

Individual's Health - Clinical Outcomes

PIH1

IN-HOSPITAL MORTALITY, LOS, AND COSTS FOR SYSTEMIC-TO-PULMONARY SHUNT PROCEDURES: RESULTS FOR THE NEWBORN POPULATION FROM THE HCUP KIDS' INPATIENT DATABASE

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Objectives: Systemic-to-pulmonary pediatric shunts are typically used in the first stage of palliative therapy to improve blood oxygenation in infants with cyanotic congenital heart defects. The repair is associated with a high economic burden and patients tend to develop severe complications often resulting in high mortality. This analysis estimates the in-hospital mortality, length of stay (LOS) and inpatient costs in newborn patients (≤ 1 month old) who had shunt procedures with and without complications. **Methods:** The 2016 Kids' Inpatient Database was used to identify newborn patients who had a shunt procedure, identified with ICD10-PCS codes as primary or secondary. The sample was further refined with ICD10-CM diagnosis codes associated with this disease such as Tetralogy of Fallot, pulmonary artery atresia and Hypoplastic Left Heart Syndrome. The cohort was then separated into successful versus complicated procedures, which were identified by ICD10-CM T82 codes that describe complications of prosthetic devices. We further identified complicated patients that required an ECMO since ECMO results in significant cost burden. Patient and hospital characteristics, in-hospital mortality, LOS and average costs per admission were estimated. **Results:** There were 1,267 admissions for shunt procedures in newborn patients in 2016. Of these, 531 cases were identified as successful shunt patients (37.5% female, 72% treated at a hospital >325 beds, 49% Medicaid insurance) and 63 cases were identified as complicated patients (45% female, 66% treated at a hospital >325 beds, 51% Medicaid insurance). In-hospital mortality, LOS and costs per admission were higher for the complicated cohort (in-hospital mortality 7% versus 9%, LOS 42 days versus 65 days, costs \$231,536 versus \$380,463). For ECMO cases ($N=10$), in-hospital mortality, LOS and costs were 16%, 112 and \$484,926, respectively. **Conclusions:** Newborn patients with shunt procedures have high in-hospital mortality, LOS and costs. Complicated cases result in increased LOS and 64% higher costs per admission.



PIH2

EFFICACY AND SAFETY OF MIDAZOLAM ORAL SOLUTION FOR SEDATIVE-HYPNOSIS AND ANTI-ANXIETY IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives: To explore the efficacy and safety of midazolam oral solution for sedation and hypnosis in children. **Methods:** Relevant studies were identified through searches of PubMed, Embase (Ovid), Cochrane Library, CINAHL, International Pharmaceutical, and four Chinese electronic databases. Two reviewers independently selected trials, assessed trial quality, and extracted the data. **Results:** Eighty-nine RCTs comparing midazolam oral solution with placebo or blank ($n=33$), dexmedetomidine ($n=15$), ketamine ($n=11$), different midazolam doses ($n=10$), midazolam injection ($n=8$), chloral hydrate ($n=7$), diazepam ($n=5$), N₂O ($n=5$), triclofos ($n=4$), butorphanol ($n=2$), fentanyl ($n=2$), hydroxyzine ($n=1$), and thiopental ($n=1$) were identified. Meta-analysis showed no significant difference in the success rate and duration of sedation and hypnosis between midazolam oral and injectable solution ($P>0.05$). No significant difference was found in the success rate of sedation and hypnosis, mask acceptance and parental separation between midazolam oral solution and dexmedetomidine ($P>0.05$), and the result of one cohort study was consistent. The results of RCTs and prospective cohort study showed the incidence of ADR was 19.57% (189/966). Incidence of ADR between (0.25, 0.5] mg/kg and (0.5, 1.0] mg/kg dose groups were similar [Pf (95% CI) =0.10(0.04, 0.24) and Pf (95% CI) =0.09(0.02, 0.39) respectively], higher than that of (0, 0.25] mg/kg dose group [Pf (95% CI) =0.01(0.00, 0.19)]. **Conclusions:** Available evidence suggests that midazolam oral solution is as good as midazolam injection and dexmedetomidine, and is better than ketamine. Based on efficacy and safety results, the dose of oral midazolam solution is recommended 0.5-1 mg/kg for children.



