CONCLUSIONS: The FSS scale is an instrument reliable and valid to measure muscular fatigue in Brazilian patients with myopathy.

PN068
SOCIAL ECONOMIC BURDEN AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RARE DISEASES IN EUROPE (BURQOL-RD PROJECT): METHODS OF SELECTION OF 10 DISEASES FOR A EUROPEAN SURVEY
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OBJECTIVES: The BURQOL-RD project is intended to develop a disease based model capable of quantifying the socio-economic burden and Health-Related Quality of Life (HRQOL) for patients with rare diseases (RD) and their caregivers in Europe. We described the methodology used to select a set of 10 RD to be approached in a pilot study.
METHODS: BURQOL-RD project counts with 20 partners, from 8 European countries (Spain, UK, France, Germany, Sweden, Italy, Hungary and Bulgaria). Two rounds Delphi process was used to generate consensus in the selection of the 10 RD among the project participants. The wide variability and dispersion of the responses received in the two Delphi rounds of prioritization suggested that an additional procedure should be implemented to improve the representativeness of selected diseases. The Carroll’s trilateral diagram was applied based on three determinants. RESULTS: The two rounds of Delphi panel yielded into a prioritised list, to which the Carroll diagram was applied, taking into account three determinants: prevalence, availability of effective treatment and need for care. The final set of 10 RD was obtained to be targeted in the pilot study of BURQOL-RD. This methodology permitted to obtain an equilibrated set of RD for the pilot study of BURQOL-RD project. The model that will be generated will not only be suitable to apply in a wide range of medical and social care systems of EU member states.
Urinary/Kidney Disorders – Clinical Outcomes Studies

CONCLUSIONS: The FSS scale is an instrument reliable and valid to measure muscular fatigue in Brazilian patients with myopathy.

PN069
A MIXED-EFFECTS PIEWISKE LINEAR MODEL OF THE RATE OF LUNG FUNCTION DECLINE BEFORE AND AFTER THE CLINICAL USE OF DORNASE ALFA IN AN OBSERVATIONAL STUDY OF CYSTIC FIBROSIS
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OBJECTIVES: To evaluate lung function decline before and after the initiation of dornase alfa (DA) through a multivariable mixed-effects piecewise linear model using data from the Epidemiologic Study of Cystic Fibrosis (ESCF). METHODS: Patients in the 2003–2010 cohort included in ESCF for 2 or more years prior to initial treatment with DA were selected if they remained on treatment for at least 2 years. A comparator group including cystic fibrosis patients not yet reported to have received DA. FEV1 percent predicted (pp) was analyzed before and after an index measurement with a post-bronchodilator (DA group) or an encounter within 1 year following the 8th or subsequent even-numbered birthday (comparator group). For each patient, we fit a regression line to FEV1 pp separately for the pre-index and post-index periods (both 2 years in duration) using a mixed-effects piecewise linear model adjusted for age, gender, pulmonary exacerbations, respiratory therapies, and nutritional supplements. Patients were categorized by age, gender, and nutritional status. RESULTS: The DA group (n=2,230) had a lower FEV1 pp at index and a more rapid decline during the pre-index period. There was an acute improvement in FEV1 pp (change in intercept) associated with the initiation of DA therapy. Furthermore, the mean rate of FEV1 pp decline was more attenuated for the DA group than for the comparator group (n=5,970) across age groups and deciles. CONCLUSIONS: The use of DA for a 2-year period is associated with both an acute improvement in FEV1 pp (previously shown in clinical trials) and a slower rate of FEV1 pp decline (shown for the first time). These results demonstrate the value of using mixed-effects piecewise linear models in observational studies to evaluate the effect of instituting a therapy on both the slope and intercept of a continuous outcome.

CONCLUSIONS: The FSS scale is an instrument reliable and valid to measure muscular fatigue in Brazilian patients with myopathy.

