Brodszky V (ed.): Systematic review and analysis of evidences on clinical efficacy and cost-effectiveness of biological drugs for the treatment of Psoriatic Arthrtis

Appendix 8.8.

Results of the health economic literature search (references and abstracts)

Ovid MEDLINE(R) 1946 to Present with Daily Update (8 hits)

Results 8
1. **EXLUDED / METHODOLOGICAL PAPER**
Modelling correlated clinical outcomes in health technology appraisal.
Epstein D. Sutton A.
Value in Health. 14(6):793-9, 2011 Sep-Oct.
[Journal Article. Research Support, Non-U.S. Gov't]
UI: 21914498
OBJECTIVES: Many clinical treatments have multiple effects that can only be effectively captured on multiple outcome scales. It might be important to understand how these outcomes are correlated to evaluate the effectiveness and cost-effectiveness of treatments in decision models.
METHODS: The probabilities are estimated that both, one, or neither outcome occurs, given estimates of the marginal probability for each outcome and information about the correlation between them. Methods are shown for different measures of association. Lower and upper bounds for the correlation coefficient are calculated for given values of the marginal probabilities. The approach is illustrated using a simplified decision model based on a recent evaluation of adalimumab, a biologic drug for psoriatic arthritis.
RESULTS: Assuming the outcomes are positively correlated, the probability of both a skin and arthritis response after adalimumab was estimated to be 0.387 (95% confidence interval 0.210-0.570). The incremental cost-effectiveness ratio (ICER) of adalimumab versus no biologic is Pound18,500 per quality-adjusted life-year (QALY). The ICER increases to Pound19,500 per QALY if the responses are independent.
CONCLUSION: Estimates of ICERs can be sensitive to assumptions about how multiple outcomes are correlated. These assumptions should be explored in univariate and probabilistic sensitivity analyses.

Status
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Date Created
20110914
Year of Publication
2011
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21914498

2. INCLUDED
Modelling the cost-effectiveness of biologic treatments for psoriatic arthritis.
Bojke L. Epstein D. Craig D. Rodgers M. Woolacott N. Yang H. Sculpher M.
Rheumatology. 50 Suppl 4:iv39-iv47, 2011 Sep.
[Journal Article. Research Support, Non-U.S. Gov't]
UI: 21859705
OBJECTIVES: A probabilistic model was developed to determine the cost-effectiveness of three

biologics, etanercept, infliximab and adalimumab, compared with palliative care for the treatment of active and progressive PsA in patients who have an inadequate response to standard treatment (including DMARDs).
METHODS: A previous model was revised to evaluate the impact of biologics on both skin and joint disease and to include new evidence from the clinical review and evidence synthesis. Initial response to biologics was determined using the PsA response criteria. The impact of biologics on the arthritis component of the disease is then modelled via a change in the HAQ and the impact of the psoriasis component measured using the Psoriasis Area and Severity Index.
RESULTS: For PsA patients with mild to moderate skin disease, the incremental cost-effectiveness ratio (ICER) for etanercept vs palliative care is around Pound18 000, and the ICER for infliximab vs etanercept is around Pound44 000 per quality-adjusted life year (QALY). Adalimumab is extendedly dominated. The probability that etanercept is cost effective is 0.436 at a threshold of Pound20 000 per QALY. Etanercept is also likely to be cost effective for patients with moderate to severe psoriasis or negligible skin involvement.
CONCLUSIONS: Further investigation is required to reduce uncertainties around a number of model parameters, in particular the length of time over which biologics are assumed to be effective and the progression of HAQ on and off treatment.
Status
MEDLINE
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Bojke, Laura. Epstein, David. Craig, Dawn. Rodgers, Mark. Woolacott, Nerys. Yang, Huiqin. Sculpher, Mark.
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20110823
Year of Publication
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Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21859705

3. EXLUDED / THIS REVIEW ARTICLE WAS THE BASIS OF OUR SEARCH
Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. [Review]
Rodgers M. Epstein D. Bojke L. Yang H. Craig D. Fonseca T. Myers L. Bruce I. Chalmers R. Bujkiewicz S. Lai M. Cooper N. Abrams K. Spiegelhalter D. Sutton A. Sculpher M. Woolacott N. Health Technology Assessment (Winchester, England). 15(10):i-xxi, 1-329, 2011 Feb.
[Journal Article. Research Support, Non-U.S. Gov't. Review]
UI: 21333232
BACKGROUND: Etanercept, infliximab and adalimumab are licensed in the UK for the treatment of active and progressive psoriatic arthritis (PsA) in adults who have an inadequate response to standard treatment.
OBJECTIVE: To determine the clinical effectiveness, safety and cost-effectiveness of these biologic agents in the treatment of active and progressive PsA.
DATA SOURCES: Systematic reviews were performed, with data sought from 10 electronic databases (MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Science Citation Index, Conference Proceedings Citation Index - Science, ClinicalTrials.gov, metaRegister of Current Controlled Trials, NHS Economic Evaluation Database, Health Economic Evaluations Database and EconLit) up to June 2009.
REVIEW METHODS: Full paper manuscripts of titles/abstracts considered relevant were obtained and assessed for inclusion by two reviewers according to criteria on study design, interventions, participants and outcomes. Data on study and participant characteristics, efficacy outcomes, adverse effects, costs to the health service and cost-effectiveness were extracted, along with baseline data where reported. The primary efficacy outcomes were measures of anti-inflammatory response, skin lesion response and functional status, and the safety outcome was the incidence of serious adverse events. The primary measure of cost-effectiveness was incremental cost per additional quality-adjusted life-year (QALY). Standard meta-analytic techniques were applied to efficacy data. Published cost-effectiveness studies and the economic analyses submitted to the National Institute for Health and Clinical Excellence (NICE) by the biologic manufacturers were reviewed. An economic model was developed by updating the model produced by the York Assessment Group for the previous NICE appraisal of biologics in PsA.
RESULTS: Pooled estimates of effect demonstrated a significant improvement in patients with PsA for all

joint disease and functional status outcomes at 12-14 weeks' follow-up. The biologic treatment significantly reduced joint symptoms for etanercept [relative risk (RR) 2.60, 95% confidence interval (CI) 1.96 to 3.45], infliximab (RR 3.44, 95% CI 2.53 to 4.69) and adalimumab (RR 2.24, 95% CI 1.74 to 2.88), with 24-week data demonstrating maintained treatment effects. Trial data demonstrated a significant effect of all three biologics on skin disease at 12 or 24 weeks. Evidence synthesis found that infliximab appeared to be most effective across all outcomes of joint and skin disease. The response in joint disease was greater with etanercept than with adalimumab, whereas the response in skin disease was greater with adalimumab than with etanercept, although these differences are not statistically significant. Under base-case assumptions, etanercept was the most likely cost-effective strategy for patients with PsA and mild-to-moderate psoriasis if the threshold for cost-effectiveness was Pound20,000 or Pound30,000 per QALY. All biologics had a similar probability of being cost-effective for patients with PsA and moderate-to-severe psoriasis at a threshold of Pound20,000 per QALY.
LIMITATIONS: Limited available efficacy data and difficulty in assessing PsA activity and its response to biologic therapy.
CONCLUSIONS: The data indicated that etanercept, infliximab and adalimumab were efficacious in the treatment of PsA compared with placebo, with beneficial effects on joint symptoms, functional status and skin. Short-term data suggested that these biologic agents can delay joint disease progression and evidence to support their use in the treatment of PsA is convincing. Future research would benefit from long-term observational studies with large sample sizes of patients with PsA to demonstrate that beneficial effects are maintained, along with further monitoring of the safety profiles of the biologic agents.
FUNDING: The National Institute for Health Research Health Technology Assessment programme.
Status
MEDLINE
Authors Full Name
Rodgers, M. Epstein, D. Bojke, L. Yang, H. Craig, D. Fonseca, T. Myers, L. Bruce, I. Chalmers, R. Bujkiewicz, S. Lai, M. Cooper, N. Abrams, K. Spiegelhalter, D. Sutton, A. Sculpher, M. Woolacott, N.
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20110221
Year of Publication
2011
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21333232

4. **EXCLUDED / NOT CU ANALYSIS**
A 3 mg/kg starting dose of infliximab in active spondyloarthritis resistant to conventional treatments is efficient, safe and lowers costs.
Tenga G. Goeb V. Lequerre T. Bacquet-Deschryver H. Daragon A. Pouplin S. Lanfant-Weybel K. Le Loet X. Dieu B. Vittecoq O.
Joint, Bone, Spine: Revue du Rhumatisme. 78(1):50-5, 2011 Jan.
[Journal Article]
UI: 20646950
OBJECTIVE: We assessed the efficacy, tolerance and cost of a 3 mg/kg starting dose of infliximab for ankylosing spondylitis (AS) and psoriatic arthritis (PsA).
METHODS: We retrospectively followed-up 45 biologic-naive consecutive patients (11 with axial AS, 24 with axial and peripheral [mixed] AS and 10 with PsA) who were treated between 2002 and 2005 with a 3 mg/kg dose of infliximab after failure of conventional therapies. The following variables were recorded: visual analog scale (VAS) scores of patient's global (G) and pain (P) assessment, duration of early morning stiffness (EMS), disease activity (BASDAI) and functional disability (BASFI). Treatment responses were assessed at 6 and 12 months using the AS assessment score (ASAS)-20% and -40% criteria and BASDAI-50.
RESULTS: Baseline characteristics of the 29 men and 16 women were (median [range]): G-VAS, 70 [13-100]; P-VAS, 70 [13-100]; EMS, 60 [0-180] minutes; BASDAI, 64.4 [23.9-100]; BASFI, 57.2 [3.5-98.5]. All manifestations regressed significantly ($p<0.0001$) for 39 (86.7%) and 24 (53.5%) patients at 6 and 12 months, respectively; 26 (57.8%) had achieved ASAS-20 responses at 6 months that persisted at 1 year for 20 (44.4%); 19 (42.2%) and 12 (26.7%) satisfied BASDAI 50 criteria at 6 and 12 months, respectively. Interestingly, almost 30% still received low-dose infliximab after 4 years of follow-up.
CONCLUSION: An initial dose of 3 mg/kg of infliximab significantly attenuated AS and PsA manifestations in>40% of the patients, making use of this dose highly advantageous in terms of safety and 33% lower cost.

reserved.
Status
MEDLINE
Authors Full Name
Tenga, Ginette. Goeb, Vincent. Lequerre, Thierry. Bacquet-Deschryver, Helene. Daragon, Alain. Pouplin, Sophie. Lanfant-Weybel, Karine. Le Loet, Xavier. Dieu, Bernard. Vittecoq, Olivier.
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http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20646950

5. **INCLUDED**
Cost-effectiveness of infliximab for the treatment of active and progressive psoriatic arthritis.
Cummins E. Asseburg C. Punekar YS. Shore E. Morris J. Briggs A. Fenwick E.
Value in Health. 14(1):15-23, 2011 Jan.
[Journal Article. Meta-Analysis. Research Support, Non-U.S. Gov't]
UI: 21211482
BACKGROUND: Despite its proven efficacy, infliximab is often considered to be an expensive treatment for patients with psoriatic arthritis.
OBJECTIVES: To estimate the cost-effectiveness of infliximab among patients with active and progressive psoriatic arthritis.
METHODS: A decision analytic model was constructed to simulate disease progression in hypothetical cohorts of patients with psoriatic arthritis receiving infliximab maintenance treatment. The primary response measure was change in Health Assessment Questionnaire score from a baseline estimated from mixed treatment models drawn from published clinical trials. Palliative care, comprising nonbiologic disease-modifying antirheumatic drugs, was used as a comparator. The primary outcome was quality-adjusted life years. The dose of infliximab was estimated for a range of 60 to 80 kg per patient body weight. The costs and outcomes were discounted at 3.5% for a period of 40 years. Uncertainty around the results was explored with probabilistic sensitivity analysis.
RESULTS: The mixed treatment comparison showed a significant reduction in Health Assessment Questionnaire score across all patients. The tumor necrosis factor alpha inhibitors were significantly superior to palliative care but comparable with one another. The incremental cost-effectiveness ratios for etanercept, adalimumab, and infliximab relative to palliative care were Pound17,327; Pound19,246; and Pound16,942 to Pound23,022, respectively, across all patients with psoriatic arthritis and Pound16,613; Pound18,170; and Pound15,788 to Pound21,736, respectively, in the subgroup with significant psoriasis.
CONCLUSION: Infliximab represents a cost-effective treatment option well within the National Institute for Health and Clinical Excellence threshold relative to palliative care. In light of equivalent outcomes with other tumor necrosis factor alpha inhibitors, its position in the treatment pathway is likely to be governed by treatment costs. Copyright Copyright 2011 International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc. All rights reserved.
Status
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Cummins, Ewen. Asseburg, Christian. Punekar, Yogesh Suresh. Shore, Emily. Morris, James. Briggs, Andrew. Fenwick, Elisabeth.
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Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=21211482

6. **EXCLUDED / METHODOLOGICAL PAPER**
Eliciting distributions to populate decision analytic models.
Bojke L. Claxton K. Bravo-Vergel Y. Sculpher M. Palmer S. Abrams K.
Value in Health. 13(5):557-64, 2010 Aug.
[Journal Article. Meta-Analysis. Research Support, Non-U.S. Gov't]
UI: 20345548
BACKGROUND: Elicitation can be used to characterize structural uncertainty within a decision analytic model. This allows the value of acquiring further evidence to resolve these uncertainties to be established.
AIM: This article demonstrated the use of expert elicitation for this purpose and also compared the elicited results with the results from alternative assumptions previously used to characterize the uncertainties.
MATERIALS AND METHODS: Distributions for two unknown parameters were elicited. These were used within a model developed to assess the cost-effectiveness of infliximab and etanercept for the treatment of active psoriatic arthritis (PsA), compared with palliative care. The experts' distributions were synthesized using two approaches: linear pooling and random effects meta-analysis. Weighting of experts is also explored.
RESULTS: The four methods produce broadly similar results, and in each, the choice of optimum strategy is between etanercept and palliative care (incremental cost-effective ratio for etanercept is between pound29,021 and pound39,259 per costs and quality adjusted life years). Decision uncertainty, at a pound30,000 threshold, is high in all of the synthesis models thus generating high values of further research at between pound141 and pound634 million. In each model, the greatest value of further research was for the short-term effectiveness of treatment (pound47- pound406 million).
DISCUSSION: Although the cost-effectiveness results do not differ substantially between the models using the elicited values and the original scenarios, there are some stark contrasts in terms of the values of further research generated.
CONCLUSION: Elicitation offers a feasible method to generate evidence for the missing information but there are a number of key issues for which further research is required.
Status
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Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20345548

7. **Excluded / NOT CU ANALYSIS**
Listeria endocarditis in a patient with psoriatic arthritis on infliximab: are biologic agents as treatment for inflammatory arthritis increasing the incidence of Listeria infections?. [Review] [48 refs]
Kelesidis T. Salhotra A. Fleisher J. Uslan DZ.
Journal of Infection. 60(5):386-96, 2010 May.
[Case Reports. Journal Article. Review]
UI: 20176052
The use of anti-tumor necrosis factor agents such as infliximab as treatment modalities of inflammatory joint diseases has widely spread over the past few years. However, increasing numbers of reports of infectious complications during TNF-a blockade have also highlighted the fact that an increased rate of sometimes life-threatening complications may be the price paid for superior therapeutic efficacy. We report the first case report of Listeria endocarditis associated with infliximab use and the second published case of Listeria infection associated with infliximab in patients with psoriatic arthritis. We also summarize the literature regarding the association of Listeria infection with use of infliximab. Further studies are needed to elucidate the contribution of anti-TNF-a therapy to development of listeriosis. Physicians should be aware of the possibility of Listeria infection in individuals receiving anti-TNF therapy. 2010 The British Infection Society. Published by Elsevier Ltd. All rights reserved. [References: 48]
Status
MEDLINE
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Kelesidis, Theodoros. Salhotra, Amandeep. Fleisher, Jorge. Uslan, Daniel Z.

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Date Created
20100503
Year of Publication
2010
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=20176052

8. EXCLUDED / NOT CU ANALYSIS
Real-world anti-tumor necrosis factor treatment in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: cost-effectiveness based on number needed to treat to improve health assessment questionnaire.
Barra L. Pope JE. Payne M.
Journal of Rheumatology. 36(7):1421-8, 2009 Jul.
[Journal Article. Research Support, Non-U.S. Gov't]
UI: 19487267
OBJECTIVE: To determine the effectiveness and cost-effectiveness of anti-tumor necrosis factor (anti-TNF) medications in a real-world environment for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) using the Health Assessment Questionnaire (HAQ).
METHODS: We created a database of patients with RA, PsA, or AS treated with anti-TNF agents (etanercept, infliximab, or adalimumab) at a large outpatient rheumatology clinic. Patient characteristics, baseline HAQ prior to treatment, subsequent yearly HAQ, and reasons for termination were collected. The cost based on percentage of patients achieving >or= 0.2 improvement in HAQ (minimal clinically important difference, MCID) was calculated using the 2008 direct cost (Cdn) of the medication.
RESULTS: Data were available on 297 patients (206 with RA, 57 PsA, 34 AS). The mean age was 55 years, with 12 years of disease, and the mean baseline HAQ (standard error, SE) was 1.37 (0.04). The changes in HAQ (SE) at Years 1, 2, and 3 were -0.31 (0.04), -0.24 (0.06), and -0.27 (0.07) for annual cost to achieve MCID of $41,636, $42,077, and $42,147, respectively. The number needed to treat (NNT) was 1.94 (RA), 1.88 (PsA), and 2.30 (AS). There were no statistical differences between the diseases studied.
CONCLUSION: We obtained data on the effectiveness and cost-effectiveness of anti-TNF drugs using the HAQ score, which is known to be an excellent predictor of work disability, morbidity, and mortality. HAQ scores decreased with treatment and were sustained throughout the 3-5 years of followup. The NNT of approximately 2 seems favorable and was similar between diseases.
Status
MEDLINE
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Barra, Lillian. Pope, Janet E. Payne, Michael.
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Date Created
20090701
Year of Publication
2009
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=medl&AN=19487267

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <March 30, 2012> (8 hits)

1. **INCLUDED**
Golimumab for the treatment of psoriatic arthritis: a NICE single technology appraisal.
Yang H. Craig D. Epstein D. Bojke L. Light K. Bruce IN. Sculpher M. Woolacott N.
Pharmacoeconomics. 30(4):257-70, 2012 Apr 1.
[Journal Article. Research Support, Non-U.S. Gov't]
UI: 22283690
The National Institute for Health and Clinical Excellence (NICE) invited the manufacturer of golimumab (Schering-Plough/Centocor) to submit evidence for the clinical and cost effectiveness of this drug for the treatment of active and progressive psoriatic arthritis (PsA) in patients who have responded inadequately to previous disease-modifying anti-rheumatic drugs (DMARDs). The Centre for Reviews and Dissemination and the Centre for Health Economics at the University of York were commissioned to act as the Evidence Review Group (ERG) to critically appraise the evidence presented by the manufacturer. This article provides a description of the company submission, the ERG review and the resulting NICE guidance. The ERG critically reviewed the evidence presented in the manufacturer's submission and identified areas requiring clarification, for which the manufacturer provided additional evidence. The main clinical effectiveness data were derived from a single phase III randomized controlled trial (GO-REVEAL) that compared golimumab with placebo for the treatment of active and progressive patients who were symptomatic despite the use of previous DMARDs or NSAIDs. The 14-week data showed that, compared with placebo, golimumab 50[THIN SPACE]mg significantly improved joint disease response as measured by American College of Rheumatology (ACR) 20 (relative risk [RR] 5.73, 95% CI 3.24, 10.56) and Psoriatic Arthritis Response Criteria (PsARC) [RR 3.45, 95% CI 2.49, 4.87], and significantly improved skin disease response as measured by Psoriasis Area and Severity Index (PASI) 75 (RR 15.95, 95% CI 4.62, 59.11). The 24-week absolute data showed that these treatment benefits were maintained. There was a significant improvement in patients' functional status as measured by Health Assessment Questionnaire change from baseline at 24 weeks (-0.33; p[THIN SPACE]<[THIN SPACE]0.001). The open-label extension data showed that these beneficial effects were also maintained at 52 and 104 weeks. The ERG identified several issues relating to the clinical effectiveness results. Analyses of the 24-week data were less robust, failing to adjust for treatment contamination due to patient crossover at week 16. It was also unclear if these results were generalizable to clinical practice. No randomized controlled trial compared the effectiveness of different biologic therapies head-to-head. To compare the effectiveness of the biologics etanercept, infliximab, adalimumab and golimumab, the manufacturer conducted a network meta-analysis, including the comparator palliative care (usual care including use of NSAIDs or DMARDs). The ERG considered the assumption of exchangeability between the trials for the purpose of the network meta-analysis to be acceptable and the statistical approach to be reliable. The results indicated somewhat lower efficacy with golimumab than with comparator biologics. The ERG identified a number of issues relating to the cost-effectiveness results. The manufacturer calculated incremental cost-effectiveness ratios (ICERs) incorrectly by comparing golimumab with palliative care instead of the most cost-effective alternative (etanercept). Despite the manufacturer's claim that golimumab was a cost-effective treatment option, the manufacturer's own model showed that golimumab was unlikely to be cost effective, relative to currently accepted thresholds, when the ICERs were correctly calculated using an incremental analysis (i.e. comparing each treatment to the next best alternative). None of the sensitivity analyses carried out by the manufacturer or the ERG regarding uncertainty in the estimates of clinical effectiveness, the acquisition and administration cost of drugs, the cost of treating psoriasis and the utility functions estimated to generate health outcomes changed this conclusion. However, a key area in determining the cost effectiveness of biologics was whether they should be treated as a class. The ERG concluded that if all biologics were considered equally effective, then etanercept, adalimumab and golimumab had almost equal costs and equal QALYs, and all had an ICER of about Pound15[THIN SPACE]000 per QALY versus palliative care, whilst infliximab, with a higher acquisition cost, was dominated by the other biologics. The Appraisal Committee altered its position between the Appraisal Consultation Document and the Final Appraisal Determination. It ultimately recommended that golimumab be provided as an option for the treatment of active and progressive PsA in adults only if (i) it is used as described for other tumour necrosis factor inhibitor treatments in 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis' (NICE clinical guideline 199); and (ii) the manufacturer provides the 100[THIN SPACE]mg dose of golimumab at the same cost as the 50[THIN SPACE]mg dose.
Status
In-Process

