

outcomes, RCT estimates may overestimate the effectiveness of treatments in practice. Instrumental Variable (IV) estimation techniques applied to retrospective healthcare data can yield unbiased treatment estimates for patients at the “extensive margin” of practice. As a result, it can be shown that IV estimates are better suited to evaluate the cost-effectiveness of policies that modify existing treatment rates.

**OBJECTIVE:** To estimate cost-effectiveness ratios using treatment estimates from IV techniques and contrast these results to cost-effectiveness ratios obtained using RCT estimates.

**METHODS:** Data from 18,795 Iowa Medicaid eligible children with an index event of acute otitis media (AOM) from 1989 to 1995 were collected. Instrumental variables were constructed for each patient based on their relative access to various provider types. IV estimates were used to estimate cost-effectiveness ratios for AOM patients on the extensive margin.

**RESULTS:** For these patients, IV estimates of the difference in cure rates between patients that were treated with antibiotics and those not treated ranged from 11% to 13% and were statistically significant from zero at the 1% level. These estimates are less than 15% difference in cure rates from RCTs (Rosenfeld et al. *Journal of Pediatrics*. 1994). Using the average antibiotic prescription charge observed from our sample, IV estimates translate into cost-effectiveness ratios between \$123 and \$145 per additional cured patient. In contrast, the RCT estimate yields a cost-effectiveness ratio of \$107 per additional cured patient.

**CONCLUSION:** If patients are heterogeneous with respect to treatment outcomes, cost-effectiveness ratios estimated using RCT treatment estimates will understate the costs per outcome from changing existing treatment rates. IV estimation with retrospective data provides a useful alternative for policy-makers to evaluate costs per outcome at the margins of practice.

**ID2****CHRONIC HEPATITIS C: COST-EFFECTIVENESS OF INTERFERON AND RIBAVIRIN**

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**OBJECTIVE:** Cost-effectiveness of strategies for treating hepatitis C.

**METHODS:** A decision analytic Markov model was created comparing strategies employing interferon and interferon + ribavirin: 1) IFN = interferon, 12 months; 2) IFN/CMB = interferon 12 months, followed by 6 months of combination therapy (interferon + ribavirin) for IFN failures; 3) IFN/CMB-R = interferon 12 months, followed by 6 months of combination therapy for IFN relapsers; 4) CMB = combination therapy, 6 months; 5) CMB-G = genotyping, followed by 12 months of combination therapy for genotype 1, 6 months for others. Interferon therapy was stopped after 3 months for non-

responders. Sustained virologic response (SVR) 6 months post-treatment was considered to be a cure. There were seven Markov states: well, chronic hepatitis C, compensated cirrhosis, decompensated cirrhosis, hepatic cellular carcinoma, liver transplantation, dead. Only direct medical costs were considered. Model parameters were from published literature, utility assessments of patients, Medicare fee schedules, and wholesale drug prices. Patients were followed until death. Costs and health benefits were discounted at 3%. Sensitivity analyses were performed using 95% CIs for probabilities, doubling and halving cost parameters, and wide ranges for utilities.

**RESULTS:** The genotyping (CMB-G) strategy produced the highest SVR. Despite having the highest cost, its incremental cost-effectiveness ratio (ICER) was just \$7552/QALY (quality-adjusted life-year) compared to the second best strategy, IFN/CMB. All other strategies were dominated. The model was only sensitive to the response of genotype 1 to combination therapy. As the initial response rate of genotype 1 approaches the lower limit of the 95% CI, interferon followed by combination therapy (IFN/CMB) became cost-effective, with the ICER of genotyping reaching \$137,000/QALY.

**CONCLUSION:** Combination therapy, with duration based on genotype, is the most cost-effective treatment of chronic hepatitis C.

**ID3****ADDITIONAL ANTIBIOTIC UTILIZATION IN A RANDOMIZED TRIAL OF CLARITHROMYCIN (CLARI) COMPARED WITH AZITHROMYCIN (AZI) FOR THE TREATMENT OF S. PYOGENES PHARYNGITIS/TONSILLITIS**

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**OBJECTIVE:** To compare additional antibiotic usage for subjects randomized to Clari or Azi for the treatment of *S. pyogenes* pharyngitis/tonsillitis.

**METHOD:** Subjects with symptoms of streptococcal pharyngitis/tonsillitis and *S. pyogenes* positive were enrolled in a randomized, multicenter, investigator blind, parallel comparative control study of 10 days Clari (250mg bid) versus 5 days Azi (250mg bid on day 1 then qd on days 2–5). Subjects were evaluated at the end of the treatment, at 2 weeks and at 5 weeks. Clinical and bacteriological evaluations as well as additional or concomitant antibiotics were evaluated at each visit.

**RESULTS:** A total of 525 subjects aged 12 years and older were enrolled and randomized (Clari n = 260; Azi n = 265). The bacteriological eradication and clinical cure rates for Clari and Azi were 94% [195 of 207] versus 77% [155 of 202] (p < 0.001) and 98% [200 of 205] versus 90% [182 of 202] (p < 0.002), respectively, based on per-protocol analysis. A total of 445 subjects (Clari n = 221; Azi n = 224) were evaluable for the intent-to-treat analysis. There was a greater rate of additional antibiotic usage