increasing MS severity and its impact on relapsing-remitting (RRMS) and secondary progressive (SPMS) MS patients. **METHODS:** Data were drawn from the Adelphi MS Disease Specific Programme, a global (France, Germany, Italy, Spain, UK, USA) cross-sectional study with 2965 RRMS and 494 SPMS patients. Multiple logistic, linear and partial proportional odds regressions determined the association between physician-reported MS severity ('very mild' [RRMS only], 'mild', 'moderate', 'severe') and presence of an informal caregiver, weekly informal caregiver hours, and employment status, respectively. Regressions adjusted for age, gender, BMI and number of comorbid conditions. Reference category was 'very mild' and 'mild' for RRMS and SPMS, respectively. **RESULTS:** For RRMS patients, the likelihood of part-time employment or unemployment, increased with MS severity (mild: OR = 1.51; moderate: OR = 3.28; severe: OR = 17.39; p<0.001 for all) and (mild: OR = 1.18, p=0.143; moderate: OR = 2.45, p<0.001; severe: OR = 8.53, p<0.001), respectively. Similar results were observed in SPMS patients (moderate: OR = 3.41, p=0.002; severe: OR = 16.85, p<0.001) and (moderate: OR = 3.41, p=0.002; severe: OR = 16.85, p<0.001). Increasing level of severity was associated with a higher likelihood of informal care (RRMS: mild: OR = 1.60, p=0.040; moderate: OR = 4.27, p<0.001; severe: OR = 15.31, p<0.001; SPMS: moderate: OR = 6.70, p<0.001; severe: OR = 14.93, p<0.001) and higher weekly informal caregiver hours (RRMS: mild: +0.97, p=0.014; moderate: +4.52, p<0.001; severe: +13.27, p<0.001; SPMS: moderate: +8.45, p=0.006; severe: +18.81, p<0.001). **CONCLUSIONS:** Increased MS severity is associated with significantly lower employment as well as increased caregiver burden. MS patients should start effective treatments early to delay disease progression.

PND64

COMPARING RESOURCE USE IN ALZHEIMER'S DISEASE ACROSS THREE EUROPEAN COUNTRIES - 18-MONTH RESULTS OF THE GERAS STUDY

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OBJECTIVES: To compare resource utilization drivers of societal costs for Alzheimer's disease (AD) over 18-months in three countries participating in an observational study. **METHODS:** GERAS is a prospective, multi-centre, non-interventional cohort study in France (n=419), Germany (n=550) and the UK (n=526). Resource use of AD patients and caregivers (including informal caregiving time and institutionalization), contributing to >1% total societal costs (comprising patient health and social care costs and informal caregiver costs - based on 2010 prices) were identified and assessed for country differences using Generalised Linear Models of repeated measures or Cox models, adjusting for key patient and caregiver characteristics. **RESULTS:** 18-month societal costs per patient: France €33,300, Germany €38,200 and UK €37,900. Caregiver time spent assisting patient with basic and instrumental activities of daily living (ADL) made the largest contribution to total societal costs in each country (55-69%). Caregivers in France spent less time on basic and instrumental ADLs and were less likely to miss work. Patients in France used more community care services and were more likely to spend time in respite care, whereas German patients were less likely to use respite care and had slower time to institutionalization (Hazard Ratio 0.59 (95% CI 0.41-0.84) Germany, 0.84 (0.60-1.18) France, reference UK; p-value 0.0143). UK caregivers spent more time on instrumental ADLs while patients used fewer outpatient resources but were more likely to receive financial support. No country differences in hospital stays or use of AD medication were seen. **CONCLUSIONS:** Caregiver time was consistently the

main contributor to societal costs. Although time on basic and instrumental ADLs differed across countries, some of this may be explained by use of community care services and institutionalization. Other resources had different patterns of use across countries, reflecting country-specific health and social care systems.

