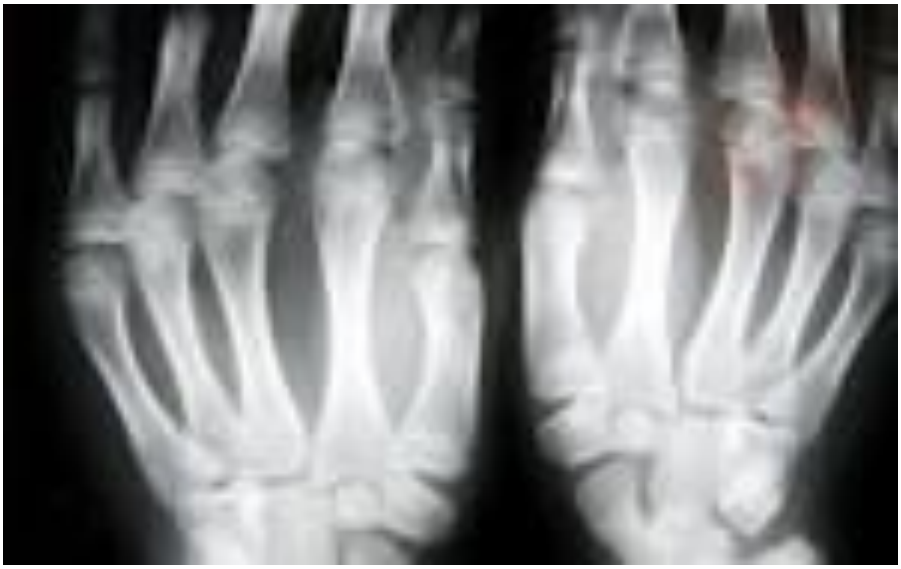
University Hospitals Bristol NHS
NHS Foundation Trust

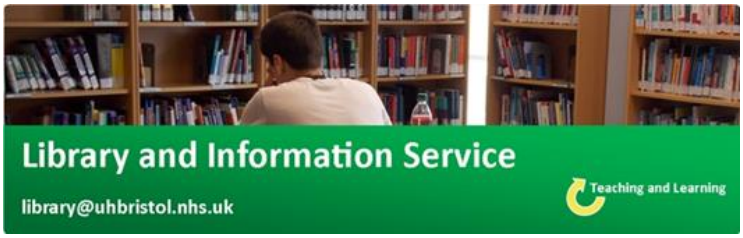
Rheumatology

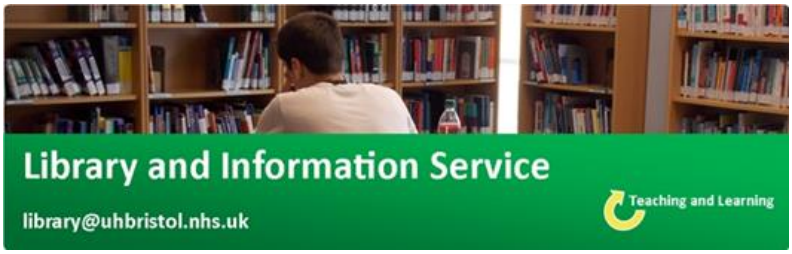
Current Awareness Newsletter



May 2016

Respecting everyone
Embracing change
Recognising success
Working together
Our hospitals.





Outreach

Your Outreach Librarian can help facilitate evidence-based practise for all Rheumatology staff, as well as assisting with academic study and research. We can help with **literature searching, obtaining journal articles and books**, and setting up individual **current awareness alerts**.

Literature Searching

We provide a literature searching service for any library member. For those embarking on their own research it is advisable to book some time with one of the librarians for a 1 to 1 session where we can guide you through the process of creating a well-focused literature research and introduce you to the health databases access via NHS Evidence.

Critical Appraisal Training

We also offer **one-to-one or small group training** in literature searching, accessing electronic journals, and critical appraisal/Statistics. These are essential courses that teach how to interpret clinical papers.

For more information, email: katie.barnard@uhbristol.nhs.uk

Books

Books can be searched for using SWIMS our online catalogue at www.swims.nhs.uk. Books and journals that are not available on site or electronically may be requested from other locations. Please email requests to: library@uhbristol.nhs.uk

Contents

Librarians on demand!

Do you urgently need to find evidence to support your treatment of a patient? Would you like immediate information about a particular therapy, practice, condition, or other clinical need?

The Library can provide swift assistance with a range of our services, including literature searches and access to full text articles.

