Selected reviews of Economic Evaluations relating to Dermatology

Economic evaluation of etanercept in the management of chronic plaque psoriasis

**Study Question:** To assess the cost-effectiveness of etanercept 50 mg twice weekly (biw) for the treatment of chronic plaque psoriasis, and to explore characteristics of patients who benefited most from 50 mg dosing. An economic model was constructed to estimate the incremental cost per quality-adjusted life year (QALY) gained from the perspective of the U.K. National Health Service (NHS).

**Patient Group:** The model considered patients with chronic plaque psoriasis who had both Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) of 10 or higher who were unable to take standard systemic therapies. Patients entered the model when etanercept therapy was initiated. Three treatment regimens were compared: etanercept 50 mg; etanercept 25 mg; and no systemic therapy. After 12 weeks, patients on etanercept who did not achieve a reduction in PASI of at least 50% were regarded as non-responders. Patients who achieved a PASI 75 response were regarded as responders. Patients who had a reduction in PASI of 50-74% after 12 weeks of treatment received a further 12 weeks of etanercept at a dose of 25 mg biw, and were viewed as responders if they achieved a PASI 75 at 24 weeks. All responders entered a treatment-free period and received re-treatment with 12 weeks of etanercept 25 mg biw after a median treatment interruption of 29 days.

**Key Results:** The incremental cost per QALY for etanercept 50 mg biw compared with no systemic therapy was found to be £6217 (95% confidence interval £5396-7486). The incremental cost per QALY for etanercept 50 mg biw compared with 25 mg biw was £11,710 (95% CI £8407-26,642) and the incremental cost per QALY for the etanercept 25 mg biw regimen compared with no systemic therapy was £4,297 (95% CI £3,671-5,231). The cost-effectiveness of 50 mg dosing was more attractive in patients with baseline PASI > or = 20 (£5,163) or baseline DLQI > or = 20 (£4,599). The cost-effectiveness of both etanercept regimens was sensitive to the assumed requirement for hospitalization in untreated individuals and to the response rate achieved in re-treatment. The model reported a high degree of confidence that comparing etanercept 50 mg biw with no systemic therapy, the incremental cost per patient over a 10-year period would be between £5,000 and £6,000 and that the QALYs gained would be between 0.7 and 1.2. The authors conclude that etanercept 50 mg biw is cost effective in the U.K. This regimen was particularly appropriate for patients with severe disease or poor quality of life at baseline.

Cost-effectiveness analysis of linezolid vs. vancomycin in treating methicillin-resistant Staphylococcus aureus complicated skin and soft tissue infections using a decision analytic model
**Study Question:** To assess the cost-effectiveness of vancomycin vs. linezolid in complicated skin and soft tissue infections (cSSTIs) with methicillin-resistant Staphylococcus aureus (MRSA) using a decision analytic (DA) model. DA modelling was used to evaluate the most cost-effective strategy among four treatment strategies (linezolid intravenous (i.v.) to oral (LIN), vancomycin i.v. inpatient treatment (VAN-1), vancomycin i.v. switch to oral linezolid (VAN-2) and vancomycin i.v. switch to outpatient vancomycin i.v. (VAN-3)). This study was conducted from the perspective of the healthcare system in the USA.

**Patient Group:** Patients with cSSTIs. Four strategies were assessed: MRSA culture is positive/responder/no-relapse; MRSA culture is positive/responder/relapse; MRSA culture is positive/non-responder/switch to alternative antibiotic; and MRSA culture is negative/switch to an alternative antibiotic.

