PGI23

STAPLED HAEMORRHOIDOPEXY IN THE TREATMENT OF HAEMORRHOIDAL PROLAPSE—COMPARISON OF HTA REPORTS, FOR TWO ITALIAN REGIONS

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OBJECTIVES: Surgical management of Haemorrhoidal Disease includes Milligan-Morgan (MM) haemorrhoidectomy and Stapled Haemorrhoidopexy (PPH). Scope of work was to compare HTA Reports for PPH vs. MM (especially cost and budget impact analyses) for two Italian Regions: Lombardia and Toscana. **METHODS:** Literature search; identification of the surgical course (intervention, hospital admission) and global course (clinical evaluation, surgical phase, follow-up) at the local hospital level; micro-costing for PPH vs. MM at 3 hospitals per Region; comparison of direct medical costs, reimbursement tariffs and budgetary impact in 2008 Euro values. **RESULTS:** PPH surgical pattern generates costs to Hospitals of €2,306 and €2,177/case, respectively in Lombardia and Toscana; MM surgery costs are €1558 and €1277/case, respectively. Higher unitary costs of personnel and operating theatre in Lombardia drive higher surgical intervention costs, irrespective of procedure type. Whereas hospital admission costs were similar for PPH (€698 vs €638), the gap between Lombardia and Toscana widens for MM hospitalization costs (€812 vs €638), because of longer length of stay in full admission setting. The Lombardia DRG158 tariff (€1209) is not sufficient to recap costs of both alternatives, whilst the Toscana tariff (€1400) is remunerative only for MM, but not when applying higher levels of operating theatre unit cost. The global course generates costs of €2532 (PPH-Lombardia) and €2400 (PPH-Toscana) vs €1781 (MM-Toscana) and €1527 (MM-Toscana). Sensitivity analyses on literature data confirmed the robustness of basecase results. Budget impact analysis, based on regional statistics for haemorrhoidal surgery and suggested extra-tariffs for PPH, estimated the need for additional funding ranging 1.7%–16% for Lombardia and 2.2%–20.4% for Toscana, over the current Regional expenditure. **CONCLUSIONS:** Analysis of management courses showed the inadequacy of current regional funding for PPH and MM. Current regionalization of the Italian NHS prompts for implementation of HTA at the Regional level.

MENTAL HEALTH – Clinical Outcomes Studies

PMH1

COMPLIANCE WITH ANTIPSYCHOTIC DRUGS AND HOSPITALIZATION: A NESTED CASE-CONTROL ANALYSIS IN A COHORT OF PEOPLE WITH SCHIZOPHRENIA

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OBJECTIVES: To assess the association between compliance with antipsychotic drug therapy and mental health-related hospitalization in people with schizophrenia. **METHODS:** A nested case-control study using the Quebec Health Insurance Board databases. The source cohort was made of people with schizophrenia who initiated an antipsychotic treatment between January 1, 2000 and March 31, 2007. Cases were cohort members who were hospitalized for a mental health-related problem during their follow-up period. Five matched (for sex, age and year of treatment initiation) controls were selected using density sampling method thus allowing a control's observation period to equal its case's period. Compliance was assessed using the medication possession ratio (MPR). A paired multivariate logistic regression model was used to calculate adjusted odds ratios (OR). Co-variates included: mental health co-morbidities, patient characteristics at treatment initiation; antipsychotics and other drugs used as well as health services used during the observation period and current use of any antipsychotic at the end of the observation period. **RESULTS:** A total of 2429 cases were identified and matched to 11,988 controls. Compared to individuals with a MPR ≥ 80%, those with a MPR ≥ 40% and <80% (OR: 1.4; 95% confidence interval (CI): 1.1–1.7) and those with a MPR < 40% (OR: 1.9; CI: 1.5–2.4) were more likely to be hospitalized. Were also more likely to be hospitalized: past antipsychotic users (OR: 1.4; CI: 1.1–1.7), those with low SES (OR: 1.3; CI: 1.2–1.4)) and those with more medical visits (2nd tertile: OR: 1.5; CI: 1.3–1.7, 3rd tertile: OR: 2.0; CI: 1.8–2.3). Likewise, having bipolar disorder (OR: 1.7; CI: 1.4–2.0) as well as having another psychosis diagnosis (OR: 1.4; CI: 1.2–1.7) increase the likelihood of hospitalization. **CONCLUSIONS:** Among people with schizophrenia, compliance with antipsychotic treatment does influence the risk of hospitalization.

