second reviewer was up to 3% more sensitive than the first. In the ovarian cancer, anti-infectives, hyperlipidemia, and clinical breast cancer reviews, the second reviewer was up to 2% more specific than the first; all were significant differences apart from the clinical breast cancer review. In the cases where the second reviewer was less sensitive or specific than the first, these differences were non-significant. CONCLUSIONS: While first and second reviewers tend to have similar sensitivity in including citations, second reviewers tend to be more accurate at excluding citations. This may be explained by the fact that, since more caution is exercised in excluding citations than including them, reviewers may wait until they have gained sufficient experience to make this decision.

MENTAL HEALTH—Clinical Outcomes Studies

PREVALENCE OF TIC DISORDERS AND COEXISTENCE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN A GERMAN COMMUNITY SAMPLE

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OBJECTIVES: To determine 12-months administrative prevalence rate of tic disorders (TD) and Tourette syndrome (TS), as well as their coexistence with ADHD in a large German community sample, against the background of the clinical importance of this association. METHODS: Data for patients with a diagnosis of any tic disorder (F95, ICD-10), Tourette disorder (F95.2), or ADHD (F90.0 and/or F90.1) were extracted from the Nordbaden claims database, covering the complete subpopulation insured by Statutory Health Insurance (2.238 million lives in 2003; for comparison: total German population insured by SHI in 2003, 70.2 million) in Nordbaden in South-Western Germany (representing 82% of the total regional population). RESULTS: A total of 3,618 patients with a diagnosis of any TD (hereof, 215 with TS) and 11,875 patients with ADHD were identified, corresponding to overall administrative prevalence rates (across all age groups) of 0.16% (TD), 0.01% (TS), and 0.53% (ADHD). Males were generally more often afflicted with any of the disorders analyzed than females (TD, 0.19% versus 0.13% for females; TS, 0.02% versus 0.01%; ADHD, 0.83% versus 0.27%). TD and TS were most prevalent among children 7–12 years (0.79% and 0.04%, respectively), and were significantly associated with presence of ADHD. ADHD was reported in 1.12% of children aged ≤12 years with TD (boys, 15.4%; girls, 4.5%), compared to 3.1% (boys, 4.4%; girls, 1.7%) in the community covered. Among adolescents (age 13–18 years), a diagnosis of ADHD was tenfold more likely in patients with TD (15.1%; boys, 18.5%; girls, 7.7%) compared with the community group (1.5%; boys, 2.3%; girls, 0.7%). CONCLUSIONS: These data extend the epidemiological database by providing for the first time information from Germany on the administrative prevalence of TD, TS, and ADHD, as well as their coexistence, hereby highlighting the relevance of taking comorbidity into account when designing health care utilization and burden of disease studies.

DIRECT AND INDIRECT TREATMENT EFFECTS ON SLEEP DISTURBANCE IN GENERALIZED ANXIETY DISORDER: A STATISTICAL MEDIATION MODEL ANALYSIS

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OBJECTIVES: The majority (50–80%) of patients with generalized anxiety disorder (GAD) suffer from a variety of sleep problems. The objective of this study was to measure the direct effect of anxiolytic treatment and, separately, its indirect effect mediated by anxiety symptoms on sleep disturbance in patients with GAD. METHODS: Data were obtained from an 8-week, double-blind, randomized, flexible-dose, placebo- and active-control study in 372 GAD patients. Patients were assigned to pregabalin (300–600 mg/day), venlafaxine XR (75–225 mg/day), or placebo. Anxiety symptoms were measured by clinician-administered HAM-A scale at baseline and on weeks 1–4, 6, and 8 and sleep disturbances were measured using the 4-item sleep disturbance subscale on Medical Outcomes Study Sleep Scale (MOS-SS), a validated patient-reported outcome measure. Statistical mediation modeling was used to estimate the direct effects of pregabalin and venlafaxine XR (relative to placebo) and the indirect effects via anxiety symptoms, the mediator variable, as measured by HAM-A total score. All available data from the trial were used in the statistical analyses. RESULTS: Patients were predominantly female (61%) and had a mean age of 41 years. Path coefficients for direct and indirect (mediated) paths for patients in the pregabalin group indicated less sleep disturbance with treatment. Fifty-three percent of the reduction in sleep disturbance was due to the direct effect of pregabalin (p = 0.007). The remainder of the reduction in sleep disturbance (47%, p = 0.015) was mediated via anxiety symptoms. In contrast, there was no difference in sleep disturbance (p = 0.58) between patients treated with venlafaxine XR or placebo. CONCLUSIONS: The underlying relationships between treatment, anxiety symptoms, and sleep disturbance are explicitly described and partitioned through mediation modeling. About half of the total improvement in sleep disturbance was identified as being due to the direct effect of pregabalin independent of an effect on anxiety symptoms.

RISPERIDONE LONG-ACTING INJECTION (RLAI) IN THE TREATMENT OF SCHIZOPHRENIA: 3 MONTH PRELIMINARY RESULTS FROM THE ELECTRONIC SCHIZOPHRENA TREATMENT ADHERENCE REGISTRY (E-STAR) IN RUSSIA

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OBJECTIVES: To evaluate preliminary treatment outcomes of Russian patients enrolled in the electronic-Schizophrenia Treatment Adherence Registry (e-STAR) following up for three months after initiating treatment with risperidone long-acting injectable (RLAI). METHODS: e-STAR is an international, prospective, observational study of schizophrenia patients initiated on RLAI. Psychiatric hospitalisations and medication use are collected retrospectively for one year and prospectively every three months for two years. Clinical and functioning outcomes, which are measured by the Clinical Global Impression Severity (CGI-S) Scale and the Global Assessment of Functioning (GAF) Scale, respectively, are assessed prospectively every three months for two years. McNemar’s test and paired-t test were used to evalu-
ate changes in categorical and continuous variables, respectively.

