Conduct a systematic review in schizophrenia relapse prevention, using randomized controlled trials (RCTs) to compare the efficacy of antipsychotics in the prevention of relapse (OR versus placebo). The review was conducted using Markov Chain Monte Carlo simulation. No firm conclusions can be made from the analysis due to the limited number of trials.

PMH5

USING TREETMAPS TO ASSESS PHYSICAL COMORBIDITY RISK IN PATIENTS WITH BIPOLAR DISORDER

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OBJECTIVES: Research has shown bipolar patients are at greater risk for somatic illnesses than the rest of the population. This study assesses the incidence and relative risk (RR) of physical comorbid disease among patients with bipolar disorder.

METHODS: A large US longitudinal claims database and medical episode grouping software was used to construct disease specific episodes of care for the years 2006–2007. Patients were identified as having an episode of care during 2005 with an episode of bipolar disorder and at least 12 months of continuous enrollment (CE). The control population were year-, age-, and sex-matched individuals with no mental health or substance abuse episodes and at least 12 months CE. A total of 102,670 cases and 205,340 controls were enrolled in the study. Of the total cases, 102,248 were with bipolar I disorder. The remaining 422 cases were classified as initiators of DLX (n = 10,239), or OSSRI (n = 1,191). Nearly all systemic disease classes and individual pain diseases were most prevalent in DLX patients, followed by VLX and ECP patients, with OSSRI patients being the least affected.

CONCLUSIONS: In routine clinical settings, mild to moderate AD patients who received donepezil had fewer total and GI symptoms versus patients treated with rivastigmine or galantamine.

PMH6

IMPACT OF COMORBIDITIES ON ANTIDEPRESSANT INITIATION: DULOXETINE, VENLAFAXINE, AND ESCLITOLAPRAM VERSUS OTHERS

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OBJECTIVES: Although efficacy and safety are 2 key issues to be taken into account when choosing an antidepressant, many other factors may also influence treatment initiation. The purpose of the study was to examine the impact of comorbidities on the initiation of antidepressants: duloxetine (DLX), venlafaxine (VLX), and escitalopram (ECP) versus other SSRIs (OSSRI) in patients with major depressive disorder (MDD). METHODS: A total of 44,026 MDD patients from a large commercial administrative claims database were classified as initiators of DLX (n = 10,239), or OSSRI (n = 11,911) during the study period. All patients were matched for the year 2006; 109,124 cases and 218,248 controls were matched using propensity score models. Cases were recorded, with similar incidences of events found across the different AChEIs. In all studies, low numbers of CNS and cardiovascular AEs were reported lowest OR for withdrawal due to other reasons, respectively. The model was considered a good fit for relapse and discontinuation due other reasons but not for DAE. CONCLUSIONS: When NICE’s schizophrenia guideline was in production, quetiapine (XR) was not licensed in the UK and therefore excluded from the health economic model. However, it is now available and the above analysis suggests that treatment with quetiapine (XR) could potentially provide benefit in the management of schizophrenia relapse prevention. No firm conclusions can be made from the analysis DAE.

PMH8

CLINICAL EFFECTIVENESS AND SAFETY OF DULOXETINE IN COMPARISON WITH PLACEBO IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER IN POLAND

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OBJECTIVES: The objective of this study was to compare the clinical effectiveness and safety of duloxetine with placebo in the treatment of major depressive disorder in Poland. METHODS: Comparison was based on a systematic review and meta-analysis according to guidelines published by the Cochrane Collaboration and the Agency for Health Technology Assessment in Poland. The most important medical databases (MEDLINE, EMBASE, CENTRAL) were searched. Two reviewers independently screened 14 RCTs were included. The quality of evidence was assessed using the Hamilton Rating Scale for Depression (HAM-D) and quality of life were measured. Percentage of patients responding to treatment (defined as ≥50% improvement in HAM-D) and percentage of patients achieving total remission (defined as ≥7 points HAM-D) were also reported. Head-to-head comparisons based on randomized controlled trials (RCTs) were performed both for safety and efficacy analysis. RESULTS: The results of 14 RCTs were included in the analysis. After 7 to 9 weeks of treatment duloxetine allowed better improvement than placebo in HAM-D scores (WMD = −3.24 [−2.94; −1.57]) and in quality of life (WMD = −3.60 [−4.89; −2.31]). Percentage of patients with response to treatment (RR = 1.42 [1.29; 1.56]), NNT = 6.95 [5.53; 9.37], and with total remission (RR = 1.45 [1.29; 1.64]), NNT = 8.92 [6.80; 12.93]) was also statistically significantly higher for duloxetine adverse event group. Although risk of suicidal adverse event was significant among treatment patients (RR = 1.19 [1.13; 1.24], NNH = 8.60 [6.75; 11.84], no differences in the incidence of serious adverse events were observed (RR = 0.55 [0.49; 1.84]). Withdrawals due to adverse events were significantly more frequent in duloxetine than in placebo group (RR = 2.11 [1.61; 2.77], NNH = 17.31 [12.87 26.44]). CONCLUSIONS: Duloxetine is efficacious drug in the treatment of patients with major depressive disorder. Safety profile seems to be acceptable (slightly worse than placebo).