You can discuss your **urgent literature search** needs with a librarian immediately by calling extension 20105. A librarian can also be with you in your clinical area usually within 15 minutes.

For **speedy article requests** and other library services, email library@uhbristol.nhs.uk. If you specify your urgent need, we will prioritise this.

Tables of Contents from Rheumatology journals

The links below will take you to the full Tables of Contents.

If you require full articles please email: library@uhbristol.nhs.uk

Rheumatology
May 2016, Volume 55, Issue 5

Annals of Rheumatic Disease
May 2016, Volume 75, Issue 5

Arthritis & Rheumatology
May 2016, Volume 68, Issue 5

Journal of Rheumatology
May 2016, Volume 43, Issue 5

Osteoporosis International
May 2016, Volume 27, Issue 5

New NICE Guidance

QS121	Antimicrobial stewardship
NG46	Controlled drugs: safe use and management
NG45	Routine preoperative tests for elective surgery

Quick Exercise

Heterogeneity

Heterogeneity is the extent to which studies brought together in a systematic review demonstrate variation across a range of key variables.

Match the different types of heterogeneity:

1. Statistical heterogeneity (conventionally just known as 'heterogeneity')
2. Methodological heterogeneity
3. Clinical heterogeneity

A. Variability in the participants, interventions and outcomes studied
B. Variability in study design and risk of bias
C. Variability in the intervention effects being evaluated in the different studies

Answers: 1C, 2B, 3A

Upcoming Lunchtime Drop-in Sessions

The **Library and Information Service** provides free specialist information skills training for all UHBristol staff and students. To book a place, email: **library@uhbristol.nhs.uk**

If you're unable to attend we also provide **one-to-one** or **small group** sessions. Contact **library@uhbristol.nhs.uk** or **katie.barnard@uhbristol.nhs.uk** to arrange a session.

May (1pm)

Weds 4th	**Understanding articles**
Thurs 12th	**Statistics**
Fri 20th	**Information resources**
Tues 31st	**Literature Searching**

June (12pm)

Weds 8th	**Understanding articles**
Thurs 16th	**Statistics**
Fri 24th	**Information resources**

Current Awareness database articles

If you require full articles please email: library@uhbristol.nhs.uk

Title: Self-Reported Knee Instability Before and After Total Knee Replacement Surgery.
Citation: Arthritis care & research, Apr 2016, vol. 68, no. 4, p. 463-471, 2151-4658 (April 2016)
Author(s): Fleeton, Genevieve, Harmer, Alison R, Nairn, Lillias, Crosbie, Jack, March, Lyn, Crawford, Ross, van der Esch, Martin, Fransen, Marlene

Abstract: To determine the prevalence and burden of pain and activity limitations associated with retaining presurgery self-reported knee instability 6 months after total knee replacement (TKR) surgery and to identify early potentially modifiable risk factors for retaining knee instability in the operated knee after TKR surgery. A secondary analysis was performed using measures obtained from 390 participants undergoing primary unilateral TKR and participating in a randomized clinical trial. Self-reported knee instability was measured using 2 items from the Activities of Daily Living Scale of the Knee Outcome Survey. Outcome measures were knee pain (range 0-20) and physical function (range 0-68) on the Western Ontario and McMaster Universities Arthritis Index (WOMAC), stair-climb power, 50-foot walk time, knee range of motion, and isometric knee flexion and extension strength. In this study, 72% of participants reported knee instability just prior to surgery, with 32% retaining instability in the operated knee 6 months after surgery. Participants retaining operated knee instability had significantly more knee pain and activity limitations 6 months after surgery, with mean ± SD WOMAC scores of 4.8 ± 3.7 and 17.5 ± 11.1, respectively, compared to participants without knee instability, with 2.9 ± 3.1 and 9.8 ± 9.2. The multivariable predictor model for retained knee instability included a high comorbidity score (>6), low stair-climb power (<150 watts), more pain in the operated knee (>7 of 20), and younger age (<60 years). Self-reported knee instability is highly prevalent before and after TKR surgery and is associated with a considerable burden of pain and activity limitation in the operated knee. Increasing lower extremity muscle power may reduce the risk of retaining knee instability after TKR surgery. © 2016, American College of Rheumatology.

