lack of an RCT makes formal technology assessment vs. alternative treatment (e.g., best supportive care [BSC]) challenging. In such instances, naive indirect comparison based on historical controls is typically employed. We present a method for estimating outcomes for untreated patients when appropriate historical controls are not available, by matching historical responders in an uncontrolled trial. METHODS: 1) Olfatumumab was licensed for fludarabine- and alemtuzumab-refractory chronic lymphocytic leukemia (FA-Ref CLL) based on results of an uncontrolled trial (Hx-CD20-406). To evaluate the cost-effectiveness of olfatumumab vs. BSC from the UK National Health Service perspective of the payer, a decision-analytical model was developed. Progression free survival (PFS) and overall survival (OS) for olfatumumab were estimated by fitting Weibull survival functions to failure time data for all FA-Ref patients in Hx-CD20-406. Following a literature search, no suitable historical control representing BSC could be identified; therefore hazard ratios (HR) for OS and HR for BSC vs. olfatumumab were estimated by fitting Cox regression models to data for non-responders as well as all FA-Ref patients. Costs and utilities were taken from both published and unpublished sources. RESULTS: BCS: patients (approximated by non-responders) were estimated to achieve 4.7 months PFS, 11.3 months OS, 0.50 QALYs, and expected lifetime costs of £4,876. Olfatumumab patients were estimated to reach 6.5 months PFS, 17.9 months OS, 0.77 QALYs, with expected lifetime costs of £43,828. CONCLUSIONS: The novel approach presented permits a practical alternative for estimating cost-effectiveness when neither an RCT nor appropriate historical control can be identified. Further research should be conducted using established data sets to validate the methodology, and to address potential limitations, e.g., unobserved differences between treatment groups, and potential benefits of treatment in patients classified as non-responders.

**PMC3**

**A NOVEL APPROACH TO MATCHING ADJUSTED INDIRECT COMPARISON ANALYSIS USING COMMON SAS 9.2 PROCEDURES**

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OBJECTIVES: While randomized control trials (RCT) are the gold standard for drug approval, there is often a lack of data directly comparing different treatment options. An indirect comparison of the treatment effects may serve as a proxy for a head-to-head RCT, however, naively comparing treatments using published trial data without adjusting for distribution differences in patient characteristics and prognostic factors can result in misleading conclusions. A novel matched-adjusted approach to indirectly compare absolute survival estimates (median overall survival (OS) or progression free survival (PFS)) for competitive treatment options is presented. METHODS: This proposed approach requires patient-level data for one of the treatments and summary data of patient characteristics and survival outcomes for the comparator of interest. Using this proposed method, the researcher would first decide on one or two matching variables that are prognostic for survival, and apply a program involving an extension of a common SAS 9.2 procedure, Proc Surveyselect, to select 1000 random repeated subsamples from the original population with the same distribution of matched variables. The analysis also requires programming statements using ODS and survival analysis procedures. The median OS or PFS estimates are computed for each bootstrapped sample and a 95% confidence interval (CI) is inferred around the mean of the sampled survival estimates. These absolute survival estimates, based on the adjusted population, can then be compared to the absolute survival survival estimates reported in published literature of the comparator treatment. CONCLUSIONS: In the absence of head-to-head RCT data, an adjusted indirect comparison accounts for observed differences between populations making them more comparable and results in an effect of treatment exposure on survival outcomes that is less likely due to confounders.

**PMC4**

**COST ESTIMATION IN HEALTH ECONOMIC EVALUATIONS IN GERMANY: A SYSTEMATIC REVIEW**

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OBJECTIVES: The objectives of this study are: 1) to systematically review the methods used in developing cost estimates in the recent German health economic literature and 2) to examine the methodological approaches in terms of analytical framework, cost components, resource use and cost data sources in light of the national Institute for Quality and Efficiency in Healthcare guidelines. METHODS: The MEDLINE database was searched for studies published between 1-Jan-2006 and 31-Dec-2008 estimating direct and/or indirect costs of health care interventions in Germany. A systematic literature search, no suitable historical control representing BSC could be identified; therefore hazard ratios (HR) for OS and HR for BSC vs. olfatumumab were estimated by fitting Cox regression models to data for non-responders as well as all FA-Ref patients. Costs and utilities were taken from both published and unpublished sources. RESULTS: BCS: patients (approximated by non-responders) were estimated to achieve 4.7 months PFS, 11.3 months OS, 0.50 QALYs, and expected lifetime costs of £4,876. Olfatumumab patients were estimated to reach 6.5 months PFS, 17.9 months OS, 0.77 QALYs, with expected lifetime costs of £43,828. CONCLUSIONS: The novel approach presented permits a practical alternative for estimating cost-effectiveness when neither an RCT nor appropriate historical control can be identified. Further research should be conducted using established data sets to validate the methodology, and to address potential limitations, e.g., unobserved differences between treatment groups, and potential benefits of treatment in patients classified as non-responders.