PMH2

EVIDENCE FOR SSRI IN THE TREATMENT OF DEPRESSION: EARLY KNOWLEDGE GAIN—LATE CONSEQUENCES IN ROUTINE CARE?

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OBJECTIVES: This study aims to determine since when the evidence on the two most important groups of antidepressants SSRI and TCA could be valued as a sufficient basis for medical decision making regarding the preference for one of them. Furthermore, it was analyzed whether the utilization of SSRI in Germany from this point onward was adequate and to what extent health gains might have been foregone due to a limited use of SSRI. **METHODS:** To determine since when the beneficial effect of SSRI was known, cumulative metaanalyses of RCT derived from systematic reviews were conducted. The evidence base was considered as established, when significant (5%-level) results favoring SSRI or TCA regarding two main outcome criteria (antidepressive efficacy and treatment termination due to side-effects) were observed. Utilization figures for SSRI and epidemiological estimates were taken from published sources. **RESULTS:** Findings on n = 4031 patients of 31 studies on the antidepressive efficacy from 1983 to 2001 could be considered. The cumulative metaanalysis showed no significant difference between SSRI and TCA regarding the antidepressive efficacy (RR 0.05; 95%-KI –0.01–0.12). On the other hand, in the course of time, SSRI were consistently superior regarding unwanted side-effects since 1985 (RR 0.69; 95%-KI 0.62–0.77). **CONCLUSIONS:** Regarding the comparison of the efficacy of both substance groups, our findings are in line with the common clinical appraisal. The superiority of SSRI in terms of lower rates of treatment termination has become known in the mid 1980s. The analysis of the utilization data suggests a considerable delay in the consequences of this appreciation for routine care. Factors like cost considerations and lack in knowledge dissemination might have contributed to this phenomenon. Limitations of the present analysis are primarily associated with uncertainties of epidemiological estimates and the application of study results to the entire patient population.

PMH3

OVERCOMING THE CHALLENGES OF MODELLING SCHIZOPHRENIA: A UK CASE STUDY OF THE COST-EFFECTIVENESS OF OLANZAPINE LONG-ACTING INJECTION VS. RISPERIDONE LONG-ACTING INJECTION

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OBJECTIVES: Schizophrenia is a complex and heterogeneous psychiatric disorder with usual onset in early adulthood leading to a lifetime of morbidity and chronic disability that affects a person's ability to perceive, think and feel. The disease heterogeneity and chronic course presents significant challenges for realistic economic modelling. We present a cost-effectiveness model of schizophrenia applied to the UK, which overcomes the limitations of previous modelling techniques. **METHODS:** Given the heterogeneous and progressive nature of schizophrenia, accurate modelling needs to capture patient history and, in particular, the complex interactions between treatment discontinuation and relapse, and the impact of past relapses on the risk of future relapse. For these reasons, a discrete event simulation (DES) model was built comparing the cost-effectiveness of olanzapine long-acting injection (OLAI) against risperidone long-acting injection (RLAI). The model considered a real-world patient population utilising data from real-world sources such as open-label studies rather than randomised controlled trials. An indirect comparison was used to calculate relapse and treatment discontinuation rates. Key outcomes of interest included relapse, discontinuation, treatment switching, side effects, quality-adjusted life years, and treatment and resource use costs. **RESULTS:** The DES model captured outcomes that other modelling techniques would struggle to achieve. Among these were patient time on/off different treatments, occurrence of side effects including post-injection syndrome, and the number of relapses and treatment discontinuations. By modelling a real-world patient population, the evaluation generated patient-level findings directly relevant to clinical practice and accentuated the benefits of OLAI for reducing the risk of treatment discontinuation and in turn relapses. **CONCLUSIONS:** Key modelling challenges for schizophrenia include capturing patient history and time-dependent variables such as relapse and discontinuation. Real-world modelling to inform decision-making is growing in importance, and therefore requires the application of advanced simulation techniques.

