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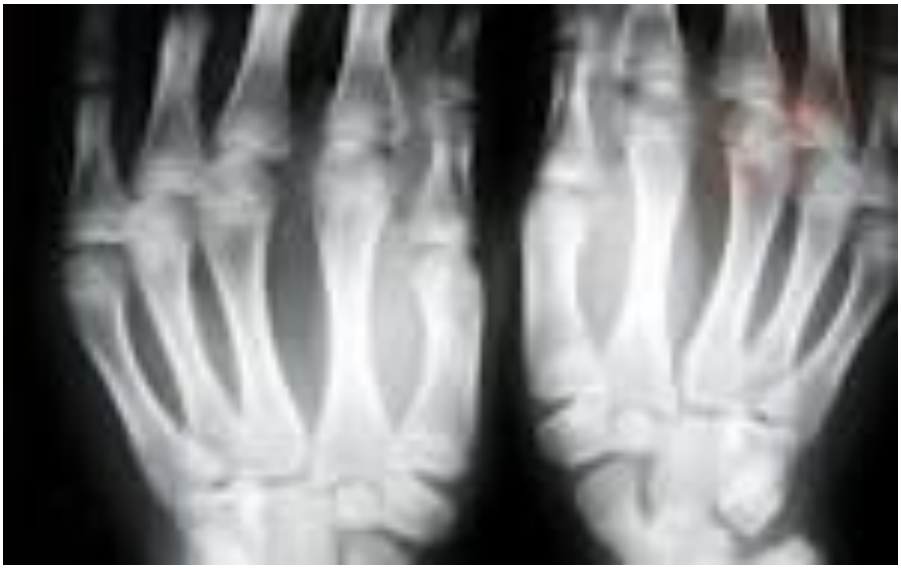
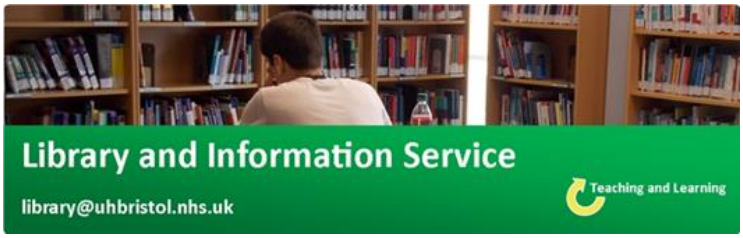
Rheumatology

Current Awareness Newsletter



Winter 2016

Respecting everyone
Embracing change
Recognising success
Working together
Our hospitals.



Training Sessions 2016/17

All sessions are 1 hour

December (12.00)

Fri 16th	**Literature Searching**
Mon 20th	**Critical Appraisal**

January (13.00)

Tues 10th	**Literature Searching**
Wed 18th	**Critical Appraisal**
Thur 26th	**Statistics**

February (12.00)

Fri 3rd	**Literature Searching**
Mon 6th	**Critical Appraisal**
Tues 14th	**Statistics**
Wed 22nd	**Literature Searching**

Your Outreach Librarian – Jo Hooper

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Contents

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New Additions to NICE, the Cochrane Library and UptoDate

NICE National Institute for Health and Care Excellence

BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding. Part I : standard and biologic disease modifying anti-rheumatic drugs and corticosteroids [PDF]

Source: British Society for Rheumatology - BSR - 10 January 2016 - Publisher: British Society for Rheumatology (BSR)

This guideline is intended for use by healthcare professionals who are currently (or considering) treating women who are planning pregnancy, currently pregnant or breastfeeding with any of the drugs listed in this document. Recommendations for men trying to...

Read Summary
- **More:** Guidance

Secukinumab for active ankylosing spondylitis after treatment with non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors - guidance (TA407)

Source: National Institute for Health and Care Excellence - NICE - 28 September 2016

Evidence-based recommendations on secukinumab (Cosentyx) for ankylosing spondylitis (spondyloartritis) that has not responded well enough to conventional....

Read Summary
- **More:** Guidance
- **More:** Medicines Current Awareness
- **More:** Drug Best Practice Guidance

Cochrane Library

Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying anti-rheumatic drugs for rheumatoid arthritis: A network meta-analysis.

Glen S Hazlewood , Cheryl Barnabe , George Tomlinson , Deborah Marshall , Daniel JA Devoe and Claire Bombardier

Online Publication Date: August 2016

UpToDate®

OpenAthens login required. Register here: https://openathens.nice.org.uk/

- **Overview of biologic agents and kinase inhibitors in the rheumatic diseases**
  - TNF inhibition
  - IL-1 inhibition
  - IL-6 inhibition
  - Biosimilars for biologic agents
  - Summary
- **Treatment of rheumatoid arthritis in adults resistant to initial nonbiologic DMARD therapy**
  - Approach to treatment with DMARDs
  - Resource-poor settings
  - Principles of management
  - Reevaluation and monitoring
  - Summary and recommendations
- **Cytokine networks in rheumatic diseases: Implications for therapy**
  - Anti-TNF antibodies
  - Soluble TNF receptors

Summary

BSR The British Society for Rheumatology

NICE accredited www.nice.org.uk/accreditation

http://www.rheumatology.org.uk/resources/guidelines/

Current guidelines	Produced	Due for revision
NEW BSR and BHPR guideline for the treatment of axial spondyloarthritis (including ankylosing spondylitis) with biologics **Executive summary** **Full Guideline**	2016 NICE accredited	2019
BSR and BHPR guideline for the treatment of systemic sclerosis **Executive summary** **Full guidelines**	2016 NICE accredited	2019

Prescribing for rheumatological conditions in pregnancy and breastfeeding. **Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids.** **Part II: analgesics and other drugs used in rheumatology practice.**	2016 NICE accredited	2019

Current Awareness Database Articles

Below is a selection of articles related to Rheumatology recently added to the healthcare databases.

If you would like any of the following articles in full text, or if you would like a more focused search on your own topic, then get in touch: library@uhbristol.nhs.uk

The Effects of Yoga on Pain, Mobility, and Quality of Life in Patients with Knee Osteoarthritis: A Systematic Review

Source: Evidence-based Complementary and Alternative Medicine; 2016; vol. 2016

Publication Type(s): Journal: Review

Author(s): Kan L.; Yang Y.; Wang P.; Zhang J.