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20120313
Year of Publication
2012
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=22283690

2. **EXCLUDED / NOT CU ANALYSIS**
Annual costs of tumor necrosis factor inhibitors using real-world data in a commercially insured population in the United States.
Schabert VF. Watson C. Gandra SR. Goodman S. Fox KM. Harrison DJ.
Journal of Medical Economics. 15(2):264-75, 2012.
[Journal Article. Research Support, Non-U.S. Gov't]
UI: 22115327
OBJECTIVE: To calculate annual cost per treated patient of tumor necrosis factor (TNF) inhibitors etanercept, adalimumab, and infliximab for common approved indications, based on actual TNF-inhibitor use in clinical practice.
METHODS: Adults with >=1 claim for etanercept, adalimumab, or infliximab between January 2005 and March 2009 were identified from the IMS LifeLinkTM Health Plan Claims Database. Patients new to therapy or continuing therapy (i.e., a prior claim for a TNF-inhibitor) were analyzed separately. Included patients had been enrolled from 180 days before the first TNF-inhibitor claim (index date) through 360 days after the index date and had a diagnosis during the pre-index period for rheumatoid arthritis, psoriasis, psoriatic arthritis, or ankylosing spondylitis. Patients with Crohn's disease, ulcerative colitis, or juvenile idiopathic arthritis were excluded. Annual costs were calculated using wholesale acquisition costs for the TNF-inhibitor and Medicare Physician Fee Schedule for drug administration. Costs from restarting or switching TNF-inhibitor therapy during the first year were included.
RESULTS: A total of 27,704 patients (11,528 new, 16,176 continuing) had claims for etanercept, adalimumab, or infliximab, most commonly (65%) for treatment of rheumatoid arthritis. The most commonly used agent was etanercept (14,777 patients; 53%), followed by adalimumab (6862 patients; 25%) and infliximab (6065 patients; 22%). Annual cost per treated patient was etanercept $14,873, adalimumab $17,766, and infliximab $21,256 across all indications. Annual cost per treated patient by disease was (etanercept/adalimumab/infliximab): rheumatoid arthritis ($14,314/$17,700/$20,390), psoriasis ($17,182/$17,682/$23,935), psoriatic arthritis ($15,030/$18,483/$24,974), and ankylosing spondylitis ($14,254/$16,925/$23,056). New and continuing patients showed similar results, with etanercept having the lowest costs.
LIMITATIONS: This analysis is limited to three TNF-inhibitors and a US managed-care population.
CONCLUSIONS: Based on this analysis of real-world use of TNF-inhibitors among patients in nationwide clinical practice settings, the annual TNF-inhibitor cost per treated patient was lowest for etanercept across all indications.
Status
In-Process
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3. INCLUDED

Golimumab for the treatment of psoriatic arthritis.
Yang H. Epstein D. Bojke L. Craig D. Light K. Bruce I. Sculpher M. Woolacott N.
Health Technology Assessment (Winchester, England). 15 Suppl 1:87-95, 2011 May.
[Journal Article. Research Support, Non-U.S. Gov't]
UI: 21609657
This paper presents a summary of the evidence review group (ERG) report into the use of golimumab for the treatment of psoriatic arthritis (PsA). The main clinical effectiveness data were derived from a single phase III randomised controlled trial (RCT: GO-REVEAL) that compared golimumab with placebo for treating patients with active and progressive PsA who were symptomatic despite the use of previous disease-modifying antirheumatic drugs or non-steroidal anti-inflammatory drugs. The 14-week data showed that, compared with placebo, golimumab 50 mg significantly improved joint disease response as measured by American College of Rheumatology (ACR) 20 [relative risk (RR) 5.73, 95% confidence interval (CI) 3.24 to 10.56] and Psoriatic Arthritis Response Criteria (PsARC) (RR 3.45, 95% CI 2.49 to 4.87), and skin disease response as measured by the Psoriasis Area and Severity Index (PASI) 75 (RR 15.95, 95% CI 4.62 to 59.11). The 24-week absolute data showed that these treatment benefits were maintained. There was a significant improvement in patients' functional status as measured by the Health Assessment Questionnaire (HAQ) change from baseline at 24 weeks (-0.33, $p < 0.001$). The open-label extension data showed that these beneficial effects were also maintained at 52 and 104 weeks. However, PASI 50 and PASI 90 at 14 weeks, and all of the PASI outcomes at 24 weeks, were not performed on the basis of intention-to-treat analysis. Furthermore, analyses of the 24-week data were less robust, failing to adjust for treatment contamination due to patient crossover at week 16. The manufacturer conducted a mixed treatment comparison (MTC) analysis. The ERG considered the assumption of exchangeability between the trials for the purpose of the MTC analysis to be acceptable, and the statistical approach in the MTC analysis to be reliable. Regarding the safety evaluation of golimumab, the manufacturer failed to provide longer-term data or to consider adverse event data of golimumab from controlled studies in other conditions, such as rheumatoid arthritis and ankylosing spondylitis. Although the adverse effect profile of golimumab appears similar to other anti-tumour necrosis factor (TNF) agents, the longer-term safety profile of golimumab remains uncertain. The manufacturer's submission presented a decision model to compare etanercept, infliximab, golimumab and adalimumab versus palliative care for patients with PsA. In the base-case model, 73% of the cohort of patients were assumed to have significant psoriasis (> 3% of body surface area). Estimates of the effectiveness of anti-TNF agents in terms of PsARC, HAQ change and PASI change were obtained from an MTC analysis of RCT data. The manufacturer failed to calculate incremental cost-effectiveness ratios (ICERs) correctly by comparing golimumab with palliative care instead of the most cost-effective alternative (etanercept). Despite the manufacturer's claim that golimumab is a cost-effective treatment option, the manufacturer's own model showed that golimumab is not cost-effective compared with other biologics when the ICERs are correctly calculated. None of the sensitivity analyses carried out by the manufacturer or the ERG regarding uncertainty in the estimates of clinical effectiveness, the acquisition and administration cost of drugs, the cost of treating psoriasis and the utility functions estimated to generate health outcomes changed this conclusion. However, a key area in determining the cost-effectiveness of anti-TNF agents is whether they should be treated as a class. If all anti-TNF agents are considered equally effective then etanercept, adalimumab and golimumab have very nearly equal costs and equal quality-adjusted life-years (QALYs), and all have an ICER of about Pound 15,000 per QALY versus palliative care, whereas infliximab with a higher acquisition cost is dominated by the other biologics.
Status
In-Process
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20110525
Year of Publication
2011
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=21609657

4. **EXCLUDED / NOT CU ANALYSIS**

Cost per treated patient for etanercept, adalimumab, and infliximab across adult indications: a claims analysis.
Bonafede MM. Gandra SR. Watson C. Princic N. Fox KM.
Advances in Therapy. 29(3):234-48, 2012 Mar.
[Journal Article]
UI: 22411424
INTRODUCTION: This paper aims to estimate the annual cost of etanercept, adalimumab, and infliximab per treated patient across adult indications using US-managed care drug use data.
METHODS: Adult patients who used etanercept, adalimumab, or infliximab were identified in the Thomson Reuters MarketScan[REGISTERED] Commercial Claims and Encounters Database (Thomson Reuters Healthcare, Ann Arbor, MI, USA) between January 1, 2005 and June 30, 2009. The index event was the first use of etanercept, adalimumab, or infliximab preceded by a diagnosis for rheumatoid arthritis, psoriasis, psoriatic arthritis, or ankylosing spondylitis. Patients were defined as either newly initiating or continuing tumor necrosis factor (TNF) blocker treatment based on their use during the 6 months before the index event. Annual cost per treated patient was the sum of the etanercept, adalimumab, and infliximab medication and administration costs during the 12 months following the index claim. Annual costs were calculated across all patients as well as within each indication group and patient type (new initiator or continuing).
RESULTS: In total, 21,652 patients met the study criteria (etanercept n = 12,065; adalimumab n = 5,685; infliximab n = 3,902); 43% of patients were new initiators. Patient characteristics were similar across treatment groups in terms of age (mean = 49, SD = 10) and gender (66% female). Across indications, the mean annual TNF-blocker cost per treated patient was $15,345 for etanercept, $18,046 for adalimumab, and $24,018 for infliximab. In new initiators, the TNF-blocker cost per treated patient across indications was $14,543 for etanercept, $16,978 for adalimumab, and $21,086 for infliximab; among patients continuing therapy, annual costs were $15,836 for etanercept, $19,457 for adalimumab, and $25,748 for infliximab.
CONCLUSION: Patients on etanercept had the lowest TNF-blocker cost per treated patient for adult indications when applying actual drug use from a US-managed care population. TNF-blocker costs per treated patient on adalimumab and infliximab were approximately 18% and 57% higher than etanercept, respectively, using real-world drug use data.
Status
In-Data-Review
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Date Created
20120321
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2012
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=22411424

5. **EXLUDED / NOT CU ANALYSIS**
Complement system in psoriatic arthritis: a useful marker in response prediction and monitoring of anti-TNF treatment.
Chimenti MS. Perricone C. Graceffa D. Di Muzio G. Ballanti E. Guarino MD. Conigliaro P. Greco E. Kroegler B. Perricone R.
Clinical & Experimental Rheumatology. 30(1):23-30, 2012 Jan-Feb.
[Journal Article]
UI: 22260811
OBJECTIVES: Treatment with anti-TNF agents is well established in psoriatic arthritis (PsA). Anti-TNF agents are capable of modulating complement activity in vitro but there are no data on the in vivo effect. Anti-TNF have high costs and potential risks, thus, there is an urgent need for accurate predictors of response. We aimed at studying the usefulness of erythrocyte-sedimentation-rate (ESR), C-reactive protein (CRP), and complement for response prediction and monitoring of anti-TNF treatment in PsA patients.
METHODS: Fifty-five patients were included consecutively before starting etanercept or adalimumab. ESR, CRP, plasma complement C3, C4, and C3 and B cleavage fragments were evaluated at baseline and after 22 weeks of anti-TNF treatment. Disease activity was measured with DAS28 and response to therapy with EULAR criteria. Complement was evaluated at baseline in 30 healthy subjects as well.
RESULTS: At baseline, C3 and C4 levels were significantly higher than in controls (C3 126.9+/-22 vs. 110+/-25 mg/dl, p=0.000002; C4 31.2+/-9.2 vs. 22.7+/-8.3 mg/dl, p=0.0003). After anti-TNF therapy, C3 and C4 levels were significantly reduced to normalization (p=0.0009 and 0.0005, respectively) and ESR, CRP and

DAS28 showed a significant reduction (p=0.002, 0.004 and 0.0001, respectively). Split products of C3 and B were not observed at baseline and after 22 weeks. Higher baseline C3 levels were associated with EULAR non-response (p=0.011).
CONCLUSIONS: PsA patients with moderate to severe disease show elevated C3 and C4 levels, reverted by anti-TNF treatment. High C3 may be considered a hallmark of inflammation and C3 revealed the highest predictive value for response to anti-TNF.
Status
In-Data-Review
Authors Full Name
Chimenti, Maria Sole. Perricone, Carlo. Graceffa, Dario. Di Muzio, Gioia. Ballanti, Eleonora. Guarino, Maria Domenica. Conigliaro, Paola. Greco, Elisabetta. Kroegler, Barbara. Perricone, Roberto.
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6. **EXCLUDED / NOT CU ANALYSIS**
Efficacy and safety of adalimumab treatment in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. [Review]
Poddubnyy D. Rudwaleit M.
Expert Opinion on Drug Safety. 10(4):655-73, 2011 Jul.
[Journal Article. Review]
UI: 21554150
INTRODUCTION: In the last couple of years, the number of patients with chronic inflammatory rheumatic diseases being treated with TNF alpha antagonist has increased dramatically. Adalimumab, a fully human monoclonal antibody against TNF alpha, is one of the most frequently administered TNF alpha antagonists. Yet, unresolved issues are the long-term safety of TNF alpha antagonists and high treatment costs. AREAS COVERED: The authors summarize the available data on short- and long-term efficacy and safety of adalimumab in the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. The reader will find a comprehensive overview on the safety and efficacy of adalimumab for these conditions. Clinically relevant questions of adalimumab therapy are discussed. A special focus of this review is on the safety of adalimumab therapy. EXPERT OPINION: Adalimumab is effective and reasonably safe in the short- and long-term treatment of patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis who do not respond to the standard therapy. It inhibits radiographic progression in rheumatoid and psoriatic arthritis. Treatment with a TNF alpha inhibitor such as adalimumab is associated with high treatment costs.
Status
In-Process
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Date Created
20110613
Year of Publication
2011
Link to the Ovid Full Text or citation:
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=21554150

7. **EXCLUDED / NOT PsA**
Therapy of moderate and severe psoriasis.
Claes C. Kulp W. Greiner W. von der Schulenburg JM. Werfel T.
GMS Health Technology Assessment. 2:Doc07, 2006.
[Journal Article]
UI: 21289958

OBJECTIVE AND METHODS: This health technology assessment (HTA) report synthesises systematically randomized controlled studies (RCT) on the therapy of moderate and severe psoriasis vulgaris which were published between 1999 and 2004; it includes some important clinical studies which have been published after 2004 and thus updates the English HTA report by Griffiths et al. [1]. The major objective is the evaluation of the medical effectiveness of different therapeutical approaches and the cost effectiveness with relevance for Germany.
RESULTS: The major conclusions from the results of medical RCT on moderate and severe psoriasis vulgaris are: Oral fumarates are effective in the treatment of moderate to severe psoriasis vulgaris. However, fumarates quiet frequently cause moderate side effects. Cyclosporine and methotrexate are both effective in the treatment of severe psoriasis vulgaris. Both substances have a different spectrum of side effects which may limit the individual applicability. Acetritin is only moderately effective in the treatment of severe psoriasis of the plaque type. Calcipotriol or UV-radiation used at the same time can increase the clinical effectiveness of acetritin. Systemic PUVA, balneo-PUVA and UVB therapy are all effective for the treatment of severe psoriasis. The combination of UV therapy with vitamin D3 analogues or with topical steroids is more effective than the treatment with UV radiation alone. Saltwater baths increase the effectiveness of UVB therapy. No RCT on the therapeutical effects of topical tar or of dithranol in combination with UV therapy have been published so far. A continuous therapy with PUVA should not be applied due to its proven photocarcinogenicity. Three substances from the group of biologicals (Efalizumab, Etanercept, and Infliximab) are now available in Europe and a further substance (Alefacept) is available in the USA for the treatment of moderate to severe psoriasis. All biologicals have been effective in placebo controlled studies. The substances differ in the times until a clinical effect is observable, in the spectrum of side effects and in their efficiency on psoriasis arthritis. From health-economic studies considering both costs and clinical efficiency oral fumarates appear to be superior to acitretin or cyclosporine (although cyclosporine appears to be more effective in severe psoriasis). From the health economic view methotrexate is equivalent with UVB or PUVA and superior to cyclosporine. The therapy options UVB, UVB plus calcipotriol and PUVA are equivalent and superior to balneo-phototherapy. Biologicals are cost intensive and should be used when other approaches are not sufficient or are not applicable due to their side effects. The HTA report summarizes some health-economic studies on dithranol, on calcipotriol and on the combination with tar and UV light. No RCT have been published for the treatment of severe psoriasis with these agents alone but it appears to be certain that these substances are effective in severe psoriasis as well.
DISCUSSION: The spectrum of therapeutical options has fortunately increased during the last years. It must be emphasized that a number of therapeutical procedures exist which are not discussed in detail in this HTA. This is due to the search strategy of literature: Only RCT performed with patients with moderate and/or severe psoriasis vulgaris were included into this evaluation. This led to the exclusion of a number of substances which are traditionally used alone or in combination for the treatment of moderate or severe psoriasis vulgaris (e.g. dithranol, salicyc acid, tar, corticosteroids and topical retinoids). Moreover, other approaches which include neither drugs nor UV light are not discussed in this HTA although the authors believe in the importance of psychotherapeutical interventions, educational approaches and combined medical and non-medical approaches in rehabilitational medicine in the management of psoriasis vulgaris. The transferability of the health economic evaluations is strongly limited by the fact that all included health economic evaluations except one were not aligned to a German setting. A future research question will be the evaluation of the duration of remission and relapse ratios in the context of different therapy options of moderate and severe psoriasis. Moreover, the consideration of combined outcomes such as the improvement of psoriatic symptoms and the decrease of symptoms in accompanying psoriasis arthritis represents a future requirement of health assessment.
CONCLUSIONS: From the clinical point of view it is positive that the spectrum of therapeutic procedures for a chronic severe skin disease has increased continuously during the last years. In cases of individual contraindications or individual inefficacies it is now possible to try alternative approaches. Moreover the risk of long-term side effects can be reduced by changing the therapeutical procedure after some time (so-called rotation therapy). The therapeutical algorithm for severe psoriasis vulgaris now includes photo(chemo-)therapy in combination with topical substances, oral fumaric acid esters, retinoids (in combination with phototherapy or topical substances), methotrexate, cylosporine and the new biologics. Future studies should address therapeutical approaches which can not easily be studied by RCT, e.g. physical, balneological, climate approaches, educational programs and complex rehabilitation therapy which all may have positive effects on individuals with severe psoriasis. As in medical therapy management of moderate and severe psoriasis the economic evaluation also points out the way of a strategic therapy concept which corresponds to a large extent to the algorithm in medical practice.
Status
In-Data-Review
Authors Full Name
Claes, Christa. Kulp, Werner. Greiner, Wolfgang. von der Schulenburg, Johann-Matthias. Werfel, Thomas.

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Other ID
Source: NLM. PMC3011355
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20110203
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2006
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http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=21289958

8. **EXCLUDED / NOT PsA**
Pharmacoeconomics of adalimumab for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and Crohn's disease.
Gladman DD. Brown RE.
Expert Review of Pharmacoeconomics & Outcomes Research. 8(2):111-25, 2008 Apr.
[Journal Article]
UI: 20528400
Adalimumab is a monoclonal antibody that inhibits TNF, an osteogenic cytokine involved in the pathogenesis of chronic, disabling inflammatory diseases. Adalimumab is indicated for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and Crohn's disease. It alleviates the symptoms of these diseases, prevents disease progression in some patients and, in the case of Crohn's disease, induces and maintains remission. Compared with traditional disease-modifying antirheumatic drugs that offer significantly less benefit, adalimumab is much more costly. However, most studies to date demonstrate the cost-effectiveness of adalimumab treatment. Cost-effectiveness data for newer indications of adalimumab, including ankylosing spondylitis and Crohn's disease, are needed. As longer term data for adalimumab become available, the cost-effectiveness data will have greater precision.
Status
In-Data-Review
Authors Full Name
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http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=prem&AN=20528400

Web of knowledge (34 hits)

Record 1 of 34 **EXCLUDED / NOT CU ANALYSIS**

Title: Use of anti-tumor necrosis factor-a therapy in hepatitis B virus carriers with psoriasis or psoriatic arthritis: A case series in Taiwan

Author(s): Cho, YT (Cho, Yung-Tsu); Chen, CH (Chen, Chien-Hung); Chiu, HY (Chiu, Hsien-Yi); Tsai, TF (Tsai, Tsen-Fang)

Source: JOURNAL OF DERMATOLOGY Volume: 39 Issue: 3 Pages: 269-273 DOI: 10.1111/j.1346-8138.2011.01434.x Published: MAR 2012

Abstract: The use of anti-tumor necrosis factor (TNF)-a therapy in patients with psoriasis who are hepatitis B virus (HBV) carriers is usually not recommended, and routine antiviral prophylaxis is suggested for those who need the treatment. We report our experience on the safety of anti-TNF-a therapy in patients with psoriasis who are HBV carriers in our clinic using HBV viral load as a guide for HBV treatment. Between 2007 and 2011, seven HBV carriers receiving TNF-a inhibitors for psoriasis in our clinic were collected retrospectively. The HBV viral load and aminotransferase levels were regularly monitored. Two of the seven patients were inactive HBV carriers, and the other five patients had chronic hepatitis B. Only one patient received antiviral agents before the anti-TNF-a treatment. The mean duration of the anti-TNF-a treatment was 26.6 months (range, 1445 months). These patients were followed up from the start of the anti-TNF-a therapy for a mean duration of 28.9 months (range, 1445 months). HBV reactivation was observed in three patients, one of whom required antiviral treatment. No HBV reactivation-related hepatitis was observed. In conclusion, prevention of HBV reactivation by monitoring of HBV viral load is cost-effective and may decrease the risk of developing drug resistance from routine anti-HBV prophylaxis treatment. It can be considered as an alternative in psoriasis patients treated by TNF-a inhibitors, especially in areas with a high HBV burden and in hepatitis B e-antigen-negative patients who have a lower risk of viral reactivation.