RESULTS: Total of 102 patients who were followed up for 3 months are included in this analysis. Of which, 43.1% were male, mean age was 38.5 ± 12.6 years old, and mean time since diagnosis was 8.9 ± 8.4 years. The first reasons for initiating RLAI were insufficient response to previous medication (43.1%) and need for maintenance (24.5%). At 3-months, 98% of patients were still on RLAI treatment. Comparing the first 3-month treatment of RLAI to the 3-month period prior to the initiation of RLAI for the 102 patients, significant decreases were observed in the proportion of patients hospitalized (26.5% vs. 2.9%, p < 0.001) and the mean number of days in hospital (10.2 days vs. 1.3 days, p < 0.001). By 3-months, there were significant improvements in disease severity and patient functioning; the average CGI-S score significantly decreased from 3.74 at baseline to 1.3 days (p < 0.001) and the mean GAF score significantly increased from 51.5 at baseline to 56.0 at 3 months (p < 0.001). CONCLUSIONS: Based on the 3-month interim results, treatment with RLAI was associated with reductions in hospitalizations and improvements in disease severity and patient functioning in Russian patients with schizophrenia.


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OBJECTIVES: Atypical antipsychotics are widely used in the pharmacologic management of schizophrenia. A meta-analysis of oral atypical antipsychotics was conducted to assess the relative effectiveness of a newly introduced agent, paliperidone extended-release (ER). METHODS: Randomized placebo-controlled studies of risperidone, olanzapine, quetiapine and aripiprazole were identified via a database search (MEDLINE, Embase, the Cochrane Library, PsycINFO and the Cumulative Index to Nursing & Allied Health Literature). Baseline demographic, efficacy and safety data were extracted and combined in the meta-analysis using the DerSimonian and Laird approach [1]. Random effects meta-regression was used to assess potential confounding by patient mean age, gender ratio and duration of therapy on variability in efficacy and safety. RESULTS: Atypical antipsychotics as a group had lower odds of withdrawal for any reason than placebo treatment (OR 0.52, 95% CI 0.46, 0.58), with paliperidone ER having lower odds than the antipsychotic class as a whole (OR 0.43, 95% CI 0.34, 0.53). Odds of withdrawal due to adverse events were lower with paliperidone ER (OR 0.88, 95% CI 0.71, 1.15) than with risperidone (OR 2.09, 95% CI 0.80, 5.41) and with the atypical antipsychotics as a class (OR 1.02, 95% CI 0.83, 1.25). Paliperidone ER was associated with a lower odds of somnolence (OR 1.33, 95% CI 0.92, 1.94) than the atypical class (OR 1.70, 95% CI 1.39, 2.09) and a lower odds of weight gain (OR 1.75, 95% CI 1.29, 2.37) than all of the atypical antipsychotics, including risperidone (OR 3.08, 95% CI 1.53, 6.20). The predominant factor in the observed variability in efficacy was the specific antipsychotic, rather than patient-related factors or duration of therapy. CONCLUSIONS: Within the spectrum of efficacy and safety of the class, Paliperidone ER demonstrates a unique efficacy and tolerability profile. Owing to the heterogeneity within the class, information on individual benefit/risk profiles of atypical antipsychotics is necessary for selecting a specific treatment for each patient. [1] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.

Comparison of Risk of Upper Gastrointestinal Hemorrhage Among SSRI-Users Within U.S. Managed Care Population

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OBJECTIVES: Serotonin is critical for maintaining platelet haemostatic function such as aggregation. SSRI-induced upper gastrointestinal hemorrhage (UGIH) may occur through SSRI-induced inhibition of serotonin reuptake by platelets, leading to depletion of serotonin after several weeks of antidepressant (i.e. SSRI) treatment. The risk of SSRI-induced-UGIH has not been documented in a U.S. managed care population. The purpose of this study was to compare the incremental likelihood of UGIH events with use of SSRIs and in combination with NSAIDs in a managed care population. METHODS: A retrospective study was designed using data from a large managed care claims database. Subjects were identified anytime between October 1, 2005 to September 30, 2006 (index-period) and classified into SSRI-users, NSAID-users or SSRI-NSAID concomitant users. Each subject was matched to a control (non-SSRI/NSAID-user) based on their index date. All subjects were treatment naïve 12 months prior to their pre-index period and followed for 12 months post index date to determine the risk of any UGIH event based on ICD-9-CM code. RESULTS: A total of 87,054, 275,476, 27,696, and 386,248 subjects were identified as SSRI-users, NSAID-users, concomitant-users and controls at index-period. The control group was significantly (p < 0.001) younger than the drug cohorts (31vs. 42years), lower (p < 0.001) proportions of females (47% vs. 57%), and lower (p < 0.001) burden of comorbid illness as measured by Charlson Comorbidity Index (0.15 vs. 0.50). Compared to the controls, concomitant-users had 1.0% (OR = 3.32; 95% CI = 2.90–3.79), SSRI-users had 0.8% (RR = 2.59; 95% CI = 2.36–2.86), and NSAID-users had 0.5% (RR = 1.83; 95% CI = 1.69–1.97) cases with a diagnoses of UGIH. CONCLUSIONS: Current SSRIs that are recommended as first line therapy for depression is associated with a risk of UGIH within first 12-months either alone or in combination with NSAIDs. Future research needs to estimate the economic burden of such bleeding events to managed care.