PIH3

ANGIOTENSIN I CONVERTING ENZYME INHIBITORS REDUCE RISK OF PNEUMONIA IN HOSPITALIZED ELDERLY PATIENTS

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Objectives: Pneumonia is associated with increased mortality and morbidity, particularly among elderly and debilitated hospitalized patients. Previous research indicated a protective effect of ACE inhibitors (ACEi) on pneumonia risk but the literature lacks strength and is controversial. The objective of this study was to validate early findings of ACEi protective effect on pneumonia among elderly



hospitalized patients. **Methods:** To assess the association between chronic ACEi and risk of pneumonia among elderly hospitalized patients without selected neurological disorders, a case-control study was conducted using data from University of Utah Data Warehouse. Inclusion criteria were hospitalized patients aged ≥ 65 years without ICD-diagnostic codes associated with dysphagia with a diagnosis of pneumonia between January 2012 and December 2016. Controls were propensity score matched to cases based on age, gender and Charlson's Comorbidity Index. Patient records were reviewed for the use of ACEi 3 months, 6 months and 9 months prior to the admission date with estimations of risk of developing pneumonia. Odds ratios (OR) were calculated using multivariable conditional logistic regression. This data was used to validate our previous medical claims study of ACEi effect in a similar population from 2000-2002 from the Medstat MarketScan®/Medicare Supplemental and Coordination of Benefits. **Results:** The study population comprised 1,635 cases and 1,635 matched controls. After matching for confounders, chronic ACEi use was associated with a decreased risk of pneumonia (adjusted odds ratio (OR) 0.87 [95% confidence interval (CI) (0.84 - 0.89)]. The 2019 data compares favorably to 2000 claims data with chronic ACEi reduced pneumonia risk with an OR 0.71 [0.68-0.75]. **Conclusions:** Chronic ACE inhibitor use is associated with 13-29% lower risk of pneumonia in elderly hospitalized patients without neurological disorders affecting swallowing. These findings substantially add to the body of evidence about the effect of ACE inhibitors on pneumonia.

PIH4

NUMBER NEEDED TO TREAT (NNT) WITH FENFLURAMINE TO ACHIEVE A CLINICALLY MEANINGFUL REDUCTION IN CONVULSIVE SEIZURE FREQUENCY IN PATIENTS WITH DRAVET SYNDROME: HEALTH ECONOMIC IMPLICATIONS

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Objectives: Families of patients with Dravet syndrome (DS) experience substantial financial and humanistic burdens, driven by seizures and poor neurodevelopmental outcomes. We determined the number needed to treat (NNT) with fenfluramine to achieve "clinically meaningful" reductions in monthly convulsive seizure frequency (MCSF), as determined by Clinical Global Impression of Improvement (CGI-I) ratings and improvement on Behavior Rating Inventory for Executive Function (BRIEF®-2) Index Scores. **Methods:** Using data from a Phase 3 and long-term extension study for adjunctive fenfluramine (NCT02682927/NCT02826863/NCT02823145), we assessed: (1) the degree of seizure frequency reduction associated with "Very much improved" caregiver CGI-I ratings via receiver operating characteristic (ROC) analysis and (2) the proportion of patients with clinically meaningful, ≥ 10 -point improvement on BRIEF®-2 index scores (Behavior, Emotion, Cognition, Global), comparing patients with $<25\%$ (negligible) vs $\geq 75\%$ (profound) MCSF reduction via 2-sided Mann-Whitney-U test. NNT was calculated: $1/((\text{Experimental-Responder Rate})-(\text{Control-Responder Rate}))$. **Results:** ROC analysis of CGI-I ratings identified a clinically meaningful threshold of $\geq 60\%$ MCSF reduction. There was $\geq 60\%$ MCSF reduction in 60%, 28% and 5% of patients in fenfluramine 0.7 mg/kg/day (NNT=2), fenfluramine 0.2 mg/kg/day (NNT=4), and placebo groups. Patients with $\geq 75\%$ MCSF reduction were significantly more likely to achieve ≥ 10 -point improvements in Emotion Regulation and Global BRIEF®-2 Index Scores at Year 1; 45%, 20%, and 2% of patients in fenfluramine 0.7 mg/kg/day (NNT=2), fenfluramine 0.2 mg/kg/d (NNT=6), and placebo groups achieved $\geq 75\%$ MCSF reduction. **Conclusions:** Fenfluramine treatment resulted in NNT=2 to achieve either clinically meaningful ($\geq 60\%$) or profound ($\geq 75\%$) MCSF reductions; profound reductions were associated with executive-function improvements. Prior DS antiepileptic-drug studies report NNT=5-6 for only $\geq 50\%$ MCSF reduction. Published average annual healthcare utilization costs for DS are $\sim \$27,276$, plus $\geq \$80,000$ (indirect). An NNT=2 to achieve clinically meaningful outcomes may have important positive health economic implications for both payers and patients/caregivers vs currently available treatment options.