ISSN: 0385-2407

Record 2 of 34 **EXCLUDED / NOT CU ANALYSIS**

Title: Cloning, expression, purification and characterization of a single chain variable fragment specific to tumor necrosis factor alpha in Escherichia coli

Author(s): Sushma, K (Sushma, Krishnan); Vijayalakshmi, MA (Vijayalakshmi, Mookambeswaran A.); Krishnan, V (Krishnan, Venkataraman); Satheeshkumar, PK (Satheeshkumar, Padikara Kutty)

Source: JOURNAL OF BIOTECHNOLOGY Volume: 156 Issue: 4 Special Issue: SI Pages: 238-244 DOI: 10.1016/j.jbiotec.2011.06.039 Published: DEC 20 2011

Abstract: Anti TNF-alpha molecules have been used as therapeutic agents in a variety of human diseases such as Rheumatoid arthritis, Ankylosing spondylitis, Chron's diseases, Psoriasis, etc., where high levels of TNF-alpha plays a destructive role. The limitations of the present TNF-alpha inhibitors in terms of size, tissue penetration and immunogenicity, etc., provoked the search for small anti TNF-alpha molecules. In the present study, a single chain variable fragment (ScFv) construct was made from a monoclonal antibody of the class IgG raised against TNF-alpha was used. The anti TNF-alpha ScFv was well expressed as soluble form in Escherichia coli BL21 (DE3), which was purified to homogeneity by commercial methacrylate monolith-convective interaction media (CIM) supports using two different chemistries, immobilized metal affinity chromatography (IMAC) with copper ions followed by anion exchange chromatography. The anti TNF-alpha ScFv found to be inhibiting the TNF-alpha mediated cytotoxicity in MCF-7 cells with an IC(50) of 8 mu g. Data presented here are promising and encouraging to further optimize anti TNF-alpha ScFv production in larger scale with higher recovery at a cheaper price for therapeutic purposes.

ISSN: 0168-1656

Record 3 of 34 **EXCLUDED / NOT CU ANALYSIS**

Title: Socioeconomic Burden of Immune-Mediated Inflammatory Diseases - Focusing on Work Productivity and Disability

Author(s): Jacobs, P (Jacobs, Philip); Bissonnette, R (Bissonnette, Robert); Guenther, LC (Guenther, Lyn C.)

Source: JOURNAL OF RHEUMATOLOGY Volume: 38 Pages: 55-61 DOI: 10.3899/jrheum.110901 Supplement: 88 Published: NOV 2011

Abstract: Chronic disabling conditions, such as immune-mediated inflammatory diseases (IMID), adversely af

of physical suffering and pain, impaired function, and diminished quality of life. These persistent relapsing dise significant influence on individual employment status and work-related productivity. In addition to the signific and their families, IMID represent a sizable burden to society due to high healthcare and non-healthcare relatec related, or indirect, costs primarily associated with decreased work productivity, disability payments, and early typically greater contributors than direct healthcare costs to the total costs associated with IMID. This article di socioeconomic impact of several IMID, including rheumatoid arthritis, inflammatory bowel disease, ankylosin psoriasis. (J Rheumatol 2011;38 Suppl 88:55-61; doi:10.3899/jrheum.110901)

ISSN: 0315-162X

Record 4 of 34 **EXCLUDED/METHODOLOGICAL PAPER**

Title: Modelling Correlated Clinical Outcomes in Health Technology Appraisal

Author(s): Epstein, D (Epstein, David); Sutton, A (Sutton, Alex)

Source: VALUE IN HEALTH Volume: 14 Issue: 6 Pages: 793-799 DOI: 10.1016/j.jval.2011.04.007 Published: SEP-OCT 2011

Abstract: Objectives: Many clinical treatments have multiple effects that can only be effectively captured on multiple outcome scales. It might be important to understand how these outcomes are correlated to evaluate the effectiveness and cost-effectiveness of treatments in decision models. Methods: The probabilities are estimated that both, one, or neither outcome occurs, given estimates of the marginal probability for each outcome and information about the correlation between them. Methods are shown for different measures of association. Lower and upper bounds for the correlation coefficient are calculated for given values of the marginal probabilities. The approach is illustrated using a simplified decision model based on a recent evaluation of adalimumab, a biologic drug for psoriatic arthritis. Results: Assuming the outcomes are positively correlated, the probability of both a skin and arthritis response after adalimumab was estimated to be 0.387 (95% confidence interval 0.210-0.570). The incremental cost-effectiveness ratio (ICER) of adalimumab versus no biologic is 18,500 pound per quality-adjusted life-year (QALY). The ICER increases to 19,500 pound per QALY if the responses are independent. Conclusion: Estimates of ICERs can be sensitive to assumptions about how multiple outcomes are correlated. These assumptions should be explored in univariate and probabilistic sensitivity analyses.

ISSN: 1098-3015

Record 5 of 34 **EXCLUDED / NOT CU ANALYSIS**

Title: Etanercept in spondyloarthropathies. Part II: safety and pharmacoeconomic issues

Author(s): D'Angelo, S (D'Angelo, S.); Palazzi, C (Palazzi, C.); Cantini, F (Cantini, F.); Lubrano, E (Lubrano, E.); Marchesoni, A (Marchesoni, A.); Mathieu, A (Mathieu, A.); Salvarani, C (Salvarani, C.); Scarpa, R (Scarpa, R.); Spadaro, A (Spadaro, A.); Olivieri, I (Olivieri, I.)

Source: CLINICAL AND EXPERIMENTAL RHEUMATOLOGY Volume: 29 Issue: 5 Pages: 865-870 Published: SEP-OCT 2011

Abstract: Etanercept (ETN) and other anti-TNF-alpha agents have revolutionised the management of spondyloarthropathies (SpA). With the increasingly widespread and prolonged use of these drugs an assessment of their long-term safety is extremely important. An additional concern regarding biological agents is their higher costs compared with conventional drugs. We examined safety data regarding ETN from clinical reports, clinical trials, review articles, databases and registries. In addition, evidence was reviewed about the cost effectiveness of ETN in the treatment of patients with SpA.
Our review suggests that ETN is well tolerated as long-term, continuous treatment of SpA with a favourable risk-benefit ratio maintained from 4 to 5 years. Diversity in structure and mode of action could explain some differences in the safety profile of ETN with respect to the other anti-TNF agents. In particular, ETN is less immunogenic and is less likely to induce tuberculosis re-activation than the other TNE-alpha antagonists. Although ETN is considerably more expensive than conventional therapy, it reduces direct and indirect costs associated to SpA by improving disease activity and quality of life. Recent pharmacoeconomic studies have demonstrated its cost-effectiveness in the treatment of SpA.

ISSN: 0392-856X

Record 6 of 34 INCLUDED

Title: Modelling the cost-effectiveness of biologic treatments for psoriatic arthritis

Author(s): Bojke, L (Bojke, Laura); Epstein, D (Epstein, David); Craig, D (Craig, Dawn); Rodgers, M

(Rodgers, Mark); Woolacott, N (Woolacott, Nerys); Yang, HQ (Yang, Huiqin); Sculpher, M (Sculpher, Mark)

Source: RHEUMATOLOGY Volume: 50 Pages: iv39-iv47 DOI: 10.1093/rheumatology/ker245 Supplement: 4 Published: SEP 2011

Abstract: Methods. A previous model was revised to evaluate the impact of biologics on both skin and joint disease and to include new evidence from the clinical review and evidence synthesis. Initial response to biologics was determined using the PsA response criteria. The impact of biologics on the arthritis component of the disease is then modelled via a change in the HAQ and the impact of the psoriasis component measured using the Psoriasis Area and Severity Index.
Results. For PsA patients with mild to moderate skin disease, the incremental cost-effectiveness ratio (ICER) for etanercept vs palliative care is around 18 pound 000, and the ICER for infliximab vs etanercept is around 44 pound 000 per quality-adjusted life year (QALY). Adalimumab is extendedly dominated. The probability that etanercept is cost effective is 0.436 at a threshold of 20 pound 000 per QALY. Etanercept is also likely to be cost effective for patients with moderate to severe psoriasis or negligible skin involvement.
Conclusions. Further investigation is required to reduce uncertainties around a number of model parameters, in particular the length of time over which biologics are assumed to be effective and the progression of HAQ on and off treatment.

ISSN: 1462-0324

Record 7 of 34 **EXCLUDED / NOT PsA**

Title: A pharmacoeconomic analysis of severe psoriasis therapy: a review of treatment choices and cost efficiency

Author(s): Staidle, JP (Staidle, Jonathan P.); Dabade, TS (Dabade, Tushar S.); Feldman, SR (Feldman, Steven R.)

Source: EXPERT OPINION ON PHARMACOTHERAPY Volume: 12 Issue: 13 Pages: 2041-2054 DOI: 10.1517/14656566.2011.590475 Published: SEP 2011

Abstract: Introduction: Psoriasis is a chronic, inflammatory disease afflicting 2% of the US population; it results in significant morbidity. The annual healthcare costs related to psoriasis are an estimated $ 11.3 billion and, with an expanding biologic market, an updated costs analysis is needed.
Areas covered: Current treatments, including systemic agents (acitretin, cyclosporine, methotrexate), phototherapies and all available biologics (adalimumab, etanercept, infliximab, alefacept, ustekinumab) appropriate for severe psoriasis are described mechanistically and with regard to their efficacy, quality-of-life improvements and side effects. A cost-efficacy model considering US health-system-based annual costs, clinical and quality-of-life improvements was created. Reported Psoriasis Area and Severity Index improvement of 75% from baseline (PASI-75) scores, Dermatology Life Quality Index (DLQI) improvements and estimated costs of medications are described. Annual costs ranged from $1330 for methotrexate to $48,731 for high-dose etanercept. The lowest cost per achieving DLQI minimally important difference was from phototherapy; the highest was from alefacept. The lowest costs per patient achieving PASI-75 was from methotrexate and the highest was from alefacept.
Expert opinion: Phototherapies and methotrexate offer high efficacy for their costs. Therapeutic approaches must be individualized for each patient given all considerations described.

ISSN: 1465-6566

Record 8 of 34 **EXCLUDED / NOT PsA**

Title: A one-hour infusion of infliximab during maintenance therapy is safe and well tolerated: a prospective cohort study

Author(s): Lee, TW (Lee, T. W.); Singh, R (Singh, R.); Fedorak, RN (Fedorak, R. N.)

Source: ALIMENTARY PHARMACOLOGY & THERAPEUTICS Volume: 34 Issue: 2 Pages: 181-187 DOI: 10.1111/j.1365-2036.2011.04699.x Published: JUL 15 2011

Abstract: Background
Infliximab is a chimeric monoclonal antibody to tumour necrosis factor alpha (TNF alpha) with efficacy in inducing and maintaining remission of inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis and psoriasis. Infliximab is generally administered over 2 h with a further 1-h postinfusion observation. This time interval has substantial impact on healthcare resources and is costly in terms of patient's time away from work.

Aim
To examine the safety and tolerability of a 1-h, relative to a 2-h maintenance of infusion of infliximab, and to determine the effect of corticosteroid premedication and concurrent immunosuppressor use on infusion reaction rates.
Method
A prospective cohort study with variable follow-up duration of 2165 consecutive infliximab infusions in 415 patients during 2009 was conducted. Diagnosis, infusion episode number, infusion rate, premedication, concurrent immunosuppressor therapy, the nature and the outcome of infusion reactions were examined.
Results
The majority of infusions (74%) were for management of inflammatory bowel disease. Infusion reactions clustered within the first eight infusions with subsequent sporadic reactions. The infusion reaction incidence rate per 1000 person days in 274 1-h infusions from 54 patients and 1356 2-h infusions from 256 patients were 0.08 and 0.28 respectively (P = 0.07). Poisson regression model confirmed that the concurrent use of immunosuppressor therapy was associated with a lower infusion reaction rate, whereas corticosteroid premedication was not.

ISSN: 0269-2813

Record 9 of 34 **EXCLUDED / NOT PsA**

Title: Combined treatment with etanercept 50 mg once weekly and narrow-band ultraviolet B phototherapy in chronic plaque psoriasis

Author(s): De Simone, C (De Simone, Clara); D'Agostino, M (D'Agostino, Magda); Capizzi, R (Capizzi, Rodolfo); Capponi, A (Capponi, Angela); Venier, A (Venier, Antonio); Caldarola, G (Caldarola, Giacomo)

Source: EUROPEAN JOURNAL OF DERMATOLOGY Volume: 21 Issue: 4 Pages: 568-572 DOI: 10.1684/ejd.2011.1330 Published: JUL-AUG 2011

Abstract: Background: The combination of etanercept, a tumour necrosis factor alpha inhibitor, with narrow-band ultraviolet B (NB-UVB) phototherapy has recently been reported to be effective in moderate-to-severe plaque psoriasis, yielding better results than either monotherapy. Objective: To assess the efficacy and safety of this combined treatment using the lower approved etanercept dosage. Methods: In this single-arm open-label study patients received etanercept 50 mg once weekly combined with NB-UVB phototherapy three times weekly for 8 weeks, followed by etanercept alone until week 12. We evaluated the proportion of patients achieving 75%, 90% and 100% improvement of their initial PASI score (PASI75, PASI90, and PASI100, respectively). Results: Patients were 19 men and 14 women, mean age 48.3 years +/- 12.1 standard deviation (SD) and mean baseline Psoriasis Area and Severity Index (PASI) score 22.5 +/- 7.5. On treatment weeks 4, 8, and 12, 24.2%, 66.7%, and 81.8% of patients achieved PASI75; 8.0%, 15.1%, and 57.6% reached PASI90, and 0%, 6.0%, and 24.2% attained PASI100, respectively. There were no severe side effects. Conclusion: Low-dosage etanercept combined with NB-UVB phototherapy is an effective, safe and economical approach to treat moderate-to-severe plaque psoriasis. Further studies are clearly required to assess its long-term efficacy and safety.

ISSN: 1167-1122

Record 10 of 34 **EXCLUDED / NOT CU ANALYSIS**

Title: Efficacy and safety of adalimumab treatment in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis

Author(s): Poddubnyy, D (Poddubnyy, Denis); Rudwaleit, M (Rudwaleit, Martin)

Source: EXPERT OPINION ON DRUG SAFETY Volume: 10 Issue: 4 Pages: 655-673 DOI: 10.1517/14740338.2011.581661 Published: JUL 2011

Abstract: Introduction: In the last couple of years, the number of patients with chronic inflammatory rheumatic diseases being treated with TNF alpha antagonist has increased dramatically. Adalimumab, a fully human monoclonal antibody against TNF alpha, is one of the most frequently administered TNF alpha antagonists. Yet, unresolved issues are the long-term safety of TNF alpha antagonists and high treatment costs.
Areas covered: The authors summarize the available data on short- and long-term efficacy and safety of adalimumab in the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. The reader will find a comprehensive overview on the safety and efficacy of adalimumab for these conditions. Clinically relevant questions of adalimumab therapy are discussed. A special focus of this review is on the safety of adalimumab therapy.
Expert opinion: Adalimumab is effective and reasonably safe in the short- and long-term treatment of patients

with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis who do not respond to the standard therapy. It inhibits radiographic progression in rheumatoid and psoriatic arthritis. Treatment with a TNF alpha inhibitor such as adalimumab is associated with high treatment costs.

ISSN: 1474-0338

Record 11 of 34 **EXCLUDED / NOT CU ANALYSIS**

Title: Profile of use of anti tumor necrosis factor in Colombian patients

Author(s): Machado, J (Machado, Jorge); Moncada, JC (Carlos Moncada, Juan); Pineda, R (Pineda, Ricardo)

Source: BIOMEDICA Volume: 31 Issue: 2 Pages: 250-257 Published: JUN 2011

Abstract: Introduction. Tumor necrosis factor-alpha antagonists (anti-TNF alpha) have shown an increasing consumption and generate a significant economic burden on health systems.
Objectives. The prescribing patterns of tumor necrosis factor-alpha antagonists were determined in a patient population associated with the Sistema General de Seguridad Social en Salud in Colombia.
Materials and methods. A descriptive observational study was conducted in 316 patients with respect to use of tumor necrosis factor-alpha antagonists during a treatment period from January 2008 to June 2009. The database examined contained indications of use, inclusion criteria to medication, duration of illness, co-morbidities and adverse reactions. The data were retrieved from the clinical histories. Student's t test was used for the comparison of quantitative variables, and the chi-square test was used to establish associations between categorical variables and multivariate analysis were used.
Results. Mean age was 44.6 +/- 13.9 years; 63.9% of participants were female. Of the 316 patients, 17.1% received monotherapy. The order of prescription drugs was as follows: adalimumab (37.3%), infliximab (37.3%) and etanercept (25.4%), all were prescribed in appropriately defined daily doses. Co-medication drugs most frequently prescribed were: disease-modifying anti-rheumatic (82.9%), NSAIDs (29.1%), omeprazole (22.5%), antihypertensives (21.2%), folic acid (19.9%) calcium plus vitamin D (9.8%), calcitriol (6.0%). 10.4% of patients had a record of some adverse drug reaction. The average cost of therapy per patient per year was US$23,464.
Conclusions. Anti-TNF alpha are being used at recommended doses, particularly in rheumatoid arthritis and in combination with other anti-rheumatic drugs. The direct cost of therapy was high for the country's health system.

ISSN: 0120-4157

Record 12 of 34 EXLUDED / THIS REVIEW ARTICLE WAS THE BASIS OF OUR SEARCH

Title: Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation

Author(s): Rodgers, M (Rodgers, M.); Epstein, D (Epstein, D.); Bojke, L (Bojke, L.); Yang, H (Yang, H.); Craig, D (Craig, D.); Fonseca, T (Fonseca, T.); Myers, L (Myers, L.); Bruce, I (Bruce, I.); Chalmers, R (Chalmers, R.); Bujkiewicz, S (Bujkiewicz, S.); Lai, M (Lai, M.); Cooper, N (Cooper, N.); Abrams, K (Abrams, K.); Spiegelhalter, D (Spiegelhalter, D.); Sutton, A (Sutton, A.); Sculpher, M (Sculpher, M.); Woolacott, N (Woolacott, N.)

Source: HEALTH TECHNOLOGY ASSESSMENT Volume: 15 Issue: 10 Pages: 1-+ DOI: 10.3310/hta15100 Published: FEB 2011

Abstract: Background: Etanercept, infliximab and adalimumab are licensed in the UK for the treatment of active and progressive psoriatic arthritis (PsA) in adults who have an inadequate response to standard treatment.
Objective: To determine the clinical effectiveness, safety and cost-effectiveness of these biologic agents in the treatment of active and progressive PsA.
Data sources: Systematic reviews were performed, with data sought from 10 electronic databases (MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Science Citation Index, Conference Proceedings Citation Index Science, ClinicalTrials.gov, metaRegister of Current Controlled Trials, NHS Economic Evaluation Database, Health Economic Evaluations Database and EconLit) up to June 2009.
Review methods: Full paper manuscripts of titles/abstracts considered relevant were obtained and assessed for inclusion by two reviewers according to criteria on study design, interventions, participants and outcomes. Data on study and participant characteristics, efficacy outcomes, adverse effects, costs to the health service and cost-effectiveness were extracted, along with baseline data where reported. The primary efficacy outcomes were measures of anti-inflammatory response, skin lesion response and functional status, and the safety outcome was the incidence of serious adverse events. The primary measure of cost-effectiveness was incremental cost per additional quality-adjusted life-year (QALY). Standard meta-analytic techniques were

applied to efficacy data. Published cost-effectiveness studies and the economic analyses submitted to the. National Institute for Health and Clinical Excellence (NICE) by the biologic manufacturers were reviewed. An economic model was developed by updating the model produced by the York Assessment Group for the previous NICE appraisal of biologics in PsA.
Results: Pooled estimates of effect demonstrated a significant improvement in patients with PsA for all joint disease and functional status outcomes at 12-14 weeks' follow-up. The biologic treatment significantly reduced joint symptoms for etanercept [relative risk (RR) 2.60, 95% confidence interval (CI) 1.96 to 3.45], infliximab (RR 3.44, 95% CI 2.53 to 4.69) and adalimumab (RR 2.24, 95% CI 1.74 to 2.88), with 24-week data demonstrating maintained treatment effects. Trial data demonstrated a significant effect of all three biologics on skin disease at 12 or 24 weeks. Evidence synthesis found that infliximab appeared to be most effective across all outcomes of joint and skin disease. The response in joint disease was greater with etanercept than with adalimumab, whereas the response in skin disease was greater with adalimumab than with etanercept, although these differences are not statistically significant. Under base-case assumptions, etanercept was the most likely cost-effective strategy for patients with PsA and mild-to-moderate psoriasis if the threshold for cost-effectiveness was 20,000 pound or 30,000 pound per QALY. All biologics had a similar probability of being cost-effective for patients with PsA and moderate-to-severe psoriasis at a threshold of 20,000 pound per QALY.
Limitations: Limited available efficacy data and difficulty in assessing PsA activity and its response to biologic therapy.
Conclusions: The data indicated that etanercept, infliximab and adalimumab were efficacious in the treatment of PsA compared with placebo, with beneficial effects on joint symptoms, functional status and skin. Short-term data suggested that these biologic agents can delay joint disease progression and evidence to support their use in the treatment of PsA is convincing. Future research would benefit from long-term observational studies with large sample sizes of patients with PsA to demonstrate that beneficial effects are maintained, along with further monitoring of the safety profiles of the biologic agents.