Available in full text at Evidence-based Complementary and Alternative Medicine : eCAM - from National Library of Medicine

Abstract: Objective. To systematically assess the effects of yoga on pain, mobility, and quality of life in patients with knee osteoarthritis. Methods. Pubmed, Medline, EMBASE, the Cochrane Central Register of Controlled Trials, Physiotherapy Evidence Database (PEDro), and other sources were searched systematically in this study. Two reviewers identified eligible studies and extracted data independently. Downs and Black's Quality Index were used to evaluate the methodological quality of the included studies. Results. A total of 9 articles (6 studies) involving 372 patients with knee osteoarthritis met the inclusion criteria. The most common yoga protocol is 4090 minutes/session, lasting for at least 8 weeks. The effect of yoga on pain relief and function improvement could be seen after two-week intervention. Conclusion. This systematic review showed that yoga might have positive effects in relieving pain and mobility on patients with KOA, but the effects on quality of life (QOL) are unclear. Besides, more outcome measure related to mental health of yoga effects on people with KOA should be conducted. Copyright © 2016 Laidi Kan et al.

Study of the effect of an oral formulation of fig and olive on rheumatoid arthritis (RA) remission indicators: A randomized clinical trial

Source: Iranian Journal of Pharmaceutical Research; 2016; vol. 15 (no. 3); p. 537-545

Publication Type(s): Journal: Article

Author(s): Bahadori S.; Salamzadeh J.; Kamalinejad M.; Ardekanie M.R.S.; Keshavarz M.; Ahmadzadeh A.

Abstract: This study was designed to explore the complementary effects of a combination formulation of olive oil, olive and fig fruits on RA remission indicators. A randomized controlled clinical trial was designed. Adult RA patients were randomly divided into two groups receiving routine Disease-modifying antirheumatic drugs (DMARDs) regimen (control group) and routine DMARDs regimen plus the herbal supplementary formulation of olive oil, fig and olive fruits (intervention group). Patients were followed every 4 weeks for total study period of 16 weeks. In addition to demographic and medical history of the patients, the Disease Activity Score with 28-joint counts based on Erythrocyte Sedimentation Rate (DAS28_ESR) were recorded. SPSS (version 22.0) software was used to analyze data, assuming $p<0.05$ as significance level. 56 patients (control = 27

and intervention = 29), with mean +/- sd age of 50.91 +/- 12.26 years completed the study. Repeated measures analysis revealed that differences between remission indicators in the two study groups were not statistically significant, however, there was a p = 0.03 for the within-subjects contrast test of the Patient Global Assessment (PtGA), approving a nonlinear change for PtGA with respect to time. No between groups differences in adjunct drug therapy pattern for disease flares were seen. In conclusion, although, non-significant changes in the study variable of DAS28_ESR is in agreement with few previous reports, nevertheless, trends in its reduction in the intervention group along with the significant delayed PtGA score improvements occurred in the intervention group convince us to suggest further investigations on the supplementary olive and fig products, with a longer follow up periods.

Database: EMBASE

Genetic markers as therapeutic target in rheumatoid arthritis: A game changer in clinical therapy?

Source: Rheumatology International; Nov 2016; vol. 36 (no. 11); p. 1601-1607

Publication Type(s): Journal: Review

Author(s): Ali A.M.M.T.; Vino S.

Abstract: Rheumatoid arthritis (RA) is a chronic, inflammatory, multi-systemic autoimmune disease unremitted by genetic and environmental factors. The factors are crucial but inadequate in the development of disease; however, these factors can be representative of potential therapeutic targets and response to clinical therapy. Insights into the contribution of genetic risk factors are currently in progress with studies querying the genetic variation, their role in gene expression of coding and non-coding genes and other mechanisms of disease. In this review, we describe the significance of genetic markers architecture of RA through genome-wide association studies and meta-analysis studies. Further, it also reveals the mechanism of disease pathogenesis investigated through the mutual findings of functional and genetic studies of individual RA-associated genes, which includes HLA-DRB1, HLA-DQB1, HLA-DPB1, PADI4, PTPN22, TRAF1-C5, STAT4 and C5orf30. However, the genetic background of RA remains to be clearly depicted. Prospective efforts of the post-genomic and functional genomic period can travel toward real possible assessment of the genetic effect on RA. The discovery of novel genes associated with the disease can be appropriate in identifying potential biomarkers, which could assist in early diagnosis and aggressive treatment. Copyright © 2016, Springer-Verlag Berlin Heidelberg.

The Biologic Response to Polyetheretherketone (PEEK) Wear Particles in Total Joint Replacement: A Systematic Review

Source: Clinical Orthopaedics and Related Research; Nov 2016; vol. 474 (no. 11); p. 2394-2404

Publication Type(s): Journal: Article

Author(s): Stratton-Powell A.A.; Pasko K.M.; Brockett C.L.; Tipper J.L.

Abstract: Background: Polyetheretherketone (PEEK) and its composites are polymers resistant to fatigue strain, radiologically transparent, and have mechanical properties suitable for a range of orthopaedic applications. In bulk form, PEEK composites are generally accepted as biocompatible. In particulate form, however, the biologic response relevant to joint replacement devices remains unclear. The biologic response to wear particles affects the longevity of total joint arthroplasties. Particles in the phagocytozable size range of 0.1 micro m to 10 micro m are considered the most biologically reactive, particularly particles with a mean size of < 1 micro m. This systematic review aimed to identify the current evidence for the biologic response to PEEK-based wear debris from total joint arthroplasties. Questions/purposes: (1) What are the quantitative characteristics of PEEK-based wear particles produced by total joint arthroplasties? (2) Do PEEK wear particles cause an adverse biologic response when compared with UHMWPE or a similar negative control biomaterial?

