and overseas databases including Ovid-MEDLINE, Ovid-EMBASE and Cochrane Library. A total of 274 studies were searched and 6 studies were included in the final analysis. Each of the stages from literature search and extraction of data were carried out independently by 2 researchers. RESULTS: The effectiveness of CBL gene mutation test was assessed by CBL gene mutation detection rate, relevance between CBL gene mutation and clinical outcomes, and clinical outcomes for BRACE. The CBL gene mutation detection rate was 5 to 19% among JMMI patients. The hemoglobin level and age-at-diagnosis were both significantly lower among patients with p.CBL gene mutations (p<0.01, p=0.07). There was intent to assess the impact of detecting CBL gene mutation on the medical decisions such as changes in the treatment plan and/or method; however, there were no studies reporting on this matter. CONCLUSIONS: 1. There is a need for quick and accurate diagnosis for JMMI, which will influence the strategy for disease occurring in childhood, and this test in question can be helpful in deciding on stem cell transplantation. Also, considering that CBL gene mutation occurs exclusively from other gene mutations (PTPN11, RAS, NF1, etc.) contributes to the diagnosis of JMMI, it would be deemed that even a low detection rate of 5 to 19% has clinical significance. The CBL gene mutation test is an effective test that can contribute to the diagnosis of JMMI and help determine the treatment strategy (Grade of recommendation: C).

PDN8
CONFIRMED DISABILITY IMPROVEMENT IN PATIENTS WITH ACTIVE MULTIPLE SCLEROSIS TREATED WITH FINGOLIMOD VS. BRACE: A MATCHED COMPARISON OF TREATMENTS FROM THE PANGAEA AND PEARL REGISTRY STUDIES
Alosp1,2, Bergvall N3, Connelissen C3, Vormfeldt SY3, Medin F4, Ziemssen T5
1Numerus, Wokingham, UK, 2Novartis Pharma AG, Basel, Switzerland, 3Novartis Pharma GmbH, Nuremberg, Germany, 4University Clinic Carl Gustav Carus, Dresden, Germany
OBJECTIVES: To compare confirmed disability improvement in propensity score (PS) matched cohorts receiving fingolimod or BRACE (beta-interferon or glatiramer acetate) following previous BRACE treatment, who had active multiple sclerosis (MS), using data from two German observational studies, PANGAEA and PEARL REGISTRY. METHODS: Patients with active MS (≤1 year before the study) from the PANGAEA and PEARL registries were included if they had received BRACE before participating in the studies and did not have missing relapse data in the previous year. Patients from the PANGAEA registry were excluded if they had relapsed in RA 1 year before enrolment. Patients in the PANGAEA cohort were matched in a 3:1 ratio to patients in the PEARL cohort using a PS-matching approach. Time to 3-month and 6-month confirmed disability improvement was assessed using a Kaplan-Meier approach. Hazard ratios for confirmed disability improvement (fingolimod vs BRACE) were estimated using a Cox proportional hazards model. RESULTS: After PS matching, a total of 1535 patients were included (PANGAEA, n=1163, PEARL, n=372). The proportions of patients in the PANGAEA and PEARL registries meeting confirmed disability improvement were 14.6% and 7.0%, respectively (p<0.001). Similar results were seen for 6-month confirmed disability improvement (11.0% vs 6.2%; p<0.001). The probability of 3-month confirmed disability improvement was significantly higher in PANGAEA compared with PEARL (175% increase, HR, 2.27; 95% CI, 1.82-2.45; p<0.001). The corresponding value for 6-month confirmed disability improvement was a 126% increase (2.26; 1.45-3.53; p<0.001). Similar findings were found in subgroups of patients with at least 1 year of follow-up, 2.27; 95% CI, 1.91-2.70 at 6 months and 196% increase 2.36, 1.50-3.69; p<0.001). CONCLUSIONS: This comparison of real-world cohorts of patients with MS demonstrates that fingolimod treatment is associated with statistically significantly increases in the probability of confirmed disability improvement compared with BRACE.