ISSN: 1366-5278

Record 13 of 34 INCLUDED

Title: Cost-effectiveness of infliximab for the treatment of active and progressive psoriatic arthritis

Author(s): Cummins, E (Cummins, Ewen); Asseburg, C (Asseburg, Christian); Punekar, YS (Punekar, Yogesh Suresh); Shore, E (Shore, Emily); Morris, J (Morris, James); Briggs, A (Briggs, Andrew); Fenwick, E (Fenwick, Elisabeth)

Source: VALUE IN HEALTH Volume: 14 Issue: 1 Pages: 15-23 DOI: 10.1016/j.jval.2010.10.016 Published: JAN-FEB 2011

Abstract: Background: Despite its proven efficacy, infliximab is often considered to be an expensive treatment for patients with psoriatic arthritis.
Objectives: To estimate the cost-effectiveness of infliximab among patients with active and progressive psoriatic arthritis.
Methods: A decision analytic model was constructed to simulate disease progression in hypothetical cohorts of patients with psoriatic arthritis receiving infliximab maintenance treatment. The primary response measure was change in Health Assessment Questionnaire score from a baseline estimated from mixed treatment models drawn from published clinical trials. Palliative care, comprising nonbiologic disease-modifying antirheumatic drugs, was used as a comparator. The primary outcome was quality-adjusted life years. The dose of infliximab was estimated for a range of 60 to 80 kg per patient body weight. The costs and outcomes were discounted at 3.5% for a period of 40 years. Uncertainty around the results was explored with probabilistic sensitivity analysis.
Results: The mixed treatment comparison showed a significant reduction in Health Assessment Questionnaire score across all patients. The tumor necrosis factor alpha inhibitors were significantly superior to palliative care but comparable with one another. The incremental cost-effectiveness ratios for etanercept, adalimumab, and infliximab relative to palliative care were 17,327; pound 19,246; pound and 16,942 pound to 23,022 pound, respectively, across all patients with psoriatic arthritis and 16,613; pound 18,170; pound and 15,788 pound to 21,736 pound, respectively, in the subgroup with significant psoriasis.
Conclusion: Infliximab represents a cost-effective treatment option well within the National Institute for Health and Clinical Excellence threshold relative to palliative care. In light of equivalent outcomes with other tumor necrosis factor alpha inhibitors, its position in the treatment pathway is likely to be governed by treatment costs. Copyright (C) 2011, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

ISSN: 1098-3015

Record 14 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Intestinal microsporidiosis: a hidden risk in rheumatic disease patients undergoing anti-tumor necrosis factor therapy combined with disease-modifying anti-rheumatic drugs?

Author(s): Aikawa, NE (Aikawa, Nadia Emi); Twardowsky, AD (Twardowsky, Aline de Oliveira); de Carvalho, JF (de Carvalho, Jozelio Freire); Silva, CA (Silva, Clovis A.); Silva, ILAFE (Avelino Franca e Silva, Ivan Leonardo); Ribeiro, ACD (de Medeiros Ribeiro, Ana Cristina); Saad, CGS (Schain Saad, Carla Goncalves); Moraes, JCB (Bertacini Moraes, Julio Cesar); de Toledo, RA (de Toledo, Roberto Acayaba); Bonfa, E (Bonfa, Eloisa)

Source: CLINICS Volume: 66 Issue: 7 Pages: 1171-1175 DOI: 10.1590/S1807-59322011000700008 Published: 2011

Abstract: OBJECTIVE: Immunosuppressed patients are at risk of microsporidiosis, and this parasitosis has an increased rate of dissemination in this population. Our objective was to evaluate the presence of microsporidiosis and other intestinal parasites in rheumatic disease patients undergoing anti-tumor necrosis factor/disease-modifying anti-rheumatic drug treatment.
METHODS: Ninety-eight patients (47 with rheumatoid arthritis, 31 with ankylosing spondylitis and 11 with psoriatic arthritis) and 92 healthy control patients were enrolled in the study. Three stool samples and cultures were collected from each subject.
RESULTS: The frequency of microsporidia was significantly higher in rheumatic disease patients than in control subjects (36 vs. 4%, respectively; $p<0.0001$), as well as in those with rheumatic diseases (32 vs. 4%, respectively; $p<0.0001$), ankylosing spondylitis (45 vs. 4%, respectively; $p<0.0001$) and psoriatic arthritis (40 vs. 4%, respectively; $p<0.0001$), despite a similar social-economic class distribution in both the patient and control groups ($p = 0.1153$). Of note, concomitant fecal leukocytes were observed in the majority of the microsporidia-positive patients (79.5%). Approximately 80% of the patients had gastrointestinal symptoms, such as diarrhea (26%), abdominal pain (31%) and weight loss (5%), although the frequencies of these symptoms were comparable in patients with and without this infection ($p>0.05$). Rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis disease activity parameters were comparable in both groups ($p>0.05$). The duration of anti-tumor necrosis factor/disease-modifying anti-rheumatic drugs and glucocorticoid use were also similar in both groups.
CONCLUSION: We have documented that microsporidiosis with intestinal mucosa disruption is frequent in patients undergoing concomitant anti-tumor necrosis factor/disease-modifying anti-rheumatic drug therapy. Impaired host defenses due to the combination of the underlying disease and the immunosuppressive therapy is the most likely explanation for this finding, and this increased susceptibility reinforces the need for the investigation of microsporidia and implementation of treatment strategies in this population.

ISSN: 1807-5932

Record 15 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: A 3 mg/kg starting dose of infliximab in active spondyloarthritis resistant to conventional treatments is efficient, safe and lowers costs

Author(s): Tenga, G (Tenga, Ginette); Goeb, V (Goeb, Vincent); Lequerre, T (Lequerre, Thierry); Bacquet-Deschryver, H (Bacquet-Deschryver, Helene); Daragon, A (Daragon, Alain); Pouplin, S (Pouplin, Sophie); Lanfant-Weybel, K (Lanfant-Weybel, Karine); Le Loet, X (Le Loet, Xavier); Dieu, B (Dieu, Bernard); Vittecoq, O (Vittecoq, Olivier)

Source: JOINT BONE SPINE Volume: 78 Issue: 1 Pages: 50-55 DOI: 10.1016/j.jbspin.2010.04.017 Published: JAN 2011

Abstract: Objective: We assessed the efficacy, tolerance and cost of a 3 mg/kg starting dose of infliximab for anky-losing spondylitis (AS) and psoriatic arthritis (PsA).
Methods: We retrospectively followed-up 45 biologic-naive consecutive patients (11 with axial AS, 24 with axial and peripheral [mixed] AS and 10 with PsA) who were treated between 2002 and 2005 with a 3 mg/kg dose of infliximab after failure of conventional therapies. The following variables were recorded: visual analog scale (VAS) scores of patient's global (G) and pain (P) assessment, duration of early morning stiffness (EMS), disease activity (BASDAI) and functional disability (BASFI). Treatment responses were assessed at 6 and 12 months using the AS assessment score (ASAS)-20% and -40% criteria and BASDAI-50.
Results: Baseline characteristics of the 29 men and 16 women were (median [range]): G-VAS, 70 [13-100]; P-VAS, 70 [13-100]; EMS, 60 [0-180] minutes; BASDAI, 64.4 [23.9-100]; BASFI, 57.2 [3.5-98.5]. All manifestations regressed significantly ($p < 0.0001$) for 39 (86.7%) and 24 (53.5%) patients at 6 and 12

months, respectively; 26 (57.8%) had achieved ASAS-20 responses at 6 months that persisted at 1 year for 20 (44.4%); 19 (42.2%) and 12 (26.7%) satisfied BASDAI 50 criteria at 6 and 12 months, respectively. Interestingly, almost 30% still received low-dose infliximab after 4 years of follow-up.
Conclusion: An initial dose of 3 mg/kg of infliximab significantly attenuated AS and PsA manifestations in >40% of the patients, making use of this dose highly advantageous in terms of safety and 33% lower cost.

ISSN: 1297-319X

Record 16 of 34 **EXLUDED / NOT ORIGINAL ARTICLE (CONFERENCE ABSTRACT)**

Title: COST-EFFECTIVENESS OF GOLIMUMAB IN PSORIATIC ARTHRITIS FROM THE UK PAYER PERSPECTIVE

Author(s): Cummins, E (Cummins, E.); Asseburg, C (Asseburg, C.); Prasad, M (Prasad, M.); Buchanan, J (Buchanan, J.); Punekar, Y (Punekar, Y.)

Source: VALUE IN HEALTH Volume: 13 Issue: 7 Pages: A308-A308 Published: NOV 2010

ISSN: 1098-3015

Record 17 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Utility-Based Outcomes Made Easy: The Number Needed Per Quality-Adjusted Life Year Gained. An Observational Cohort Study of Tumor Necrosis Factor Blockade in Inflammatory Arthritis From Southern Sweden

Author(s): Gulfe, A (Gulfe, Anders); Kristensen, LE (Kristensen, Lars Erik); Saxne, T (Saxne, Tore); Jacobsson, LTH (Jacobsson, Lennart T. H.); Petersson, IF (Petersson, Ingemar F.); Geborek, P (Geborek, Pierre)

Source: ARTHRITIS CARE & RESEARCH Volume: 62 Issue: 10 Pages: 1399-1406 DOI: 10.1002/acr.20235 Published: OCT 2010

Abstract: Objective. To introduce a novel, simple, utility-based outcome measure, the number needed per quality-adjusted life year (QALY) gained (NNQ), and to apply it in clinical practice in anti-tumor necrosis factor (anti-TNF)-treated patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and spondylarthritis (SpA).
Methods. The NNQ is the number of patients one has to treat in order to gain 1 QALY. It is calculated as the inverted value of the utility gain (area under the curve) over 1 year in a cohort subjected to an intervention. EuroQol Index utility data from the South Swedish Arthritis Treatment register were used.
Results. Patients with RA (n = 1,001), PsA (n = 241), and SpA (n = 255) were eligible for the study. First, second, and third treatment courses were studied. For RA, NNQ was 4.5, 6.4, and 5.2 for first, second, and third courses, respectively. For PsA and SpA, NNQ was 4.2-4.5, irrespective of treatment order. Treatment groups with <50 patients were not analyzed. During the study period 2002-2007, there were no secular trends of utility gains.
Conclusion. The NNQ is an easily derived and understandable utility-based outcome measure that may be useful for stakeholders and decision makers as well as for clinicians. It was readily applied in this study of TNF blockade across 3 arthritis diagnoses. NNQ varied little over diagnoses and treatment course order, with a possible exception in second treatment course in RA.

ISSN: 2151-464X

Record 18 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Estimation of health care costs as a function of disease severity in people with psoriatic arthritis in the UK

Author(s): Poole, CD (Poole, Chris D.); Lebmeier, M (Lebmeier, Max); Ara, R (Ara, Roberta); Rafia, R (Rafia, Rachid); Currie, CJ (Currie, Craig J.)

Source: RHEUMATOLOGY Volume: 49 Issue: 10 Pages: 1949-1956 DOI: 10.1093/rheumatology/keq182 Published: OCT 2010

Abstract: Objectives. The primary aim of this study was to estimate annual health care costs for biologic-naive patients with PsA in the UK. The relationship between disease severity, defined by physical limitations, and costs was also explored.
Methods. This study utilized data from the British Society of Rheumatology Biologics Register (BSRBR) to develop a multivariate model estimating disease severity from parameters available in routine primary care

data. The HAQ Disability Index was used to determine disease severity. This algorithm was then applied to routine data from The Health Improvement Network (THIN). Annual costs were estimated for drugs, contacts with a general practitioner and other health care professionals, tests, hospital outpatient attendances and inpatient admissions from a National Health Service perspective using official tariffs. The relationship between disease severity and health care costs was estimated using a generalized linear model.
Results. Three hundred and fifty-six cases with PsA were identified in the BSRBR and 4492 in THIN. Total mean annual health care costs ranged from 11 pound to 20 pound 782 with a mean of 1446 pound (s.d. 1756) pound. When costs were sub-grouped by the predicted HAQ score, the mean annual observed costs ranged from 548 pound per person for the least severely affected (HAQ 1.2) to 4832 pound for the most severely affected (HAQ > 2.6). Prescription costs and secondary care episodes accounted for more than a third of total care costs each (38 and 34%, respectively). When the relationship between disease severity and costs was examined, estimated HAQ was found to be a significant predictor of total health care costs.
Conclusions. Treatment of people with PsA resulted in considerable financial costs and these costs varied markedly by disease severity.

ISSN: 1462-0324

Record 19 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Golimumab: Review of the Efficacy and Tolerability of a Recently Approved Tumor Necrosis Factor-alpha Inhibitor

Author(s): Boyce, EG (Boyce, Eric G.); Halilovic, J (Halilovic, Jenana); Stan-Ugbene, O (Stan-Ugbene, Oby)

Source: CLINICAL THERAPEUTICS Volume: 32 Issue: 10 Pages: 1681-1703 DOI: 10.1016/j.clinthera.2010.09.003 Published: SEP 2010

Abstract: Background: Golimumab (GLM) is a tumor necrosis factor-alpha (TNF-alpha) inhibitor that was approved in the United States in 2009 for use with methotrexate (MTX) in adults with moderate to severe active rheumatoid arthritis (RA), and with or without MTX or other non-biologic disease-modifying antirheumatic drugs in adults with active psoriatic arthritis (PsA) or active ankylosing spondylitis (AS). GLM is administered as a 50-mg subcutaneous injection once a month.
Objectives: The goals of this article were to review the current literature on GLM and to provide recommendations for the use of GLM based on the published information.
Methods: The PubMed, Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, International Pharmaceutical Abstracts, and other databases, as well as the Web sites for the American College of Rheumatology (ACR) and the European Union League Against Rheumatism, were searched for relevant articles published in English between the inception of the databases through April 2010. Search terms included golimumab and CNTO 148. Pharmacologic, pharmacokinetic, clinical, outcomes, and economic studies as well as meta-analyses, case reports, and select abstracts were eligible for inclusion. Review articles on GLM were not used except to identify other primary papers.
Results: Seven clinical studies were identified and used to evaluate the efficacy and tolerability of GLM: 5 in patients with RA (4 subcutaneous administration and 1 intravenous administration), 1 in patients with PsA (subcutaneous), and 1 in patients with AS (subcutaneous). In MTX-naive patients with RA, the number of patients satisfying the ACR20 response criteria (>20% improvement in ACR response rate) at 24 weeks was significantly higher for the GLM + MTX groups than for the MTX-only groups (62% vs 49%, respectively; P < 0.05). In patients with active RA despite MTX therapy, ACR20 responses at 14 to 16 weeks were significantly higher for the combined GLM + MTX groups than for the MTX groups (50%-79% vs 33%-37%, respectively; P < 0.001). GLM was more effective than placebo, both with and without MTX, in patients with RA and a history of treatment with 1 or 2 TNF-alpha inhibitors (ACR20 at 14 weeks, 35%-37% vs 18%, respectively; P < 0.001). Studies of other TNF-alpha inhibitors reported ACR20 responses in 53% to 59% of patients with active RA at 24 weeks. GLM was also more effective than placebo at 24 weeks in patients with PsA (ACR20, 52%-61% vs 12%, respectively; P < 0.001) (ASAS40 [40% improvement based on Assessment in Ankylosing Spondylitis International Working Group criteria], 44%-54% vs 15%, respectively; P < 0.001). Studies of other TNF-alpha inhibitors reported ACR20 responses at 24 weeks in 55% to 57% of patients with PsA and ASAS40 responses in 46% to 47% of patients with AS. The incidence of any adverse effect appeared to be comparable in the GLM (61.2%-93.9%) and placebo groups (59.3%-85.3%), but withdrawals because of adverse effects were higher in the GLM groups (0%-12.1%) than in the placebo groups (0%-5.9%). The incidence of serious infections was comparable for GLM (0%-4.4%) and placebo (0.8%-3.5%). The most frequently reported adverse effects in the GLM groups were injection-site reactions (2.7%-37.1%), nausea (2.7%-22.9%), headache (3.8%-21.2%), nasopharyngitis (1.9%-15.0%), and upper respiratory tract infections (5.7%-13.8%).
Conclusions: Based on the results of the studies included in this review, GLM appeared to be more effective

than placebo in patients with RA, PsA, or AS. Clinical studies have not directly compared GLM with other TNF-alpha inhibitors. However, according to the available efficacy and tolerability data, GLM should be considered as the first or second TNF-alpha inhibitor for the treatment of PsA or AS and as the second or possibly first TNF-alpha inhibitor in combination with MTX for the treatment of RA. (Clin Ther. 2010;32:1681-1703) (C) 2010 Excerpta Medica Inc.

ISSN: 0149-2918

Record 20 of 34 **EXLUDED / NOT PsA**

Title: Formulary Review of 2 New Biologic Agents: Tocilizumab for Rheumatoid Arthritis and Ustekinumab for Plaque Psoriasis

Author(s): Schafer, JA (Schafer, Jeremy A.); Kjesbo, NK (Kjesbo, Nicole K.); Gleason, PP (Gleason, Patrick P.)

Source: JOURNAL OF MANAGED CARE PHARMACY Volume: 16 Issue: 6 Pages: 402-416 Published: JUL-AUG 2010

Abstract: BACKGROUND. Two autoimmune biologics were recently approved by the FDA: ustekinumab in September 2009 for the treatment of moderate to severe plaque psoriasis in adults who are candidates for phototherapy or systemic therapy and tocilizumab in January 2010 for adult patients with moderate to severe rheumatoid arthritis (RA) who have not responded adequately to 1 or more tumor necrosis factor (TNF) antagonist therapies. Both agents use new mechanisms of action and add to the growing group of autoimmune biologics.
OBJECTIVE: To critically review the phase 3 trials for ustekinumab and tocilizumab and provide managed care considerations in the context of the 9 other biologic agents on the market in the United States that are used to treat moderate to severe RA or psoriasis.
METHODS: A MEDLINE review was performed for articles published and available through January 2010 using keywords "ustekinumab" and "tocilizumab" with an emphasis on phase 3 trials. The literature search was limited to articles in English, clinical trials, randomized controlled trials, and research conducted in humans. Search results for ustekinumab included 8 articles of which 4 were excluded for not being psoriasis or psoriatic arthritis trials. Search results for tocilizumab included 16 articles of which 8 were excluded for not being RA trials or using biomarkers as primary endpoints. Additional information was obtained from the FDA website.
RESULTS: Three phase 3 trials are available for ustekinumab. Ustekinumab demonstrated superior efficacy to placebo in 2 trials for the treatment of psoriasis. In a 12-week trial, ustekinumab 45 milligrams (mg) and 90 mg demonstrated significantly higher rates of 75% improvement in the psoriasis area and severity index (PASI 75) (67.5% and 73.8%, respectively) compared with etanercept (56.8%) in the first phase 3 comparative psoriasis trial between autoimmune biologics ($P<0.05$ for both comparisons). In a phase 3 trial of RA patients who had failed prior TNF antagonist therapy, a 20% improvement in signs or symptoms according to the American College of Rheumatology criteria (ACR 20) at week 24 was achieved by significantly more study participants in the tocilizumab 8 mg per kilogram (kg) (50.0%) and 4 mg per kg (30.4%) groups than the placebo group (10.1%, $P<0.001$ for both tocilizumab groups compared with placebo) Safety data for ustekinumab are limited to use for less than 2 years, and the prescribing information contains warnings regarding infection and malignancy. Tocilizumab is associated with neutropenia, thrombocytopenia, and elevations in lipids and liver function tests. Tocilizumab has unique adverse events when compared with other autoimmune biologics and requires laboratory testing and careful monitoring.
CONCLUSIONS: Ustekinumab and tocilizumab are new additions to the treatment of autoinflammatory disease. The majority of safety data for both agents are from trials lasting 3 to 6 months Published long-term safety data for tocilizumab are limited to less than 143 patients treated longer than 5 years, and safety data for ustekinumab are scant beyond 2 years of use; therefore, clinicians should exercise caution prior to widespread adoption. The comparative efficacy and safety trial of etanercept and ustekinumab brings important clinical information to decision makers. Tocilizumab is indicated after failure or intolerance to a TNF antagonist and has unique safety concerns. Managed care plans will consider the experience and long-term data of these agents along with efficacy data and cost when establishing management programs such as prior authorization or step therapy. J Manag Care Pharm. 2010;16(6):402-16 Copyright (C) 2010, Academy of Managed Care Pharmacy. All rights reserved.

ISSN: 1083-4087

Record 21 of 34 **EXCLUDED / METHODOLOGICAL PAPER**

Title: Eliciting Distributions to Populate Decision Analytic Models

Author(s): Bojke, L (Bojke, Laura); Claxton, K (Claxton, Karl); Bravo-Vergel, Y (Bravo-Vergel, Yolanda); Sculpher, M (Sculpher, Mark); Palmer, S (Palmer, Stephen); Abrams, K (Abrams, Keith)

Source: VALUE IN HEALTH Volume: 13 Issue: 5 Pages: 557-564 DOI: 10.1111/j.1524-4733.2010.00709.x Published: JUL-AUG 2010

Abstract: Background:
Elicitation can be used to characterize structural uncertainty within a decision analytic model. This allows the value of acquiring further evidence to resolve these uncertainties to be established.
Aim:
This article demonstrated the use of expert elicitation for this purpose and also compared the elicited results with the results from alternative assumptions previously used to characterize the uncertainties.
Materials and Methods:
Distributions for two unknown parameters were elicited. These were used within a model developed to assess the cost-effectiveness of infliximab and etanercept for the treatment of active psoriatic arthritis (PsA), compared with palliative care. The experts' distributions were synthesized using two approaches: linear pooling and random effects meta-analysis. Weighting of experts is also explored.
Results:
The four methods produce broadly similar results, and in each, the choice of optimum strategy is between etanercept and palliative care (incremental cost-effective ratio for etanercept is between 29,021 pound and 39,259 pound per costs and quality adjusted life years). Decision uncertainty, at a 30,000 pound threshold, is high in all of the synthesis models thus generating high values of further research at between 141 pound and 634 pound million. In each model, the greatest value of further research was for the short-term effectiveness of treatment (47- pound 406 pound million).
Discussion:
Although the cost-effectiveness results do not differ substantially between the models using the elicited values and the original scenarios, there are some stark contrasts in terms of the values of further research generated.
Conclusion:
Elicitation offers a feasible method to generate evidence for the missing information but there are a number of key issues for which further research is required.