PMH9

A SYSTEMATIC REVIEW OF PHARMACOLOGICAL TREATMENTS FOR BIPOLAR I MANIA

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OBJECTIVES: Update a previously published systematic review of pharmacological treatments for acute mania in bipolar I disorder, to include recent publications, including new formulationquetiapine extended release (XR), and remission rates. METHODS: Systematic review of CENTRAL, EMBASE, MEDLINE, for randomised, controlled trials comparing placebo to: aripiprazole, cariprazine, divalproex, haloperidol, lithium, olanzapine, quetiapine XR, and risperidone as monotherapy, in the treatment of acute mania in bipolar I disorder, published before March 2009. Trials of combination therapy and patients non-responsive to previous therapy were also included. Data were combined through random effects meta-analyses using Comprehensive Meta Analysis. Summary effect estimates were presented as Relative Risk (RR), versus placebo and 95% Confidence Interval (95% CI). RESULTS: 408 publications were identified and overall 19 trials from 18 papers were included for the analysis. The results for remission reported that risperidone followed by quetiapine were the most effective antipsychotics: risperidone (RR:1.87, 95%CI:2.2–2.83), quetiapine XR (RR:1.46, 95%CI:0.72;2.03), olanzapine (RR:1.39, 95%CI:1.08–1.79), Schizophrenia Clinical Guideline. METHODS: Systematic review of CENTRAL, EMBASE, MEDLINE, for double-blind RCTs with, amisulpride, aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone or zotepine, (completed November 2008). Relapse and withdrawal data were extracted using individual trial definitions. Mixed treatment comparison using Markov Chain Monte Carlo simulation was conducted using a random effects model to estimate the risk of relapse, treatment discontinuation due to either intolerable adverse effects (DAE) or other reasons. Summary effect estimates are presented as Odds Ratios [OR] with 95% Credible Intervals (95%CrI) calculated versus placebo. RESULTS: Literature searching returned 488 papers that identified 18 RCTs that were of sufficient quality to be included in the analysis. Relapse analysis reported quetiapine (XR) followed by risperidone and quetiapine as most effective: quetiapine (XR) [OR: 0.151, 95%CrI: 0.021, 0.514], paliperidone [OR: 0.168, 95%CrI: 0.035, 0.304], ziprasidone [OR: 0.107, 0.69], olanzapine [OR: 0.225, 95%CrI: 0.081, 0.513], haloperidol (OR: 0.314, 95%CrI: 0.075, 0.89), ziprasidone (OR: 0.315, 95%CrI: 0.079, 0.85), paliperidone (OR: 0.362, 95%CrI: 0.058, 1.214), amisulpride (OR: 0.387, 95%CrI: 0.041, 1.497), aripiprazole (OR: 0.518, 95%CrI: 0.09, 2.815). Amisulpride, olanzapine and aripiprazole were reported lowest OR for withdrawal due to other reasons, respectively. The model was considered a good fit for relapse and discontinuation due other reasons but not for DAE. CONCLUSIONS: When NICE’s schizophrenia guideline was in production, quetiapine (XR) was not licensed in the UK and therefore excluded from the health economic model. However, it is now available and the above analysis suggests that treatment with quetiapine (XR) could potentially provide benefit in the management of schizophrenia relapse prevention. No firm conclusions can be made from the analysis DAE.
aripiprazole (RR:1.29, 95%CI:1.05–1.58), haloperidol (RR:1.29, 95%CI:1.03–1.62).

Lithium followed by divalproex ER were the most effective mood stabilizers: lithium (RR:1.73, 95%CI:1.08–2.79), divalproex ER (RR:1.40, 95%CI:1.09–1.80), and sertraline (1.12, 95%CI:0.81–1.53), carbamazepine ER (not available).

The results for other antipsychotics were as follows: risperidone (RR:1.77, 95%CI:1.50–2.09), quetiapine XR (RR:1.61, 95%CI:1.23–2.10), olanzapine (RR:1.54, 95%CI:1.23–1.92), aripiprazole (RR:1.46, 95%CI:1.26–1.70), haloperidol (RR:1.41, 95%CI:1.19–1.66). Carbamazepine ER followed by lithium were the most effective mood stabilizers: carbamazepine ER (RR:2.01, 95%CI:1.55–2.61), lithium (RR:1.57, 95%CI:1.28–1.92), divalproex ER (RR:1.46, 95%CI:1.10–1.93), divalproex ER (RR:1.45, 95%CI:1.12–1.87). Due to incomplete reporting, the pooled mean change in BMI was considered unreliable. CONCLUSIONS: Selecting the right pharmacological treatment strategy in SMD is possible in people with SMD. This is promising given the high prevalence of sedentary lifestyles and poor dietary choices and the effects of some atypical antipsychotics on weight gain. Further study of both effectiveness and cost-effectiveness (including the most cost-effective ‘dose’) of lifestyle interventions in people with SMD is required.