**Key Results:** In the base-case analysis, linezolid was associated with a large probability of patients who responded to treatment and did not relapse (49.3%) followed by the various vancomycin strategies (36%). Total direct costs for treating a patient on LIN, VAN-1, VAN-2 and VAN-3 were US$10,975, US$16,686, US$10,017 and US$9,749, respectively. Average CERs for LIN, VAN-1, VAN-2 and VAN-3 were US$22,282/cure, US$45,924/cure, US$27,626/cure and US$26,831/cure. VAN-3 was the most cost-effective strategy from the base-case analysis. From the payerÆs perspective, empirical treatment with linezolid would cost US$9488 per additional cure than with empirical treatment with VAN-3 and empirical treatment with linezolid would cost US$7371 per additional cure than with VAN-2. Univariate sensitivity analysis revealed that the model was sensitive to linezolid duration of inpatient stay and duration of i.v. vancomycin before switching to an oral agent or discharged with outpatient i.v. administration with vancomycin. Probabilistic sensitivity analysis showed that in the majority of the trial simulations (90%) LIN dominated VAN-1 but when compared with VAN-2, a total of 33% of the trial simulations reported LIN as a cost-effective strategy. Switching to an oral agent reflected reductions in hospitalization, which influenced the total costs associated with VAN-2. This was also reflected in trial simulations comparing LIN with VAN-3 where a total of 30% of the trials favoured LIN as a cost-effective strategy. Comparing VAN-2 to VAN-3 showed that 74% of the trial simulations favoured VAN-3 as the dominant strategy. For a payer to be 80% confident that LIN was cost-effective, the WTP threshold would have to be approximately US$64,000 per additional cure. The authors conclude that alternative vancomycin strategies (VAN-2 and VAN-3) that take advantage of early discharge opportunities were cost-effective compared with LIN. However, LIN’s higher efficacy would make it cost-effective for payers with a high WTP threshold.

**Economic evaluation of maintenance treatment with tacrolimus 0.1% ointment in adults with moderate to severe atopic dermatitis**


**Study Question:** To describe treatment outcomes and to evaluate resource utilization and associated cost of maintenance use of tacrolimus ointment (MU) vs. standard use of tacrolimus ointment (SU) in adults with atopic dermatitis (AD). This was done through a pan-European, phase III multicentre randomized clinical trial with patients randomized to tacrolimus 0.1% ointment (MU) or vehicle (SU) twice per week for 12 months.

**Patient Group:** Adult patients (> or = 16 years) with mild to severe AD (Rajka/Langeland score of at least 3).

**Key Results:** Of the 75 patients randomized to the maintenance use of tacrolimus ointment (MU) group, 57% had moderate and 43% severe AD. In the standard use of tacrolimus ointment (SU)
group, a total of 59 patients, 59% had moderate and 41% severe AD. In patients with moderate AD, the number of disease exacerbations in the MU arm was 2.4 vs. 5.5 in the SU arm (P<0.001); in patients with severe AD corresponding figures were 2.3 vs. 7.4 (P<0.001). Utility values in the MU group increased significantly from 0.71 to 0.79 in patients with moderate AD and from 0.67 to 0.75 in patients with severe AD. The differences were statistically significant. In the SU group the QoL changes were not statistically significant. Utility values increased from 0.69 to 0.72 in patients with moderate AD and from 0.67 to 0.71 in patients with severe AD. Mean SD total annual cost per patient was euro1525_1081 (MU) vs. euro1729_1209 (SU) in patients with moderate AD and euro2045_2013 (MU) vs. euro2904_1510 (SU) in patients with severe AD. The overall costs per patient are higher in the SU group compared with the MU arm. Approximately 66% of patients in the MU arm accrued annual total cost of less than euro2000. In the SU treatment arm, only 21% of patients accrued annual total cost of less than euro2000. The authors conclude that maintenance treatment with 0.1% tacrolimus ointment is more effective and leads to cost savings and improved health-related quality of life in comparison with standard use of 0.1% tacrolimus ointment, especially in patients with severe AD.

Willingness-to-pay stated preferences for 8 health-related quality-of-life domains in psoriasis: a pilot study