ISSN: 1098-3015

Record 22 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Challenges in Economic Evaluation of Psoriatic Arthritis

Author(s): Olivieri, I (Olivieri, Ignazio); D'Angelo, S (D'Angelo, Salvatore); Palazzi, C (Palazzi, Carlo); Padula, A (Padula, Angela)

Source: JOURNAL OF RHEUMATOLOGY Volume: 37 Issue: 6 Pages: 1086-1088 DOI: 10.3899/jrheum.100164 Published: JUN 2010

ISSN: 0315-162X

Record 23 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: The safety of infliximab infusions in the community setting

Author(s): Ducharme, J (Ducharme, James); Pelletier, C (Pelletier, Cindy); Zacharias, R (Zacharias, Ramesh)

Source: CANADIAN JOURNAL OF GASTROENTEROLOGY Volume: 24 Issue: 5 Pages: 307-311 Published: MAY 2010

Abstract: BACKGROUND: Tumour necrosis factor-alpha (TNF alpha) has an important role in the pathogenesis of inflammatory conditions such as rheumatoid arthritis, Crohn's disease, ulcerative colitis and psoriasis. Infliximab, a chimeric anti-TNF alpha monoclonal antibody, has been shown to reduce the severity of symptoms or induces remission of active disease. Infusions have generally been limited to the hospital setting due to cost and concerns for patient safety. Studies defining its efficacy and safety have, therefore, originated almost exclusively from hospital settings.
OBJECTIVE: To evaluate the safety of infliximab in a community clinic environment, across all types of patients.
METHODS: A retrospective chart review of 3161 patients who received a combined 20,976 infusions at a network of community clinics over 16.5 months was conducted. Adverse drug reaction (ADR) information was retrieved and coded for time of onset, severity and outcome. Only ADRs that occurred during or within the first 24 11 of the infusion were included.
RESULTS: A total of 524 (2.5% of all infusions) acute ADRs in 353 patients (11.2%) were recorded. Most

reactions (ie, ADRs) were mild (n=263 [50.2%, 1.3% of all infusions]) or moderate (n=233 [44.5%, 1.1% of all infusions]). Twenty-eight reactions (5.3%, 0.1% of all infusions) were severe. Emergency medical services were called to transport patients to hospital for seven of the severe reactions, of which none required admission. As per pre-established medical directives, adrenaline was administered three times. CONCLUSIONS: Infliximab infusions are safe in the community setting. Severe ADRs were rare. None required active physician intervention; nurses were able to treat all reactions by following standardized medical directives.

ISSN: 0835-7900

Record 24 of 34 **EXLUDED / NOT ORIGINAL ARTICLE (CONFERENCE ABSTRACT)**

Title: GOLIMUMAB ADMINISTERED SUBCUTANEOUSLY EVERY 4 WEEKS IN PSORIATIC ARTHRITIS PATIENTS: 52-WEEK HEALTH-RELATED QUALITY OF LIFE, PHYSICAL FUNCTION AND HEALTH ECONOMIC RESULTS OF THE RANDOMIZED, PLACEBO-CONTROLLED GO-REVEAL STUDY

Author(s): Kavanaugh, A (Kavanaugh, Arthur); Gladman, D (Gladman, Dafna); Chattopadhyay, C (Chattopadhyay, Chandrabhusan); Mease, P (Mease, Philip); McInnes, IB (McInnes, Iain B.); Beutler, A (Beutler, Anna); Zrubek, J (Zrubek, Julie); Buchanan, J (Buchanan, Jacqueline); Parasuraman, S (Parasuraman, Shreekant); Mack, M (Mack, Michael); Krueger, GG (Krueger, Gerald G.)

Group Author(s): GO-REVEAL Investigators

Source: RHEUMATOLOGY Volume: 49 Pages: I56-I56 Supplement: 1 Published: APR 2010

Conference Title: Annual Meeting of the British-Society-Rheumatology/Spring Meeting of British-Health-Professional-in-Rheumatology

Conference Date: APR 21-23, 2010

Conference Location: Birmingham, ENGLAND

Conference Sponsor(s): British Soc Rheumatol, British Hlth Profess Rheumatol

ISSN: 1462-0324

Record 25 of 34 **EXLUDED / NOT ORIGINAL ARTICLE (CONFERENCE ABSTRACT)**

Title: THE COST EFFECTIVENESS OF ETANERCEPT IN PATIENTS WITH PSORIATIC ARTHRITIS IN THE UK

Author(s): Rafia, R (Rafia, Rachid); Ara, R (Ara, Roberta); Lebmeier, M (Lebmeier, Maximilian)

Source: RHEUMATOLOGY Volume: 49 Pages: I75-I75 Supplement: 1 Published: APR 2010

Conference Title: Annual Meeting of the British-Society-Rheumatology/Spring Meeting of British-Health-Professional-in-Rheumatology

Conference Date: APR 21-23, 2010

Conference Location: Birmingham, ENGLAND

Conference Sponsor(s): British Soc Rheumatol, British Hlth Profess Rheumatol

ISSN: 1462-0324

Record 26 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Guideline on the management of psoriasis in South Africa

Author(s): Raboobee, N (Raboobee, N.); Aboobaker, J (Aboobaker, J.); Jordaan, HF (Jordaan, H. F.); Sinclair, W (Sinclair, W.); Smith, JM (Smith, J. M.); Todd, G (Todd, G.); Weiss, R (Weiss, R.); Whitaker, D (Whitaker, D.)

Group Author(s): Dermatological Soc South Africa

Source: SAMJ SOUTH AFRICAN MEDICAL JOURNAL Volume: 100 Issue: 4 Pages: 257-282 Published: APR 2010

Abstract: Background. Psoriasis vulgaris is a chronic, relapsing, immune-mediated, potentially devastating disease, influenced by genetic and environmental factors, that can cause substantial morbidity and psychological stress and have a profound negative impact on patient quality of life.
Objective. These guidelines for the management of psoriasis have been developed in an attempt to improve the outcomes of treatment of this condition in South Africa. Psoriasis has a major impact on the quality of life of sufferers, and it is expected that these guidelines, if implemented, will play a role in achieving improved

outcome.
Scope. These guidelines were developed to address the diagnosis and treatment of psoriasis, of differing degrees of severity and in patients of all ages, by all health care professionals involved with its management.
Recommendations. All health care workers involved in the management of psoriasis should take note of these guidelines and try to implement them in clinical practice as far as possible. All treatment methods and procedures not substantiated by evidence from the literature should be discontinued and avoided to decrease the financial burden of psoriasis treatment.
Validation. These guidelines were developed through general consensus by a group of 8 South African dermatologists (the 'Working Group') sanctioned by the Dermatological Society of South Africa (DSSA), by adaptation for the South African situation of the current guidelines used in the USA, the UK, Germany, Canada and Finland. Draft documents were made available for comment to the dermatological community as a whole via the official website of the DSSA, and the guidelines were presented and discussed at the annual congress of the DSSA in 2008. All input from these sources, where appropriate, were then incorporated into these guidelines.
Guidelines sponsor. Schering-Plough initiated the project and sponsored the meetings of the working group and all costs generated by these meetings.
Plans for guideline revision. The field of biologicals and cytokine modulators is in a rapid phase of development, and revision of the scope and content of these guidelines will be ongoing as longer-term data emerge.

ISSN: 0256-9574

Record 27 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Guideline on the management of psoriasis in South Africa

Author(s): Raboobee, N (Raboobee, N.); Aboobaker, J (Aboobaker, J.); Jordaan, HF (Jordaan, H. F.); Sinclair, W (Sinclair, W.); Smith, JM (Smith, J. M.); Todd, G (Todd, G.); Weiss, R (Weiss, R.); Whitaker, D (Whitaker, D.)

Group Author(s): Working Grp Dermatological Soc S

Source: SAMJ SOUTH AFRICAN MEDICAL JOURNAL Volume: 100 Issue: 4 Pages: 257-282 Part: Part 2 Published: APR 2010

Abstract: Background. Psoriasis vulgaris is a chronic, relapsing, immune-mediated, potentially devastating disease, influenced by genetic and environmental factors, that can cause substantial morbidity and psychological stress and have a profound negative impact on patient quality of life.
Objective. These guidelines for the management of psoriasis have been developed in an attempt to improve the outcomes of treatment of this condition in South Africa. Psoriasis has a major impact on the quality of life of sufferers, and it is expected that these guidelines, if implemented, will play a role in achieving improved outcome.
Scope. These guidelines were developed to address the diagnosis and treatment of psoriasis, of differing degrees of severity and in patients of all ages, by all health care professionals involved with its management.
Recommendations. All health care workers involved in the management of psoriasis should take note of these guidelines and try to implement them in clinical practice as far as possible. All treatment methods and procedures not substantiated by evidence from the literature should be discontinued and avoided to decrease the financial burden of psoriasis treatment.
Validation. These guidelines were developed through general consensus by a group of 8 South African dermatologists (the 'Working Group') sanctioned by the Dermatological Society of South Africa (DSSA), by adaptation for the South African situation of the current guidelines used in the USA, the UK, Germany, Canada and Finland. Draft documents were made available for comment to the dermatological community as a whole via the official website of the DSSA, and the guidelines were presented and discussed at the annual congress of the DSSA in 2008. All input from these sources, where appropriate, were then incorporated into these guidelines.
Guidelines sponsor. Schering-Plough initiated the project and sponsored the meetings of the working group and all costs generated by these meetings.
Plans for guideline revision. The field of biologicals and cytokine modulators is in a rapid phase of development, and revision of the scope and content of these guidelines will be ongoing as longer-term data emerge.

ISSN: 0256-9574

Record 28 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Rapid and sustained health utility gain in anti-tumour necrosis factor-treated inflammatory arthritis: observational data during 7 years in southern Sweden

Author(s): Gulfe, A (Gulfe, A.); Kristensen, LE (Kristensen, L. E.); Saxne, T (Saxne, T.); Jacobsson, LTH (Jacobsson, L. T. H.); Petersson, IF (Petersson, I. F.); Geborek, P (Geborek, P.)

Source: ANNALS OF THE RHEUMATIC DISEASES Volume: 69 Issue: 2 Pages: 352-357 DOI: 10.1136/ard.2008.103473 Published: FEB 2010

Abstract: Background: Rheumatoid arthritis (RA), psoriatic arthritis (PsA) and other spondylarthritides impose a great impact on the individual in addition to the costs on society, which may be reduced by effective pharmacological treatment. Industry-independent health economic studies should complement studies sponsored by industry.
Objective: To study secular trends in baseline health utilities in patients commencing tumour necrosis factor (TNF) blockade for arthritis in clinical practice over 7 years; to address utility changes during treatment; to investigate the influence of previous treatment courses; to study the feasibility of health utility measures and to compare them across diagnostic entities.
Methods: EuroQoL 5 dimensions (EQ-5D) utility data were collected from a structured clinical follow-up programme of anti-TNF-treated patients with RA (N = 2554), PsA (N = 574) or spondylarthritides (N = 586). Time trends were calculated. Completer analysis was used.
Results: There were weak or non-significant secular trends for increasing baseline utilities over time for RA, PsA and spondylarthritides. The maximum gain in utilities had already occurred after 2 weeks for all diagnoses and remained stable for patients remaining on therapy. The first and second anti-TNF courses performed similarly.
Conclusions: Utilities at inclusion remained largely unchanged for RA, PsA and spondylarthritides over 7 years. Improvement occurred early during treatment and not beyond 6 weeks at the group level. Improvement during the first course was not consistently greater than the second. There were no major differences between RA, PsA and spondylarthritides. EQ-5D proved feasible and applicable across these diagnoses. These "real world" data may be useful for health economic modelling.

ISSN: 0003-4967

Record 29 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Psoriatic Arthritis: A Dermatologist's Perspective

Author(s): Snyder, RA (Snyder, Robert Alan)

Source: AMERICAN JOURNAL OF CLINICAL DERMATOLOGY Volume: 11 Pages: 19-22 Supplement: 1 Published: 2010

Abstract: Psoriatic arthritis (PsA) is a common, destructive arthritis that may manifest in more than one-third of psoriasis patients. Dermatologists are in a unique position to diagnose PsA early, and to start prompt, effective treatment. Such early intervention with biological agents such as tumor necrosis factor alpha antagonists, which appear to hold particular promise in the long-term management of PsA, may significantly reduce morbidity, improve quality of life and substantially reduce the economic (patient and societal) burden of PsA.

ISSN: 1175-0561

Record 30 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Etanercept: An Evolving Role in Psoriasis and Psoriatic Arthritis

Author(s): Prodanovich, S (Prodanovich, Srdjan); Ricotti, C (Ricotti, Carlos); Glick, BP (Glick, Brad P.); Inverardi, L (Inverardi, Luca); Leonardi, CL (Leonardi, Craig L.); Kerdel, F (Kerdel, Francisco)

Source: AMERICAN JOURNAL OF CLINICAL DERMATOLOGY Volume: 11 Pages: 3-9 Supplement: 1 Published: 2010

Abstract: Tumor necrosis factor alpha (TNF alpha) plays a key pathophysiological role in psoriasis and psoriatic arthritis (PsA). Recent interest has thus focused on the clinical potential of TNF alpha antagonists (e.g. etanercept) in these settings. In psoriasis, several large pooled analyses and well-designed clinical trials documented the significant clinical efficacy and generally favorable tolerability of etanercept for up to 96 weeks. Similarly, in PsA, a large phase Ill trial showed that, etanercept significantly reduced arthritic symptoms and inhibited radiographic disease progression; sustained clinical benefit was again evident for up to 2 years. Etanercept is at the forefront of psoriatic disease management, and continued evolution and evaluation of the compound - for example, in detailed comparative studies and economic analyses - is likely to confirm a key role for etanercept in the treatment of psoriasis and PsA.

ISSN: 1175-0561

Record 31 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Treatment of moderate-to-severe plaque psoriasis

Author(s): Salgo, R (Salgo, R.); Thaci, D (Thaci, D.)

Source: GIORNALE ITALIANO DI DERMATOLOGIA E VENEREOLOGIA Volume: 144 Issue: 6 Pages: 701-711 Published: DEC 2009

Abstract: Psoriasis, a chronic common immune-mediated disease with frequent remitting/relapsing courses, has a high negative impact on the quality of life, especially in patients moderately or severely affected by the disease. It is also associated with various co-morbidities resulting in a decreased life expectancy and remarkable socioeconomic costs. At least one third of the patients who suffer from it has moderate or severe psoriasis and require continuous treatment to control disease activity. The therapeutic approach in daily practice is usually determined by the severity of the disease. Whether the definition of disease severity is not always clear, there is a considerable number of patients requiring systemic treatment to control the symptoms of psoriasis. The treatment options available for the management of moderate-severe psoriasis have dramatically increased over the past decade, and now range from phototherapy to traditional systemic treatments to biologics. Available data from clinical trials and growing number of patients treated with biologics shows that this new agent are effective and relatively safe to control psoriasis, and are coupled with improved tolerability, convenience and improvement in quality of life. This review shortly presents the characteristics, safety and efficacy profile of the conventional and newer systemic drugs used in moderate-to-severe psoriasis.

ISSN: 0026-4741

Record 32 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Regional review of patients with psoriatic arthritis in secondary care in the West Midlands: prevalence, disease activity and eligibility for anti-tumour necrosis factor therapy

Author(s): Bateman, J (Bateman, J.); Cardy, CM (Cardy, C. M.); Khan, SY (Khan, S. Y.); Menon, A (Menon, A.); Obrenovic, K (Obrenovic, K.); Rowe, IF (Rowe, I. F.); Erb, N (Erb, N.)

Source: CLINICAL AND EXPERIMENTAL RHEUMATOLOGY Volume: 27 Issue: 6 Pages: 935-939 Published: NOV-DEC 2009

Abstract: Objective
Tumour necrosis factor alpha-blockers (TNF-alpha) art licensed for the treatment of psoriatic arthritis (PsA) and their use has been approved by the National Institute for Health and Clinical Excellence (NICE) for use in the United Kingdom under a set of defined clinical criteria.
Methods
In this out-patient study we evaluated PsA in rheumatology secondary care clinics in units across the West Midlands over a 2-week period, assessing prevalence, disease activity and eligibility for anti TNF-alpha treatment as defined by the NICE criteria.
Results
Of the 1718 forms returned from the 2000 sent (86% response rate), 175 patients had PsA (10.2%). Of those, 22 (12.6%) were already on anti TNF-alpha treatment. 12 patients were noted to have purely axial disease and as per the NICE guidelines should not be assessed under the PsA criteria. A further 5 patients fulfilled the criteria for treatment with anti TNF-alpha with no contraindications. In the region 22 out of 2 7 patients (81%) with active disease were correctly on Anti TNF therapy. In total 27 (15.4%) patients with PsA met the NICE criteria for treatment of PsA with anti TNF-alpha therapy. 3 patients had previously failed anti TNF-alpha treatment. No patient fulfilling criteria for treatment were found to have any contraindications to treatment.
Conclusion
We note the relatively high proportion of PsA patients eligible for treatment with anti TNF-alpha blockers in the region (15.4%) compared to the NICE estimate (2.4%). This may be in part explained by a selection bias. However, the results may have significant implications for healthcare provision given the relatively high cost of anti-TNF-alpha agents. We comment on the limitations of such criteria and the effective use of regional collaboration for both training and audit purposes.

ISSN: 0392-856X

Record 33 of 34 EXLUDED / NOT CU ANALYSIS

Title: Real-World Anti-Tumor Necrosis Factor Treatment in Rheumatoid Arthritis, Psoriatic Arthritis, and

Ankylosing Spondylitis: Cost-Effectiveness Based on Number Needed to Treat to Improve Health Assessment Questionnaire

Author(s): Barra, L (Barra, Lillian); Pope, JE (Pope, Janet E.); Payne, M (Payne, Michael)

Source: JOURNAL OF RHEUMATOLOGY Volume: 36 Issue: 7 Pages: 1421-1428 DOI: 10.3899/jrheum.081122 Published: JUL 2009

Abstract: Objective. To determine the effectiveness and cost-effectiveness of anti-tumor necrosis factor (anti-TNF) medications in a real-world environment for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) using the Health Assessment Questionnaire (HAQ).
Methods. We created a database of patients with RA. PsA. or AS treated with anti-TNF agents (etanercept, infliximab, or adalimumab) at a large outpatient rheumatology clinic. Patient characteristics, baseline HAQ prior to treatment, subsequent yearly HAQ, and reasons For termination were collected. The cost based on percentage of patients achieving >= 0.2 improvement in HAQ (minimal clinically important difference, MCID) was calculated using the 2008 direct cost (Cdn) of the medication.
Results. Data were available oil 297 patients (206 with RA, 57 PsA. 34 AS). The mean age was 55 years, with 12 years of disease, and the mean baseline HAQ (standard error, SE) was 1.37 (0.04). The changes in HAQ (SE) at Years 1.2. and 3 were -0.31 (0.04), -0.24 (0.06). and -0.27 (0.07) for annual cost to achieve MCID of $41,636. $42,077, and $42,147, respectively. The number needed to treat (NNT) was 1.94 (RA), 1.88 (PsA), and 2.30 (AS). There were no statistical differences between the diseases studied.
Conclusion. We obtained data oil the effectiveness and cost-effectiveness of anti-TNF drugs using the HAQ score, which is known to be all excellent predictor of work disability, morbidity, and mortality. HAQ scores decreased with treatment and were sustained throughout the 3-5 years of followup. The NNT of approximately 2 seems favorable and was similar between diseases. (First Release June 1 2009; J Rheumatol 2009: 36:1421-8: doi: 10.3899/jrheum.081122)

ISSN: 0315-162X

Record 34 of 34 **EXLUDED / NOT CU ANALYSIS**

Title: Effect of Calcipotriol on Etanercept Partial Responder Psoriasis Vulgaris and Psoriatic Arthritis Patients

Author(s): Campion, E (Campion, Elena); Mazzotta, A (Mazzotta, Annamaria); Paterno, EJ (Paterno, Evelin Jasmine); Diluvio, L (Diluvio, Laura); Prinz, JC (Prinz, Joerg Christoph); Chimenti, S (Chimenti, Sergio)

Source: ACTA DERMATO-VENEREOLOGICA Volume: 89 Issue: 3 Pages: 288-291 DOI: 10.2340/00015555-0585 Published: 2009

Abstract: Patients who respond only partially to etanercept may require additional treatments that act synergistically to improve their therapeutic response while at the same time reducing the dose required and the risk of side-effects. The aim of this study was to evaluate the effectiveness of topical calcipotriol in etanercept partial responder patients. We enrolled 120 patients affected by psoriasis vulgaris and psoriatic arthritis. A 50 mg dose of etanercept was administered twice weekly for the first 12 weeks, followed by a 25 mg dose twice weekly for an additional 12 weeks. At week 12, for 45 patients who had not achieved PASI 50, calcipotriol cream was also prescribed twice daily for 4 weeks and then once daily for a further 8 weeks. At week 24, of the 45 patients in the group treated with etanercept plus calcipotriol, 14(31.1%) had achieved PASI 75, and 23 PASI 50, while 8 (17.7%) had dropped out of therapy; of the 75 patients who continued etanercept in monotherapy with a 25 mg dose twice weekly for another 12 weeks, 71 (94.6%) had achieved PASI 50 and 57 (76.0%) PASI 75. The application of calcipotriol in etanercept partial responder patients had therefore helped 37 out of 120 patients (31%) achieve at least PASI 50. This is the first report about the controlled combination of topical calcipotriol and etanercept in a large group of psoriatic patients. The efficacy and cost-effectiveness of the combined treatment is evidenced by the good response shown at week 24 by a group of etanercept low-responder patients using drugs sparingly and limiting likely toxicity.