PDN9
ADJUSTED INDIRECT COMPARISON OF ORAL MULTIPLE SCLEROSIS AGENTS
Metin H1, Huppertz H2
1Universitätsklinikum Essen, Lehrstuhl für Medizinmanagement, Essen, Germany
OBJECTIVES: BG-12 and Teriflunomide are the two oral therapies available for the treatment of Multiple Sclerosis. At the moment there is no direct comparison of these agents. The adjusted indirect comparison is a comparison of different therapies adjusted according to their direct comparison results against a common control, so that the strength of the randomised trials is preserved. METHODS: A Systematic literature search was conducted in the databases of Medline, Embase and Cochrane. Due to a lack of direct evidence an adjusted indirect comparison by Bucher in efficacy endpoints was performed. The risk of bias tool was used to assess the methodological quality of the included studies. RESULTS: 339 studies were identified in a systematic literature search. Finally four RCTs were eligible in which 4861 patients had been randomized. All included studies have a low risk of bias. There were no significant heterogeneity between the included studies in the operationalization of the relevant endpoints for AIO. Adjusted indirect comparisons could be performed in the endpoints annual relapse rate, percentage of relapse free patients and percentage of patients with EDSS progression. In the annualized relapse rate BG-12 gains a statistically significant 44% risk reduction against Laquinimod (RR=0.56; 0.52,0.60) and 26% against Teriflunomide (RR=0.74; 0.60,0.99). In no endpoints non-inferiority results were significant indicating that the relapse risk under BG-12 is less than under Laquinimod or Teriflunomide. The possible superiority of BG-12 has to be checked with the help of further direct comparative RCTs.

PDN10
COMPARATIVE EFFECTIVENESS USING A MATCHING-ADJUSTED INDIRECT COMPARISON BETWEEN DELAYED-RELEASE DIMETHYL Fumarate AND FINGOLIMOD FOR THE TREATMENT OF RELAPSING-REMITTING MULTIPLE SCLEROSIS
Fox RJ,2, Gutteridge CM,3 Chand A,4 Xiao J,5 Okwukwelu M,6 Levinson D,3 Lewin J,7 Edwards MR,4 Mararat H4
2Cleveland Clinic, Cleveland, OH, USA, 3University of Alabama at Birmingham, Birmingham, AL, USA, 4University of Birmingham, Birmingham, UK, 5Birmingham Children’s Hospital, Birmingham, Germany, 6Biogen, Cambridge, MA, USA
OBJECTIVES: Delayed-release dimethyl fumarate (DMF, also known as gastroresistant DMF) and fingolimod are oral disease-modifying treatments for relapsing-remitting multiple sclerosis (RRMS). Direct comparisons of these agents are not available. The aim of this study was to compare the effectiveness of DMF and fingolimod in Phase 3 trials using a network meta-analysis approach (NMA). RESULTS: A network meta-analysis was performed to compare the effectiveness of DMF and fingolimod in Phase 3 trials. After matching, weighted efficacy outcomes for patients treated with DMF were compared with summary efficacy outcomes for patients treated with fingolimod. RESULTS: After matching, all baseline characteristics were balanced between the pooled DMF trials and the pooled fingolimod trials. At 2 years, annualised relapse rate ratio (95% confidence interval [CI]) for DMF vs placebo was 0.52 (0.43, 0.62) and for fingolimod vs placebo was 0.48 (0.42, 0.55). Twelve-week confirmed disability progression hazard ratio (95% CI) for DMF vs placebo was 0.70 (0.57, 0.85) and for fingolimod vs placebo was 0.76 (0.61, 0.95). Additional data, including comparison of DMF vs fingolimod, will be presented. CONCLUSIONS: In a matching-adjusted indirect comparison, the efficacy of DMF was similar to that of fingolimod on clinical measures of relapse and disability progression.