NEUROLOGICAL DISORDERS – Patient-Reported Outcomes & Patient Preference Studies

PND65

ADHERENCE TO INHALED ANTIBIOTICS FOR THE TREATMENT OF CHRONIC PSEUDOMONAS AERUGINOSA INFECTION IN PATIENTS WITH CYSTIC FIBROSIS: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: To perform a systematic literature review of adherence to inhaled antibiotics for the treatment of chronic *Pseudomonas Aeruginosa* (PA) infection in patients with cystic fibrosis (CF). **METHODS:** A systematic literature search of English-language articles was conducted in April 2014 using Medline and Embase. No publication date limit was applied. The literature screening was conducted by 2 independent reviewers. All of the included studies were assessed for quality. **RESULTS:** The search yielded 192 publications, of which 9 met the inclusion criteria and underwent data extraction. Six studies focused on inhaled tobramycin, 1 on inhaled colistimethate, 1 on inhaled levofloxacin, and 1 on inhaled aztreonam lysine. Medication adherence to inhaled antibiotics was analyzed by pharmacy refill history, daily phone diary, parent and child self-reports, vials counting, or electronic monitoring. Proportion of adherent patients ($\geq 75\%/80\%$ of required doses taken) in randomized clinical trials ($n=3$) ranged from 86% to 97%; adherence rates in prospective cohort studies ($n=2$) ranged between 36% and 92%, and in retrospective studies ($n=4$) ranged between 60% and 70%. The adherence to inhaled antibiotics in CF was found to be associated with the complexity of treatment, time of drug administration, age of patients, treatment burden (i.e., adverse events, taste), and patient satisfaction. **CONCLUSIONS:** Adherence varied depending on the type of study, type of treatment, and method of measurement. In real-world trials, poor adherence to inhaled antibiotics was found in patients with CF. Regular routine adherence monitoring during CF care, discussion about sub-optimal adherence and treatment reinforcement on the basis of treatment burden, clinical status, and adverse events may help to better understand the predictors and the long-term consequences of non-adherence to inhaled antibiotics for the treatment of chronic PA infection in CF.

PND66

COMPARISON OF COMPLIANCE AND DISCONTINUATION RATES AMONG MS PATIENTS TREATED WITH FINGOLIMOD AND OTHER DISEASE-MODIFYING THERAPIES: A CANADIAN RETROSPECTIVE CLAIMS ANALYSIS

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OBJECTIVES: Pharmacological management of relapsing-remitting multiple sclerosis (RRMS) includes the use of oral, injectable, or infusible Disease Modifying Therapies (DMTs). Achieving therapeutic goals in MS requires strict adherence to medication administration schedule. To assess compliance and discontinuation rates with DMTs in Canadian patients with RRMS. **METHODS:** This non-interventional, retrospective analysis was based on private claims patient cohorts accessed through IMS Rx Dynamics®. Patients had at least one prescription filled for each DMT (oral: fingolimod, dimethyl fumarate (DMF), teriflunomide; injectable (BRACE): interferon beta-1a, interferon beta-1b, glatiramer acetate; infusible: natalizumab). Patients were compliant if the medication possession ratio (MPR) was $\geq 80\%$. Discontinuation rates were calculated based on patients who stopped therapy or who were switched to another DMT. Compliance and discontinuation rates were collected at 6-month intervals with compliance cohorts from August 2011 to December 2014 (rolling 36 months total) and discontinuation cohorts from September 2011 to January 2015. **RESULTS:** Compliance data was collected for 10315 patients (fingolimod, $n=1524$; DMF, $n=1828$; teriflunomide, $n=456$; natalizumab, $n=604$; BRACE, $n=5903$). Compliance rate across Canada was higher for fingolimod (78%) compared to other DMTs, including natalizumab (72%), DMF (70%), and BRACE (56%). In Quebec, fingolimod had a compliance rate of 80%, higher than DMF (68%) and BRACE (65%). Patients on fingolimod had the lowest discontinuation rate across Canada (22%), compared to natalizumab (30%) and BRACE (47%). In Quebec, DMF had a higher discontinuation rate (29%) than other orals (fingolimod, 20%; teriflunomide, 23%) and natalizumab (25%). **CONCLUSIONS:** In a Canadian real-world setting, the compliance rate with fingolimod was higher than for other DMTs while the discontinuation rate with fingolimod was lower compared to other DMTs. These findings may facilitate MS management strategies which may lead to improved clinical and economic outcomes. Findings based in part on data licensed from IMS Health Canada Inc. All Rights Reserved.

PND67

HOW USEFUL ARE EQ-5D AND ZBI IN ASSESSING THE IMPACT OF CARING FOR ALZHEIMER'S DISEASE PATIENTS?

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OBJECTIVES: To describe the relationship between caregiver health-related quality of life (HRQoL), caregiver burden and caregiver time for instrumental activities of

daily living (T-IADL) in carers of patients with Alzheimer's disease (AD). **METHODS:** GERAS is a prospective, non-interventional cohort study in AD patients and caregivers. The Zarit Burden Inventory (ZBI) and the EQ-5D were used to measure burden and HRQoL respectively. Spearman correlations were computed between EQ-5D, ZBI and T-IADL at baseline, 18-months and for change over 18-months. T-IADL and ZBI change scores were summarised by EQ-5D domain change category (better/stable/worse). **RESULTS:** 1495 caregivers were available at baseline [67 years (SD 12) and 64% female]. According to baseline patient severity, caregivers' EQ-5D health state values were 0.86, 0.85 and 0.82 and ZBI total scores were 25, 29 and 34 in mild, moderate and moderately severe/severe AD respectively. T-IADL increased from a mean of 79 hours (SD 89; median 60 hours) at baseline by a mean of 17 hours (SD 105; median 10 hours) over 18-months, and showed a stronger correlation with ZBI than with EQ-5D, although correlations were low for both (e.g. change scores 0.118 ZBI; 0.020 EQ-5D). Worsening within EQ-5D domains (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) was associated with the greatest increase in burden scores, although the majority of caregivers (68-90%) remained stable within each EQ-5D domain. Relative to these stable caregivers, larger increases in T-IADL over 18-months were associated with better ratings in mobility and usual activities but worsening in pain/discomfort. Larger increases in T-IADL were associated with both better and worse ratings in anxiety/depression [23.5 hours better (11%); 12.2 hours stable (68%); 24.8 hours worse (16%)]. **CONCLUSIONS:** EQ-5D health state values had low sensitivity to changes in caregiver time over an 18-month period. ZBI may better reflect the impact of caring for AD patients.