ISSN: 0001-5555

Center for Reviews and Dissemination (22 hits)

Record #1 **EXLUDED / NOT CU ANALYSIS**
TTL: TNF-alpha inhibitors for psoriatic arthritis
AUT: Golicki Dominik, Macioch Tomasz, Niewada Maciej, Jakubczyk Michal, Tlustochowicz Malgorzata, Owczarek Witold, Tlustochowicz Witold
XSO: Cochrane Database of Systematic Reviews: Protocols
PUB: John Wiley & Sons, Ltd
XYR: 2009
VOL: Issue 3
XST: This is an abstract for a Cochrane protocol
XAO: This is the protocol for a review and there is no abstract. The objectives are as follows:The aim of this review is to assess the efficacy and safety of the TNF-alpha inhibitors (adalimumab, certolizumab, etanercept, golimumab, infliximab and onercept) in patients with PsA when compared with placebo or current standard treatment.This review will address four core questions.1. What is the clinical efficacy of TNF-alpha inhibitors for the treatment of PsA in terms of:. relieving symptoms?. improving health related quality of life?. delaying disease progression?2. What are the risks (frequency and severity of adverse events) associated with use of TNF-alpha inhibitors in these patients?
XAC: 10000007940
XID: 26 Jul 2010
XUR: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD007940/frame.html
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=10000007940

Record #2 **EXLUDED / NOT CU ANALYSIS**
TTL: Combination therapy for pain management in inflammatory arthritis (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, other spondyloarthritis)
AUT: Ramiro Sofia, Radner Helga, van der Heijde Désirée, van Tubergen Astrid, Buchbinder Rachelle, Aletaha Daniel, Landewé Robert BM
XSO: Cochrane Database of Systematic Reviews: Reviews
PUB: John Wiley & Sons, Ltd
XYR: 2011
VOL: Issue 10
XST: This is an abstract for a Cochrane review
XAO: To assess the benefits and safety of combination pain therapy for people with IA (rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and other spondyloarthritis (SpA)). We planned to assess differences in effects between patients on background disease-modifying antirheumatic drug (DMARD) therapy and patients on no background therapy in subgroup analyses. Despite optimal therapy with disease-modifying antirheumatic drugs, many people with inflammatory arthritis (IA) continue to have persistent pain that may require additional therapy.
XSS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library); MEDLINE; and EMBASE. We did not impose any date or language restrictions in the search. We also handsearched conference proceedings of the American College of Rheumatology and the European League against Rheumatism (2008-10).
XDE: Two review authors independently selected trials for inclusion, assessed risk of bias and extracted data.
XRR: Twenty-three trials (total of 912 patients) met the inclusion criteria (22 in RA; one in a mixed population of RA and osteoarthritis); all except one were published before 1990. Most study populations were not taking DMARDs (e.g. methotrexate, sulphasalazine, hydroxychloroquine and leflunomide) and all studies were performed prior to the introduction of biologic therapies (e.g. etanercept, infliximab and adalimumab). All trials were at high risk of bias, heterogeneity precluded meta-analysis, and we were only able to report a general description of results.The majority (18 studies, 78%) found no differences between the combination and monotherapy treatments they studied, while five (22%) reported conflicting results, favouring either the combination or monotherapy arms.From the 12 trials on NSAID + analgesic vs NSAID, nine reported no significant difference between the interventions, while three did: in two, the combination therapy achieved better pain control; and the third trial compared combination therapy with two different dosages of monotherapy (NSAID alone) and reported that a high dose phenylbutazone was superior to combination therapy (paracetamol + aspirin), which was superior to low dose phenylbutazone.From the five studies on the combination of two NSAIDS vs one NSAID, four reported no significant differences between interventions, and one reported significantly better pain control with combination therapy.The single trial comparing a combination of opioid + neuromodulator vs opioid reported better pain control with monotherapy.The

remaining trials (NSAID + neuromodulator vs NSAID (3 trials); opioid + NSAID vs NSAID (1 trial); and opioid + analgesic vs analgesic (1 trial)) found no significant difference between combination therapy and monotherapy.Information regarding withdrawals due to inadequate analgesia and safety was incompletely reported, but in general there were no differences between combination therapy and monotherapy.No data were available that addressed the value of combination pain therapy or monotherapy for people with IA who have optimal disease suppression. There were no studies that included patients with AS, PsA or SpA.
XCL: Based on 23 trials, all at high risk of bias, there is insufficient evidence to establish the value of combination therapy over monotherapy for people with IA. Importantly, there are no studies addressing the value of combination therapy for patients with IA who have persist ent pain despite optimal disease suppression. Well designed trials are needed to address this question. COMBINING TWO OR MORE DRUGS VS ONE DRUG FOR PAIN CONTROL IN INFLAMMATORY ARTHRITIS: This summary of a Cochrane review presents what we know from research about the effect of a combination of two pain relieving drugs for pain control in inflammatory arthritis (IA).We are uncertain if two pain relieving drugs such as paracetamol (also called acetaminophen) (e.g. Panadol® and Tylenol®) plus non-steroidal anti-inflammatory drugs (NSAIDs), or paracetamol plus aspirin compared with one drug improved pain, because only single studies of low quality evidence were available. For the same reason, we do not have precise information about side effects and complications.What is IA, and what drugs are used to treat pain?IA is a group of diseases that includes rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and other spondyloarthritis (SpA). When you have IA, your immune system, which normally fights infection, attacks your joints. This makes your joints swollen, stiff and painful. In RA, the small joints of your hands and feet are usually affected first. In contrast, in AS, the joints of the spine are the most affected. PsA is characterised by inflammation of the skin, psoriasis, and joints and, depending on the disease type, can affect the small joints of the hands and feet or more the spine. There is no cure for IA at present, so the treatments aim to relieve pain and stiffness and improve your ability to move. Patients are started on disease-modifying antirheumatic drugs (DMARDs) (e.g. methotrexate, sulphasalazine, hydroxychloroquine and leflunomide) as soon as possible in an attempt to control the inflammation and to prevent the progression of the disease. Many people continue to have pain despite optimal disease treatment and have the need for specific medication to control pain.Several drugs can be used to treat pain in IA. Paracetamol/acetaminophen, is used to relieve pain but does not affect swelling; NSAIDs such as ibuprofen, diclofenac and COX-2s (e.g. celecoxib), are used to reduce pain and swelling; and opioids, such as codeine-containing Tylenol®, hydromorphone (Dilaudid), oxycodone (Percocet and Percodan), morphine and tramadol are powerful pain-relieving substances. Other drugs have some pain relieving properties and can therefore be used to mainly control pain. This is the case of the so-called neuromodulators, such as antidepressants (e.g. fluoxetine, paroxetine and amitriptyline), anticonvulsants (e.g. gabapentine and pregabaline) or muscle relaxants (e.g. diazepam). It is not clear if combining two of these drugs offers the best treatment and which drugs cause more side effects. It is known that, for instance, high doses of paracetamol/acetaminophen may cause stomach problems, such as ulcers, and NSAIDs may cause stomach, kidney or heart problems.Best estimate of what happens to people with IA who take combination therapy for painThere is insufficient evidence to establish the value of combination therapy over monotherapy for people with IA. We included 23 studies in this review, all at high risk of bias (i.e. high chance of giving invalid results). Twenty-two of the trials were in patients with RA and one in a mixed population (RA and osteoarthritis). There were no studies in patients with AS, PsA or SpA. Included studies were old (all but one were published before 1990) and patients were, in general, not on optimal disease-modifying antirheumatic drugs, as is standard current practice. Therefore, it is not possible to draw conclusions about the value of combination pain therapy over monotherapy for people with IA. Importantly, there are no studies addressing the value of combination therapy for patients with IA who have persistent pain despite optimal disease suppression. Well designed studies are needed to address this question.<Abstract truncated>
XAC: 10000008886
XID: 22 Dec 2010
XUR: http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD008886/frame.html
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=10000008886

Record #3 **EXLUDED / NOT CU ANALYSIS**
TTL: Risks and benefits of tumor necrosis factor-alpha inhibitors in the management of psoriatic arthritis: systematic review and metaanalysis of randomized controlled trials
AUT: Saad A A, Symmons D P, Noyce P R, Ashcroft D M
XSO: Journal of Rheumatology
XYR: 2008
VOL: 35(5)
PAG: 883-890

XPT: Journal article
XCC: This generally well-conducted review assessed the tumour necrosis factor-α (TNF-α) inhibitors adalimumab, etanercept and infliximab for the management of psoriatic arthritis (PsA). The authors concluded that TNF-α inhibitors were effective treatments for psoriatic arthritis with no important risks associated with short-term use. The conclusion reflected the results of the review and is likely to be reliable.
XST: This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.
XAO: To assess the efficacy and safety of tumour necrosis factor-α (TNF-α) inhibitors in the management of psoriatic arthritis (PsA).
XSS: MEDLINE, EMBASE, CINAHL and Cochrane Central Register of Controlled Trials were searched without language or publication restriction from inception to May 2007. Search terms were reported. The websites of the FDA and the European Medicines Evaluation Agency were also searched, as were the references of identified trials and reviews.
XVC: Two reviewers independently assessed the studies for validity using the Jadad scale, which awards up to 5 points for the criteria of randomisation, blinding and treatment of withdrawals and dropouts. Studies scoring fewer than 2 points were excluded from the review. Differences were resolved through discussion
XDE: Two reviewers independently performed the data extraction; disagreements were resolved through discussion. The frequency of events in each group was extracted for dichotomous data, along with the number of patients treated. The change in response from baseline, its standard deviation and the number of patients intended to be treated were extracted for continuous data.
XRR: Six RCTs (n=982) were included in the review.All three TNF-α inhibitors were significantly more effective than placebo as assessed by ACR20. The pooled RR for all trials was 4.35 (95% CI: 3.24, 5.84). Results for each individual treatment were significant (adalimumab RR 3.42, 95% CI: 2.08, 5.63, etanercept RR 5.50, 95% CI: 2.15, 14.04 and infliximab RR 5.71, 95% CI: 3.53, 9.25). The indirect comparisons found no significant differences between the treatments in achieving response assessed by ACR20. The same pattern of results was found for outcomes assessed by PsARC at 12 weeks and 24 weeks. Indirect comparisons found no significant differences in efficacy. Outcomes assessed using PASI also showed significant and consistent benefits of all three treatments. There were no significant differences between TNF-α inhibitors and placebo in the numbers of patients withdrawing from the study or withdrawing due to an adverse reaction. Nor were there significant differences in the numbers experiencing serious adverse events or respiratory tract infections. More patients experienced injection site reactions with etanercept than with placebo (RR 4.27, 95% CI: 2.25, 8.13), but no significant difference was found with adalimumab or in infusion site reactions with infliximab versus placebo. Only one incidence of malignancy (in a placebo group) was found in five trials that monitored malignancy. Quality of life outcomes were reported.
XCL: TNF-α inhibitors were effective treatments for psoriatic arthritis with no important risks associated with short-term use. There was a need for long-term risk-benefit assessment of TNF-α inhibitor use for the management of psoriatic arthritis.
XCM: The review question and the inclusion criteria were clear and specific. The authors searched several relevant databases and other sources and took steps to reduce the possibility of language or publication bias. The authors reported using methods designed to reduce reviewer bias and error in the extraction of data and the assessment of validity, but not in the selection of papers. An appropriate validity assessment was conducted, although this was not used to inform the synthesis. The decision to use meta-analysis and indirect comparisons appeared appropriate. Heterogeneity was investigated using appropriate techniques. The authors' conclusions reflected the results of the review and appear likely to be reliable.
XIM: Practice: The authors did not state any implications for practice.Research: The authors stated that there was a need for longitudinal observational studies with sufficient numbers of patients to investigate the long-term comparative safety of TNF-α inhibitors in the management of psoriatic arthritis.
KWO: Adult; Antibodies, Monoclonal /adverse effects /therapeutic use; Antirheumatic Agents /adverse effects /therapeutic use; Arthritis, Psoriatic /drug therapy; Female; Humans; Immunoglobulin G /adverse effects /therapeutic use; Male; Middle Aged; Randomized Controlled Trials as Topic; Receptors, Tumor Necrosis Factor /therapeutic use; Treatment Outcome; Tumor Necrosis Factor-alpha /antagonists & inhibitors
XAC: 12008105130
XID: 15 Jul 2009
XLA: English
XPR: 18381787
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12008105130

Record #4 **EXLUDED / NOT CU ANALYSIS**

TTL: Efficacy and tolerability of biologic and nonbiologic systemic treatments for moderate-to-severe psoriasis: meta-analysis of randomized controlled trials
AUT: Schmitt J, Zhang Z, Wozel G, Meurer M, Kirch W
XSO: British Journal of Dermatology
XYR: 2008
VOL: 159(3)
PAG: 513-526
XPT: Journal article
XCC: The authors concluded that the effects of approved systemic agents for moderate-to-severe psoriasis differed considerably. Infliximab was the most effective agent. Although the review used appropriate methods to identify and obtain data, the synthesis of data was flawed, so the conclusions about the relative efficacy of agents are not likely to be reliable.
XST: This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.
XAO: To evaluate the efficacy and tolerability of approved systemic treatments for moderate-to-severe plaque psoriasis.
XSS: Three recently published health technology assessments on systemic treatments for psoriasis were hand-searched for studies published until June 2004. MEDLINE, EMBASE, SCOPUS and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for studies published between June 2004 and December 2007. Search terms were reported. No language restrictions were applied.
XVC: Two reviewers independently assessed study validity using the Jadad criteria which assessed randomisation, blinding and reporting of withdrawals. Each trial was awarded a score up to a maximum of 5 points. Disagreements were resolved by consensus among all reviewers.
XDE: Two reviewers independently extracted data. Where only mean changes and standard deviations in Psoriasis Area and Severity Index were reported, proportions of patients achieving 75% reduction in Psoriasis Area and Severity Index response were estimated assuming a normal response distribution for Psoriasis Area and Severity Index changes. Percentages of patients with 75% reduction response in Psoriasis Area and Severity Index were reported for each treatment group. Disagreements were resolved by consensus among all reviewers.
XRR: Twenty-four RCTs were included in the review (n=9384 patients). Seventeen trials scored 5 out of 5 on the Jadad scale, two trials scored 4 points, four trials scored 3 points, three trials scored 2 points and two trials scored 1 point. Efficacy: Psoriasis Area and Severity Index 75% reduction response rates for ciclosporin varied considerably (range 28 to 97%). Meta-analyses: Sixteen double-blind RCTs were included in meta-analyses. The authors stated that infliximab (RD 77%, 95% CI 72 to 81; three trials) had significantly higher response rates for 75% reduction in Psoriasis Area and Severity Index than all other treatments. Adalimumab (RD 64%, 95% CI 61 to 68; one trial) had higher response rates than ciclosporin (RD 33%, 95% CI 13 to 52; two trials), efalizumab (RD 24%, 95% CI 19 to 30; five trials), etanercept 50mg twice weekly (RD 44, (95% CI 40 to 48; three trials) and etanercept 25mg twice weekly (RD 30%, 95% CI 25 to 35; three trials). Efalizumab (RD 24%, 95% CI 19 to 30; five trials) had a significantly lower response rate for 75% reduction in Psoriasis Area and Severity Index than fumaric acid esters (RD 48%, 95% CI 32 to 64; one trial). Tolerability: The highest withdrawal rates were for methotrexate (average monthly rate 7.3%) and fumaric acid esters (average monthly rate 10.2%). Compared to placebo, the pooled monthly incidence rate was 2.5% for infusion reactions with infliximab and 4.8% for injection site reactions with etanercept. The monthly incidence rate was 1.8% higher for upper respiratory tract infections with adalimumab compared to placebo,
XCL: The efficacy of approved systemic agents for moderate-to-severe psoriasis differed considerably. Infliximab was the most effective.
XCM: The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched and no language restrictions were applied, but no attempts were made to minimise publication or language bias. Appropriate methods were used to minimise reviewer error and bias during the review process. Only RCTs were included, validity was assessed but only aggregated scores were reported. It appeared that the decision to pool only double-blind RCTs was taken post-hoc, but a priori analysis are preferred as a method of reducing potential bias. Double-blind placebo RCTs were combined using meta-analysis and heterogeneity as assessed for trials evaluating the same agent. The authors' conclusions about relative efficacy were based on informal indirect comparisons; it was unclear how the statistical significance of differences between different agents was tested. Adjusted indirect comparison methods were not used, which suggested that the findings were subject to bias and may not be reliable. In addition, indirect comparisons are only likely to be reliable if studies are comparable in terms of design and population. Although the review used appropriate methods to identify and obtain data, the synthesis of data was flawed, so the conclusions are not likely to be reliable.Three of the authors have been investigators or consultants for various pharmaceutical

companies; they stated that this work was not directly related to this review.
XIM: Practice: The authors stated that 'published evidence questions regulatory guidelines that recommend biologics as second-line therapy for moderate-to-sever plaque psoriasis'. Research: The authors stated that studies are required to evaluate the cost-effectiveness of biological interventions such as infliximab and adalimumab. They also stated that there is a need for pragmatic RCTs that last at least two years to directly compare different biological agents with each other and with conventional systemic psoriasis treatments. The comparative efficacy of different biological agents should also be evaluated in the sub-group of patients who have failed to respond to conventional systemic treatments.
KWO: Antibodies, Monoclonal /therapeutic use; Antirheumatic Agents /therapeutic use; Biological Products /therapeutic use; Humans; Immunosuppressive Agents /therapeutic use; Practice Guidelines as Topic; Psoriasis /drug therapy /therapy; PUVA Therapy; Randomized Controlled Trials as Topic; Treatment Outcome
XAC: 12009100716
XID: 13 Jan 2010
XLA: English
XPR: 18627372
XUR: http://www3.interscience.wiley.com/journal/120749013/abstract
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12009100716

Record #5 **EXLUDED / NOT CU ANALYSIS**
TTL: Infliximab and methotrexate in the treatment of rheumatoid arthritis: a systematic review and meta-analysis of dosage regimens
AUT: Zintzaras E, Dahabreh I J, Giannouli S, Voulgarelis M, Moutsopoulos H M
XSO: Clinical Therapeutics
XYR: 2008
VOL: 30(11)
PAG: 1939-1955
XPT: Journal article
XCC: This review concluded that infliximab at 10 mg/kg in combination with methotrexate was more effective for the treatment of active rheumatoid arthritis than methotrexate alone or in combined therapy with infliximab at 3 mg/kg, without increased adverse events. This conclusion closely reflected the results of the review but its reliability may be limited by the relative narrowness of the search.
XST: This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.
XAO: To assess the efficacy and tolerability of infliximab plus methotrexate compared with methotrexate alone for the treatment of active rheumatoid arthritis; to identify subgroups of patients who benefit most from infliximab plus methotrexate treatment.
XSS: MEDLINE and the Cochrane Database of Systematic Reviews were searched from inception to November 2006 for English language studies. Search terms were reported. References of retrieved studies and rheumatology textbooks were checked.
XVC: Two reviewers independently assessed the studies for validity using blinding, allocation concealment and use of an intention-to-treat analysis.
XDE: Two reviewers independently performed the data extraction in a blinded fashion. Discrepancies were resolved through consensus with a third reviewer.
XRR: Twelve RCTs (n = 4,899) were included in the review; 3,919 patients received infliximab plus methotrexate and 980 methotrexate alone. Nine RCTs used double-blinding, seven reported adequate allocation concealment and six used an intention-to-treat analysis.Infliximab at 3 mg/kg plus methotrexate was significantly more effective than methotrexate alone on all American College of Rheumatology (ACR) efficacy measures (ACR 20 odds ratio 3.52, 95% CI: 2.14, 5.79; ACR 50 odds ratio 2.87, 95% CI: 2.28, 3.61; ACR70 odds ratio 2.42, 95% CI: 1.87, 3.13). Infliximab at 10mg/kg plus methotrexate was also significantly more effective than methotrexate alone on all American College of Rheumatology (ACR) efficacy measures (ACR20 odds ratio 5.06, 95% CI: 3.88, 6.59; ACR50 odds ratio 5.72, 95% CI: 4.05, 8.08; ACR 70 odds ratio 7.32, 95% CI: 2.28, 23.50).Regimes using higher doses of infliximab were significantly more effective on the outcome of ACR50 than lower doses (p=0.001). Subgroup results were also reported separately for treatments administered at 4 and 8 week intervals. There was some evidence of increased efficacy with 4 weekly compared to 8 weekly administration for 3 mg/kg infliximab (ACR20 p=0.03; ACR50 p>0.05; ACR70 p=0.02) but no such effect for 10 mg/kg treatments (p>0.05 in all cases).Incidence of adverse effects was not significantly different between the groups either for infliximab 3 mg/kg plus methotrexate versus methotrexate alone every eight weeks or for infliximab 10 mg/kg plus methotrexate versus methotrexate alone every eight weeks. There was no statistically

significant difference between groups treated with lower or higher doses of infliximab given every four versus every eight weeks. Further results of subgroup analyses were extensively reported, including findings of increased efficacy for high doses in patients with severe disease activity, in patients with concomitant steroid use and in trials lasting longer than 54 weeks.
XCL: Higher dose (10 mg/kg) infliximab therapy in combination with methotrexate was more effective than standard (3 mg/kg) therapy, particularly for patients with severe disease activity. Treatment benefits accrued over time and higher doses were not linked to increased adverse effect incidence. Efficacy was significantly increased by concomitant use of oral low dose steroids.
XCM: The inclusion criteria were clear. The authors searched two relevant databases and some other sources, but the restriction of the review to studies reported in English may have increased the chance of language bias and the omission of some relevant studies. The probability of publication bias was acknowledged by the authors, although not formally assessed. The authors reported using methods designed to reduce reviewer bias and error in the extraction of data and the assessment of validity, but not in the selection of studies. Validity was assessed and the influence of some aspects on results was examined. The use of meta-analysis and the assessment of heterogeneity appeared appropriate. While the conclusions closely reflected the results of the review, the relatively limited search may affect their reliability.
XIM: Practice: The authors did not state any implications for practice.Research: The authors stated that observations on the differential effectiveness of infliximab plus methotrexate in different subgroups of active rheumatoid arthritis patients should be used for hypothesis generation and the design of further RCTs.
KWO: Administration, Oral; Adult; Age Factors; Antibodies, Monoclonal /administration & dosage /adverse effects /therapeutic use; Antirheumatic Agents /administration & dosage /adverse effects /therapeutic use; Arthritis, Rheumatoid /drug therapy; Dose-Response Relationship, Drug; Drug Therapy, Combination; Female; Humans; Male; Methotrexate /administration & dosage /adverse effects /therapeutic use; Middle Aged; Randomized Controlled Trials as Topic; Time Factors; Treatment Outcome
XAC: 12009102167
XID: 01 Jul 2009
XLA: English
XPR: 19108784
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12009102167

Record #6 **EXLUDED / NOT CU ANALYSIS**
TTL: Safety and efficacy of alefacept, efalizumab, etanercept and infliximab in treating moderate to severe plaque psoriasis: a meta-analysis of randomized controlled trials
AUT: Brimhall AK, King LN, Licciardone JC, Jacobe H, Menter A
XSO: British Journal of Dermatology
XYR: 2008
VOL: 159(2)
PAG: 274-285
XPT: Journal article
XCC: This review assessed the efficacy and safety of alefacept, efalizumab, etanercept and infliximab for treatment of moderate to severe plaque psoriasis and concluded that all treatments yielded significant improvements over placebo in the short term with an increased risk of adverse events. The authors' conclusions from this generally well-conducted review reflected the evidence and are likely to be reliable.
XST: This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.
XAO: To assess the efficacy and safety of alefacept, efalizumab, etanercept and infliximab for treatment of moderate to severe plaque psoriasis.
XSS: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov were searched from inception to July 2006 for studies in English; search terms were reported. US Food and Drug Administration reports were searched and sponsors were contacted for unpublished data.
XVC: Study quality was assessed according to predefined criteria for: randomisation; allocation concealment; intention-to-treat analysis; placebo control; attrition; use of other systemic therapies; and comparable baseline demographics between placebo and treatment groups. The authors did not state how the validity assessment was performed.
XDE: Risk ratios (RRs) and their associated 95% confidence intervals (CIs) were calculated for the outcomes of interest and adverse events and serious adverse events. Data were extracted using standardised pre-piloted data extraction forms. The authors did not state how many reviewers performed the data extraction.