(3) Is the biologic response affected by particle characteristics? Methods: Embase and Ovid Medline databases were searched for studies that quantified PEEK-based particle characteristics and/or investigated the biologic response to PEEK-based particles relevant to total joint arthroplasties. The keyword search included brands of PEEK (eg, MITCH, MOTIS) or variations of PEEK types and nomenclature (eg, PAEK, CFR-PEEK) in combination with types of joint (eg, hip, knee) and synonyms for wear debris or immunologic response (eg, particles, cytotoxicity). Peer-reviewed studies, published in English, investigating total joint arthroplasty devices and cytotoxic effects of PEEK particulates were included. Studies investigating devices without articulating bearings (eg, spinal instrumentation devices) and bulk material or contact cytotoxicity were excluded. Of 129 studies, 15 were selected for analysis and interpretation. No studies were found that isolated and characterized PEEK wear particles from retrieved periprosthetic human tissue samples. Results: In the four studies that quantified PEEK-based particles produced using hip, knee, and spinal joint replacement simulators, the mean particle size was 0.23 micro m to 2.0 micro m. The absolute range reported was approximately 0.01 micro m to 50 micro m. Rod-like carbon particulates and granular-shaped PEEK particles were identified in human tissue by histologic analysis. Ten studies, including six animal models (rat, mouse, and rabbit), three cell line experiments, and two human tissue retreival studies, investigated the biologic response to PEEK-based particles. Qualitative histologic assessments showed immunologic cell infiltration to be similar for PEEK particles when compared with UHMWPE particles in all six of the animal studies identified. However, increased inflammatory cytokine release (such as tumor necrosis factor-alpha) was identified in only one in vitro study, but without substantial suppression in macrophage viability. Only one study tested the effects of particle size on cytotoxicity and found the largest unfilled PEEK particles (approximately 13 micro m) to have a toxic effect; UHMWPE particles in the same size range showed a similar cytotoxic effect. Conclusions: Wear particles produced by PEEK-based bearings were, in almost all cases, in the phagocytozable size range (0.1-10 micro m). The studies that evaluated the biologic response to PEEK-based particles generally found cytotoxicity to be within acceptable limits relative to the UHMWPE control, but inconsistent when inflammatory cytokine release was considered. Clinical Relevance: To translate new and advanced materials into clinical use more quickly, the clinical relevance and validity of preclinical tests need to be improved. To achieve this for PEEK-based devices, human tissue retrieval studies including subsequent particle isolation and characterization analyses are required. In vitro cell studies using isolated wear particles from tissue or validated joint replacement simulators, instead of manufactured particles, are also required.

A systematic review and meta-analysis on the influence of biological implant surface coatings on periimplant bone formation.

Source: Journal of biomedical materials research. Part A; Nov 2016; vol. 104 (no. 11); p. 2898-2910

Author(s): Jenny, Gregor; Jauernik, Johanna; Bierbaum, Susanne; Bigler, Martin; Grätz, Klaus W; Rücker, Martin; Stadlinger, Bernd

Abstract: This systematic review and meta-analysis evaluated the influence of biological implant surface coatings on periimplant bone formation in comparison to an uncoated titanium reference surface in experimental large animal models. The analysis was structured according to the PRISMA criteriae. Of the1077 studies, 30 studies met the inclusion criteriae. Nineteen studies examined the bone implant contact (BIC) and were included in the meta-analysis. Overall, the mean increase in BIC for the test surfaces compared to the reference surfaces was 3.7 percentage points (pp) (95% CI -3.9-11.2, p = 0.339). Analyzing the increase in BIC for specific coated surfaces in comparison to uncoated reference surfaces, inorganic surface coatings showed a significant mean increase in BIC of 14.7 pp (95% CI 10.6-18.9, p < 0.01), extracellular matrix (ECM) surface coatings showed an increase of 10.0 pp (95% CI 4.4-15.6, p < 0.001), and peptide coatings showed a statistical trend with 7.1 pp BIC increase (95% CI -0.8-15.0, p = 0.08). In this review, no statistically significant difference could be found for growth factor surface coatings (observed difference -3.3 pp, 95% CI -16.5-9.9, p = 0.6). All

analyses are exploratory in nature. The results show a statistically significant effect of inorganic and ECM coatings on periimplant bone formation. © 2016 Wiley Periodicals, Inc. J Biomed Mater Res Part A: 104A: 2898-2910, 2016. © 2016 Wiley Periodicals, Inc.

Association of the ATIC 347 C/G polymorphism with responsiveness to and toxicity of methotrexate in rheumatoid arthritis: a meta-analysis

Source: Rheumatology International; Nov 2016; vol. 36 (no. 11); p. 1591-1599

Publication Type(s): Journal: Review

Author(s): Lee Y.H.; Bae S.-C.

Abstract: This study investigated whether the 5-aminoimidazole-4-carboxamide ribonucleotide transformylase gene (ATIC) 347 C/G polymorphism can predict the response to or toxicity of methotrexate (MTX) in patients with rheumatoid arthritis (RA). We conducted a meta-analysis of studies on the association between ATIC 347 C/G polymorphism and non-responsiveness to or toxicity of MTX in RA patients, using PUBMED, EMBASE, and COCHRANE. Nine comparative studies from 6 articles including 1056 RA patients met our inclusion criteria. This final group of studies comprised 5 studies on response to MTX and 4 on toxicity of MTX in RA patients in relation to the ATIC 347 C/G polymorphism status. Meta-analysis showed association between the ATIC 347 GG + GC genotype and non-response to MTX therapy (OR = 1.572, 95 % CI 1.146-2.156, p = 0.005). Stratification by ethnicity indicated significant association between the ATIC 347 GG + GC genotype and non-response to MTX in Caucasians (OR = 1.884, 95 % CI 1.236-2.873, p = 0.003), but not in Asian patients. Similarly, associations were noted for the ATIC 347 C/G polymorphism through analysis using recessive and overdominant models. Meta-analysis revealed association between the ATIC 347 GG + GC genotype and MTX toxicity (OR = 1.454 95 % CI 1.034-2.044, p = 0.032). Stratification by ethnicity indicated significant association between the ATIC 347 GG + GC genotype and MTX toxicity in Caucasians (OR = 1.741, 95 % CI 1.080-2.806, p = 0.023), but not in Asian patients. The ATIC 347 C/G polymorphism may be associated with non-responsiveness to and or toxicity of MTX in Caucasian RA patients. Copyright © 2016, Springer-Verlag Berlin Heidelberg.

The incidence of sexually acquired reactive arthritis: a systematic literature review

Source: Clinical Rheumatology; Nov 2016; vol. 35 (no. 11); p. 2639-2648

Publication Type(s): Journal: Article

Author(s): Denison H.J.; Dennison E.M.; Curtis E.M.; Clynes M.A.; Bromhead C.; Grainger R.