PND68

SYSTEMATIC LITERATURE REVIEW OF HEALTH STATE UTILITY VALUES IN PATIENTS WITH MIGRAINE

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OBJECTIVES: This systematic literature review (SLR) aimed to identify health state utility values among migraine patients. **METHODS:** A SLR was conducted in biomedical databases and Health Technology Assessment (HTA) websites from 2000-2014. Search terms included different combinations of migraine along with utility or quality-of-life measures. References of identified SLR/meta-analyses were investigated to identify additional studies. Each study was reviewed by two independent reviewers; disagreements were resolved by a third reviewer. **RESULTS:** The search yielded 29 publications (including a submission to the National Institute for Health and Care Excellence) from which 23 studies were extracted. The studies were mainly conducted in US ($n=6$), Canada ($n=5$), or UK ($n=3$). Sample sizes varied from 14 to >8000. Age (mean: 21-47.5 years) was reported in 16 studies while disease duration (mean: 2.3-24 years) only in four. Proportion of females ranged between 70-80%. Pain and psychiatric disorders were the most common comorbidities. Migraine was primarily defined using the International Headache Society's International Classification of Headache Disorders criteria ($n=10$). Most studies used validated utility instruments: EQ-5D ($n=12$), Health Utility Index-Mark 3 ($n=7$) or SF-36 ($n=1$) to assess utility values. Three studies used the Quality of Well Being scale, and two used custom questionnaires, using Time Trade Off or Standard Gamble techniques. Utilities values were reported using the following categories: by migraine pain severity (pain-free [0.87-0.96], mild [0.66-0.84], moderate [0.51-0.77] or severe [0.39-0.54]), by number of migraine days/month (or percentage reduction in migraine frequency: <50% to $\geq 75\%$ associated with a utility increase: 0.001 to 0.010), or by migraine type (chronic [0.43-0.89]/episodic [0.62-0.91]). **CONCLUSIONS:** This SLR confirmed that increased migraine frequency and pain severity were associated with lower utility values among migraineurs. A wide range of utility values were reported; potential differences across reported estimates are likely due to different populations or different methodologies implemented to derive estimates.

PND69

TREATMENT SATISFACTION WITH DISEASE MODIFYING THERAPIES IN MULTIPLE SCLEROSIS: A SYSTEMATIC REVIEW OF STUDIES USING THE TREATMENT SATISFACTION QUESTIONNAIRE FOR MEDICATION (TSQM)

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OBJECTIVES: Treatment Satisfaction Questionnaire for Medication (TSQM) (score range 0-100) has been shown to be a reliable and valid instrument to measure patients' satisfaction with their treatment for multiple sclerosis (MS). The 14-item TSQM Version 1.4 provides scores across four domains: effectiveness, convenience, global satisfaction, and side effects. The abbreviated 9-item TSQM-9 excludes the side effects domain. Positive changes in score indicate improvement. We conducted a systematic review of clinical studies that reported MS patient satisfaction with their disease-modifying therapies (DMTs) using TSQM. **METHODS:** We systematically searched EMBASE, MEDLINE, BIOSIS Previews and Medmeme with pre-specified search terms from 2004 onwards for manuscripts and conference proceedings of prospective MS studies. The outcomes of interest included study type, change from baseline (CFB) in TSQM scores by DMT group, and differences in CFB in TSQM across treatment groups. **RESULTS:** Six studies met all study criteria (3 single-arm observational or surveillance studies and 3 randomized studies). The DMTs studied included interferon beta-1b, glatiramer acetate, fingolimod, teriflunomide, and natalizumab. Two studies used TSQM Version 1.4, while four used TSQM-9. Study length ranged from 12 weeks to 3 years. CFB at 6 months was the most commonly reported outcome. The CFB at 6 months on the effectiveness subscale ranged from 1.8 to 26.9, convenience subscale from 3.6 to 41.2, and global satisfaction subscale from 2.9 to 20.4. The CFB at 6 months was generally higher for natalizumab and fingolimod compared with injectable platform DMTs, although this finding may be confounded by the differences in study design and patient characteristics. **CONCLUSIONS:** Several MS studies have used the TSQM to measure patient satisfaction with DMTs. Comparisons across identified studies is challenging, as there is substantial heterogeneity with regards to version of TSQM used, study type and length, and type of analyses reported.