XRR: Sixteen RCTs (n=7,931, range 33 to 835) were included in the review: three trials of alefacept (n=1,289); five of efalizumab (n=3,130); four of etanercept (n=2,017); and four of infliximab (n=1,495). The included studies were considered to be of high quality.For PASI 75, all four interventions yielded significant differences over 10 to 14 weeks of treatment compared with placebo: infliximab (RR 17.40, 95% CI 6.41 to 47.19; NNT=2); etanercept (RR 11.73, 95% CI 8.04 to 17.11; NNT=3); efalizumab (RR 7.33, 95% CI 5.28 to 10.17; NNT=4); and alefacept (RR 3.70, 95% CI 2.38 to 5.75; NNT=8). The risk of one or more adverse events for each intervention compared with placebo was significantly increased for: alefacept (RR 1.09, 95% CI: 1.01, 1.18; NNH=15); efalizumab (RR 1.15, 95% CI 1.09 to 1.20; NNH=9); and infliximab (RR 1.18, 95% CI 1.07 to 1.29; NNH=9). Serious adverse events were significantly increased for efalizumab (RR 1.92, 95% CI 1.05 to 3.51; NNH=60) compared with placebo.Using PASI 90, significant differences compared to placebo were achieved for both etanercept (RR 21.44, 95% CI 9.52 to 48.26; NNT=5) and infliximab (RR 49.42, 95% CI 16.01 to 152.54; NNT=2). Non-significant differences for alefacept and efalizumab were achieved using PASI 50.
XCL: All four interventions yielded significant improvements over placebo. There was an increased risk of adverse events for alefacept, efalizumab and infliximab.
XCM: The review question and inclusion criteria were clear. A seemingly thorough literature search was restricted to publications in English and so language bias may have been present. Unpublished studies were sought. It was unclear how many of the authors were involved in study selection, data extraction and quality assessment. An appropriate assessment of the methodological quality of the included studies was undertaken. Suitable methods were used for the meta-analysis. Heterogeneity was assessed and found to be absent from the analyses for significant outcomes. Despite a lack of reporting for parts of the review process this was generally a well-conducted review. The authors conclusions reflected the evidence and are likely to be reliable.
XIM: The authors did not state any implications for practice or further research.
KWO: Antibodies, Monoclonal /adverse effects /therapeutic use; Dermatologic Agents /therapeutic use; Humans; Immunoglobulin G /adverse effects /therapeutic use; Immunosuppressive Agents /adverse effects /therapeutic use; Psoriasis /drug therapy; Randomized Controlled Trials as Topic; Receptors, Tumor Necrosis Factor /therapeutic use; Recombinant Fusion Proteins /adverse effects /therapeutic use; Treatment Outcome
XAC: 12009102350
XID: 10 Mar 2010
XLA: English
XPR: 18547300
XUR: http://www3.interscience.wiley.com/journal/120119963/abstract
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12009102350

Record #7 **EXLUDED / NOT CU ANALYSIS**
TTL: Efficacy and safety of treatments for childhood psoriasis: a systematic literature review
AUT: de Jager ME, de Jong EM, van de Kerkhof PC, Seyger MM
XSO: Journal of the American Academy of Dermatology
XYR: 2010
VOL: 62(6)
PAG: 1013-1030
XPT: Journal article
XCC: The authors concluded that calcipotriene with or without corticosteroids was the treatment of choice for childhood psoriasis, followed by dithranol. Methotrexate was the systemic treatment of choice. Evidence on specific treatments was limited: based at most on one randomised controlled trial of unknown quality plus studies of less reliable design. This means that the conclusions should be interpreted with caution.
XST: This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.
XAO: To evaluate the efficacy and safety of treatments for childhood psoriasis.
XSS: PubMed, EMBASE and Cochrane Central Register of Controlled Trials were searched from 1980 to September 2008. The main search terms were reported. The full search strategy was available from the authors. Reference lists of all identified articles were searched. Studies published in English, German or Dutch were eligible.
XVC: The authors did not state that they assessed validity. However, two reviewers independently extracted information on blinding and graded studies using a hierarchy of study design based on the Oxford Centre Evidence-Based Medicine Levels of Evidence (level one for RCTs, level two for cohort studies, level three for case-control studies, level four for case series and level five for case reports and expert opinions). Disagreements were resolved through consensus or by consultation with a third reviewer.

XDE: Two reviewers independently extracted outcome data onto a pre-designed form. The authors classified clearance as more than 90% improvement from baseline. Other levels of improvement were marked (70% to 90%), moderate (50% to 70%), slight (30% to 50%) and poor (<30%). Disagreements were resolved through consensus or by consultation with a third reviewer.
XRR: Sixty-four studies were included. Topical corticosteroids: Halobetasol cream 0.05% and clobetasol propionate emulsion 0.05% cream seemed to be effective for childhood plaque psoriasis; grade C evidence came from one open-label study (n=11), one poor-quality RCT (n=9) and one case report (n=1). Vitamin D analogues: Calcipotriene (mostly 50µg/g) was effective and reasonably well-tolerated for plaque psoriasis; grade A evidence came from one double-blind RCT (n=77), four open-label studies (n=110) and two case reports (n=2). Calcitriol seemed effective with mild side effects; grade B evidence came from one RCT (n=10) and one placebo-controlled study with the same four patients as one case series. Calcineurin inhibitors: Tacrolimus seemed effective and safe for short-term treatment of facial and intertriginous psoriasis, but there was no evidence on long-term safety; grade C evidence came from two open-label studies (n=19) and one case report (n=1). No conclusions could be reached on pimecrolimus (two case reports, n=2) due to insufficient evidence. Dithranol was effective with a good short-term side-effect profile; grade C evidence came from two open-label studies (n=99) and one case report (n=1). Phototherapy: Narrow-band ultraviolet B radiation (NB-UVB) results were good for plaque and guttate psoriasis and side effects were reasonably mild over the treatment period; grade C evidence came from two open label studies (n=30) and two case series (n=55). No conclusion could be reached on photochemotherapy UVA radiation (PUVA) due to insufficient evidence from one case series (n=2) and two case reports (n=2).Antibiotics: The authors stated that the efficacy of antibiotics remained controversial; grade C evidence came from one RCT (n=4), one open-label study (n=3), two case series (n=6) and one case report (n=1).Retinoids: Etretinate was effective for pustular and erythrodermic psoriasis, but side effects were common; grade C evidence came from three case series (n=17), one open-label study (n=3) and one case report (n=1). No conclusion could be reached on acitretin due to insufficient evidence (one case report, n=1). The authors stated that the efficacy of cyclosporine was ambiguous; grade C evidence came from two case series (n=7) and two case reports (n=2). Methotrexate was effective in moderate to severe psoriasis. Most evidence on methotrexate was about plague psoriasis. Short-term side effects were generally mild and treatable. Grade C evidence on methotrexate came from four case series (n= 45) and four case reports (n=4). Biologics: Etanercept was effective for plaque psoriasis. Short-term side effects were generally infections. Grade A evidence came from one RCT (n=211), two case series (n=7) and four case reports (n=4). No conclusion could be reached about infliximab due to insufficient evidence (four case reports, n=4).
XCL: Calcipotriene with or without corticosteroids was the treatment of choice for childhood psoriasis followed by dithranol; methotrexate was the systemic treatment of choice.
XCM: The review question was clearly stated. Inclusion criteria were broad. Three relevant databases were searched. Some attempts were made to minimise language bias. No attempts were made to minimise publication bias. Appropriate methods were used to minimise reviewer error and bias during the review process. Apart from blinding, study validity was not assessed and so results from these studies and any synthesis may not have been reliable. Given the diversity among studies, a narrative synthesis was appropriate. Evidence on specific treatments was was limited: based at most on one RCT of unknown quality plus other studies of less reliable design. The conclusions should be interpreted with caution.
XIM: Practice: The authors stated that the treatment of choice for childhood psoriasis was calcipotriene (if required combined with mild to moderate topical corticosteroids). Tacrolimus 0.1% could be added for treatment resistant flexural and/or facial psoriasis. For non-responders or patients with moderately to severe psoriasis, dithranol was recommended. Should the above be ineffective, short-term NB-UVB could be considered for adolescents. Antibiotics could be considered for guttate psoriasis and where streptococcal infection was suspected. The systemic treatment of choice was methotrexate with retinoids considered for pustular and erythematous psoriasis; cyclosporin should be considered only in exceptional cases. Etanercept should be considered as a third-line drug. Research: The authors stated that placebo-controlled RCTs were required to evaluate treatments for childhood psoriasis. They also stated that specialist centres should co-operate in developing a database to record all treatments.
KWO: Anthralin /therapeutic use; Anti-Bacterial Agents /therapeutic use; Calcineurin /antagonists & inhibitors; Calcitriol /analogs & derivatives /therapeutic use; Child; Dermatologic Agents /therapeutic use; Glucocorticoids /therapeutic use; Humans; Methotrexate /therapeutic use; Psoriasis /drug therapy
XAC: 12010003873
XID: 23 Mar 2011
XLA: English
XPR: 19900732
XUR: http://www.eblue.org/article/S0190-9622(09)00780-4/abstract
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12010003873

Record #8 **EXLCUDED / THIS ARTICLE WAS THE BASE OF OUR SEARCH**
TTL: Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation
AUT: Rodgers M, Epstein D, Bojke L, Yang H, Craig D, Fonseca T, Myers L, Bruce I, Chalmers R, Bujkiewicz S, Lai M, Cooper N, Abrams K, Spiegelhalter D, Sutton A, Sculpher M, Woolacott N
XSO: Health Technology Assessment
XYR: 2011
VOL: 15(10)
PAG: 1-134
XPT: Journal article
XST: This is a systematic review that meets the criteria for inclusion on DARE. If you would like us to consider prioritising the writing of a critical abstract for this review please e-mail CRD-DARE@york.ac.uk quoting the Accession Number of this record. Please note that priority is given to fast track requests from the UK National Health Service.
KWO: Antibodies, Monoclonal; Arthritis, Psoriatic; Humans; Immunoglobulin G; Receptors, Tumor Necrosis Factor
XAC: 12011001532
XID: 01 Jun 2011
XLA: English
XPR: 21333232
XUR: http://www.hta.ac.uk/2053
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12011001532

Record #9 **EXCLUDED / NOT CU ANALYSIS**
TTL: The risk of infection and malignancy with tumor necrosis factor antagonists in adults with psoriatic disease: a systematic review and meta-analysis of randomized controlled trials
AUT: Dommasch ED, Abuabara K, Shin DB, Nguyen J, Troxel AB Gelfand JM
XSO: Journal of the American Academy of Dermatology
XYR: 2011
VOL: 64(6)
PAG: 1035-1050
XPT: Journal article
XCC: The review concluded that there was a small increased risk of overall infections with short-term use of tumour necrosis factor antagonists for psoriasis and no difference in serious infections or malignancies. The review was generally well conducted and the authors' conclusions seem reliable. The authors noted that results were limited by the rarity of events and short follow-up.
XST: This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.
XAO: To examine the risks of infection and malignancy with use of tumour necrosis factor (TNF) antagonists in patients with psoriatic disease.
XSS: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov were searched from inception to 30 July 2009 for articles published in English. Search terms were reported. Unpublished trials were searched for in Clinical Study Results Database and by contacting industry sponsors and authors of published trials.
XVC: Validity assessment was undertaken using the Jadad criteria of randomisation, blinding and withdrawals and drop-outs to give a maximum score out of five. Trials that scored less than 3 on the Jadad scale were excluded. Two reviewers independently performed validity assessment.
XDE: Data were extracted on infections and malignancies on an intention-to-treat basis and were used to calculate odds ratios (ORs) and their 95% confidence intervals (CIs). Two reviewers independently performed data extraction.
XRR: Twenty RCTs (6,810 patients) were included in the review: seven trials of etanercept, six trials of adalimumab, five trials of infliximab, one trial of golimumab and one trial of certolizumab. Study sample sizes ranged from 60 to 1,212 patients.Infections (20 trials): Compared with placebo, TNF antagonists were associated with a statistically significant greater risk of any infection (OR 1.18, 95% CI 1.05 to 1.33, I2=21.6%, NNH=29) and a significantly greater risk of non-serious infections (OR 1.20, 95% CI 1.07 to 1.35). Subgroup analysis indicated statistically significantly more infections with TNF antagonists in patients with psoriatic arthritis (OR 1.22, 95% CI 1.06 to 1.40), but no statistically significant difference in patients with plaque

psoriasis (OR 1.09, 95% CI 0.87 to 1.37). Subgroup analysis by drug indicated that results were generally non-significant. There was no statistically significant difference in serious infections (OR 0.70, 95% CI 0.40 to 1.21). Results for incidence rate ratios were presented in the review. Malignancies (10 trials): Compared with placebo, TNF antagonists were not associated with a statistically significantly difference in malignancies (OR 1.48, 95% CI 0.71 to 3.09, I2=0%). Subgroup analysis by drug and indication were not significant. Results for incidence rate ratios were presented in the review.Sensitivity analysis using the random-effect model did not alter the results. There was no evidence of publication bias.
XCL: There was a small increased risk of overall infections with short-term use of TNF antagonists for psoriasis and no difference in serious infections or malignancies.
XCM: Inclusion criteria for the review were clearly defined. Several relevant data sources were searched. Only English language trials were included, so there was potential for language bias. Publication bias was assessed and not detected. Attempts were made to reduce reviewer error and bias during data extraction and quality assessment; the authors did not state whether the same methods were used for study selection. Study quality assessment was undertaken using a simple checklist; the authors did not report the results of this analysis, but all included trials scored at least 3. Trials were combined using appropriate statistical methods. Statistical heterogeneity was assessed. There was evidence of clinical heterogeneity, but this did not translate into statistical heterogeneity across trials. This was a well-conducted review and the authors' conclusions seem reliable. The authors noted that the results of the review were limited by the rarity of events and short duration of follow-up.
XIM: Practice: The authors did not state any implications for practice. Research: The authors stated that larger long-term studies with appropriate control groups were needed to assess the risk of infections and malignancies.
KWO: Antibodies, Monoclonal /adverse effects /therapeutic use; Arthritis, Psoriatic /drug therapy; Humans; Immunoglobulin Fab Fragments /adverse effects /therapeutic use; Immunoglobulin G /adverse effects /therapeutic use; Neoplasms /chemically induced /epidemiology; Odds Ratio; Polyethylene Glycols /adverse effects /therapeutic use; Psoriasis /drug therapy; Randomized Controlled Trials as Topic; Receptors, Tumor Necrosis Factor /therapeutic use; Tumor Necrosis Factor-alpha /antagonists & inhibitors; Tumor Necrosis Factors /antagonists & inhibitors
XAC: 12011003604
XID: 03 Feb 2012
XLA: English
XPR: 21315483
XUR: http://www.eblue.org/article/S0190-9622(10)01873-6/abstract
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12011003604

Record #10 **EXLUDED / NOT CU ANALYSIS**
TTL: Association between biologic therapies for chronic plaque psoriasis and cardiovascular events: a meta-analysis of randomized controlled trials
AUT: Ryan C, Leonardi CL, Krueger JG, Kimball AB, Strober BE, Gordon KB, Langley RG, de Lemos JA, Daoud Y, Blankenship D, Kazi S, Kaplan DH, Friedewald VE, Menter A
XSO: JAMA
XYR: 2011
VOL: 306(8)
PAG: 864-871
XPT: Journal article
XCC: The authors concluded that, compared with placebo, anti-interleukin 12 and 23 or anti-tumour necrosis factor alpha treatment did not significantly affect the rate of major adverse cardiovascular events, in patients with chronic plaque psoriasis, but the trials might have been underpowered to detect significant differences. This was a well-conducted review and the authors' conclusions reflect the evidence and seem appropriate.
XST: This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.
XAO: To assess the effects of biologic therapies for chronic plaque psoriasis, in terms of major adverse cardiovascular events (MACEs).
XSS: MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov were searched for articles from inception to May 2011, without language or publication status restrictions. Search terms were reported.
XVC: Six reviewers assessed trial quality based on adequacy of randomisation, allocation concealment, and blinding. Disagreements were resolved by consensus.

XDE: Six reviewers extracted the number of MACEs in patients receiving at least one dose of the intervention or placebo. Disagreements were resolved by consensus.
XRR: Twenty-two RCTs (10,183 patients) were included in the review; 7,037 patients received an intervention and 3,146 received placebo. All trials were adequately randomised and all were double blind. Fourteen RCTs (64%) reported adequate allocation concealment.For the overall analysis, there were no statistically significant differences in MACEs between patients given placebo and those treated with an anti-interleukin 12 and 23 (RD 0.012 events per person-year, 95% CI -0.001 to 0.026; nine RCTs), or with an anti-TNFα (RD -0.0005 events per person-year, 95% CI -0.010 to 0.009; 15 RCTs). Subgroup analyses by agent showed similar results. The sensitivity analyses did not significantly alter the results. There was no evidence of statistical heterogeneity for any comparison (I2 was zero).There was no evidence of publication bias.
XCL: Compared with placebo, an anti-interleukin 12 and 23 or an anti-TNFα treatment did not significantly affect the rate of MACEs in patients with chronic plaque psoriasis. The evidence highlighted the limitations of the RCTs in reliably interpreting the significance of rare events, as the trials were often underpowered and too short to detect rare or long-term adverse events.
XCM: The review question was clear and was supported by clearly defined inclusion criteria. A satisfactory literature search was undertaken and steps were taken to reduce the potential for language and publication bias. Publication bias was formally assessed and no evidence was found. The authors acknowledged that the reliability of their findings might have been reduced due to many of the trials reporting no events.Quality assessment of the trials suggested generally high quality, but withdrawals and intention-to-treat analysis were not assessed. Each stage of the review process was performed in duplicate, thereby reducing the potential for reviewer error and bias. There was no evidence of statistical heterogeneity and the analyses seem to have been appropriate. It was unclear if combining all doses of each agent affected the results, and there were approximately twice as many patients in the intervention group compared with the placebo group.This was a well-conducted review and the authors' conclusions reflect the evidence and seem appropriate.
XIM: Practice: The authors reported that the briakinumab trials had been discontinued pending investigations into possible links with MACEs and, until more definitive data become available, extreme vigilance for cardiovascular risk should be exercised when initiating anti-interleukin 12 and 23 agents in patients with psoriasis. The authors suggested that the limitations of RCTs in reliably detecting the significance of rare events should be considered for the benefit of the patients in these trials and those treated once the drugs are approved.Research: The authors did not state any implications for research.
KWO: Adolescent; Adult; Aged; Antibodies, Monoclonal /adverse effects /therapeutic use; Cardiovascular Diseases /chemically induced; Double-Blind Method; Humans; Immunoglobulin G /adverse effects /therapeutic use; Immunologic Factors /adverse effects /therapeutic use; Interleukin-12; Interleukin-23; Middle Aged; Myocardial Infarction /chemically induced; Placebos; Psoriasis /drug therapy; Randomized Controlled Trials as Topic; Receptors, Tumor Necrosis Factor /therapeutic use; Risk; Stroke /chemically induced; Tumor Necrosis Factor-alpha; Young Adult
XAC: 12011004961
XID: 07 Sep 2011
XLA: English
XPR: 21862748
XUR: http://jama.ama-assn.org/content/306/8/864.short
DBN: DARE
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=12011004961