Study Question: To pilot test a new method to measure quality of life (QOL) impact in psoriasis and identify the areas of life most affected by psoriasis. This was done through a study of patients with psoriasis at outpatient clinics in the USA.
Patient Group: Forty participants with a history of psoriasis who were aged 18 years of age or older and spoke English.
Key Results: A quarter of the sample were aged 40 years or less, 52.5% 40-60 years and 22.5% >60 years, 48% were female, 60% had a college degree or further education, and 38% had an income level over US$45,000/year. Psoriasis-related disease-severity varied widely in the sample, with the percent of BSA covered by plaques at a patients last dermatology visit ranging between 1-80% and a median 20%. Physical comfort, social comfort, and emotional health were highly ranked by more than 75% of respondents. Ability to concentrate was least likely to be affected by psoriasis with just a quarter (25.7%) of respondents ranking this domain as important. The median amount patients were willing to pay for a hypothetical cure of psoriasis specific to a particular domain was highest for physical comfort (US$2000, 25th quartile = US$500, 75th quartile = US$5500) and emotional health (US$2000, 25th quartile = US$250, 75th quartile = US$5000), and lowest for ability to sleep (US$625, 25th quartile = US$50, 75th quartile = US$5000). Median WTP was greater for younger patients (<40 years) in the social and emotional domains. The authors conclude that the study successfully pilot tested a willingness-to-pay method and a ranking task and found that physical comfort, social comfort, and emotional health were the domains of health most affected by psoriasis.

The impact of psoriasis on health care costs and patient work loss

Study Question: To estimate both the incremental direct costs (i.e, medical and prescription drug costs) and indirect work loss costs (i.e, value of sick days, other missed work time, and disability
payments) associated with psoriasis. The study uses data from a de-identified claims database from 31 self-insured employers and adopts an employer's perspective. Each psoriasis patient is matched with 3 non-psoriasis patients of the same age and sex, and the incremental costs of psoriasis estimated using a two-part regression model.

**Patient Group:** 12,280 psoriasis patients with at least 2 psoriasis claims and 36,840 non-psoriasis patients. Patients aged 65 years or older were excluded.

**Key Results:** Compared to non-psoriasis patients, the incremental direct and indirect costs of psoriasis were approximately US$900 and US$600 per patient per year, respectively (P < .001). The authors conclude that the annual incremental cost of psoriasis represents a substantial economic burden. They encourage additional multivariate studies by researchers with access to large nationally representative samples of patients, particularly if the data allow them to add additional cost categories, control variables, or both to the analysis.

**Costs of skin and skin structure infections due to Staphylococcus aureus: an analysis of managed-care claims**

Marton J P, Jackel J L, Carson R T, Rothermel C D, Friedman M, Menzin J; *Current Medical Research and Opinion* 2008; 24(10):2821-2828

**Study Question:** To assess the costs of a treatment episode for skin and skin structure infections (SSSIs) due to Staphylococcus aureus (SA) (SA-SSSIs) and to determine rates of use of antibiotics and predictors of cost. The study uses retrospective data from a nationwide managed-care claims database to assess treatment with selected antibiotics (i.e. vancomycin, oral linezolid, and daptomycin - termed 'study antibiotics').

**Patient Group:** 1997 patients aged at least 18 years with a new SA-SSSI diagnosis. Patients with a diagnosis of osteomyelitis up to 6 months before the first SSSI diagnosis were excluded.

**Key Results:** The mean (+/- SD) overall episode cost was US$8865 (+/- US$20,003), and was primarily composed of inpatient and outpatient medical services. Significant positive predictors of overall cost were treatment failure (i.e. study antibiotic switching or hospitalisation), younger age, a diagnosis of bacteraemia, osteomyelitis, or multiple complications during the episode, treatment with daptomycin, and greater Charlson co-morbidity score. Significant negative predictors of cost were treatment with oral linezolid and hospitalization before the start of the outpatient treatment episode. Mean (+/- SD) SSSI-related costs were US$4551 (+/- US$11,058). The authors conclude that the costs of treating SA-SSSIs are substantial and vary by failure rates, co-morbidities, and type of antibiotic therapy.

**How complicated skin and soft tissue infections are treated in Italy: economic evaluation of inpatient intravenous antibiotic treatment in seven hospitals**


**Study Question:** The main objective of this study was to evaluate the costs and outcomes of antibiotic therapy for the treatment of complicated skin and soft tissue infections (cSSTIs) in Italy from the hospital perspective. The results of this study will provide decision makers with relevant base data that could be used to assess the introduction of newer antibiotics. Only direct hospital costs were identified and measured. Seven hospitals were selected across the country and each hospital was asked to recruit patients retrospectively. A bottom-up micro costing approach was
considered to measure consumption of antibiotics. Continuous variables were analysed using descriptive statistics, one-way analysis of variance (ANOVA) or Student’s t-test.