PMH4

A SYSTEMATIC REVIEW OF THE REAL-WORLD STUDY EVIDENCE COMPARING THE SAFETY AND TOLERABILITY OF DONEPEZIL, RIVASTIGMINE AND GALANTAMINE FOR THE TREATMENT OF MILD TO MODERATE ALZHEIMER'S DISEASE

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OBJECTIVES: The acetylcholinesterase inhibitors (ChEIs) donepezil, rivastigmine and galantamine are recommended for symptomatic treatment of mild to moderate Alzheimer's Disease (AD). Despite AChEI efficacy being demonstrated in randomised clinical trials (RCTs), this study design has limited validity in relation to real-world patient care. Observational studies of routine patient care can be valuable sources of adverse event (AE) data in chronic conditions such as AD. A systematic review was undertaken to compare the safety of the AChEIs in treating AD in routine clinical care. **METHODS:** Cochrane Library, MEDLINE, and EMBASE searches were conducted together with searches of selected bibliographies and conference proceedings to identify head-to-head, non-randomised AChEI studies. Two reviewers independently extracted data from relevant articles. **RESULTS:** Twelve studies (N = 6 prospective; N = 6 retrospective) met the pre-specified inclusion criteria. Due to study design heterogeneity, a narrative data analysis was conducted. Four studies reporting total AE data found consistently fewer AEs in donepezil versus other AChEI patients, the difference being statistically significant in the largest study (N = 5462; $p < 0.001$). In three of four studies, fewer donepezil-treated patients withdrew due to AEs compared to patients receiving the other two AChEIs, with a statistically significant difference

reported in the largest study (N = 407; p < 0.01). In four studies reporting total gastrointestinal (GI) AE data, donepezil was consistently associated with a lower incidence of GI AEs compared to rivastigmine, with three of these reporting a lower incidence for donepezil compared to galantamine. In the largest study reporting total GI AEs (N = 5462), the incidence was donepezil 6%, rivastigmine 14%, and galantamine 24%. In all studies, low numbers of CNS and cardiovascular AEs were recorded, with similar incidences of events found across the different AChEIs. **CONCLUSIONS:** In routine clinical settings, mild to moderate AD patients who received donepezil had fewer total and GI AEs versus patients treated with rivastigmine or galantamine.

PMH5

USING TREEMAPS 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. The case population consisted of individuals <65 years 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 matched for the year 2006; 109,124 cases and 218,248 controls were matched in 2007. Treemaps produced by SAS v. 9.1 are used to convey the relative rankings of disease incidence and RR of disease as compared to persons without mental health disorders. **RESULTS:** Compared to controls, cases had elevated RR of disease ranging from 1.25 (conditions of the female reproductive system) to 3.14 (trauma or iatrogenic conditions). Among the specific trauma and iatrogenic conditions, poisoning, adverse drug reactions and injury the RRs at least 2.5 times higher than controls. Cases had a RR of 1.69 for endocrine and metabolic diseases (e.g diabetes, hypothyroidism, hypoglycemia). Musculoskeletal conditions and ear, nose and throat conditions were the most common types of physical comorbidities among both cases and controls, however, RR was 1.59 times higher for cases. **CONCLUSIONS:** Compared to patients with no mental health diagnoses, patients with bipolar disorder are at greater risk for a wide range of physical comorbidities. Treemaps are a valuable tool for visualizing the relative impact of a broad range of diseases across two populations.