Abstract: Reactive arthritis (ReA) is an inflammatory spondyloarthritis occurring after infection at a distant site. Chlamydia trachomatis is proposed to be the most common cause of ReA, yet the incidence of sexually acquired ReA (SARA) has not been well established. We therefore carried out a systematic literature review to collate and critically evaluate the published evidence regarding the incidence of SARA. MEDLINE and EMBASE databases were searched using free-text and MeSH terms relating to infection and ReA. The title and abstract of articles returned were screened independently by two reviewers and potentially relevant articles assessed in full. Data was extracted from relevant articles and a risk of bias assessment carried out using a validated tool. Heterogeneity of study methodology and results precluded meta-analysis. The search yielded a total of 11,680 articles, and a further 17 were identified from review articles. After screening, 55 papers were assessed in full, from which 3 met the relevant inclusion criteria for the review. The studies reported an incidence of SARA of 3.0-8.1 % and were found to be of low to moderate quality. More studies are required to address the lack of data regarding the incidence of SARA. Specific and sensitive classification criteria must be developed in order for consistent classification and valid conclusions to be drawn. In clinical practice, it is recommended clinicians discuss the possibility of ReA developing

at the time of STI diagnosis and to encourage patients to return if they experience any relevant symptoms.

Benefit of health education by a training nurse in patients with axial and/or peripheral psoriatic arthritis: A systematic literature review

Source: Rheumatology International; Nov 2016; vol. 36 (no. 11); p. 1493-1506

Publication Type(s): Journal: Review

Author(s): Candelas G.; Villaverde V.; Garcia S.; Guerra M.; Leon M.J.; Canete J.D.

Abstract: The aim of this study was to systematically review the literature available about the benefit of health education by a training nurse in patients with axial and/or peripheral psoriatic arthritis in the framework of the drawing up of the axial spondyloarthritis and psoriatic arthritis guidelines of the "Spanish Society of Rheumatology". Electronic databases (Cochrane Central Register of Controlled Trials, EMBASE, Medline/PubMed, CINAHL) were systematically searched from inception to 2014 using medical subject headings and keywords. Only articles in English, Spanish and French were included. The patients studied had to be diagnosed of psoriatic arthritis (all ages, both sexes) with axial involvement and/or peripheral arthritis who had received health education by a specialized nurse. We included in the search randomized clinical trials, cohort observational studies, descriptive studies and case series and qualitative research studies. Measured outcomes were those related to the education provided in a nursing consultation such as increased adherence to biological therapy, conducting exercises, smoking cessation and patient satisfaction. Eight studies were included, five randomized clinical trials with moderate level of quality and three intervention studies with no control group with low level of quality. Meta-analyses were not undertaken due to clinical heterogeneity. According to our results, it can be concluded that although there is little evidence on the role of a trained nurse in patients with psoriatic arthritis, this role can be beneficial to the patients because it can increase the rate of adherence to treatment prescribed by a rheumatologist, promotes patient self-management of their disease and increases patient satisfaction. Copyright © 2016, Springer-Verlag Berlin Heidelberg.

Efficacy of mesenchymal stem cells in treating patients with osteoarthritis of the knee: A meta-analysis

Source: Experimental and Therapeutic Medicine; Nov 2016; vol. 12 (no. 5); p. 3390-3400

Publication Type(s): Journal: Article

Author(s): Cui G.-H.; Wang Y.Y.; Li C.-J.; Shi C.-H.; Wang W.-S.

Abstract: To assess the clinical efficacy and safety of mesenchymal stem cell (MSC) treatment for osteoarthritis of the knee (KOA), a systematic electronic literature search was performed on PubMed, EMBASE and Web of Science. Studies published in English from the earliest record to December 2014 were searched using the following keywords: Cartilage defect, cartilage repair, osteoarthritis, KOA, stem cells, MSCs, bone marrow concentrate (BMC), adipose-derived mesenchymal stem cells, synovial-derived mesenchymal stem cells and peripheral blood-derived mesenchymal stem cells. The effect sizes of selected studies were determined by extracting pain scores from the visual analog scale and functional changes from International Knee Documentation Committee and Lysholm and Western Ontario and McMaster Universities Osteoarthritis Index before and after MSCs or reference treatments at 3, 6, 12, and 24 months. The factors were analyzed and the outcomes were modified after comparing the MSC group pooled values with the pretreatment baseline or between different treatment arms. A systematic search identified 18 clinical trials on this topic, including 10 single-arm prospective studies, four quasi-experimental studies and four randomized controlled trials that used BMCs to treat 565 patients with KOA in total. MSC treatment in patients with KOA showed continual efficacy for 24 months compared with their

pretreatment condition. Effectiveness of MSCs was improved at 12 and 24 months post-treatment, compared with at 3 and 6 months. No dose-responsive association in the MSCs numbers was demonstrated. However, patients with arthroscopic debridement, activation agent or lower degrees of Kellgren-Lawrence grade achieved improved outcomes. MSC application ameliorated the overall outcomes of patients with KOA, including pain relief and functional improvement from basal evaluations, particularly at 12 and 24 months after follow-up.

Effect of IL-6 receptor blockade on high-sensitivity troponin T and NT-proBNP in rheumatoid arthritis

Source: Atherosclerosis; Nov 2016; vol. 254 ; p. 167-171

Publication Type(s): Journal: Article

Author(s): Welsh P.; Sattar N.; Tuckwell K.; McInnes I.B.

Abstract: Background and aims Observational associations between inflammation and cardiovascular disease are interesting, but randomised experimental data are lacking. We investigated the effect of the IL-6 receptor blocker tocilizumab on N terminal pro B type natriuretic peptide (NT-proBNP) and high sensitivity troponin T (hsTnT) in rheumatoid arthritis (RA) patients. Methods A post-hoc study was performed in a subset of patients with moderate to severe RA participating in a randomised controlled trial. The effect of tocilizumab on cardiac biomarkers was determined using stored serum (baseline and 24 weeks) in recipients of tocilizumab (8 mg/kg every 4 weeks plus DMARDs; n = 225) or placebo (every 4 weeks plus DMARDs; n = 132). Results Median NT-proBNP and hsTnT concentrations at baseline were 100 pg/ml and 5.7 pg/ml, respectively. NT-proBNP decreased in both study arms (median at 24 weeks 77 pg/ml in the placebo arm, 79 pg/ml in the tocilizumab arm; p<0.001 for the decrease in both arms), and decreased to a similar extent comparing study arms (tocilizumab effect: -5.5%, p=0.55). hsTnT also decreased in both study arms (median at 24 weeks 3.1 pg/ml in the placebo arm, 4.4 pg/ml in the tocilizumab arm; p<0.001 for the decrease in both arms). The extent of the reduction in hsTnT was greater in the placebo group (tocilizumab effect: +23.3%, p=0.002). Change in NT-proBNP, but not hsTnT, correlated modestly with change in CRP (r = 0.17, p=0.013). Conclusions These data argue against a rapid preferential benefit of IL-6 blockade on these specific surrogate markers of cardiovascular risk, but may be consistent with a general cardiovascular benefit of improved RA treatment. Clinical trials.gov identifier NCT00106574. Copyright © 2016 The Authors

Septic arthritis in children in resource limited and non-resource limited countries: an update on diagnosis and treatment

Source: Expert Review of Anti-Infective Therapy; Nov 2016; vol. 14 (no. 11); p. 1087-1096

Publication Type(s): Journal: Review

Publisher: Taylor and Francis Ltd (E-mail: info@expert-reviews.com)

Author(s): Chiappini E.; Mastrolia M.V.; Galli L.; De Martino M.; Lazzeri S.