Individual's Health - Economic Evaluation

PIH5

ANNUAL HEALTH INSURANCE TREATMENT COST OF FEMALE INFERTILITY BASED ON ROUTINELY COLLECTED FINANCING DATA

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Objectives: The prevalence of female infertility and the use of assisted reproductive technology in the treatment of women of reproductive age have been increasing. Several endocrinological diseases may play a role in the development of female infertility. Our aim was to determine the annual health insurance treatment cost of female infertility in Hungary. **Methods:** Data were derived from the financial database of the NHIFA, for the year 2018. Data analysed included annual health insurance costs, patient numbers and cost distribution calculated for age groups and sex. The



following cost categories were included into the study: general practice care, home care, in- and outpatient care, medical imaging, laboratory diagnostics, pharmaceuticals and medical aids. Patients with female infertility were identified with the following code of the International Classification of Diseases 10th revision: N97. **Results:** In 2018, the Hungarian National Health Insurance Fund Administration spent 6.91 billion Hungarian Forints (HUF) on the treatment of patients with female infertility, which equals 25.57 million American Dollars (USD), or 21.67 million Euros (EUR). 99.97% of costs was spent on the treatment of female patients. The highest patient numbers were in outpatient care: 30,112 patients. Acute inpatient care (53.2% of total health insurance costs), pharmaceuticals (42.2%) and outpatient care (3% in women) were the main cost drivers, while all other forms of medical care amounted to 1.6% in women. Annual health care treatment cost per patient was 229,387 HUF (849 USD/719 EUR) for women. **Conclusions:** Acute inpatient care was the major cost driver in the treatment of female infertility. The treatment of patients aged 25–44 accounted for 96.2% of costs.

PIH6

PREFERENCES AND WILLINGNESS TO PAY FOR EARLY DIAGNOSIS OF ENDOMETRIOSIS TO REDUCE THE ADVERSE RISK OUTCOMES: A DISCRETE CHOICE EXPERIMENT

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Objectives: Endometriosis is a gynecological disease that mainly affects women of reproductive age worldwide. It imposes clinical and economic burden on patients, their families and the society as a whole. Patients' perspectives are increasingly used in healthcare decision making. In this study, we aim to evaluate women's preferences and willingness to pay regarding early diagnosis and treatment of endometriosis. **Methods:** A discrete choice experiment (DCE) was designed and administered to elicit women's preferences and WTP for early diagnosis of endometriosis. Women ages 18 and older were selected to participate in the study. The attributes (and levels) considered were diagnosis (immediate/postponed), chance of advanced endometriosis and more serious illness (low/high), time away from daily living activities (8 days, 15 days, 22 days and 30 days), and out-of-pocket costs (\$0, \$15, \$60 and \$210). Data were summarized. A mixed logit model was used to analyze the effects of the individual attributes on elicited preferences and estimate the WTP. The effects of participants' characteristics on the preference for early diagnosis were modeled using a Tobit model. **Results:** A total of 66 women with (2) or at-risk (64) of endometriosis completed the experiment. The age range of women participated were 19–69 years. Respondents preferred scenarios with lower risk and out of pocket costs. They also preferred to spend less time away from work, education, and other daily living activities. While respondents preferred lower out of pocket costs, they were willing to give up some out-of-pocket costs in order to avoid the risk of adverse outcomes. The respondents' age and insurance statuses significantly influenced their preference or choice for early diagnosis. **Conclusions:** The results suggest that preferences for treatment attributes for endometriosis vary widely. This highlights the importance of accounting for individual preferences in order to improve decision-making for the diagnosis and treatment of endometriosis.

PIH7

ANNUAL HEALTH INSURANCE TREATMENT COST OF CERVICAL CANCER BASED ON ROUTINELY COLLECTED NATIONWIDE REAL-WORLD FINANCING DATA IN HUNGARY

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Objectives: Cervical cancer represents a significant burden for the individual and the society. The aim of our study was to determine the annual health insurance treatment cost of cervical cancer in Hungary. **Methods:** Data were derived from the financial database of the Hungarian National Health Insurance Fund Administration (NHIFA), for the year 2018. Data analysed included annual health insurance costs, patient numbers and cost distribution calculated for age groups and sex. The following cost categories were included into the study: general practice care, home care, in- and outpatient care, medical imaging, laboratory diagnostics, pharmaceuticals and medical aids. Patients with cervical cancer were identified with the following code of the International Classification of Diseases 10th revision: C53. **Results:** In 2018, the Hungarian National Health Insurance Fund Administration spent 1.238 billion Hungarian Forints (HUF) on the treatment of patients with endometriosis, which equals to 4.58 million American Dollars (USD), or 3.88 million Euros (EUR). We found he highest patient numbers in outpatient care: 5,208 patients, resulting in a prevalence of 53.3 patients/100,000 female population. Acute inpatient care (60.0% of total health insurance costs), CT imaging examinations (18.2%) and reimbursement of pharmaceuticals (6.9%) were the main cost drivers, while all other forms of medical care amounted to 14.9%. Annual health care treatment cost per patient was 237,675 HUF (879 USD/745 EUR) for women. **Conclusions:** Acute inpatient care was the major cost driver in the treatment of cervical cancer primarily, due to the surgical interventions often required for its treatment. CT imaging examinations play important role in the diagnosis of disease and in the

monitoring of treatment. The treatment of patients aged 45–74 accounted for 70.0% of costs.

