simple and useful tool for quantifying and exploring the (combined) uncertainty associated with decision-making about adopting guidelines and implementation strategies and, therefore, for informing decisions about efficient resource allocation to change clinical practice.


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OBJECTIVES: Estimation of cost-of-illness typically involves the analysis of skewed medical costs that include large outliers. Log transformations are frequently used to overcome these problems. Linear regression models (OLS) are then applied to the transformed data. The estimated model coefficients are retransformed back to the linear scale using the smearing approach. Implementing this approach in statistical packages requires customized programming. We propose an alternative to using log transformations: Generalized Linear Models (GLM) with a log link function. We compare the performance of both models in estimating cost-of-illness.

METHODS: We derived data from a large administrative database representing 143,593 discharges from 39 US hospitals from January 2004 to December 2005. We estimated total medical costs among hospitalized patients attributable to hyponatremia. Using a cross-validation approach, we compared the performance of two models: log transformed OLS with smearing and GLM with a log link function and a normal error distribution. We used the Root Mean Squared Error (RMSE) and the Mean Absolute Error (MAE) to assess model performance. Covariates in both models included patient age, gender, race, geographic region, Deyo-Charlson comorbidity index, primary diagnosis, teaching status of hospital, and admission source. All analyses were contacted using SAS®.

RESULTS: The GLM with log-link and a normal error distribution had both the smallest RMSE (23,688) and MAE (11,304) compared to the log transformed OLS with smearing (24,057 and 11,392, respectively). Furthermore, by using GLM, there was no need to compute a retransformation estimate, since the log link function relates the response mean to the original scale. CONCLUSIONS: In this cross-validation study, GLM outperformed OLS with smearing. GLM is easier to implement using SAS® with no need for retransformation estimates. Because of its ease of use and statistical accuracy, GLM is a useful alternative to log-transformed OLS models with smearing, when estimating cost-of-illness.

**A Framework for Real-World Economic Evaluation by Incorporating Implementation Parameters**

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OBJECTIVES: Reimbursement decisions are often supported by economic evaluations based on randomised controlled trials (RCTs). A problem with RCTs is that they usually deviate from daily practice. Hence, reimbursement decisions are based on perfect-world assessments of cost-effectiveness. In daily practice, the technology is likely to be less cost-effective for instance due to lower compliance. To make real-world reimbursement decisions, factors that potentially influence the cost-effectiveness should be considered. These factors are implementation factors, and stochastic in nature. This study presents a framework that incorporates the implementation of a technology directly into the economic evaluation, thus anticipating on potentially less than perfect implementation. This results in real-world economic evaluations.

METHODS: The framework allows for a stepwise consideration of the net benefit (NB) of a technology in different states of the world: 1) perfect-world (NB under perfect implementation); 2) real-world (NB under expected implementation); and 3) improved-world (NB after intervention to improve implementation). Step 1 tells us whether the technology could be cost-effective. Step 2 gives us the real world cost-effectiveness. The difference between the NB of step 1 and 2 gives the upper bound of the value of improving implementation. Step 3 tells us whether it is cost-effective to invest in specific interventions to improve implementation. The implementation factors are stochastic, therefore in each step parameter uncertainty is addressed in probabilistic sensitivity analyses, and the value of reducing uncertainty is examined in value of information analyses.

RESULTS: As a case we used a Markov model that examines the cost-effectiveness of direct hearing aid provision versus provision by referral. Two stochastic implementation parameters were incorporated: patient compliance and professional uptake. The upper bound of the value of improving implementation was €50 million (patient compliance), €23 (professional uptake) and €72 million in total. This suggests that implementation interventions may be valuable (results presented at the conference).

METHODS: CONCLUSIONS: This framework allows for real-world economic evaluations to inform policy decisions.

**In or Out? Empirical Evidence on Income Losses in Health State Valuations and Implications for Economic Evaluations**

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In 1996 the Washington Panel controversially recommended valuing productivity costs (PC) in terms of QALYs. While this recommendation was criticised, the Panel’s assumption, that respondents in health state valuation (HSV) exercises take income losses into account, could not be countered since there was no evidence regarding what people consider in HSV exercises. If they do consider income losses and if this changes HSV’s, then all past economic evaluations that have included PC in the numerator may have double counted these costs. Alternatively, if respondents do not consider income losses then all past economic evaluations that have not included PC in the numerator have failed to account for sizeable societal costs.

OBJECTIVES: To recapture the debate surrounding the appropriate method for including PC in health economic evaluations, to identify empirical evidence addressing the assumptions made by the Washington Panel and to recommend a research agenda for the future.

METHODS: In this review we first present and discuss the human capital and friction cost approaches for capturing PC. Then, the Washington Panel approach is highlighted and discussed. Next, we identify, outline and critically appraise the existing empirical studies that attempt to address the assumption that respondents to HSV exercises take income effects into account. Finally, we outline a research agenda for the future that will help to determine the most appropriate method for including PC.

RESULTS AND CONCLUSIONS: Only six empirical studies were identified. The studies differ substantially in methods and results and drawing general conclusions from them is difficult. Overall, it seems that not explicitly mentioning the inclusion of income will induce a minority of respondents to
include these effects and this appears not to influence results in general. More empirical work is needed, using generic instruments, larger and more relevant samples, and perhaps using the interview method of administration.