PDN11
RANKING OF DISEASE-MODIFYING THERAPIES FOR MULTIPLE SCLEROSIS
Fogarty E1, Schmitt 5, Walsh C2, Barry M1
1National Centre for Pharmaceuticals, Dublin, Ireland, 2Trinity College Dublin, Dublin, Ireland, 3University of Limorick, Limorick, Ireland
OBJECTIVES: Relapses and disability progression are the clinical hallmarks of MS and the two most commonly assessed endpoints for therapeutic interventions in clinical trials. For many patients relapses are the initial defining feature of MS. However, the accumulation of disability has the greatest long-term clinical, social and economic impact on patients and society. This study evaluated the comparative efficacy of therapies for multiple sclerosis, and ranked each therapy based on probabilities of being among the best treatments for each outcome. METHODS: A network meta-analysis was conducted within a Bayesian framework to estimate comparative annualised relapse rates (ARR) and risks of disability progression (disability free 1-4 months follow-up from relapse) 12-month disability free follow-up (delayed Dunbar interval). Cumulative ranking analysis, using the Surface Under the Cumulative Rank curve (SUCRA) method, provided a ranking of treatments for each outcome. RESULTS: Alemtuzumab and natalizumab both scored relatively highly for ARR (>90%) and disability progression confirmed after three months (>80%), while IFN-β-1a 30mcg ranked lowest among active treatments for these outcomes. Disability progression was affected by the definition of disability progression largely due to the conflicting results of IFN-β-125 mcg, ranking among the most efficacious treatments for disability progression confirmed after six months (>90%) and among the least efficacious for disability progression confirmed after three months (<40%). Alemtuzumab and natalizumab scored highly for disability progression confirmed after six months. Notable variation in ranking across outcomes was observed for fingolimod (>70% for ARR, <50% for the disability progression outcomes). CONCLUSIONS: The magnitude of treatment effects and associated uncertainty varied between DMTs, and across outcomes. While natalizumab and alemtuzumab demonstrated consistently high ranking for both relapse and progression, with older interferon-beta and glatiramer acetate products ranking lower. CONCLUSIONS: In disability progression definition leads to variation in the relative ranking of treatments.

PND13
EPIDEMIOLOGY AND CURRENT TREATMENT OF NEUROMYELITIS OPTICA: A SYSTEMATIC REVIEW
Likhar N, Mothe RK, Exam H, Kintra G, Shah C, Dang A
MarkMan Healthcare Solutions LLP (HEOR and RWE Consulting), Navi Mumbai, India
OBJECTIVES: Neuromyelitis Optica (NMO) has been described as a disease clinically characterised by severe optic neuritis and transverse myelitis. There are very few epidemiological and clinical studies in NMO and no randomised controlled studies that guide therapy. The aim of this review is to determine epidemiology of NMO and to provide an algorithm of treatment. METHODS: A systematic search was conducted of the relevant published evidence from Embase, MEDLINE, and Cochrane. Search limits were articles in English and in human. Retrieved citations were screened by two independent reviewers according to inclusion criteria: NMO, incidence, prevalence, and treatments reported in population base and observational studies. The analyses of pooled and varied trials were carried out under careful appraisal of the studies. RESULTS: A total 16 studies met the inclusion criteria including six studies reported epidemiological data while 10 other studies reported treatment algorithm. The incidence of NMO was reported to range per year in United Kingdom (UK) to 0.4 per 100,000 in Southern Denmark. Prevalence was ranged from 0.44 per 100,000 in UK to 4.4 per 100,000 in Southern Denmark. Peak incidence of NMO occurs among the people at 40-49 years of age. Low level evidence recommended inpatient 1mg/d dose for 1 to 2 weeks of plasmapheresis per week, up to 7 sessions for acute attacks of NMO. Nine studies observed the improvements in the reduction of mean annualized relapse rate. CONCLUSIONS: There is limited evidence on current available treatment thera-
corticosteroid pulse and plasmapheresis may help in acute attacks of NMO. Further well designed, adequately powered studies are required in this context.

PND14

VARIATION IN STATE-LEVEL VS. NATIONAL INCIDENCE IN RARE GENETIC DISEASE: A MONTE CARLO SIMULATION IN CONGESTION ALADRENAL HYPERPLASIA AS A PRIMARY EXPLANATION IN CONGENITAL ADRENAL HYPERPLASIA