Title: Prognosis of Pain and Physical Functioning in Patients With Knee Osteoarthritis: A Systematic Review and Meta-Analysis.
Citation: Arthritis care & research, Apr 2016, vol. 68, no. 4, p. 481-492, 2151-4658 (April 2016)
Author(s): de Rooij, Mariëtte, van der Leeden, Marike, Heymans, Martijn W, Holla, Jasmijn F M, Häkkinen, Arja, Lems, Willem F, Roorda, Leo D, Veenhof, Cindy, Sanchez-Ramirez, Diana C, de Vet, Henrica C W, Dekker, Joost

Abstract: To systematically summarize the literature on the course of pain in patients with knee osteoarthritis (OA), prognostic factors that predict deterioration of pain, the course of physical functioning, and prognostic factors that predict deterioration of physical functioning in persons with knee OA. A search was conducted in PubMed, CINAHL, Embase, Psych-INFO, and SPORTDiscus up to January 2014. A meta-analysis and a qualitative data synthesis were performed. Of the 58 studies included, 39 were of high quality. High heterogeneity across studies (I(2) >90%) and within study populations (reflected by large SDs of change scores) was found. Therefore, the course of pain and physical functioning was interpreted to be indistinct. We found strong evidence for a number of prognostic factors predicting deterioration in pain (e.g., higher knee pain at baseline, bilateral knee symptoms, and depressive symptoms). We also found strong evidence for a number of prognostic factors predicting deterioration in physical functioning (e.g., worsening in radiographic OA,

worsening of knee pain, lower knee extension muscle strength, lower walking speed, and higher comorbidity count). Because of high heterogeneity across studies and within study populations, no conclusions can be drawn with regard to the course of pain and physical functioning. These findings support current research efforts to define subgroups or phenotypes within knee OA populations. Strong evidence was found for knee characteristics, clinical factors, and psychosocial factors as prognostics of deterioration of pain and physical functioning.

Title: Long-Term Outcomes of Patients With Recent-Onset Rheumatoid Arthritis After 10 Years of Tight Controlled Treatment: A Randomized Trial.
Citation: Annals of internal medicine, Apr 2016, vol. 164, no. 8, p. 523-531, 1539-3704 (April 19, 2016)
Author(s): Markusse, Iris M, Akdemir, Gülsah, Dirven, Linda, Goekoop-Ruiterman, Yvonne P M, van Groenendael, Johannes H L M, Han, K Huub, Molenaar, T H Esmeralda, Le Cessie, Saskia, Lems, Willem F, van der Lubbe, Peter A H M, Kerstens, Pit J S M, Peeters, André J, Ronday, H Karel, de Sonnaville, Peter B J, Speyer, Irene, Stijnen, Theo, Ten Wolde, Saskia, Huizinga, Tom W J, Allaart, Cornelia F

Abstract: Treat-to-target therapy is effective for patients with rheumatoid arthritis (RA), but long-term results of continued targeted treatment are lacking. To evaluate long-term outcomes in patients with early RA after 10 years of targeted treatment in 4 treatment strategies. Randomized trial. (Nederlands Trial Register: NTR262 and NTR265). The Netherlands. 508 patients with early active RA. Sequential monotherapy (strategy 1), step-up combination therapy (strategy 2), or initial combination therapy with prednisone (strategy 3) or with infliximab (strategy 4), all followed by targeted treatment aiming at low disease activity. Functional ability (Health Assessment Questionnaire [HAQ] score) and radiographic progression (Sharp-van der Heijde score) were primary end points. Survival in the study population was compared with the general population using the standardized mortality ratio. 195 of 508 of patients (38%) dropped out of the study (28% in strategy 4 vs. 40% to 45% in strategies 1 to 3, respectively). At year 10, mean HAQ score (SD) was 0.57 (0.56); 53% and 14% of patients were in remission and drug-free remission, respectively, without differences among the strategies. Over 10 years, mean HAQ scores were 0.69, 0.72, 0.64, and 0.58 in strategies 1 to 4, respectively (differences not clinically relevant). Radiographic damage was limited for all strategies, with mean Sharp-van der Heijde estimates during follow-up of 11, 8, 8, and 6 in strategies 1 to 4, respectively (P = 0.15). Standardized mortality ratio was 1.16 (95% CI, 0.92 to 1.46) based on 72 observed and 62 expected deaths, with similar survival among the 4 strategies (P = 0.81). Dropout rate varied by strategy. In patients with early RA, initial (temporary) combination therapy results in faster clinical improvement and targeted treatment determines long-term outcomes. Drug-free remission, with prevention of functional deterioration and clinically relevant radiographic damage, and normalized survival are realistic outcomes. Dutch College of Health Insurance Companies, Schering-Plough, and Janssen.