**PMC5**

**DEVELOPMENT OF A WEB-BASED SOFTWARE TOOL TO EVALUATE THE ECONOMIC IMPACT OF LOST PRODUCTIVITY DUE TO PREMATURE MORTALITY IN DEVELOPED AND EMERGING NATIONS**

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OBJECTIVES: Economic analyses that take a societal perspective need to incorporate estimates of lost productivity due to premature death. Such estimates are likely to vary substantially across countries, making it a challenge to assess the value of alternative medical interventions on a global basis. Our goal was to develop a generic, web-based software tool based on rigorous analytic methods that would enable researchers to assess the expected discounted present value of lost productivity for persons who die prematurely at various ages in selected developed and emerging nations. METHODS: An analytic model framework was developed to estimate the expected present value of lost productivity due to premature mortality from a societal perspective using a human capital approach (with value attached to household work, as data permitted). Key model inputs included life tables, labor force participation rates, wages and discount rates. Default input parameter values were based on each country’s national statistics, as available, or via generic “global” estimates when such data were lacking. RESULTS: Model results were generated for 20 countries around the world, and varied substantially based on patient age at death and the economic region in which a country is located. For illustration purposes, the illustration presents the discounted present value of lost productivity for a person who dies at age 23-29 in the US, Brazil, and Sweden were estimated to be $US 945,162, 124,795, and 805,740, while the corresponding values for those who die at age 45-49 were 622,248, 78,976, and 480,480. The web-based interface allows researchers to select the country of interest, modify default values, and conduct sensitivity analyses. CONCLUSIONS: This generic web-based software tool allows researchers to easily incorporate the value of lost productivity due to premature mortality into economic analyses that take a societal perspective, and provides estimates for many different developed and emerging countries.

**PMC6**

**ASSESSING PRODUCTIVITY AND ACTIVITY IMPAIRMENT DUE TO ILLNESS IN POLAND**

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OBJECTIVES: The inclusion of loss productivity costs in pharmacoeconomic studies is still a subject of considerable debate. The aim of this study was to quantify the work impairment due to general health status in Poland with the Productivity and Activity Impairment: General Health (WPAI-GH) Questionnaire. METHODS: Data were obtained from a survey that incorporated the WPAI-GH questionnaire and information on impairment of work and activity related to a chronic disease on a representative sample of the Polish general population aged more than 16 years. There were 13,700 participants in total, gathered in two waves in January and May 2010. RESULTS: The total population comprised 795 subjects in paid jobs. Subjects reported 4.5% work time missed (absenteeism) during the past 7 days. Impairment while at work (presenteeism) amounted to 13.9% of total time. The overall work productivity loss (absenteeism plus presenteeism) equaled 15.2%. Impairment in performing daily activity was 15.6% in the past 7 days. Observed percentages were in general higher in subject from the first wave of study [January 2010] than from second wave (May 2010)—differences did not reach statistical significance. The general tendency of a higher absenteeism and a lower presenteeism values among men than among women were observed. CONCLUSIONS: Productivity and Activity Impairment measured by WPAI-GH in the Polish population are similar to these observed in other European countries and the U.S. Moderate differences between values estimated in January and May suggest limited impact of seasonal diseases such as influenza on productivity.

**PMC7**

**TARIFF LISTS FROM SPANISH AUTONOMOUS COMMUNITIES: AN ASSESSMENT OF ITS STRUCTURE, CONTENTS, AND TARIFF LEVELS**

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OBJECTIVES: There exists no standardised list of unit costs (UC) for use in economic evaluations in Spain. Tariffs published by the 17 Autonomous Communities (ACs) are often used as a proxy for costs. We explored the structure and contents of AC tariffs lists and tariff ranges for common resource use items. METHODS: Current tariff lists responders in an untitled bulleted 16 Spanish ACs were retrieved. Tariffs for key health services in the following categories were extracted: specialist and A&E visits, hospitalization, investigations, procedures, laboratory tests, and episodes of care (DRGs). We qualitatively assessed structure and contents of tariffs lists, item content for selected items. Ranges, normal mean and weighted mean (according to

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demographic size of ACs) were calculated for selected tariffs. RESULTS: We observed lack of consistency in structure and content of tariffs lists and in tariff levels, as exemplified by: different categorization of services; incomplete listing of services; different terminologies; different levels of detail for common services (e.g. M.R. 2–127 optimized by 60% of the ACs, and/or complexity); wide-range of tariffs for most specialty visit: £65–£191, general ward per diem: £82–£4569, simple M.R. £110-£634). Wide variations were also observed for other diagnostic investigations, (non-surgical) procedures, laboratory tests and DRGs. CONCLUSIONS: Wide ranges in tariffs for health resources commonly used in economic evaluations were identified across ACs with a difference between minimum and maximum values of at least factor 2. There exists no evidence on how tariffs are calculated and if they reflect real cost. Available AC tariffs should be used with caution and a simple or weight average across AC tariffs may be used as poor cost-hits. Elaboration of a nationwide-wide list would avoid possible bias from analysts in the selection of cost values to obtain given results.