**PMC16**

**EXPENSIVE DRUGS FOR RARE DISORDERS AND THE LOGIC OF COST-EFFECTIVENESS**

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**OBJECTIVES:** Expensive drugs for rare disorders (EDRDs; “orphan drugs”) do not usually meet widely applied cost-effectiveness benchmarks (“lambdas”). Adopting the standard decision rules of the logic of cost-effectiveness cannot be reconciled with granting reimbursement status for many EDRDs and would inevitably deprive patients with very rare disorders from any chance to get access to effective treatment, given the high fixed / low variable cost structure of the pharmaceutical industry. On the other hand, public policies have been established to provide incentives to support development of orphan drugs. This (and some further observations) suggests a serious mismatch between the logic of cost-effectiveness and societal preferences. Decision-makers have responded; for instance, the National Institute for Health and Clinical Excellence (NICE) attempts to define a special subcategory of “ultra-orphans”—while maintaining that budgetary impact analysis is not part of its appraisal decisions (but limited to implementation support). This policy, however, does not appear to adequately address the underlying problem.

**METHODS:** First, “ultra-orphans” are not a distinct, well-defined category—they rather represent one extreme of a continuous spectrum, and “orphan drugs” and some cancer treatments pose the same fundamental problem. Second, size of a patient population eligible for treatment is directly linked to budgetary impact (and hence the opportunity for manufacturers to recoup fixed costs), whereas the logic of cost-effectiveness is impaired by not taking into account the size of the numerator and the denominator of the incremental cost-effectiveness ratio (ICER), which has been described as “the silence of the lambda.” Policy makers might address these issues by explicitly taking budgetary impact into account when deciding on maximum reimbursement prices or by price-volume agreements. RESULTS: Both approaches, albeit perhaps pragmatic, cannot satisfy from a theoretical economic perspective. CONCLUSIONS: Rigorous normative analysis and empirical research are required to further explore the mapping of individual health-related utilities into societal preferences (willingness-to-pay).

**PMC17**

**VALIDITY OF ELECTRONIC PRESCRIPTION CLAIMS RECORDS: A COMPARISON OF ELECTRONIC PBM CLAIMS RECORDS WITH PHARMACY PROVIDER DERIVED RECORDS**

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**OBJECTIVES:** To determine if and to what extent records obtained from PBM pharmacy claims differ from source documents obtained directly from pharmacy providers. Also this study sought to explore possible associations between patient, pharmacy benefit, and pharmacy provider characteristics and the likelihood a patient would have missing prescription claims.

**METHODS:** This study used a cross sectional survey of 1,484 patients residing in a single state with a common pharmacy benefit. Patient profiles describing all prescriptions filled in a pharmacy between January 1, 2002 through June 30, 2002 of these patients were requested directly from their pharmacy providers. Logistic regression was used to explore the factors associated with a person receiving a prescription that did not appear on the PBM claims. RESULTS: Of the 1484 eligible recipients sampled, profiles were obtained for 323 (22%) persons and there were analyzable profiles for 315 (21%) persons. Of those 2,977 prescriptions filled for the 315 persons, 207 (7.0%) were missing from the claims files indicating that 93% were captured. Prescription drugs such as iron products, digoxins, diuretics, sulfonylureas, and antigout were more likely to be missing from the PBM claims. Only prescription volume consistently influenced the likelihood a patient would have a missing prescription from the PBM claims (OR = 1.08; 95% CI: 1.05–1.12). CONCLUSIONS: Claims obtained from pharmacy benefit companies capture approximately 93% of prescription records when verified with records obtained from pharmacy providers. The rate of missing records from PBM claims does not appear to be meaningfully influenced by most finance based pharmacy benefit design features, however, certain drugs available over the counter and less expensive drugs may have less complete claims records compared to other classes of drugs. Higher prescription utilization is more likely to have prescription records filled that are not captured by PBMs.

**PMC18**

**CONCEPTUALISING DISEASE: BUILDING UNIFYING MODELS TO SUPPORT THE DEVELOPMENT OF PROS AND COST-EFFECTIVENESS ANALYSES. A CASE STUDY IN ALZHEIMER’S DISEASE (AD)**

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**OBJECTIVE:** The core of a cost effectiveness model should be guided by the underlying disease process, natural history and how particular interventions impact on disease. The development of conceptual models within PRO research is based on the same rationale. The objective of this study was to explore the overlap between cost effectiveness modelling and conceptual models for PROs, using AD as an example. METHODS: A conceptual model of AD was reviewed alongside a cost effectiveness model by a team of PRO researchers and health economists. Areas of commonality and divergence were documented and discussed. RESULTS: Points of overlap were identified which included the impact of AD on day to day functioning of the patient and associated caregiver burden. This will influence the ability of the caregiver to work and impact on other resource utilisation. This may, also have an impact on the time to institutionalisation, which is a major financial burden in AD. One major area of divergence is the emphasis in economic models on the use of generic quality of life data; whereas conceptual models are commonly developed to measure disease specific PRO burden. CONCLUSIONS: The commonalities between PRO conceptual models and health economic models indicates the potential for developing PRO and HE models simultaneously. This is likely to increase the validity of each of the models as well as having a positive impact on related research e.g., through the development of health state utilities. As a next step we are prospectively developing a conceptual model of disease which is specifically