CONCLUSIONS: Extrapyramidal symptoms (EPS), sexual dysfunction, sedation, and weight gain, as the outcomes considered by patients taking atypical antipsychotics were the most troublesome. This research was designed to compare the tolerability of the new extended release quetiapine to the existing quetiapine immediate release formulation on these outcomes in addition to orthostatic hypotension, which could be a significant cause of morbidity. METHODS: Systematic review of CENTRAL, BIOSIS, EMBASE and MEDLINE for randomised controlled trials (RCTs) in patients with acute bipolar disorder treated with quetiapine was conducted in May 2008. Meta-analyses of quetiapine vs placebo used a random effects model. The results from the individual meta-analyses formed the basis of an adjusted indirect comparison of the two quetiapine formulations using placebo as a common comparator. Summary effect estimate for each outcome was calculated as relative risk (RR) with 95% confidence interval (95% CI) where RR < 1 favoured extended release and RR > 1 favoured immediate release. RESULTS: Of the 331 papers initially identified in the literature search, 5 RCTs compared quetiapine with placebo with a common daily dose of 300mg (4 RCTs immediate release and 1 RCT extended release). Adjusted indirect comparison identified no significant differences between the two formulations of quetiapine in the outcomes assessed. Individual results were as follows: EPS RR 0.34 (95% CI: 0.04 to 12.07); orthostatic hypotension RR 1.81 (95% CI: 0.19 to 57.84); prolactin RR 1.92 (95% CI: 0.11 to 123.24); sedation RR 1.09 (95% CI: 0.51 to 6.29); weight gain RR 0.26 (95% CI: 0.05 to 6.86). CONCLUSIONS: This adjusted indirect comparison of five placebo-controlled clinical trials suggests that the tolerability profile of extended release quetiapine is consistent with that of the immediate release formulation. Further research will need to be conducted to determine if these results are replicated in real-life clinical practice.

PMH9
TOLERABILITY OF ATYPICAL ANTIPSYCHOTICS IN THE TREATMENT OF SCHIZOPHRENIA AND BIPOLAR DISORDER: A SYSTEMATIC REVIEW OF RANDOMISED CONTROLLED TRIALS

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OBJECTIVES: To compare the tolerability profiles of atypical antipsychotics assessed in randomised controlled trials (RCTs).

METHODS: Systematic review of BIOSIS, CENTRAL, EMBASE, MEDLINE, PsycINFO for RCTs comparing two or more atypical antipsychotics (aripiprazole—ARI, olanzapine—OLZ, quetiapine—QTP, risperidone—RSD, ziprasidone—ZPD).

Searching was restricted to English-language publications and was completed in December 2007. Data were extracted on the following outcomes: anxiety or depression, bodily anxiety or restlessness, dizziness or nausae, extrapyramidal symptoms (EPS), sexual dysfunction, stiffness or tremor, tiredness or weakness, weight gain. Data were recalculated if not presented in an intention-to-treat format. Mixed treatment comparisons were conducted by Bayesian Markov Chain Monte Carlo simulation using uninformed priors. Summary effect estimates (Odds Ratios [OR], 95% credible intervals [95%CrI]) were calculated compared to RSD. RESULTS: Of the 2963 papers identified in the literature search, 50 were found to provide data on 48 RCTs comparing two or more atypical antipsychotics. The results presented a wide spectrum of tolerability among the atypical antipsychotics with no single treatment being identified as consistently better tolerated than all other. The outcomes that could be considered statistically significant at the 5% level were: decrease in
bodily anxiety or restlessness with QTP (OR 0.506, 95%CrI: 0.290, 0.789), decrease in EPS with QTP (OR 0.441, 95%CrI: 0.129, 0.910), increase in weight gain with OLZ (OR 2.139, 95%CrI: 1.764, 2.626), and decrease in weight gain with ZPD (OR 0.466, 95%CrI: 0.317, 0.657). CONCLUSIONS: The results of this systematic review paint a complex picture akin to the nature of schizophrenia and bipolar disorder, reinforcing the importance of treatment choice. To achieve optimal outcomes, physicians need to consider efficacy and tolerability together with the patient’s psychiatric history, preferences and values when making treatment decisions.

TOLERABILITY OF ONCE-DAILY EXTENDED RELEASE QUETIAPINE COMPARED TO QUETIAPINE IMMEDIATE RELEASE: A META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS IN SCHIZOPHRENIA

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OBJECTIVES: In 2002, the National Institute for Health and Clinical Excellence (NICE) highlighted extrapyramidal symptoms (EPS), sexual dysfunction, sedation, and weight gain, as the outcomes considered by patients taking atypical antipsychotics to be the most troublesome. This research was designed to compare the tolerability of the new extended release quetiapine to the existing quetiapine immediate release formulation on these outcomes in addition to orthostatic hypotension, which could be a significant cause of morbidity. METHODS: A meta-analysis of the four regulatory randomised controlled trials (Study 041, 133, 132 and 146) comparing quetiapine extended release with the immediate release formulation using a fixed effect model. Summary effect estimate was calculated as relative risk (RR) with 95% confidence interval (95% CI) where RR < 1 favours extended release and RR > 1 favours immediate release. All comparisons were conducted on a mg-for-mg basis (300 mg, 400 mg 600 mg and 800 mg) for the two formulations. Statistical heterogeneity was tested for using a chi-square test. A sensitivity analysis was conducted using a random effects model. RESULTS: All outcomes were measured in the trials included in the analyses. There were no significant differences between the two formulations of quetiapine for any outcomes assessed. Individual results were as follows: EPS RR 1.067 (95%CI: 0.694 to 1.641; p = 0.767); orthostatic hypotension RR 1.089 (95%CI: 0.744 to 1.595; p = 0.661); sedation RR 0.781 (95%CI: 0.569 to 1.073; p = 0.128); weight gain RR 0.784 (95%CI: 0.521 to 1.180; p = 0.244); prolactin RR 0.708 (95%CI: 0.465 to 1.077; p = 0.107). Significant heterogeneity was not detected in any comparison (all p > 0.42) and the effect of using a random effects model made no difference to the summary effect estimates. CONCLUSIONS: The meta-analysis suggests that the tolerability profile of extended release quetiapine is consistent with that of the immediate release formulation.