DIFFERENCES BETWEEN CHILDREN AND ADOLESCENTS IN TREATMENT RESPONSE TO ATOMOXETINE AND THE CORRELATION BETWEEN QOL AND ADHD CORE SYMPTOMS

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OBJECTIVES: To explore differences between age subgroups in QOL in atomoxetine treated patients and evaluate correlations between ADHD core symptoms and QOL. METHODS: Pooled data of 5 similar clinical atomoxetine trials (8–12 weeks follow-up, 3 placebo-controlled, 2 open-label) were included in the analysis. All studies used the ADHD-RS and the CHC-PE instruments. Treatment group differences (effect size vs. placebo) in CHC-PE score changes were compared between different age groups (≥12 vs <12 years). RESULTS: A total of 611 children (<12 yrs) and 183 adolescents (≥12 yrs) were included. Baseline CHC-PE total scores (mean ± SD) were: 10.3 ± 4.7 in children (n = 534) and 12.2 ± 4.3 in adolescents (n = 77) (p < 0.001). Greater impairments in the CHC-PE ‘achievement’ domain were seen in adolescents than in children (t-scores 53.1 ± 10.26 and 26.9 ± 10.71, respectively; p < 0.05); there were no clinically relevant differences in other domains. For the CHC-PE ‘risk avoidance’ domain, the effect size of atomoxetine was higher in adolescents than in children (0.83, p < 0.001 and 0.37, p = 0.005; age treatment interaction p = 0.05); age group differences for other domains and CHC-PE total scores were not clinically relevant. ADHD-RS/CHC-PE correlations were low at baseline but moderate for changes from baseline similar in age groups. Only the ‘risk avoidance’ domain showed a trend towards lower correlation of change in adolescents (r = –0.384 and r = –0.145).

CONCLUSIONS: Both age groups showed a clinically relevant improvement of QoL at baseline. Differences in similar for adolescents and similar for children in four out of the five CHC-PE domains. In both groups, atomoxetine was effective in improving QoL. For the ‘risk avoidance’ domain, the effect size of atomoxetine was larger in adolescents than in children, while the ADHD-RS/CHC-PE correlation was lower in adolescents, indicating a lower association with core symptoms.

COMPARISON OF POLYPHARMACY VS MONOTHERAPY ON OCCURRENCE OF RELAPSE IN SCHIZOPHRENIC PATIENTS – ADVANTAGE OF PROPENSITY SCORING ADJUSTMENT

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OBJECTIVES: To evaluate time to optimization of dose in children with ADHD in The Netherlands. METHODS: Claims data from the PHARMO medical record linkage system database from 48 geo-demographic areas in The Netherlands (2003–2006). The study cohort was defined as all ADHD patients aged 6–18 years who were followed for at least 12 months after treatment initiation with methylphenidate or atomoxetine. Demographic and medication characteristics at treatment initiation, and concurrent psychotropic treatments in the year before ADHD treatment initiation were recorded. For this analysis, only patients with ≥5 dispensings for any ADHD drug during follow-up and no missing information on type of drug, strength, and number of pills per day were included. Optimized dosing regimen was defined as no change in type of drug, strength, and number of pills per day for 5 consecutive dispensings (no time restriction between dispensings). Time to optimized dosing regimen was defined as the number of days between the first dispensing for an ADHD drug (cohort entry date) and the first of five unchanged dispensings. RESULTS: Of 4909 children initiating treatment from 2003–2006, 3159 met selection criteria. The proportion of patients reaching dosing optimization with initial treatment was 65.8% for atomoxetine (ATX; n = 37, 74.8% for short-acting methylphenidate and 82.4% for long-acting methylphenidate (LA); n = 262, P = 0.05 for both ATX and SA vs LA). The median number of days required to reach optimal dosing regimen was 49 across the total sample. Among patients achieving dose optimization, those initiating treatment with LA had a significantly shorter time to dose optimization (14 days) than patients initially treated with SA (56 days; P < 0.001) or ATX (31 days; P = 0.05). CONCLUSIONS: Time to optimization of dosing regimen in children with ADHD in The Netherlands varied according to treatment chosen at initiation and was shortest for long-acting methylphenidate. Supported by funding from Shire Development Inc.