Title: What are the effects of medication adherence interventions in rheumatic diseases: a systematic review.
Citation: Annals of the rheumatic diseases, Apr 2016, vol. 75, no. 4, p. 667-673, 1468-2060 (April 2016)
Author(s): Galo, Jessica S, Mehat, Pavandeep, Rai, Sharan K, Avina-Zubieta, Antonio, De Vera, Mary A

Abstract: Consistent reports of suboptimal treatment adherence among patients with inflammatory arthritis underscore the importance of understanding how adherence can be promoted and supported. Our objectives were to identify and classify adherence interventions; and assess the evidence on the effects of adherence interventions on outcomes of patients with rheumatic diseases. We conducted a mapped search of Medline, Embase and International Pharmaceutical Abstract databases to identify studies meeting inclusion criteria of: (1) patient population with inflammatory arthritis; (2) evaluation of an intervention or programme targeting medication adherence directly or indirectly; (3) reporting of one or more measures of medication adherence and disease outcome; (4) publication in English, French or Spanish. For our first objective, we applied a structured framework to classify interventions according target (patient vs provider), focus (educational vs behavioural vs affective), implementation (generalised vs tailored), complexity (single vs multifaceted) and provider. For the second objective, we appraised the evidence of effects of interventions on adherence and disease outcomes. We identified 23 studies reporting adherence interventions that directly or indirectly addressed treatment adherence in rheumatic diseases and further appraised included RCTs. Interventions that were shown to impact adherence outcomes were generally interventions directed at adherence, tailored to patients and delivered by a healthcare provider. For interventions that were not shown to have impacts, reasons may be those related to the intervention itself, patient characteristics or study methodology. Our systematic review shows limited research on adherence interventions in rheumatic diseases with inconsistent impacts on adherence or disease outcome. Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://www.bmj.com/company/products-services/rights-and-licensing/

Title: Does disease activity at start of biologic therapy influence work-loss in RA patients?
Citation: Rheumatology (Oxford, England), Apr 2016, vol. 55, no. 4, p. 729-734, 1462-0332 (April 2016)
Author(s): Olofsson, Tor, Johansson, Kari, Eriksson, Jonas K, van Vollenhoven, Ronald, Miller, Heather, Petersson, Ingemar F, Askling, Johan, Neovius, Martin

Abstract: To compare work-loss in RA patients starting their first biologic with high vs moderate disease activity. We identified all RA patients aged 20-63 years in the Swedish Biologics Register who started their first biologic 2007-09 with high disease activity (DAS28 >5.1; n = 868) or moderate disease activity (DAS28 3.2-5.1; n = 854). Work days lost, defined as sick leave and disability pension days from the Swedish Social Insurance Agency, were assessed over 5 years after first bio-start. We estimated between-group mean differences adjusted for age, sex, calendar year, education level, disease duration, comorbidities and work-loss the month before bio-start. During 5 years after anti-TNF start, mean monthly work days lost declined from 16.0 to 9.2 (42%; P < 0.001) in patients with high disease activity at baseline and from 12.0 to 7.2 (40%; P < 0.001) in patients with moderate disease activity, with no between-group difference (adjusted mean difference 0.81; 95% CI - 0.44, 2.05). Accumulated 5-year work-loss was, however, higher in the high activity group (724 vs 548 days; adjusted mean difference 70; 95% CI 20, 120), but after stratification on baseline disability pension status, no differences in accumulated work-loss were detected. Substantial work-loss was seen in both patients with high and patients with moderate disease activity at anti-TNF start, with a 5-year decline in mean monthly work days lost by ∼40% in both groups and no between-group difference. Accumulated work-loss over 5 years was higher in the high-activity group, which may be explained by differences in baseline disability pension status. © The Author 2015. Published by

---

Title: Pulsed electromagnetic fields in knee osteoarthritis: a double blind, placebo-controlled, randomized clinical trial.
Citation: Rheumatology (Oxford, England), Apr 2016, vol. 55, no. 4, p. 755-762, 1462-0332 (April 2016)
Author(s): Bagnato, Gian Luca, Miceli, Giovanni, Marino, Natale, Sciortino, Davide, Bagnato, Gian Filippo