**Patient Group:** A total of 307 patients (>= 18 years) enrolled in a retrospective, multicentre, incidence-based, observational study and eligible to receive antibiotic therapy for complicated skin and soft tissue infections (cSSTIs) were considered for the present analysis. The target population consisted of hospitalised patients eligible to receive intravenous antibiotic therapy for cSSTI. Excluded were patients with minor or superficial infections, perirectal abscess, gangrene, multiple infected ulcers at distant sites, or infections of third-degree burns and patients with bacteremia, required curative surgery or had concomitant infections at another site.

**Key Results:** Study findings suggest that efforts must be made to reduce the failure rate of the initial antibiotic option as much as possible and to choose the quickest antibiotics, whilst keeping safety and effectiveness as high as possible. The authors believe that the correct choice of first-line antibiotics can save up to Euros 2,850 per patient in the case of failure avoided, of which Ç671 are avoidable costs; that is, they can actually be saved in the very short term. This could be ultimately increased by Ç74 for each hospital data avoided because of faster antibiotic action. Findings of this study should be interpreted with caution as the study has some limitations including the lack of representativeness and generalizability.

**Annual direct and indirect health care costs of chronic idiopathic urticaria**

**Study Question:** This study estimates the direct and indirect costs, including travel and work losses, for patients with chronic idiopathic urticaria (CIU) managed with usual treatments. Patients taking corticosteroids or other immunosuppressants in the month before enrollment were not included.

**Patient Group:** 50 adults with chronic idiopathic urticaria

**Key Results:** This paper reports estimates of direct and indirect costs, including travel and work losses, for patients with chronic idiopathic urticaria (CIU) managed with usual treatments. Patients with CIU had total costs of US$2,047 per annum. Medication costs accounted for 62 per cent, or US$1,280. Other costs included outpatient visits at US$280, other hospital visits at US$148, and US$17 for laboratory costs. Indirect costs accounted for 16 per cent, or US$322 of costs, consisting of an average of US$252 wages lost due to absence from work, and an average of US$70 of wages lost due to travel to outpatient services. Costs are said to compare to other skin diseases.

**Advanced cutaneous malignant melanoma: a systematic review of economic and quality-of-life studies**

**Study Question:** Metastatic melanoma (MM), a major concern for health care providers, is increasing. The aim of this study was to carry out a systematic review of published articles describing the impact of interventions (drugs and screening) on quality of life (QoL) in patients with MM. The literature review involved searching secondary databases including MEDLINE, Embase, CINAHL, Cochrane, and DARE from inception to 2006. The review found 13 QoL and five economic studies (three cost-effectiveness and two cost-utility).

**Patient Group:** Adult patients with metastatic melanoma, including stage III (nonresectable) or IV, as defined by the American Joint Committee on Cancer Staging.
Key Results: No strong evidence was found in this review for cost-effectiveness of interferons in Canada (incremental cost per quality adjusted life year (QALY) gained of Can$55,090) or temozolomide in the United States (incremental cost per life-year gained of Can$36,990 based on nonsignificant efficacy differences). Melanoma screening was not cost-effective in the United States (Can$150,000-Can$931,000 per life-saved) or Germany (no survival benefit). From the 13 quality of life (QoL) studies, eight-measured baseline QoL; six studied the same population, generating similar results using different approaches/outcomes. Baseline QoL scores ranged from 0.60 to 0.69. In the five-randomised trials analysing QoL in patients treated with different drugs, little difference was found in QoL scores between drugs or between baseline and end point. Based on these findings, the authors conclude that cost-effectiveness has not been widely demonstrated for treatment of metastatic melanoma (MM). Only two studies with unimpressive results exist for treatments. Screening was not cost-effective in the United States or Germany. Generally, no significant improvements in QoL were found for any alternative for treating MM. A need exists for effective treatments that improve duration and QoL.