Abstract: Introduction: Septic arthritis (SA) is an orthopedic emergency in childhood. It is uncommon in high resource settings. However, an incidence of 5-20 per 100,000 children has been reported in low-income countries. Area covered: The predictive value of serum markers is still under debate and the proposed diagnostic algorithms for SA are not sufficiently validated in children. Recent data suggest that short-course intravenous treatment, followed by oral therapy, is as effective as traditional long-term treatment. Results from three randomized controlled trials suggest that the addition of systemic steroids may accelerate clinical improvement. Minimally invasive surgical techniques have been proposed for treatment in recent years. Expert commentary: The causes and the epidemiology of septic arthritis will continue to mutate according to the changes in

immunization practices, bacterial resistance patterns and the implementation of PCR techniques. Future research should focus on the assessment of appropriate antibiotic regimens and surgical procedures.

The role of high-resolution peripheral quantitative computed tomography as a biomarker for joint damage in inflammatory arthritis

Source: Journal of Rheumatology; Oct 2016; vol. 43 (no. 10); p. 1911-1913

Publication Type(s): Journal: Review

Author(s): Tam L.-S.

Abstract: Since 2011, members of the SPECTRA Collaboration (Study grouP for xtrEme-Computed Tomography in Rheumatoid Arthritis) have investigated the validity, reliability, and responsiveness of high-resolution peripheral quantitative computed tomography (HR-pQCT) as a biomarker for joint damage in inflammatory arthritis. Presented in this series of articles are a systematic review of HR-pQCT-related findings to date, a review of selected images of cortical and subchondral trabecular bone of metacarpophalangeal (MCP) joints, results of a consensus process to standardize the definition of erosions and their quantification, as well as an examination of the effect of joint flexion on width and volume assessment of the joint space.

16. Hylan G-F 20 Versus Low Molecular Weight Hyaluronic Acids for Knee Osteoarthritis: A Meta-Analysis

Source: BioDrugs; Oct 2016; vol. 30 (no. 5); p. 387-396

Publication Type(s): Journal: Review

Author(s): Zhao H.; Liu H.; Liang X.; Li Y.; Wang J.; Liu C.

Abstract: Background: Hyaluronic acid injection has been reported to decrease pain compared with baseline levels in knee joint osteoarthritis. Hylan G-F 20 is distinguished from the other products by its chemical structure and relatively higher molecular weight. Many trials have compared hylan G-F 20 and low molecular weight hyaluronic acids (LMWHAs); however, their relative efficacy and safety are still debated. Objective: The aim was to compare the effectiveness and safety of intra-articular injection of hylan G-F 20 and LMWHA in the treatment of knee joint osteoarthritis. Methods: A comprehensive search of the literature up to February 2016 was performed; multiple databases were searched with 'Synvisc' or 'hylan' or 'hyaluronan' as free word terms. The pain-related outcomes and treatment-related adverse events from intent-to-treat analyzed studies were pooled for meta-analysis; other functional outcomes were included in the qualitative analysis. Results: Twenty trials with a total of 3034 patients and 3153 knees were included, with a pooled dropout rate of 7.2 %. The pooled pain-related outcomes at 2 to 3 months reached a statistically significant difference in favor of hylan G-F 20 (I<ovid:sup>2</ovid:sup> = 88 %; random effects; P = 0.02), and the significance still existed with exclusion (in order to eliminate heterogeneity) of the three studies that most favored hylan G-F 20 (I<ovid:sup>2</ovid:sup> = 51 %; fixed effect; P = 0.03). No significant difference was reached for other group and subgroup analyses. No significant difference was reached in comparing the patients with treatment-related adverse events (seven trials; 2025 patients; P = 0.13) or the treatment-related adverse events (six trials; 1633 patients; P = 0.14). Conclusion: According to the current results, limited evidence showed a superior effect favoring hylan G-F 20 over LMWHA in the period from 2 to 3 months post-injection for pain-related outcomes. There was no evidence of increased risk of treatment-related adverse events for hylan G-F 20 injections.

Improving the power of clinical trials of rheumatoid arthritis by using data on continuous scales when analysing response rates: An application of the augmented binary method

Source: Rheumatology (United Kingdom); Oct 2016; vol. 55 (no. 10); p. 1796-1802

Publication Type(s): Journal: Article

Author(s): Wason J.M.S.; Jenkins M.

Abstract: Objective. In clinical trials of RA, it is common to assess effectiveness using end points based upon dichotomized continuous measures of disease activity, which classify patients as responders or non-responders. Although dichotomization generally loses statistical power, there are good clinical reasons to use these end points; for example, to allow for patients receiving rescue therapy to be assigned as non-responders. We adopt a statistical technique called the augmented binary method to make better use of the information provided by these continuous measures and account for how close patients were to being responders. Methods. We adapted the augmented binary method for use in RA clinical trials. We used a previously published randomized controlled trial (Oral SyK Inhibition in Rheumatoid Arthritis-1) to assess its performance in comparison to a standard method treating patients purely as responders or non-responders. The power and error rate were investigated by sampling from this study.Results. The augmented binary method reached similar conclusions to standard analysis methods but was able to estimate the difference in response rates to a higher degree of precision. Results suggested that CI widths for ACR responder end points could be reduced by at least 15%, which could equate to reducing the sample size of a study by 29% to achieve the same statistical power. For other end points, the gain was even higher. Type I error rates were not inflated.Conclusion. The augmented binary method shows considerable promise for RA trials, making more efficient use of patient data whilst still reporting outcomes in terms of recognized response end points.