Record #11 **EXLUDED / NOT PsA**
TTL: Economic evaluation of etanercept in the management of chronic plaque psoriasis
AUT: Lloyd A, Reeves P, Conway P, Reynolds A, Baxter G
XSO: British Journal of Dermatology
XYR: 2009
VOL: 160(2)
PAG: 380-386
XPT: Journal article
XST: This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.
AUC: The authors concluded that etanercept 50mg biw was cost-effective from the perspective of the UK NHS, especially in patients with severe disease or poor quality of life at baseline.
CMO: Cost-utility analysis
COM: Interventions: The authors justified their selection of the comparators. The 50mg biw dose was selected because a previous economic evaluation carried out by the National Institute of Health and Clinical Excellence

(NICE) considered only the 25mg biw dose. The selection of no intervention was appropriate as the background comparator as this patient population had already received conventional systemic therapy.Effectiveness/benefits: The use of three RCTs to derive efficacy data was appropriate as their design should ensure the validity and rigour of the clinical estimates. The authors stated that the trial samples were homogeneous with respect to their baseline characteristics, which enabled the pooling of data to provide a large sample of patients. The sensitivity analysis showed that the use of individual RCT data did not change the authors' conclusions. Apart from the baseline characteristics of the patient groups, no information on the methods of the three trials was provided. The use of the DLQI was appropriate because such a tool was validated for assessment of health-related quality of life in psoriasis. QALYs are a valid measure, which not only capture the impact of the interventions on quality of life, but also allow cross-disease comparisons to be made.Costs: The economic analysis was carried out satisfactorily. The cost categories were consistent with the perspective as were the sources of data, which reflected NHS official sources. Details on the unit costs, resource use, price year, and use of discounting were clearly reported, enhancing the transparency of the economic analysis. Key economic inputs were varied in the sensitivity analysis.Analysis and results: The methods used to synthesise the costs and benefits and to investigate the issue of uncertainty were appropriate. The results of both the base case and the sensitivity analyses were clearly presented. The authors compared the results of their study with other published evidence, which showed similar findings. The authors briefly discussed some potential limitations of their analysis, mainly related to the short-term clinical evidence, and stated that there was a need for future long-term naturalistic studies on etanercept.Concluding remarks: The study was well conducted and clearly presented, especially for the economic data. The authors' conclusions appear to be valid.
INT: The regimen of 12 weeks of etanercept 50mg biw was compared with no systemic therapy, and with 12 weeks of etanercept 25mg biw. Patients who responded to therapy were assumed to continue on etanercept 25mg biw intermittently.
LOC: UK/primary care.
RES: In the base case, for patients with a PASI and a DLQI of 10 or more at baseline, the 10-year costs were £47,587 with etanercept 50mg, £44,855 with 25mg, and £41,985 with no systemic therapy. The QALYs were 1.61 with 50mg, 1.37 with 25mg, and 0.70 with no therapy. Thus, the incremental cost per QALY was £6,217 (95% CI: 5,396 to 7,486) with 50mg over no therapy, £4,297 (95% CI: 3,671 to 5,231) with 25mg over no therapy, and £11,710 (95% CI: 8,407 to 26,642) with 50mg over 25mg.The sensitivity analysis showed that these findings were sensitive to variations in the assumed requirement for hospitalisation in untreated individuals and in the response rate achieved in re-treatment. Other alternative assumptions did not substantially alter the base-case findings. The incremental cost per QALY for etanercept 50mg always remained lower than £15,000 compared with no therapy and £20,000 compared with etanercept 25mg.The analysis identified a positive correlation between the incremental cost and incremental benefit, as successful treatment was associated with both higher benefits and increased management costs.
SUM: This study examined the cost-effectiveness of etanercept 50mg twice weekly in adults with moderate to severe plaque psoriasis, who were unable to take standard systemic therapies. The authors concluded that etanercept 50mg was cost-effective from the perspective of the UK National Health Service, especially in patients with severe disease or poor quality of life at baseline. The study was well conducted and clearly presented, especially for the economic data. The authors' conclusions appear to be valid.
XFU: Not stated.
XOP: Woolacott N, Bravo Vergel Y, Hawkins N, et al. Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. Health Technol Assess 2006;10:1-239.Papp KA, Tyring S, Lahfa M, et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. Br J Dermatol 2005;152:1304-12.Leonardi CL, Powers JL, Matheson RT, et al. Etanercept as monotherapy in patients with psoriasis. N Engl J Med 2003;349:2014-22.
CO1: United Kingdom
KWO: Adult; Anti-Inflammatory Agents, Non-Steroidal /economics /therapeutic use; Chronic Disease; Cost-Benefit Analysis; Drug Administration Schedule; Female; Humans; Immunoglobulin G /economics /therapeutic use; Male; Middle Aged; Models, Economic; Patient Selection; Psoriasis /drug therapy; Randomized Controlled Trials as Topic; Receptors, Tumor Necrosis Factor /therapeutic use; Severity of Illness Index
XAC: 22009100633
XID: 07 Oct 2009
XLA: English
XPR: 18808413
XUR: http://www3.interscience.wiley.com/cgi-bin/fulltext/121414238/PDFSTART
DBN: NHS EED
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=22009100633

Record #12 **EXLUDED / THIS ARTICLE WAS THE BASE OF OUR SEARCH**
TTL: Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation
AUT: Rodgers M, Epstein D, Bojke L, Yang H, Craig D, Fonseca T, Myers L, Bruce I, Chalmers R, Bujkiewicz S, Lai M, Cooper N, Abrams K, Spiegelhalter D, Sutton A, Sculpher M, Woolacott N
XSO: Health Technology Assessment
XYR: 2011
VOL: 15(10)
PAG: 1-329
XPT: Journal article
XST: This is an economic evaluation that meets the criteria for inclusion on NHS EED. If you would like us to consider prioritising the writing of a critical abstract for this economic evaluation please e-mail: CRD-NHSEED@york.ac.uk quoting the Accession Number of this record. Please note that priority is given to fast track requests from the UK National Health Service.
CO1: United Kingdom
KWO: Antibodies, Monoclonal /economics /therapeutic use; Anti-Inflammatory Agents /economics /therapeutic use; Anti-Inflammatory Agents, Non-Steroidal /economics /therapeutic use; Arthritis, Psoriatic /drug therapy /economics; Cost-Benefit Analysis; Humans; Immunoglobulin G /economics /therapeutic use; Receptors, Tumor Necrosis Factor /therapeutic use; Recombinant Fusion Proteins /economics /therapeutic use; Treatment Outcome; Tumor Necrosis Factor-alpha /economics /therapeutic use
XAC: 22011000397
XID: 22 Jun 2011
XLA: English
XPR: 16948890
DBN: NHS EED
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=22011000397

Record #13 INCLUDED
TTL: Cost-effectiveness of infliximab for the treatment of active and progressive psoriatic arthritis
AUT: Cummins E, Asseburg C, Punekar YS, Shore E, Morris J, Briggs A, Fenwick E
XSO: Value in Health
XYR: 2011
VOL: 14(1)
PAG: 15-23
XPT: Journal article
XST: This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.
AUC: The authors concluded that, infliximab was clinically effective and could be cost-effective compared with palliative care without biologic DMARDs.
CMO: Cost-utility analysis
COM: Interventions: The therapies were described and might be feasible in other settings.Effectiveness/benefits: It was unclear if a systematic review was undertaken to identify the effectiveness data, making it uncertain if all the best available evidence was used. The clinical trials included in the study should be consulted to assess their quality. The clinical effectiveness of the drugs and the utility values were based on indirect comparisons, which introduces uncertainty. These methods are likely to have been the best possible, but caution should be taken when interpreting the results.Costs: The costs appear to have been appropriate to the perspective. The resource quantities and unit costs were clearly presented. Assumptions were made in measuring these resources, but they appear to have been reasonable and comprehensive. The unit costs were from sources available to the general public, and they appear to have been of good quality.Analysis and results: The analytic approach was well described and appears to have been appropriate. The methods and results were well reported and the results were adequately assessed for uncertainty. The results of the one-way sensitivity analyses were fully reported, allowing the assessment of the impact of variations in key inputs. Some limitations were acknowledged, including the omission of adverse events, which it was considered would not significantly impact on the results.Concluding remarks: The methods, analyses, and results were clear and comprehensive. The conclusions reached by the authors appear to be appropriate.
INT: Infliximab, a tumour necrosis factor alpha (TNF-α) inhibitor, was administered twice weekly, as maintenance treatment, at the licensed dose of 5mg per kg. This was compared with palliative care,

which included non-biologic DMARDs without TNF-α inhibitors.
LOC: UK/community care.
RES: Compared with palliative care, the incremental cost per QALY ratios ranged from £16,942 to £23,022 for infliximab, depending on patient weight (60 to 80kg), and were £17,327 for etanercept, and £19,246 for adalimumab.For the subgroup of patients with significant psoriasis at baseline, the ratios ranged from £15,788 to £21,736 for infliximab, and were £16,613 for etanercept, and £18,170 for adalimumab.In the one-way sensitivity analyses, the results were sensitive to changes in the utility estimates, the HAQ score rebound after drug withdrawal, and halving the rate of natural HAQ score progression. Based on the probabilistic analysis, infliximab could be cost-effective at a willingness-to-pay as low as £12,000 per QALY in typical patients with psoriatic arthritis.
SUM: This study examined the costs and health outcomes of infliximab for the treatment of adults with active and progressive psoriatic arthritis, weighing 60 to 80kg, for whom treatment with at least two disease-modifying anti-rheumatic drugs (DMARDs) had failed. The authors concluded that, infliximab was clinically effective and could be cost-effective compared with palliative care without biologic DMARDs. The methods, analyses, and results were clear and comprehensive. The conclusions reached by the authors appear to be appropriate.
XOP: Bravo Vergel Y, Hawkins N, Claxton K, et al. The cost-effectiveness of etanercept and infliximab for the treatment of patients with psoriatic arthritis. Rheumatology 2007; 46: 1729-1735.
XFU: Funded by Schering-Plough Ltd.
CO1: United Kingdom
KWO: Antibodies, Monoclonal /economics /therapeutic use; Antirheumatic Agents /economics /therapeutic use; Arthritis, Psoriatic /drug therapy /economics; Cost-Benefit Analysis; Decision Support Techniques; Disease Progression; Female; Great Britain; Health Care Costs; Humans; Immunoglobulin G; Male; Middle Aged; Models, Econometric; Palliative Care /economics; Quality-Adjusted Life Years; Receptors, Tumor Necrosis Factor; Tumor Necrosis Factor-alpha /antagonists & inhibitors
XAC: 22011000617
XID: 22 Jun 2011
XLA: English
XPR: 21211482
XUR: http://www.sciencedirect.com/science/article/pii/S1098301510000173
DBN: NHS EED
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=22011000617

Record #14 INCLUDED
TTL: Modelling the cost-effectiveness of biologic treatments for psoriatic arthritis
AUT: Bojke L, Epstein D, Craig D, Rodgers M, Woolacott N, Yang H, Sculpher M
XSO: Rheumatology
XYR: 2011
VOL: 50(Supplement 4)
PAG: iv39-iv47
XPT: Journal article
XST: This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.
AUC: The authors concluded that etanercept appeared to be the most cost-effective treatment for active and progressive psoriatic arthritis. Further investigation was required to reduce the uncertainty around a number of key model parameters.
CMO: Cost-utility analysis
COM: Interventions: The interventions appear to have been appropriate comparators and to have included the usual practice in the authors' setting. These comparators might be suitable for other settings.Effectiveness/benefits: A systematic review and a Bayesian mixed-treatment comparison were conducted for the effectiveness data, which should have included all the best available evidence. Very little information was reported on this systematic review and evidence synthesis, and the other publication should be consulted to fully assess their quality. Most of the effectiveness data were from randomised controlled trials, which should have high validity. QALYs were an appropriate benefit measure, capturing the impact of the interventions on quality of life and survival. The details of the derivation of the utility values would have been useful to fully assess their validity.Costs: The perspective was clearly stated and those costs relevant to this perspective appear to have been included. The sources for the cost data were clearly reported and appear to have been appropriate for the setting. Most of the costs were presented as category totals, rather than individual items, which reduces the transparency of

the analysis. The costs were appropriately discounted and adjusted for inflation.Analysis and results: The costs and outcomes were synthesised in a probabilistic model, which was described and a diagram was given. The results were clearly reported. The impact of uncertainty in the inputs on the results was explored in probabilistic and one-way sensitivity analyses. The authors identified and discussed a number of limitations to their analysis, and these generally related to the lack of appropriate data.Concluding remarks: The methods appear to have been valid, and they and the results were clearly reported. The authors' conclusions seem appropriate.
INT: Palliative care, which did not include biologic therapy, was compared with adalimumab, etanercept, or infliximab.
LOC: UK/secondary care.
RES: The expected lifetime costs were £42,205 for palliative care, £66,408 for adalimumab, £72,178 for etanercept, and £89,107 for infliximab. The projected QALYs were 5.241 for palliative care, 6.642 for adalimumab, 7.115 for etanercept, and 7.430 for infliximab.Adalimumab was extendedly dominated, as its incremental cost-effectiveness ratio (ICER) was higher than that of the next more effective option (etanercept). The ICER for etanercept, compared with palliative care, was £15,986. The ICER for infliximab, compared with etanercept, was £53,750.At a willingness-to-pay (WTP) threshold of £20,000 per QALY, the probability that etanercept was cost-effective was 0.524. At a threshold of £30,000 per QALY, this increased to 0.566. The results were sensitive to a number of parameters including the length of the effect for biologic treatments, and the prescription costs.
SUM: The objective was to determine the cost-effectiveness of etanercept, infliximab, and adalimumab, compared with palliative care, for active and progressive psoriatic arthritis in patients with mild-to-moderate disease that had inadequately responded to standard treatment. The authors concluded that etanercept appeared to be most cost-effective, but further investigation was required for a number of key model parameters. The methods appear to have been valid, and they and the results were clearly reported. The authors' conclusions seem appropriate.
XFU: Funded by the NIHR Health Technology Assessment programme, UK.
CO1: United Kingdom
KWO: Adult; Antibodies, Monoclonal /economics /therapeutic use; Antirheumatic Agents /economics /therapeutic use; Arthritis, Psoriatic /drug therapy /economics; Biological Products /economics /therapeutic use; Cost-Benefit Analysis; Drug Costs /statistics & numerical data; Humans; Immunoglobulin G /economics /therapeutic use; Middle Aged; Models, Econometric; Quality-Adjusted Life Years; Receptors, Tumor Necrosis Factor /therapeutic use; Severity of Illness Index; Treatment Outcome; Tumor Necrosis Factor-alpha /antagonists & inhibitors
XAC: 22011001570
XID: 07 Dec 2011
XLA: English
XPR: 21859705
XUR: http://rheumatology.oxfordjournals.org/content/50/suppl_4/iv39.abstract
DBN: NHS EED
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=22011001570

Record #15 **EXLUDED / NOT CU ANALYSIS**
TTL: Adalimumab for the treatment of moderate to severe psoriatic arthritis
AUT: Bravo Vergel Y, Palmer S, Erhorn S, Young V, Brent S, Dyker A, Horsley W, Macfarlane K, Martin J, Reddy B, White S, Thomas S
XSO: Health Technology Assessment
PUB: NIHR Health Technology Assessment programme
XPT: HTA Technology Assessment Report
XST: This is a bibliographic record of a published health technology assessment from a member of INAHTA. No evaluation of the quality of this assessment has been made for the HTA database.
CO1: United Kingdom
KWO: Antibodies, Monoclonal; Anti-Inflammatory Agents; Arthritis, Psoriatic; Humans; Psoriasis; Tumor Necrosis Factor-alpha
XAC: 32010000051
XID: 03 Mar 2010
XLA: English
XUR: http://www.hta.ac.uk/1646
DBN: HTA
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32010000051

Record #16 **EXCLUDED / THIS ARTICLE WAS THE BASE OF OUR SEARCH**
TTL: Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation
AUT: Rodgers M, Epstein D, Bojke L, Yang H, Craig D, Fonseca T, Myers L, Bruce I, Chalmers R, Bujkiewicz S, Lai M, Cooper N, Abrams K, Spiegelhalter D, Sutton A, Sculpher M, Woolacott N
XSO: Health Technology Assessment
PUB: NIHR Health Technology Assessment programme
XYR: 2011
VOL: 15(10)
PAG: 1-329
XPT: HTA Technology Assessment Report
XST: This is a bibliographic record of a published health technology assessment from a member of INAHTA. No evaluation of the quality of this assessment has been made for the HTA database.
XAO: To determine the clinical effectiveness, safety and cost-effectiveness of etanercept, infliximab and adalimumab for the treatment of active and progressive PsA in patients who have an inadequate response to standard treatment (including DMARD therapy).
CO1: United Kingdom
KWO: Antibodies, Monoclonal; Anti-Inflammatory Agents; Arthritis, Psoriatic; Humans; Tumor Necrosis Factor-alpha
XAC: 32010000260
XID: 14 Apr 2010
XLA: English
XUR: http://www.hta.ac.uk/2053
DBN: HTA
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32010000260

Record #17 **EXLUDED / NOT CU ANALYSIS**
TTL: Etanercept for psoriasis and psoriatic arthritis
XSO: Lansdale, PA: HAYES, Inc
PUB: HAYES, Inc.
XYR: 2009
XPT: Report
XST: This is a bibliographic record of a published health technology assessment. No evaluation of the quality of this assessment has been made for the HTA database.Report may be purchased from http://www.hayesinc.com.
CO1: United States
KWO: Arthritis, Psoriatic; Humans; Immunoglobulin G; Immunosuppressive Agents; Psoriasis; Receptors, Tumor Necrosis Factor
XAC: 32010000858
XID: 01 Sep 2010
XLA: English
XUR: http://www.hayesinc.com/
DBN: HTA
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32010000858

*Record #18 **EXLUDED / NOT CU ANALYSIS**
TTL: [Infliximab in patients with arthritis psoriatic: systematic review of the clinical and economic literature]
AUT: Brodszky V, Pentek M, Gulacsi L
XSO: Budapest: Unit of Health Economics and Technology Assessment in Health Care (HUNHTA)
PUB: Unit of Health Economics and Technology Assessment in Health Care (HunHTA)
XYR: 2007
XPT: Report
XST: This is a bibliographic record of a published health technology assessment. The agency responsible for the publication, formerly a member of INAHTA, has subsequently been disbanded. No evaluation of the quality of this assessment has been made for the HTA database.
CO1: Hungary
KWO: Antibodies, Monoclonal; Antirheumatic Agents; Arthritis, Psoriatic; Humans; Review
XAC: 32010001762
XID: 05 Jan 2011
XLA: Hungarian, English

XUR: http://hecon.uni-corvinus.hu/download/english/publ/infliximab.hta.AP.2007.december.pdf
DBN: HTA
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32010001762

Record #19
TTL: Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis
AUT: National Institute for Health and Clinical Excellence
XSO: London: National Institute for Health and Clinical Excellence (NICE)
PUB: National Institute for Health and Clinical Excellence (NICE)
XYR: 2010
XPT: Report
XST: This is a bibliographic record of a published health technology assessment. No evaluation of the quality of this assessment has been made for the HTA database.
CO1: United Kingdom
KWO: Antibodies, Monoclonal; Antirheumatic Agents; Arthritis, Psoriatic; Humans; Receptors, Tumor Necrosis Factor; Tumor Necrosis Factor-alpha
XAC: 32011000069
XID: 26 Jan 2011
XLA: English
XUR: http://www.nice.org.uk/nicemedia/live/13110/50422/50422.pdf
DBN: HTA
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32011000069

Record #20 **EXCLUDED / TIHS HTA WAS REPLACED BY ANOTHER HTA WHICH SERVED AS BASE FOR OUR SEARCH (RODGERS ET AL 2011)**
TTL: Adalimumab for the treatment of psoriatic arthritis (replaced by TA199 etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis)
AUT: National Institute for Health and Clinical Excellence
XSO: London: National Institute for Health and Clinical Excellence (NICE)
PUB: National Institute for Health and Clinical Excellence (NICE)
XYR: 2007
XPT: Report
XST: This is a bibliographic record of a published health technology assessment. No evaluation of the quality of this assessment has been made for the HTA database.
CO1: United Kingdom
KWO: Antibodies, Monoclonal /therapeutic use; Anti-Inflammatory Agents /therapeutic use; Arthritis /drug therapy; Humans
XAC: 32011000415
XID: 23 Mar 2011
XLA: English
XUR: http://guidance.nice.org.uk/TA125
DBN: HTA
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32011000415

Record #21 **EXCLUDED / THIS IS A GUIDANCE**
TTL: Golimumab for the treatment of psoriatic arthritis
AUT: National Institute for Health and Clinical Excellence
XSO: London: National Institute for Health and Clinical Excellence (NICE)
PUB: National Institute for Health and Clinical Excellence (NICE)
XYR: 2011
XPT: Report
XST: This is a bibliographic record of a published health technology assessment. No evaluation of the quality of this assessment has been made for the HTA database.
CO1: United Kingdom
KWO: Antibodies, Monoclonal; Arthritis, Psoriatic; Humans
XAC: 32011000522
XID: 18 May 2011
XLA: English
XUR: http://www.nice.org.uk/nicemedia/live/13441/54169/54169.pdf
DBN: HTA

RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32011000522

Record #22 **EXCLUDED / ONGOING PROJECT**
TTL: Golimumab for the treatment of psoriatic arthritis
XSO: Health Technology Assessment
PUB: NIHR Health Technology Assessment programme
XPT: HTA Technology Assessment Report
XST: This is a bibliographic record of an ongoing health technology assessment being undertaken by a member of INAHTA. Links to the published report and any other relevant documentation will be added when available.
CO1: United Kingdom
KWO: Antibodies, Monoclonal /therapeutic use; Arthritis, Psoriatic /drug therapy; Humans
XAC: 32011000774
XID: 15 Jun 2011
XLA: English
XUR: http://www.hta.ac.uk/2320
DBN: HTA
RUR: http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?ID=32011000774

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