Cost comparisons of managing complex facial basal cell carcinoma: Canadian study

Study Question: Based on a prospective study, the aim of this study was to calculate the costs of managing high-risk Basal cell carcinomas (BCCs) using radiotherapy (RT) in comparison with Mohs micrographic surgery (MMS). Basal cell carcinoma (BCC) is the most common human malignancy and accounts for over 60,000 new cases of cancer in Canada annually. The authors indicate that although expensive to the health care system, no Canadian studies have reported the costs involved in management. A radiation oncologist reviewed each case retrospectively. The costs of MMS were the actual costs of the procedure, with an additional amount added to account for the technical costs of the surgery. The perspective adopted in the economic analysis was that of the payer, and the setting was secondary care in Canada.

Patient Group: The patient group comprised 49 consecutive complex Basal cell carcinoma (BCC) cases presenting to a skin cancer referral center. The mean age was 67 (34-86) with five patients being excluded because radiation was not recommended (age <50 years or radiation would overlap with a previous radiation field). All BCCs were located on the head and neck and were either recurrent disease or located in "at risk" sites such as the eye, ear, lip, or nose. All patients eventually underwent Mohs micrographic surgery (MMS).

Key Results: The baseline results showed that the direct cost of treating a patient with a single Basal cell carcinoma (BCC) was CN$871 (range CN$630-1,159) using Mohs micrographic surgery (MMS) and CN$3,625 (range CN$3,430-3,971) using radiotherapy (RT). The costs were found to be significantly higher for patients with multiple tumors with both modalities (p = .02 for both). The direct costs of a "5-year cure" were CN$952 (range CN$644-1,647) for MMS and CN$3,758 (range CN$3,564-4,675) for RT. The authors also undertook subgroup analysis, which revealed independent associations between aggressive histology, larger tumor size, and complexity of surgical closure and higher costs. A sensitivity analysis was performed to determine the ranges using known 5-year recurrence rates (for single tumors) and upper and lower bounds for costs, derived from the literature. The findings indicated that, although a trend toward greater costs in patients with recurrent disease, in males, younger patients, and tumors present for > 1 year, was present, they did not reach significance with the relatively small sample size used in the study. The authors highlight a
limitation of their analysis in that treatment costs may be center and provincially dependent. They suggest this preliminary report will initiate further study into comparing Canadian costs of managing skin cancer.

Cost-effectiveness of biologic treatments for psoriasis based on subjective and objective efficacy measures assessed over a 12-week treatment period


**Study Question:** To determine the cost-effectiveness of biologic agents in cost per patient achieving a Dermatology Life Quality Index, minimally important difference (DLQI MID) and cost per patient achieving a 75% reduction in baseline Psoriasis Area Severity Index (PASI-75), assessed over a 12-week period. Efficacies of the agents were determined through a literature review; treatment paradigms and associated costs were determined. The analysis was undertaken from a third-party payer perspective in the USA

**Patient Group:** Persons receiving systemic psoriasis treatment (phototherapy, systemic therapy, biologic therapy) who were compared to a placebo group.

**Key Results:** The objective of this study is to determine the cost-effectiveness of biologic agents in cost per patient achieving a Dermatology Life Quality Index, minimally important difference (DLQI MID) and cost per patient achieving a 75% reduction in baseline Psoriasis Area Severity Index (PASI-75), assessed over a 12-week period. Etanercept at a dose of 25 mg administered subcutaneously (SQ) once weekly was the most cost-effective agent in cost per patient achieving DLQI MID; infliximab at a dose of 3 mg/kg administered intravenously (IV) for 3 infusions, adalimumab at a dose of 40 mg SQ every other week, and etanercept at a dose of 25 mg SQ twice weekly were the next most cost-effective agents in cost per patient achieving the DLQI MID. Intravenous infliximab at a dose of 3 mg/kg was the most cost-effective agent in terms of cost per patient achieving PASI-75 improvement; intravenous infliximab at a dose of 5 mg/kg and adalimumab at a dose of 40 mg SQ every other week were the next most cost-effective agents in cost per patient achieving PASI-75 improvement. The cost-effectiveness ratios were sensitive to variations in average wholesale price and DLQI efficacy at a level of +/- 5% in one-way sensitivity analysis. When sensitivity analyses were performed, multiple agents had overlapping cost-effectiveness ratios at relatively low levels of variance; thus it may not be accurate to differentiate the cost-effectiveness of these agents. The authors conclude that infliximab and adalimumab appear to be the most cost-effective agents.