Biologic Therapies and Risk of Infection and Malignancy in Patients With Inflammatory Bowel Disease: A Systematic Review and Network Meta-analysis

Source: Clinical Gastroenterology and Hepatology; Oct 2016; vol. 14 (no. 10); p. 1385

Publication Type(s): Journal: Article

Author(s): Bonovas S.; Fiorino G.; Allocca M.; Lytras T.; Nikolopoulos G.K.; Peyrin-Biroulet L.;

Abstract: Background & Aims Safety issues are a major concern for patients considering treatments for inflammatory bowel disease (IBD). We performed a systematic review and meta-analysis to determine whether biologic agents affect the risk of infection or malignancy in adults with IBD. Methods We searched PubMed, Embase, Scopus, Cochrane IBD Group Specialized Trials Register, World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov through March 2016 for randomized placebo-controlled or head-to-head trials of biologic agents approved for treatment of adults with IBD (ie, adalimumab, certolizumab, golimumab, infliximab, natalizumab, or vedolizumab). Two reviewers independently extracted study data and outcomes (serious infections, opportunistic infections, tuberculosis, any infection, and malignancies) and rated each trial's risk of bias. We used conventional meta-analysis to synthesize direct evidence and a network meta-analysis for adjusted indirect treatment comparisons. Results We identified 49 randomized placebo-controlled studies comprising 14,590 participants. Synthesis of the evidence indicated that patients treated with biologics had a moderate increase in risk of any infection (odds ratio [OR], 1.19; 95% confidence interval [CI], 1.10-1.29) and a significant increase in risk of opportunistic infections (OR, 1.90; 95% CI, 1.21-3.01). Risk of serious infections was not increased in patients treated with biologics (OR, 0.89; 95% CI, 0.71-1.12). On the contrary, biologics appeared to significantly reduce risk of serious infections in studies with low risk of bias (OR, 0.56; 95% CI, 0.35-0.90). We did not find an increased risk of malignancy with use of biologic agents (OR, 0.90; 95% CI,

0.54-1.50), but data were insufficient in terms of exposure and follow-up times. None of the indirect comparisons, either among the individual agents or between the anti-tumor necrosis factor and anti-integrin classes, reached significance for any of the outcomes analyzed. Conclusions On the basis of a systematic review and meta-analysis, biologic agents increase the risk of opportunistic infections in patients with IBD, but not the risk of serious infections. It is necessary to continue to monitor the comparative and long-term safety profiles of these drugs. Copyright © 2016 AGA Institute

Real-world effectiveness of anti-TNF switching in psoriatic arthritis: a systematic review of the literature

Source: Clinical Rheumatology; Oct 2016 ; p. 1-12

Publication Type(s): Journal: Article In Press

Author(s): Reddy S.M.; Crean S.; Martin A.L.; Burns M.D.; Palmer J.B.

Abstract: Anti-tumor necrosis factors (Anti-TNFs) are a class of biologic disease-modifying anti-rheumatic drugs indicated for the treatment of moderate-to-severe psoriatic arthritis (PsA). Refractory patients are commonly managed by switching from one anti-TNF to another. To assess the evidence on the effectiveness of anti-TNF cycling in PsA patients, a systematic review of the literature was conducted. MEDLINE- and Embase-indexed English-language publications were systematically searched from 1995 to 2015 for studies assessing real-world effectiveness outcomes of anti-TNF cycling in PsA patients. Of 1086 citations identified, 18 studies were included; most conducted in Europe. Six of seven studies testing between lines found significant differences in effectiveness between earlier and subsequent lines of anti-TNF therapy. First-line therapy yielded better results compared with second-line therapy, and significant differences were observed between second- and third-line anti-TNF treatments. In the only study with multivariate regression testing for predictors of response, Danish registry patients were less likely to respond (American College of Rheumatology 20 % or 50 % response) to a second anti-TNF course if safety, rather than lack of effect, caused them to switch (odds ratio [OR] 0.04; p = 0.003 and OR 0.05; p = 0.03, respectively). Effectiveness of anti-TNFs at second line and later is reported in a small number of real-world studies of PsA patients. Subsequent treatment lines may be associated with less response in some measures. More research is needed to quantify the effectiveness of sequential anti-TNF lines in this progressive population and to compare these effects with responses to drugs with different mechanisms of action. Copyright © 2016 International League of Associations for Rheumatology (ILAR)

Comparative effectiveness of biologics for the management of rheumatoid arthritis: systematic review and network meta-analysis

Source: Clinical Rheumatology; Oct 2016 ; p. 1-10

Publication Type(s): Journal: Article In Press

Author(s): Alfonso-Cristancho R.; Arjunji R.; Ganguly R.; Armstrong N.; Riemsma R.; Worthy G.; Kleijnen J.

Abstract: Our aim was to establish the comparative effectiveness of rheumatoid arthritis (RA) biologics, using a systematic review and network meta-analysis. The systematic review used randomized controlled trials (RCTs) in adults with RA who failed treatment with conventional disease-modifying agents for rheumatoid disease (cDMARDs). We compared the effectiveness of abatacept, adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, and rituximab to tocilizumab, a recent biologic with a different mechanism of action (anti-IL-6 receptor). A network meta-analysis (NMA) included the indirect and direct evidence previously selected. In total, 207 articles were included describing 68 RCTs. The NMA showed that tocilizumab monotherapy was superior to standard care (ACR20, OR 13.27, 95 % CrI [3.958, 43.98]; ACR50, 17.45 [10.18, 31.24];

ACR70, 37.77 [7.226, 216.3]; EULAR, 10.42 [1.963, 54.8]); and methotrexate (MTX; ACR50, OR 5.44 [4.142, 7.238]; ACR70, 7.364 [1.4, 30.83]; EULAR, 4.226 [1.184, 15.58]) at 26 weeks. Similarly, the combination of tocilizumab + MTX was significantly better than standard care/placebo and MTX alone for ACR20, ACR50, ACR70, and EULAR at 26 weeks (OR 18.63 [5.32, 66.81]; 24.27 [14.5, 41.91]; 46.13 [10.08, 277]; 14.23 [2.493, 84.02]; 4.169 [2.267, 7.871]; 5.44 [4.142, 7.238]; 8.731 [4.203, 19.29]; 7.306 [4.393, 13.04], respectively). At 52 weeks, compared to MTX alone, tocilizumab + MTX was significantly better for ACR20 and ACR50 response. Few significant differences were found between tocilizumab (alone or in combination) and any other biologics. Results must be considered in context with the limitations of the available evidence. This NMA suggests that tocilizumab was superior to cDMARDs and as effective as other biologics for RA.