MENTAL HEALTH—Cost Studies

DRUG-RELATED PUBLIC EXPENDITURE IN EUROPE: THE BUDGET IMPACT OF ILLEGAL DRUGS

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OBJECTIVES: By testing a methodology that combines labelled and non-labelled public expenditure, this report aims to produce first estimates of the amounts European governments spend on the illegal drug problem. METHODS: The European Information Network on Drugs and Drug Addiction (REITOX) was asked to list any budgeted labelled drug-related fund found after reviewing government budgets for the year 2005 in 30 countries. In order to ensure consistency in comparing figures over time and across countries, labelled expenditure was classified according to the International Classification of the Functions of Government (COFOG). Since not all drug-related expenditure is identified as such in budgets, modelling approaches were used to estimate the amount embedded in other programmes and interventions. Non-labelled drug-related expenditure was obtained by using a top-down costing approach to estimate the proportion of expenditure causally attributable to drug use. Wherever possible, REITOX explored feasible definitions of ‘attributable proportions’ for estimating non-labelled drug-related expenditure under two COFOG functions: public order and safety and health. RESULTS: On the whole, countries have a considerable amount of quality information available on this type of costs, although calculating the non-labelled constituent is often an arduous task. Estimates from reporting countries extrapolated to European level arrived at a total cost of drug-related public expenditure in 2005 of €34 billion, which is equivalent to 0.3% of the sum of the GDP of all of the countries. This represents an average expenditure of €60 per European citizen per year. CONCLUSIONS: Whilst such figures should still be used with caution (the methodology still needs refining and country data is in no way uniform), one observation the report makes is that the disbursements identified mainly refer to public expenditure made at central government level. The future inclusion of sub-national government expenditure will certainly increase the amounts of public expenditure estimated.

BUDGET IMPACT OF GENERIC ANTIPSYCHOTIC SUBSTITUTION—A DATABASE ANALYSIS IN GERMANY

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Cost containment in Germany is to a large extent regulated by fixed doctor’s budgets (Richtgrößen) for treatment of patients in statutory health insurance (SHI). With Olanzapine (OLA) and Oral Risperidone (RIS) two of the most often used second generation antipsychotics (SGA) lost patent in 2007. Generic substitution could lead to significant cost savings. OBJECTIVES: Aim of this database analysis was to estimate the budget impact of prescribing generic OLA and RIS and to evaluate the potential for a more individualized therapy in schizophrenia without exceeding budgets. METHODS: Using the IMS Disease Analyzer based on the electronic medical records of 112 psychiatrist practices in Germany, a retrospective analysis of drug expenditures for schizophrenia was conducted. As reference data from QIV 2007 were used. Budget impact was then estimated based on a scenario assuming generic prices being 20% (RIS) or 30% (OLA) of original and an overall generic patient share of 80%. RESULTS: Data of 93.844 SHI-insured patients were analyzed. Mean drug expenditures of psychiatrists could be explained by SGA prescriptions. A total of 55.1% of those with drug prescriptions in QIV 2007 were found, with 65.028 of those with drug prescriptions in QIV 2007 were used. Budget impact was then estimated based on a scenario assuming generic prices being 20% (RIS) or 30% (OLA) of original and an overall generic patient share of 80%. RESULTS: Data of 93.844 SHI-insured patients were analyzed, 65.028 of those with drug prescriptions in QIV 2007 were used. Budget impact was then estimated based on a scenario assuming generic prices being 20% (RIS) or 30% (OLA) of original and an overall generic patient share of 80%. RESULTS: Data of 93.844 SHI-insured patients were analyzed, 65.028 of those with drug prescriptions in QIV 2007 were used. Budget impact was then estimated based on a scenario assuming generic prices being 20% (RIS) or 30% (OLA) of original and an overall generic patient share of 80%. RESULTS: Data of 93.844 SHI-insured patients were analyzed, 65.028 of those with drug prescriptions in QIV 2007 were used. Budget impact was then estimated based on a scenario assuming generic prices being 20% (RIS) or 30% (OLA) of original and an overall generic patient share of 80%. RESULTS: Data of 93.844 SHI-insured patients were analyzed, 65.028 of those with drug prescriptions in QIV 2007 were used. Budget impact was then estimated based on a scenario assuming generic prices being 20% (RIS) or 30% (OLA) of original and an overall generic patient share of 80%. RESULTS: Data of 93.844 SHI-insured patients were analyzed, 65.028 of those with drug prescriptions in QIV 2007 were used. Budget impact was then estimated based on a scenario assuming generic prices being 20% (RIS) or 30% (OLA) of original and an overall generic patient share of 80%.