Alinefasah A, Rittenhouse B
McGill University, Bath, MA, USA

OBJECTIVES: The cost-effectiveness of CAH screening (a state-level policy) was assessed by Yoo and Grosse (2009) using national incidence (NATL). Incidence of rare genetic diseases often varies geographically, however, it is likely that some state variation is due to sampling error. This resulted in the underestimation of sampling error explanation through a series of simulations. METHODS: We obtained actual state-level incidence (ASI) for the 50 US states plus DC for 2006. For the simulation we assumed that state equalized national incidence and constructed a Beta distribution with alpha parameter equaling predicted state cases, and Beta parameter equaling state births minus predicted cases. We then ran a Monte Carlo simulation of 1000 iterations and calculated the proportion of iterations for which the state prevalence was more extreme than the ASI (i.e. draw > ASI or ASI > NATL or draw < ASI if ASI < NATL). Small numbers of iterations more extreme than the ASI are consistent with the ASI not equaling NATL. Extreme was defined as less than 5% of draws in the simulation less than the ASI if ASI > NATL or greater than the ASI (if ASI > NATL). RESULTS: ASI per 1000 births ranged from 0 to 343 (median, 0.38). There were 21 states with ASI < NATL (including 13 values of 0) and 25 states with ASI > NATL. The median 95% CI for ASI was 46 cases reporting ASI, 21 (45%) had an “extreme” ASI by our definition. CONCLUSIONS: State incidence vary significantly according to Korean Standard Classification of Disease (KICD-10 code : G20) are selected from National Patients Sample Dataset. The characteristics of age, sex, length of stay for inpatients, the number of outpatient visit and medical cost were analyzed by using a dataset extracted. SAS 9.2 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis. RESULTS: The number of patients with Parkinson’s disease for the analysis was 4,137, and that of claims cases for 12 months was 34,259. The average age of the patients with Parkinson’s disease was 66 years old and the female to male ratio was 1.07. The prevalence level of Parkinson’s disease was about 1.5 times that of the male patients. The prevalence rate of Parkinson’s disease per 1,000 populations was 3.4% in 2013. Based on 1-year claims dataset, outpatient visits for patients were 9,831 and inpatient hospitalization days were 75.3. The annual direct medical costs were USD 487 for an outpatient and USD 10,429 for an inpatient. CONCLUSIONS: As the result, the Parkinson’s disease is the economic burden in aging society in Korea. The limitation that the sample data used for the research is smaller than the raw data should be considered. Therefore further analysis on Parkinson’s disease in aging society is needed.

PND16

FORECASTING THE PREVALENCE OF STATUS EPILEPTICUS AND ITS SUBTYPES IN EUROPE, 2015–2024

Smita M
Deerfield Institute, New York, NY, USA

OBJECTIVES: To estimate the prevalence of status epilepticus (SE), refractory status epilepticus (RSE), and super-refractory status epilepticus (SRSE) in five major European Union (5EU) markets (France, Germany, Italy, Spain, and the United Kingdom) using the Health Insurance Claims dataset (HIRA-NPS 2013), which is one of the secondary sources and Summary of Product Characteristics documentation. Switching rates and further treatment patterns were based on manufacturer’s projections. RESULTS: An estimated 5,084 people with MS received GA 20 mg/ml once-daily in Spain in 2014 (5 EU, 1% of those receiving DMTs) and were assumed to switch to more expensive newly-introduced first-line and second-line DMTs at an annual rate of 8%. Assuming these people received GA 40 mg/ml three times a week instead, and – due to receiving fewer injections – switched at an annual rate of 5%, total expenditure on DMTs and related costs was reduced by between €5.9 million and €7.2 million annually, with savings totalling €32.8 million over five years: a 21% reduction in total expenditure related to DMTs. Incremental BI of perampanel was €1,537 M RUB. Savings were primarily driven by lower acquisition costs of GA compared with other DMTs, and also from lower initiation, administration and monitoring requirements. CONCLUSIONS: Introducing GA 40 mg/ml three times a week may limit switching from GA to other DMTs, but will not change the economic impact of newly-introduced first- and second-line DMTs, potentially generating cost savings.

PND17

GLATIRAMER ACETATE 40 MG/ML THREE TIMES A WEEK FOR THE TREATMENT OF RELAPSING FORMS OF MULTIPLE SCLEROSIS: POTENTIAL COST BENEFTS OF A SWITCHING STRATEGY 1ST AND 2ND LINE THERAPY VS. A STAND-MINIMUM

Tremblay G1, Patel V2, Forsythe A2, Moiseev A3, Belousov D4
Pharmaceuticals Europe B.V., Amsterdam, The Netherlands