INVESTIGATING WHAT IT REALLY MATTERS? Jurado A1, Garcia-Alba A2, Alvarez-Martín E3, Gáñova-Malauras R4, Morant-Ginestar C5, Parouty M6

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OBJECTIVES: We examined the association between economic evaluation studies performed in Spain in 1983-2008 and the burden of disease in the population. METHODS: Cross-sectional observational study. Electronic databases (PubMed/MEDLINE, SCOPUS, BI Web of Knowledge, CRD, IME, IBECS) and reports from public policies were systematically reviewed. Inclusion and exclusion criteria and a set of variables were defined to analyze the characteristics of the papers selected. Using the Global Burden of Disease (GBD) study classification the following measures were calculated: years of life lost (YLLs), years lived with disability (YLDs), disability-adjusted life-years (DALYs), and mortality by cause. Correlation and linear regression models were used. RESULTS: Cardiovascular diseases (15.7%), infectious and parasitic diseases (15.3%), and malignant neoplasms (13.2%) were the conditions most commonly addressed. Accidents and injuries, congenital anomalies, oral conditions, nutritional deficiencies and other neoplasms were the categories with a lowest number of studies (0.6% from the total for each of them). The disease sub-categories most prevalent in the studies were lower respiratory infections (5.7%), ischemic heart disease (5.7%), hepatitis B and C (3.3%) and HIV/AIDS (3.1%). For GBD categories (n = 20), a correlation was seen with: mortality 0.67 (p = 0.001), DALYS 0.63 (p = 0.003), YLLs 0.54 (p = 0.014), and YLDs 0.51 (p = 0.018). By disease sub-categories (n = 51), the correlations were low and non statistically significant. CONCLUSIONS: There is a mild-moderate association of economic evaluations with the main causes of burden of disease. For some conditions, the data show over or under-representation of studies related to their burden generated. The burden of disease is a criterion that, in combination with efficiency and equity, would allow to set recommendations to guide debates on health research priority setting.

ARE THRESHOLD RANGES FOR COST PER QALY A BARRIER TO RESEARCH FOR LIFE EXTENDING TREATMENTS? Roberts Gi, de Nigris E

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As they are currently used thresholds for cost per QALY may provide a disincentive for companies to invest in research for therapies that prolong life in conditions with an already high treatment cost. Cost per QALY thresholds, although not the sole basis for decision making are a major influence on whether a technology is considered cost-effective by NICE. Discussions have centred on the most appropriate threshold level and how its value should be determined. However a consequence of cost per QALY thresholds that is not discussed is the impact they may have on future health care research. The cost per QALY for renal dialysis has been estimated at £30,000, higher of what NICE considers acceptable. We have therefore reached the ceiling for the cost of treating renal disease. Assuming that utility is not improved a treatment that extends life will be at additional and huge cost which raise the cost per QALY greater than £30,000. Manufacturers of health care technologies may consider that the risk of not getting a product approved on cost-effectiveness grounds is not worth the financial investment in its development. As health care costs continue to grow the manufacture costs of more conditions will exceed £20,000 per year and future research may be stifled as manufacturers seek to develop products that replace rather than add to current treatments. Since the background treatment cost would cancel out in an incremental analysis a treatment could be more cost-effective than the one it replaces but conversely can still be cost-effective on the increased cost which raise the cost per QALY of standard treatment above £20,000 or £30,000. As treatment costs for more conditions increase to threshold values (even if they are raised) manufacturers may be advised to consider realigning their portfolio and investment to other diseases.

ASSESSMENT OF THE WORKLOAD REAL TIME DEDICATED TO EACH PATIENT IN INTENSIVE CARE UNITS (ICU): PRELIMINARY RESULTS OF THE CRÈA study

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OBJECTIVES: The objective of the CRÈa study is to assess the real daily cost of a patient’s stay in ICU in France. We present here preliminary results regarding the average time spent per patient by different health caregivers. METHODS: A prospective multicentric health economic study was performed in 23 ICUs of different French hospitals randomly selected from the PMSI database (French National Hospital database) over a one day study, 5 adults patients were randomly selected among patients with a simplified severity score ≥ 15 in each ICU. Data on all the resources used, treatments administered, biological tests performed, etc. and time spent by different health caregivers to take care of each patient over a 24 hour period (direct and indirect interventions) were collected throughout the data entry. Data were analyzed considering the professionals themselves. RESULTS: A total of 109 patients (median age = 66 years, 65% males) of 22 intensive care units (15 polyvalent, 3 surgical and 4 medical ICUs) were included. 104 of them were followed over 24 hours (there were 2 deaths and 3 early withdrawals). On the day of the study, 84% of patients were mechanically