PIH8

UNDERSTANDING THE ECONOMIC BURDEN OF COMORBIDITIES ASSOCIATED WITH MALE HYPOGONADISM: A COST MODEL IN ENGLAND

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Objectives: Male hypogonadism is closely associated with a number of comorbidities such as type 2 diabetes (T2DM) and cardiovascular disease (CVD), increasing the complexity and burden of disease. Evidence demonstrates testosterone therapy improves patient outcomes, both in terms of improvements in parameters relating to hypogonadism and the rate of comorbidities. However, there is little evidence on the economic impact of reducing comorbidity rates. **Methods:** A cost model was developed to estimate the economic benefits of testosterone therapy for male patients with hypogonadism with four major comorbidities; T2DM, osteoporosis, obesity and CVD in England, compared to no treatment. The model utilized a ten-year time horizon. Only direct costs were considered. Comorbidity rates were from published literature, and costs for each comorbidity were an average of the related NHS national tariff. No potential drug costs associated with the comorbidities were included. **Results:** In total, treatment resulted in cost savings of £3,045 per treated individual per year, versus no treatment. For patients treated with testosterone therapy, individual yearly costs of £324, £134, and £229 for treatment, administration, and monitoring are outweighed by a £3,732 reduction in the cost of treating comorbidities. Of this, £823 is attributed to treating obesity (22%), £967 on osteoporosis (26%), £216 on T2DM (6%) and £1,727 on CVD (46%). **Conclusions:** The cost model demonstrates that reduction of comorbidity rates in patients treated with testosterone therapy versus no treatment translates into an economic benefit through cost savings. This analysis is likely to underestimate savings as drug costs for treatment of comorbidities are not included. Therefore, treatment of hypogonadism has additional advantages related to reducing comorbidities beyond improving testosterone levels and it is important to take this wider benefit into account when making clinical decisions regarding screening for hypogonadism and testosterone therapy.

PIH9

BUDGET IMPACT ANALYSIS VS. COST EFFECTIVENESS ANALYSIS - HORMONAL CONTRACEPTIVES AS AN ILLUSTRATIVE CASE

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Objectives: Globally, over 200 million women are using hormonal contraceptives (HCs). Unintended pregnancies pose a major economic burden on low and middle income countries (LMIC). Budget impact analyses (BIAs) are beneficial for LMICs as they aim to make large public health investments in family planning. The objective of this study was to review cost-effectiveness analyses (CEAs) and BIAs published on HCs to assess whether future CEAs could be extended to examine national budget impact. **Methods:** A systematic literature search was conducted using PubMed and EMBASE to identify CEAs conducted on HCs until December 2018. The selected articles were screened to assess methodological characteristics and extent of quality budget impact information. The modified BIA checklist for CEAs based on the ISPOR Task Force Recommendations was used to examine the extent to which CEAs could be used to create BIAs. **Results:** A total of 22 CEAs and 2 BIAs resulted from the literature search. CEAs were conducted in 6 countries (12 USA, 6 United Kingdom and 1 each from Singapore, Iran, France and Canada). Of the 22 CEAs, 20 were conducted from a payer perspective. The 2 BIAs from USA and South Africa used a managed care and public provider perspective, respectively. Both the BIAs and CEAs examined direct medical costs with 2 CEAs each reporting direct non-medical costs and indirect costs. Actual costs of side effects were mentioned in 5 CEAs, but not in the BIAs. The majority of the CEAs met the criteria of the BIA checklist for CEAs. The BIAs adhered well to ISPOR's best-practice recommendations for BIA quality. **Conclusions:** This review using HCs highlights that BIAs are lacking in the literature. Current CEAs can be optimized to provide budget impact data which may be useful for LMICs as they work towards addressing resource allocation decisions to reduce the unmet need for contraception.

PIH10

COST-EFFECTIVENESS ANALYSIS OF IMRECOXIB, CELECOXIB AND DICLOFENAC IN OSTEOARTHRITIS IN CHINA

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Objectives: Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely prescribed to patients with osteoarthritis (OA), it was assumed that both cyclooxygenase-2 (COX-