Abstract: This trial aimed to test the effectiveness of a wearable pulsed electromagnetic fields (PEMF) device in the management of pain in knee OA patients. In this randomized [with equal randomization (1:1)], double-blind, placebo-controlled clinical trial, patients with radiographic evidence of knee OA and persistent pain higher than 40 mm on the visual analog scale (VAS) were recruited. The trial consisted of 12 h daily treatment for 1 month in 60 knee OA patients. The primary outcome measure was the reduction in pain intensity, assessed through VAS and WOMAC scores. Secondary outcomes included quality of life assessment through the 36-item Medical Outcomes Study Short-Form version 2 (SF-36 v2), pressure pain threshold (PPT) and changes in intake of NSAIDs/analgesics. Sixty-six patients were included, and 60 completed the study. After 1 month, PEMF induced a significant reduction in VAS pain and WOMAC scores compared with placebo. Additionally, pain tolerance, as expressed by PPT changes, and physical health improved in PEMF-treated patients. A mean treatment effect of -0.73 (95% CI - 1.24 to - 0.19) was seen in VAS score, while the effect size was -0.34 (95% CI - 0.85 to 0.17) for WOMAC score. Twenty-six per cent of patients in the PEMF group stopped NSAID/analgesic therapy. No adverse events were detected. These results suggest that PEMF therapy is effective for pain management in knee OA patients and also affects pain threshold and physical functioning. Future larger studies, including head-to-head studies comparing PEMF therapy with standard pharmacological approaches in OA, are warranted. ClinicalTrials.gov, http://www.clinicaltrials.gov, NCT01877278. © The Author 2015. Published by Oxford University Press on behalf of the British Society for Rheumatology.

Title: Efficacy and safety of biological agents for systemic juvenile idiopathic arthritis: a systematic review and meta-analysis of randomized trials.
Citation: Rheumatology (Oxford, England), Apr 2016, vol. 55, no. 4, p. 669-679, 1462-0332 (April 2016)
Author(s): Tarp, Simon, Amarilyo, Gil, Foeldvari, Ivan, Christensen, Robin, Woo, Jennifer M P, Cohen, Neta, Pope, Tracy D, Furst, Daniel E

Abstract: To define the optimal biologic agent for systemic JIA (sJIA) based on safety and efficacy data from a randomized controlled trial (RCT). Through a systematic literature search, sJIA RCTs evaluating biologic agents were identified. The primary efficacy outcome was defined as a 30% improvement according to the modified American College of Rheumatology Paediatric 30 response criteria (JIA ACR30). The primary safety outcome was defined as serious adverse events (SAEs). Outcomes were analysed by pairwise and network meta-analyses. The quality of evidence between biologic agents was assessed by applying the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. From the 493 citations originally identified, 5 RCTs were eligible for inclusion-one each for anakinra, canakinumab and tocilizumab and two for rilonacept: all vs placebo. While all were effective, the network meta-analysis indicated with low-quality evidence (due to indirect comparison and inconsistency) that rilonacept-treated patients were less likely to respond than those treated with canakinumab [odds ratio (OR) 0.10 (95% CI 0.02,

0.38), P = 0.001] or tocilizumab [OR 0.12 (95% CI 0.03, 0.44), P = 0.001]. Risks of SAEs were similar among the biologic agents (supported by very low-quality evidence) and not different from placebo. Despite heterogeneous eligibility criteria and study designs across the five studies and different modified JIA ACR30 criteria, this meta-analysis of short-term RCTs presents empirical evidence that canakinumab and tocilizumab are more effective than rilonacept. Biologic agents in sJIA seem safe and comparable with respect to SAE risk in the short term.

Title: The majority of patients do not store their biologic disease-modifying antirheumatic drugs within the recommended temperature range.
Citation: Rheumatology (Oxford, England), Apr 2016, vol. 55, no. 4, p. 704-709, 1462-0332 (April 2016)
Author(s): Vlieland, Nicolaas D, Gardarsdottir, Helga, Bouvy, Marcel L, Egberts, Toine C G, van den Bemt, Bart J F

Abstract: To monitor whether biologic DMARD (bDMARD) home storage temperatures comply with the manufacturers' Summary of Product Characteristics (SmPC) recommendations. This observational study included consenting adult patients from eight Dutch pharmacies who received their bDMARDs with a validated temperature logger. Patients were instructed to store their packages according to standard label instructions and to return the temperature logger(s) after use. Primary outcome was defined as the proportion of patients that stored their bDMARDs within the SmPC recommended temperature range. In addition, the proportion of patients storing bDMARDs below 0°C or above 25 °C for longer than two consecutive hours was estimated. A total of 255 (87.0%) patients (mean age 53.2 (s.d.; 13.1) years, 51.4% female) returned their temperature logger(s) to the pharmacy. Of these, 17 patients (6.7%) stored their bDMARD within the recommended temperature range. The proportion of the patients that stored their bDMARD for more than 2 h consecutive time below 0°C or above 25°C was respectively 24.3% (median duration: 3.7 h (IQR 2.2 h; range 2.0-1,097.1 h) and 2.0% (median duration: 11.8 h (IQR 44.3 h; range 2.0-381.9 h). The majority of patients do not store their bDMARDs within the SmPC-recommended temperature range. © The Author 2015. Published by Oxford University Press on behalf of the British Society for Rheumatology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