PMH6

IMPACT OF COMORBIDITIES ON ANTIDEPRESSANT INITIATION: DULOXETINE, VENLAFAXINE, AND ESCITALOPRAM VERSUS OTHER SSRIS

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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), valenfaxine (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 = 7,567), VLX (n = 6,106), ECP (n = 10,239), or OSSRI (n = 20,114) during the year 2006. Patients were classified on their first index medication during the study period. All patients had no active prescription of the same medication(s) in the prior 3 months. On the basis of ICD-9-CM, 17 systemic disease classes and 21 individual diseases in the prior 12 months were identified. **RESULTS:** Patients receiving DLX were more likely than those receiving VLX, ECP, and OSSRI to be female (75.1% vs. 71.5%, 69.7%, 70.5%, p < 0.001) and aged 46 years or above (62.3% vs. 54.6%, 49.8%, 50.5%, p < 0.001). 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. Most significant predicting comorbid diseases (OR > 1.40) of DLX initiation versus OSSRI were fibromyalgia (OR = 1.86), low back pain (OR = 1.54), and bipolar disorder (OR = 1.43) after adjustment for demographics and other comorbidities. However, no comorbid diseases with an OR > 1.40 were associated with VLX and ECP initiation versus OSSRI. **CONCLUSIONS:** Patients initiating DLX have the most comorbid diseases, followed by VLX, ECP, with patients initiating OSSRI having the least. Specifically, the presence of chronic pain diseases and bipolar disorder appear to be most significant predictors of DLX initiation relative to OSSRI.

PMH7

EFFICACY OF ANTIPSYCHOTICS IN THE PREVENTION OF SCHIZOPHRENIA RELAPSE: A SYSTEMATIC REVIEW OF DOUBLE BLIND RANDOMISED CONTROLLED TRIALS

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OBJECTIVES: Conduct a systematic review in schizophrenia relapse prevention, using the same methodology as the recent National Institute for Clinical Excellence (NICE) 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 Odd 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 zotepine as most effective: quetiapine (XR) (OR: 0.151, 95%CrI: 0.021, 0.52), risperidone (OR: 0.168, 95%CrI: 0.035, 0.52), zotepine (OR: 0.17, 95%CrI: 0.017, 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), apripazole (OR: 0.518, 95%CrI: 0.09, 1.702). Amisulpride, olanzapine and ziprasidone reported lowest OR for DAE. Amisulpride, quetiapine (XR) and olanzapine 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 EFFICACY 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 analysis was to compare efficacy and safety of duloxetine with placebo in the treatment of major depressive disorder in Poland. **METHODS:** Comparison was based on a systematic review, carried out 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 had selected trials, assessed their quality and extracted data. For efficacy analysis improvements in 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-17) 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 = −2.26 [−2.94; −1.57]) and in quality of life (WMD = −3.60 [−4.89; −2.31]). Percentage of patients with response to treatment (RB = 1.42 [1.29; 1.56]), NNT = 6.95 [5.53; 9.37]), and with total remission (RB = 1.45 [1.29; 1.64]), NNT = 8.92 [6.80; 12.93]) was also statistically significantly higher for duloxetine group. Although risk of adverse events was significantly higher in duloxetine treated 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 = 0.95 [0.49; 1.84]). Withdrawals due to adverse events were significantly more frequent in duloxetine group 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[1] of pharmacological treatments for acute mania in bipolar I disorder, to include recent publications, including new formulation quetiapine extended release (XR), and remission rates. **METHODS:** Systematic review of CENTRAL, EMBASE, MEDLINE, for randomised, controlled trials comparing placebo to: aripiprazole, carbamazepine, 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 excluded. 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 in the analysis. The results for remission reported that risperidone followed by quetiapine XR were the most effective antipsychotics: risperidone (RR:1.87, 95%CI:1.22–2.85), quetiapine XR (RR:1.46, 95%CI:1.07–2.01), olanzapine (RR:1.39, 95%CI:1.08–1.79),