OBJECTIVES: To evaluate treatment costs and treatment discontinuation rates, with the proportion receiving DMTs calculated using market research data. Medication costs were based on published data, and treatment initiation, administration and monitoring costs were calculated from published Spanish sources. The number of patients with Parkinson’s disease for the analysis was 4,137, and that of claims cases for 12 months was 34,259. The average age of the patients with Parkinson’s disease was 66 years old and the female to male ratio was 1.07. The prevalence level of Parkinson’s disease was about 1.5 times that of the male patients. The prevalence rate of Parkinson’s disease per 1,000 populations was 3.4% in 2013. Based on 1-year claims dataset, outpatient visits for patients were 9,831 and inpatient hospitalization days were 75.3. The annual direct medical costs were USD 487 for an outpatient and USD 10,429 for an inpatient. CONCLUSIONS: As the result, the Parkinson’s disease is the economic burden in aging society in Korea. The limitation that the sample data used for the research is smaller than the raw data should be considered. Therefore further analysis on Parkinson’s disease in aging society is needed.

NEUROLOGICAL DISORDERS – Cost Studies

PND18

BUDGET IMPACT OF PERAMПLEAN FOR THE TREATMENT OF PATIENTS WITH PARTIAL-ONSET SEIZURES (POS) IN RUSSIA

Tremblay G1, Patel V2, Forsythe A2, Moiseev A3, Belousov D4
Pharmaceuticals Europe B.V., Amsterdam, The Netherlands

OBJECTIVES: The primary objective of this study was to estimate the incremental budget impact (BI) of utilizing perampanel to treat partial-onset seizures (POS) in patients who are 12 years of age and older in Russia. METHODS: The incremental BI was estimated by comparing the cost of POS seizures with and without perampanel. Direct (drug, healthcare provider visits, emergency room visits, hospitalizations) and indirect (overhead) costs were included. The model was developed from a societal perspective. The time horizon is 5 years. Costs are reported in rubles (RUB). RESULTS: An estimated 351,582 patients ages 12 years and older are on a treatment with first-line DMTs in Russia. Approximately 53% are refractory persistent seizures despite current treatment. The market share uptake of perampanel in POS patients is estimated to be 3%, 5%, 10%, 15% and 20% in years 1 to 5, respectively. Using these five years, the adoption of perampanel is projected to increase overall costs by 305M, 510M, 1,022M, 1,537M and 2,055M RUB, respectively. Due to seizures reductions with perampanel, 27% of the drug cost increase (5,428M RUB) over 5 years is offset by the lower utilization of direct medical resources (RUB 253M) and lower overall work impairment (RUB -1,012M), yielding an overall BI of 2.5% over 5 years. CONCLUSIONS: With a budget impact of only 2.5% over a period of 5 years and demonstrated efficacy benefits in refractory POS patients (63% median reduction in secondarily generalized seizures and 13% seizure freedom rate), perampanel should be considered a valuable treatment.

PND19

COST OFFSETS ASSOCIATED WITH REBIF USE IN FIRST-LINE BRMS: AN ANALYSIS BASED ON THE COCHRANE COLLABORATION REVIEW AND REAL-WORLD PERSISTENCE DATA

Waters J, Fuji P, Beckerman B
EMD Serono, Inc, Billerica, MA, USA, 2CBPartners, New York, NY, USA

OBJECTIVES: To project the number and costs of relapses and escalations to second-line therapy over 2 years for subcutaneous (SC) interferon beta (IFN-β) (Rebif®, intramuscular (IM) IFN-β) (IFN-β 1a, 1b, and glatiramer acetate (GA) in the treatment of first-line relapsing-remitting multiple sclerosis (RRMS) from the perspective of the UK National Health Service (NHS). METHODS: A four-state (initial therapy, alternate first-line, second-line, and second-line) Markov model was constructed to simulate a cohort of 1,000 newly-diagnosed RRMS patients. Transition probabilities were based on real-world persistence data from the NHS PAMI database and Markov model was calibrated to French and British registries. A decision analytic model was performed to test the robustness of the model results. RESULTS: Treatment with SC IFN-β 1a is projected to avoid 94, 7, and 7 additional relapses compared with IM IFN-β 1a, IFN-β 1b, and GA, respectively, resulting in savings of £20,460, £5369, and £20,677 over 2 years in a hypothetical cohort of 1,000 newly-diagnosed RRMS patients. Treatment with