Title: Why Do Patients with Chronic Inflammatory Rheumatic Diseases Discontinue Their Biologics? An Assessment of Patients' Adherence Using a Self-report Questionnaire.
Citation: The Journal of rheumatology, Apr 2016, vol. 43, no. 4, p. 724-730, 0315-162X (April 2016)
Author(s): Betegnie, Anne-Laure, Gauchet, Aurélie, Lehmann, Audrey, Grange, Laurent, Roustit, Matthieu, Baudrant, Magalie, Bedouch, Pierrick, Allenet, Benoît

Abstract: Concerns have been raised about nonadherence behavior among patients with chronic inflammatory rheumatic diseases (CIRD) receiving biologics. This nonadherence may be caused by various factors. The main objective was to explain why patients discontinue their biologics of their own accord. A quantitative and descriptive study was performed using a self-report questionnaire that was sent through the Internet to members of different patient associations. Sociodemographic data, medical and therapeutic history, management of biologic administration, previous experiences, and patients' beliefs and perceptions about treatment efficacy and side effects were studied to explain self-discontinuation (SD). A total of 581 patients answered the questionnaire between June 16, 2012, and July 4, 2012, including patients with ankylosing spondylitis (351/581,

60.4%), rheumatoid arthritis (196/581, 33.7%), psoriatic arthritis (30/581, 5.2%), and other CIRD (4/581, 0.7%). More than 1000 different biologics were described by the 581 patients, with a median of 2 lines per patient. Eighty-six patients discontinued their biologics of their own accord (14.8%). In a multivariate analysis, factors that were significantly related to SD were low level of pain, more than 1 line of biologics tried, self-administration of biologics, negative beliefs about the treatment, and a lack of medical and social support. Five predictive factors of this SD were identified, which should be assessed in routine with patients with CIRD receiving biologic treatment: pain, treatment history, self-administration of injections, negative beliefs about treatment, and a lack of perceived medical and social support.

Title: Tailored first-line biologic therapy in patients with rheumatoid arthritis, spondyloarthritis, and psoriatic arthritis.
Citation: Seminars in arthritis and rheumatism, Apr 2016, vol. 45, no. 5, p. 519-532, 1532-866X (April 2016)
Author(s): Cantini, Fabrizio, Niccoli, Laura, Nannini, Carlotta, Cassarà, Emanuele, Kaloudi, Olga, Giulio Favalli, Ennio, Becciolini, Andrea, Biggioggero, Martina, Benucci, Maurizio, Li Gobbi, Francesca, Grossi, Valentina, Infantino, Maria, Meacci, Francesca, Manfredi, Mariangela, Guiducci, Serena, Bellando-Randone, Silvia, Matucci-Cerinic, Marco, Foti, Rosario, Di Gangi, Marcella, Mosca, Marta, Tani, Chiara, Palmieri, Fabrizio, Goletti, Delia, Italian board for the TAilored BIOlogic therapy (ITABIO)

Abstract: A multidisciplinary expert panel, the Italian board for the TAilored BIOlogic therapy (ITABIO), was constituted to formulate evidence-based decisional statements for the first-line tailored biologic therapy in patient with rheumatoid arthritis (RA), spondyloarthritis (SpA), and psoriatic arthritis (PsA). Systematic review of the literature to identify English-language articles on the variables influencing the first-line biologic choice, including the efficacy and safety of the drug, the route of administration, the availability of response predictor biomarkers, the need of monotherapy, the patient socio-economic status, lifestyle, cultural level, personality, fertility and childbearing potential in women, the presence of comorbidities, the host-related risk factors for infection and latent tuberculosis infection (LTBI) reactivation, the cardiovascular (CV) risk, and costs. Some variables, including the patients' preference, the indication for anti-TNF monotherapy in potential childbearing women, and the intravenous route with dose titration in obese subjects resulted valid for all the three rheumatic conditions. Further, evidence of a better cost-effectiveness profile for etanercept (ETN) and biosimilar infliximab (IFX) in RA was found. Any biologic may be employed in absence of choice driving factors in RA. Otherwise, a high infection risk or LTBI positivity drive the choice toward abatacept (ABA), tocilizumab (TCZ), or ETN. TCZ should be the first choice if monotherapy is required. High rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) titers should drive the choice toward TCZ or ABA, while in patients at high CVD risk anti-TNF choice, with preference for ETN, seems appropriate. Presence of anterior uveitis or inflammatory bowel disease drives the choice to monoclonal antibody anti-TNFs (MoAb anti-TNFs). In PsA, ustekinumab (UTK), and to a lesser extent ETN, represents the first choice in patients at high infection and TB risk. Anti-TNFs or UTK choice is guided by skin or articular disease severity, enthesitis, and dactylitis, whereas ETN should be preferred if metabolic syndrome or high CV risk complicate PsA. Taking in account of multiple choice driving variables, first-line biologic therapy may be optimized in patients with RA, SpA, and PsA.