PN070
ESTIMATES OF TOLTERODINE AND FESOTERODINE REDUCTIONS OF URGENCY URINARY INCONTINENCE EPISODES RELATIVE TO PLACEBO
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OBJECTIVES: To explore potential sources of heterogeneity among estimates of tolterodine (TOL) and fesoterodine (FESO) efficacy relative to placebo (PBO) in patients with overactive bladder and urgent urinary incontinence (UUI) from randomized controlled trials (RCTs) published from 2001 – 2010. METHODS: RCTs evaluating TOL 4mg, solifenacin 5mg and/or 10mg, or FESO 4mg or 8mg compared to PBO reporting mean reduction of UUI episodes/d from baseline to endpoint were identified. Treatment response was defined as a reduction in mean UUI episodes/d of at least 2.0 episodes. RESULTS: Treatment response effect size estimates were tested for heterogeneity using Cochran’s Q statistic. Where heterogeneity was present, other study variables (baseline UUI, baseline micturitions, gender, age, diary evaluation days, publication year, and study duration) were evaluated for potential confounding using linear regression methods. RESULTS: Statistical heterogeneity was found among the 17 PBO responses (mean reduction of UUI) of the included studies. PBO response increased with publication year, which accounted for more than 27% of response variation. Publication year (p<0.003), gender (p<0.003), and study duration (6-week vs. other) (p=0.006) were significant predictors of PBO effect size (TOL and FESO) and treatment response estimates were also heterogeneous. Among the nine TOL trials, treatment responses remained constant over publication year while PBO responses increased, resulting in a net decline in TOL treatment effect (p=0.0928). The majority of this decline was explained by publication year and study duration (adj. R2=0.7039). The four FESO 4mg UUI responses also displayed a publication year-dependent decrease leading to a decreasing treatment effect relative to PBO. However, this trend was almost perfectly predictable by differential baseline UUI episodes (adj. R2=0.9721).
CONCLUSIONS: Publication year, gender, 6-week duration, and baseline UUI were found to be significant predictors of PBO response or treatment effect. Additional research should be done to understand why PBO response has increased over time

forms of tacrolimus with belatacept. RESULTS: Thirty-five studies from an initial list of 1095 citations were included in the analysis. Results show CNI avoidance leads to higher incidence of acute rejection (RR 2.52, 95% CI 1.11–5.73), which is a known predictor for graft loss, but reduced chronic allograft nephropathy. Tacrolimus produces better rejection prophylaxis compared with ciclosporin (RR 0.38, 95% CI 0.21–0.70), and ciclosporin produces lower acute rejection compared with belatacept (RR 0.32, 95% CI 0.13–0.79). Indirect analysis showed that tacrolimus is superior to belatacept in acute rejection prophylaxis (RR 0.18, 95% CI 0.08–0.39), but leads to more cases of a decrease in glomerular filtration rate (GFR) (RR 1.37, 95% CI 0.92–2.03); however, the long-term impact of a reduction in GFR in the context of a CNI avoidance regimen is not clear at present. CONCLUSIONS: Direct and indirect comparisons demonstrate that CNIs, and in particular tacrolimus, remain superior even against more recent compounds for preventing acute rejection. However, more research needs to be done to find the optimum combination of therapies.

PUK2
COMPARATIVE EFFECTIVENESS OF INVESTIGATIONAL COMPOUNDS AND FERUMOXYTOL FOR THE TREATMENT OF IRON DEFICIENCY ANEMIA IN CHRONIC KIDNEY DISEASE: SYSTEMATIC REVIEW AND MIXED TREATMENT COMPARISON
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OBJECTIVES: To evaluate the comparative therapeutic effects of investigational compounds and ferumoxytold for the treatment of iron deficiency anaemia (IDA) associated with chronic kidney disease (CKD) compared to alternative iron replacement therapies (IRT). Primary interest was the improvement in haemoglobin (Hb) from baseline levels. METHODS: A comprehensive systematic review was conducted to identify and independently assess the evidence generated to investigate the effectiveness of the treatment of IDA in CKD where efficacy is defined as Hb change from baseline and IRTs included intravenous (IV) and oral treatments. Twelve electronic databases were searched up to November 2010 (language unrestricted). Two reviewers independently assessed each identified reference and conducted subsequent data extraction. Method quality of each included trial was also independently assessed in accordance with NICE guidelines. A standard meta-analysis comparing oral iron to ferumoxytold was initially conducted, reflecting the trial programme. The full network meta-analysis that included both IRTs and oral iron therapies was synthesised using a mixed treatment comparison (MTC). The random effects model showed ‘predicting superiority’ to the fixed effects model and was thus utilised. Mean efficacy was estimated through analysing standardised effect sizes of trials and back-translating them to Hb values via a standard effect size vector and standard deviation. RESULTS: Seventeen published trials and one unpublished clinical study provided the heterogeneous trial base for MTC analysis. Ferumoxytold was significantly favoured when compared to oral iron therapy by conventional meta-analysis (0.61, 95% CI: 0.44, 0.79; P value <0.0001) which was supported by results from the MTC efficacy analysis (0.48, 95% CI: 1.24–3.2). Significant differences in efficacy were not observed between ferumoxytold and any of the alternative IV iron therapies. CONCLUSIONS: The results from the conventional meta-analysis showed that the model favoured investigational compound ferumoxytold, in terms of increasing Hb, compared to the oral iron therapy. We suggested a modelled equivalence to currently approved alternative IV iron treatments.