Total ankle arthroplasty versus ankle arthrodesis for the treatment of end-stage ankle arthritis: a meta-analysis of comparative studies

Source: International Orthopaedics; Oct 2016 ; p. 1-9

Publication Type(s): Journal: Article In Press

Author(s): Kim H.J.; Ahn H.S.; Suh D.H.; Han S.W.; Choi G.W.; Yang J.H.; Lee J.W.

Abstract: Purpose: Total ankle arthroplasty (TAA) and ankle arthrodesis (AA) are the main surgical treatment options for end-stage ankle arthritis. Although the superiority of each modality remains debated, there remains a lack of high-quality evidence-based studies, such as randomized controlled clinical trials, and meta-analyses of comparative studies. We performed a meta-analysis of comparative studies to determine whether there is a significant difference between these two procedures in terms of (i) clinical scores and patient satisfaction, (ii) re-operations, and (iii) complications. Methods: We conducted a comprehensive search in the MEDLINE, EMBASE, and Cochrane library databases. Only retrospective or prospective comparative studies were included in this meta-analysis. The literature search, data extraction, and quality assessment were conducted by two independent reviewers. The primary outcomes were clinical scores and patient satisfaction. We also investigated the prevalence of complications and the re-operation rate. Results: Ten comparative studies were included (four prospective and six retrospective studies). There were no significant differences between the two procedures in the American Orthopaedic Foot and Ankle Society ankle-hindfoot score, Short Form-36 physical component summary and mental component summary scores, visual analogue scale for pain, and patient satisfaction rate. The risk of re-operation and major surgical complications were significantly increased in the TAA group. Conclusions: The meta-analysis revealed that TAA and AA could achieve similar clinical outcomes, whereas the incidence of re-operation and major surgical complication was significantly increased in TAA. Further studies of high methodological quality with long-term follow-up are required to confirm our conclusions.

Safety of Repeated Injections of Sodium Hyaluronate (SUPARTZ) for Knee Osteoarthritis: A Systematic Review and Meta-Analysis.

Source: Cartilage; Oct 2016; vol. 7 (no. 4); p. 322-332

Publication Type(s): Journal Article

Author(s): Bannuru, Raveendhara R; Brodie, Christopher R; Sullivan, Matthew C; McAlindon, Timothy E

Abstract: Though there is no consensus on its efficacy, knee osteoarthritis is symptomatically managed with intra-articular hyaluronic acid (IAHA). Recent reports suggest that IAHA may delay the need for total knee replacement, with the magnitude of delay proportional to the number of injection series. However, the safety of repeated injection series is reported to vary between

commercial products. This report describes a systematic review of safety data on repeated treatment courses of SUPARTZ. We performed a systematic search of MEDLINE, Cochrane database, EMBASE, Web of Science, Google Scholar, and unpublished data. We included all human randomized controlled trials or observational studies with adverse event (AE) data for SUPARTZ in knee osteoarthritis. Two independent reviewers extracted data and evaluated study quality. Data were analyzed separately for the first and subsequent series of injections. The primary sources for repeated-injection data on SUPARTZ were a postmarket registry (N = 7404), 4 prospective studies (N = 127 total), and a retrospective study (N = 220). None of the sources reported increased frequency or severity of AEs with repeated injections. In the registry, 95% of multiple-injection-series patients who reported an AE did so during the first series. None of the AEs was serious, and most resolved spontaneously without medical intervention. The overall adverse event rate after repeat courses of SUPARTZ was 0.008 (95% confidence interval: 0.001-0.055). Multiple courses of SUPARTZ injections appear to be at least as safe, and probably safer, than the first course. This study supports the safety of repeat courses of SUPARTZ injections for knee osteoarthritis.

Safety and efficacy of intra-articular injections of a combination of hyaluronic acid and mannitol (HAnOX-M) in patients with symptomatic knee osteoarthritis: Results of a double-blind, controlled, multicenter, randomized trial.

Source: The Knee; Oct 2016; vol. 23 (no. 5); p. 842-848

Publication Type(s): Journal Article

Author(s): Conrozier, Thierry; Eymard, Florent; Afif, Naji; Balblanc, Jean-Charles;

Abstract: To compare both safety and efficacy of a novel intra-articular viscosupplement made of intermediate molecular weight (MW) hyaluronic acid (HA) mixed with high concentration of mannitol with a marketed high MW HA, in patients with knee osteoarthritis (OA). Patients with symptomatic knee OA, with radiological OARSI grades 1 to 3, were enrolled in a controlled, double-blind, parallel-group, non-inferiority trial. They were randomized to receive three intra-articular injections, at weekly intervals, of either HAnOX-M made of a combination of HA (MW one to 1.5MDa, 31mg/2ml) and mannitol (70mg/2ml) or Bio-HA (MW 2.3 to 3.6MDa, 20mg/2ml). The primary outcome was six-month change in the WOMAC pain subscale (0 to 20). Sample size was calculated according to a non-inferiority margin of 1.35. Secondary endpoints included six-month change in function and walking pain, analgesic consumption and safety. The intention-to-treat (ITT) and per-protocol (PP) populations consisted of 205 and 171 patients. HAnOX-M and Bio-Ha groups did not differ statistically at baseline. The primary analysis was conducted in the PP population, then in the ITT population. The average WOMAC pain score at baseline was 9.5 in both groups. Mean (SD) variations in WOMAC pain score were -4.4 (3.8) and -4.5 (4.3) mm, for HAnOX and Bio-HA respectively, satisfying the claim for non-inferiority. Similar results were obtained for all other secondary endpoints. Treatment with of HAnOX-M is effective to alleviate knee OA symptoms and to improve joint function over six months, with similar safety than conventional HA viscosupplement.

Shared Biologic Pathways Between Alzheimer Disease and Major Depression: A Systematic Review of MicroRNA Expression Studies.

Source: The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry; Oct 2016; vol. 24 (no. 10); p. 903-912

Publication Type(s): Journal Article

Author(s): Mendes-Silva, Ana Paula; Pereira, Kelly Silva; Tolentino-Araujo, Gesiane Thamire; Nicolau, Eduardo de Souza; Silva-Ferreira, Camila Moreira; Teixeira, Antonio Lucio; Diniz, Breno S

Abstract: The clinical-epidemiological relationship between major depressive disorder (MDD) and Alzheimer disease (AD) suggests that they may share common neurobiologic abnormalities. The authors conducted a systematic review and identified microRNAs abnormally expressed in both AD and MDD. The pattern of microRNA regulation in each disorder and the genes regulated by each microRNA and the biologic processes and pathways regulated by these genes were identified. Seventy-four microRNAs were abnormally expressed in AD and 30 in MDD; 7 were common for both disorders (hsa-let-7f-5p, hsa-miR-664a-3p, hsa-miR-361-5p, hsa-let-7g-5p, hsa-let-7d-5p, hsa-miR-191-5p, hsa-miR-26b-5p). These microRNAs interact with 45 validated genes, and the main biologic pathways and processes regulated by them were proteostasis control, maintenance of genomic integrity, regulation of transcriptional activity, immune-inflammatory control, and neurotrophic support. The current results suggest that the maintenance of genomic integrity, proteostasis control, immune-inflammatory regulation, and neurotrophic support are key neurobiologic links between these conditions. A comprehensive hypothetical model for the interaction between MDD, aging, and the development of AD is provided.