Title: Cerebrovascular Disease in Rheumatic Diseases: A Systematic Review and Meta-Analysis.
Citation: Stroke; a journal of cerebral circulation, Apr 2016, vol. 47, no. 4, p. 943-950, 1524-4628 (April 2016)
Author(s): Wiseman, Stewart J, Ralston, Stuart H, Wardlaw, Joanna M

Abstract: Some rheumatic diseases are associated with stroke. Less is known about associations with stroke subtypes or stroke risk by age. We quantified the association between stroke, its subtypes, and rheumatic diseases and identified when stroke risk is greatest. Searches of EMBASE (from 1980) and MEDLINE (from inception) to end 2014 and manual search of reference lists for studies of stroke and stroke subtypes in rheumatic diseases as well as studies measuring cerebrovascular disease from magnetic resonance imaging. Prior published meta-analyses and new pooled analyses of any stroke in rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, gout, and psoriasis show an excess risk of stroke over the general population with odds ratio (OR) ranging from 1.51 (95% confidence interval: 1.39-1.62) to 2.13 (1.53-2.98). New meta-analyses of stroke subtypes in rheumatoid arthritis [ischemic: OR, 1.64 (1.32-2.05); hemorrhagic: OR, 1.68 (1.11-2.53)] and systemic lupus erythematosus [ischemic: OR, 2.11 (1.66-2.67); hemorrhagic: OR, 1.82 (1.07-3.09)] show an excess risk of stroke over the general population. Stroke risk across rheumatic diseases is highest in those aged <50 years [OR, 1.79 (1.46-2.20)] and reduces relatively with ageing [>65 years: OR, 1.14 (0.94-1.38); difference P<0.007]. Inflammatory arthropathies conveyed higher stroke risk than noninflammatory diseases (OR, 1.3, 1.2-1.3). It was not possible to adjust ORs for risk factors or treatments. Risk of any stroke is higher in most rheumatic diseases than in the general population, particularly <50 years. Rheumatoid arthritis and systemic lupus erythematosus increase ischemic and hemorrhagic stroke risk by 60% to 100% relative to the general population. © 2016 American Heart Association, Inc.

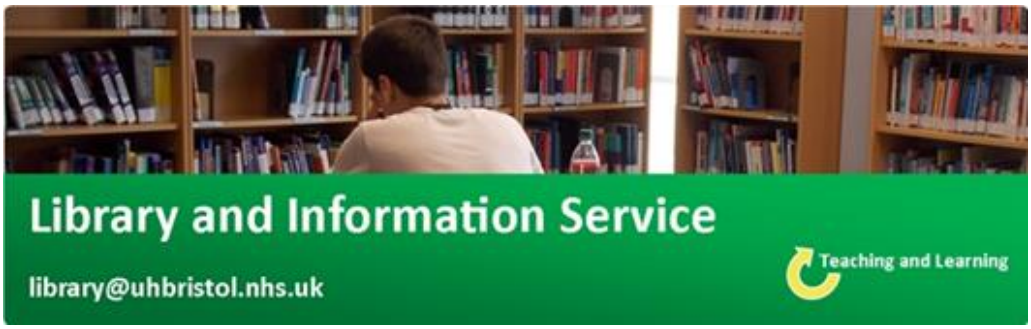
Title: The Challenge of Treating Early-Stage Rheumatoid Arthritis: The Contribution of Mixed Treatment Comparison to Choosing Appropriate Biologic Agents.
Citation: BioDrugs : clinical immunotherapeutics, biopharmaceuticals and gene therapy, Apr 2016, vol. 30, no. 2, p. 105-115, 1173-8804 (April 2016)
Author(s): Migliore, Alberto, Bizzi, Emanuele, Petrella, Lea, Bruzzese, Vincenzo, Cassol, Maurizio, Integlia, Davide