Puk3
SOURCES OF HETEROGENEITY AMONG OVERACTIVE BLADDER CLINICAL TRIAL ESTIMATES OF TOLTERODINE AND FESOTERODINE REDUCTIONS OF URGENT URINARY INCONTINENCE EPISODES RELATIVE TO PLACEBO
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OBJECTIVES: To systematically identify and summarise the evidence of renal transplant and adverse events related to the most effective options. In particular, comparing tacrolimus, the cornerstone of renal transplantation therapy, with newer therapies that have been introduced since 2003. METHODS: An electronic literature search of MEDLINE, Current Contents and the Cochrane Library. A search was conducted, plus manual reference checks of all articles involving controlled trials of kidney transplants and immunosuppressive therapy between 2003 and July 2010. Studies were assessed for eligibility and quality by two reviewers who extracted data independently. Studies were classified according to (CNI avoidance or reduction, steroid avoidance, and induction therapies. Results were expressed as risk ratio (RR) with 95% confidence intervals (CI). Where necessary, indirect comparison techniques were used to compare different
and future trials should compare to real-world treatments wherever possible to demonstrate clinically-meaningful differences.

PUK4

COMPARING PROJECTED OUTCOMES OF RENAL TRANSPLANT RECIPIENTS BASED ON TRAIAL ENDPOINT OF RENAL FUNCTION AND RECEIVING DIFFERENT IMMUNOSUPPRESSIVE REGIMENS IN THE UNITED STATES

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OBJECTIVES: Enhancements in renal transplant have led to reduced rates of acute rejection leading to a shift to kidney function as an accepted endpoint in efficacy trials. Characterizing long-term benefits requires modeling to project long-term outcomes based on kidney function endpoints. The goal of this study was to assess the long-term project rates of graft failure and quality adjusted life years over the lifetimes of hypothetical patients receiving belatacept (a recently-introduced selective co-stimulation blocker), cyclosporine or tacrolimus. METHODS: We developed a simulation with two phases that integrated trial-based information with a long-term four-state Markov model (functioning graft, graft failure on dialysis, functioning re-graft, and death). In the first phase, three-year distributions of patients in four estimated glomerular filtration rate (eGFR) categories (≥60, 45-59, 30-44 and 15-29, with graft failure assumed at eGFR <15 mLs/min/1.73m2) were estimated using a mixed treatment comparison of cyclosporine, belatacept, and tacrolimus. The Markov phase was populated using transplant recipient data from the United States Renal Data System (n=34,130). Utilities for adjusting life-years were obtained from a study of US renal transplant patients. RESULTS: Over a 20-year model horizon, the predicted mean long-term 1,000 hypothetical patients, belatacept was associated with 551 graft failures, and 96 quality-adjusted life years. Relative to cyclosporine, belatacept was associated with 0.9 additional quality-adjusted life years, and 56 fewer graft failures. Relative to tacrolimus, belatacept was associated with 0.9 additional quality-adjusted life years, and 18 fewer graft failures. CONCLUSIONS: This is the first long-term follow-up model of renal transplant patients to be based on trial-based graft function endpoints and include all relevant comparators. This long-term extrapolation of differences in kidney function observed at three years shows clinically important differences between treatments. While validation of these models will require long-term follow-up of patients, it is anticipated that evaluation of renal function may prove to be a useful method of projecting long-term outcomes.

PUK5

MIXED TREATMENT COMPARISONS OF IMMUNOSUPPRESSANTS FOLLOWING RENAL TRANSPLANT

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BACKGROUND: Belatacept is a first-in-class co-stimulation blocker developed for primary maintenance immunosuppression following renal transplantation. Data is widely available comparing belatacept to cyclosporine, limited data is available comparing it with other immunosuppressants. OBJECTIVES: Estimate belatacept’s efficacy and safety relative to tacrolimus. METHODS: A systematic review was conducted to randomised controlled trials (RCTs) published between January 1990 and September 2010. Data extraction captured study duration, quality, baseline data, treatment and clinical outcomes. Efficacy and safety outcomes included glomerular filtration rate (GFR), graft- and patient-survival, and acute rejection (AR). The data were analysed with fixed- and random-effects models. Linear models with random-effects for GFR were assessed for logistic and continuous measures, unlike the other variables which are dichotomous in nature. Logistic models were used for these other outcomes (summary measure being odds ratios). Sensitivity analyses (SAs) were conducted based on trial durations and sub-populations. RESULTS: We identified twenty-six RCTs comparing cyclosporine with tacrolimus, three RCTs comparing cyclosporine with belatacept, and no trials comparing tacrolimus with belatacept. Most trials were 12 months in duration (range: 6 to 60 months). MTC results using 36 month belatacept data suggested benefits with belatacept on patient survival (OR = 0.62 95% CI: 0.31,1.24), and difference in GFR (85.50 mL/min/1.73 m2; 95% CI = 4 – 22.20;44), versus tacrolimus, with AR outcomes favouring tacrolimus (OR = 2.43; 95% CI: 1.08,5.34). MTC results indicated reduced graft-survival with belatacept at 36 months (OR = 1.18 95% CI: 0.51,2.85). However, when using data at 12 months post-transplant demonstrated a benefit for belatacept on graft-survival (OR=0.89 95% CI: 0.36.2,16). Benefits on graft-survival were also seen at 12 and 24 months in the standard-criteria donor population. SAs on the other outcomes resulted in similar conclusions to those of the base case. CONCLUSIONS: This approach showed improved efficacy and benefits in graft- and patient survival in comparison to tacrolimus despite increased risks for AR.

PUK6

BPH PATIENTS TREATED WITH PHYTOTHERAPY IN PORTUGAL: RESULTS AT SIX MONTHS

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OBJECTIVES: To elucidate patient and economic burden associated with chronic kidney disease (CKD) across countries. METHODS: A targeted literature review using PubMed and desktop research was performed. Current conversions were adjusted to 2010. RESULTS: North American, European, and Asian studies were identified; most reports were from the United States (US). Advanced CKD (stages 3-5) adversely affects outcomes. As patient-reported outcomes (PROs) deteriorate, resource utilization (RU) and costs escalate. Across studies, patients with CKD report increased health impairment, sleep impairment and anxiety, decreased HRQOL. RU and costs to healthcare systems and employers increase with CKD severity. Prior to (12-24 months) dialysis initiation, costs increase substantially due to hospitalization. Annual US total cost per patient (c/p/p) with CKD (stages 3-5) range from $6,026 (4,927) to $30,398 (24,855), annual Germany total c/p/p (stages 1-4) is €3,581 ($4,379), compared to €1,272 ($1,555) in those without CKD. The cost burden of CKD is rising. From 1993 to 2007, Medicare costs for patients with CKD increased by ~5-fold. High healthcare costs (HC) and reduced productivity (P) are reported. For employees with CKD (US), HCs range from $1,187 (€791) (stage 3) to $21,826 (€17,846) (stage 5) and work-hours missed per week often exceeds 10. The impact of CKD on patient and economic burden across countries is evident. CONCLUSIONS: Patient and economic burden associated with CKD is considerable across countries. With disease progression and kidney function decline, unfavorable outcomes arise. As evidenced by the high patient and economic burden of CKD, a large unmet need exists for new therapies and employee CKD-management programs.

PUK9

COMPARATIVE COST ANALYSIS OF TREATMENT FOR RENAL ANEMIA WITH METHOXY POLYETHYLENE GLYCOL ERYTHROPOIETIN BETA (MIRCERA®) VERSUS ERYTHROPOIETIN BETA (NEORECORMON®)

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OBJECTIVES: Evaluate if the use of Methoxy polyethylene-glycol erythropoietin beta (MGP-beta) offers better health outcomes and costs with respect to erythropoietin multidoose presentation (50,000 IU). METHODS: Analysis of incrementen.