Abstract: Use of biologic drugs is approved for treatment in rheumatoid arthritis (RA), both in established disease and at the early stage of RA (ERA). Identification of ERA and an early therapeutic strategy would lead to greater clinical improvement. Only a few indirect comparisons of the efficacy of different biologic agents in established RA have been performed and, to date, no studies reporting direct comparisons have been performed in ERA. The aim of this study was to compare, by use of a mixed treatment comparison (MTC), the efficacy profiles of biologic agents in ERA. An extensive literature search was performed to identify results of randomized, controlled trials (RCTs) evaluating biologic agents at licensed doses to treat patients affected by ERA. The primary end points for the analysis were the American College of Rheumatology 20 % improvement (ACR20), ACR50, and ACR70 responses from baseline to various times of follow-up. WinBUGS 1.4 software (MRC Biostatistics Unit, Cambridge, UK) was used to perform the analyses. The MTC results are reported as the relative risk of a response for every single treatment coadministered with methotrexate, versus methotrexate plus placebo, which was used as a comparator in all RCTs. Ten scientific papers met the study inclusion criteria and were included in the analysis. Data on the use of infliximab, adalimumab, etanercept, abatacept, golimumab, and rituximab were included. No studies reported on the use of certolizumab pegol or tocilizumab in ERA. All biologic agents coadministered with methotrexate proved to be more efficacious than methotrexate plus placebo in inducing ACR20, ACR50, and ACR70 responses. The biologic agent characterized by the highest probability of inducing an ACR70 response was adalimumab (33.28 %). Etanercept was the biologic agent with the highest probability of inducing ACR20 and ACR50 responses, in comparison with all other biologic agents, with probability rates of 62.95 and 37.1 %, respectively. In our analysis, adalimumab proved to be the biologic agent with the highest probability of inducing an ACR70 response in patients affected by

ERA, while etanercept was the biologic agent with the highest probability of inducing ACR50 and ACR20 responses.

Title: An indirect comparison and cost per responder analysis of adalimumab, methotrexate and apremilast in the treatment of methotrexate-naïve patients with psoriatic arthritis.
Citation: Current medical research and opinion, Apr 2016, vol. 32, no. 4, p. 721-729, 1473-4877 (April 2016)
Author(s): Betts, Keith A, Griffith, Jenny, Friedman, Alan, Zhou, Zheng-Yi, Signorovitch, James E, Ganguli, Arijit

Abstract: Objective Apremilast was recently approved for the treatment of active psoriatic arthritis (PsA). However, no studies compare apremilast with methotrexate or biologic therapies, so its relative comparative efficacy remains unknown. This study compared the response rates and incremental costs per responder associated with methotrexate, apremilast, and biologics for the treatment of active PsA. Methods A systematic literature review was performed to identify phase 3 randomized controlled clinical trials of approved biologics, methotrexate, and apremilast in the methotrexate-naïve PsA population. Using Bayesian methods, a network meta-analysis was conducted to indirectly compare rates of achieving a ≥20% improvement in American College of Rheumatology component scores (ACR20). The number needed to treat (NNT) and the incremental costs per ACR20 responder (2014 US$) relative to placebo were estimated for each of the therapies. Results Three trials (MIPA for methotrexate, PALACE-4 for apremilast, and ADEPT for adalimumab) met all inclusion criteria. The NNTs relative to placebo were 2.63 for adalimumab, 6.69 for apremilast, and 8.31 for methotrexate. Among methotrexate-naïve PsA patients, the 16 week incremental costs per ACR20 responder were $3622 for methotrexate, $26,316 for adalimumab, and $45,808 for apremilast. The incremental costs per ACR20 responder were $222,488 for apremilast vs. methotrexate. Conclusion Among methotrexate-naive PsA patients, adalimumab was found to have the lowest NNT for one additional ACR20 response and methotrexate was found to have the lowest incremental costs per ACR20 responder. There was no statistical evidence of greater efficacy for apremilast vs. methotrexate. A head-to-head trial between apremilast and methotrexate is recommended to confirm this finding.



The Library

Level 5

Education Centre

University Hospitals Bristol

Staffed: 8.00 am—17.00 pm, Monday to Friday

Swipe Access: 7.00 am—23.00pm, 7 days a week

Contact the Rheumatology Outreach librarian:

katie.barnard@uhbristol.nhs.uk

www.uhbristol.nhs.uk/for-clinicians/

library-and-information-service