Prevalence and risk factors of low bone mineral density in psoriatic arthritis: A systematic review.

Source: Seminars in arthritis and rheumatism; Oct 2016; vol. 46 (no. 2); p. 174-182

Publication Type(s): Journal Article Review

Author(s): Chandran, Shelly; Aldei, Ali; Johnson, Sindhu R; Cheung, Angela M; Salonen, David; Gladman, Dafna D

Abstract: Prevalence and impact of low bone mineral density (BMD) in psoriatic arthritis (PsA) is not well understood. We aimed to synthesize current evidence regarding the prevalence, impact, and risk factors for low BMD and fractures in PsA. A systematic literature search limited to human studies was conducted without language restriction. Data on BMD, prevalence of osteoporosis, osteopenia and fractures, risk factors, morbidity, and mortality due to low BMD in PsA patients were collected. A total of 21 studies (16 case-control, 4 cross-sectional, and 1 prospective cohort) were reviewed after screening 639 titles and abstracts. In all, 17 studies compared PsA patients with one or more control group (four normal controls, five psoriasis, and eight other rheumatic diseases with or without healthy controls). The number of PsA patients in the studies ranged from 8 to 2212 with a mean (standard deviation) age of 35 (10) to 63.4 (6.2), and mean PsA duration of 2.25-13.65 years. Reported prevalence of osteoporosis varied from 1.4% to 68.8%. Low BMD was identified as a significant problem in 13 of the 21 studies. Age, female sex, postmenopausal status, PsA duration, presence of erosions, and cumulative steroid dose were associated with lower BMD. Fractures (12-40%) were associated with postmenopausal status and axial disease. No studies reported on hospitalization and mortality due to low BMD. This systematic review synthesizes current evidence on BMD and its impact in PsA. High likelihood of bias and inconsistent results suggest a need for well-designed longitudinal studies on bone health in PsA.

Osteoarthritis and mortality: A prospective cohort study and systematic review with meta-analysis.

Source: Seminars in arthritis and rheumatism; Oct 2016; vol. 46 (no. 2); p. 160-167

Publication Type(s): Journal Article

Author(s): Veronese, Nicola; Cereda, Emanuele; Maggi, Stefania; Luchini, Claudio; Solmi, Marco;

Abstract: Osteoarthritis (OA) is a leading cause of disability, but the relationship with premature mortality remains uncertain. We aimed to investigate the relationship between OA and mortality from any cause and from cardiovascular disease (CVD). Electronic literature databases searches were

conducted to identify prospective studies comparing mortality in a sample of people with and without OA. Risk of all-cause and CVD mortality were summarized using adjusted hazard ratios (HRs) for joint specific (hand, hip, and knee) and joint non-specific OA. New data from the Progetto Veneto Anziani (PRO.V.A.) study were also included. From the PRO.V.A. study (N = 2927), there was no significant increase in mortality risk for participants with any joint OA (N = 1858) compared to non-OA (all-cause, HR = 0.95, 95% CI: 0.77-1.15 and CVD, HR = 1.12, 95% CI: 0.82-1.54). On meta-analysis, seven studies (OA = 10,018/non-OA = 18,541), with a median 12-year follow-up, reported no increased risk of any-cause mortality in those with OA (HR = 1.10, 95% CI: 0.97-1.25). After removing data on hand OA, a significant association between OA and mortality was observed (HR = 1.18, 95% CI: 1.08-1.28). There was a significant higher risk of overall mortality for (1) studies conducted in Europe, (2) patients with multi-joint OA; and (3) a radiological diagnosis of OA. OA was associated with significantly higher CVD mortality (HR = 1.21, 95% CI: 1.10-1.34). People with OA are at increased risk of death due to CVD. The relationship with overall mortality is less clear and may be moderated by the presence of hand OA.

Clinical benefit of intra-articular saline as a comparator in clinical trials of knee osteoarthritis treatments: A systematic review and meta-analysis of randomized trials.

Source: Seminars in arthritis and rheumatism; Oct 2016; vol. 46 (no. 2); p. 151-159

Publication Type(s): Journal Article

Author(s): Altman, Roy D; Devji, Tahira; Bhandari, Mohit; Fierlinger, Anke; Niazi, Faizan;

Abstract: Hyaluronic acid and corticosteroids are common intra-articular (IA) therapies widely used for the management of mild to moderate knee osteoarthritis (OA). Many trials evaluating the efficacy of IA administered therapies commonly use IA saline injections as a placebo comparator arm. Using a systematic review and meta-analysis, our objective was to assess the clinical benefit associated with use of IA saline in trials of IA therapies in the treatment of patients with painful knee OA. MEDLINE and Embase databases were searched for articles published up to and including August 14th, 2014. Two reviewers assessed the eligibility of potential reports and the risk of bias of included trials. We analyzed short (≤3 months) and long-term (6-12 months) pain reduction of the saline arm of included trials using standardized mean differences (SMDs; estimated assuming a null effect in a comparator group) that were combined and weighted using a random effects model. Treatment-related adverse events (AEs) were tabulated and presented using descriptive statistics. From 40 randomized controlled trials (RCTs) eligible for inclusion only 38 provided sufficient data to be included in the meta-analysis. Based on data with moderate inconsistency IA saline was found to significantly improve short-term knee pain in 32 studies involving 1705 patients (SMD = -0.68; 95% CI: -0.78 to -0.57; P < 0.001; I(2) = 50%). Long-term knee pain was significantly decreased following IA injection with saline in 19 studies involving 1445 patients (SMD = -0.61; 95% CI: -0.76 to -0.45; P < 0.001) with a substantial degree of inconsistency (I(2) = 74%). Overall, 29 of the included trials reported on adverse events, none of which found any serious treatment-related AEs following IA injection with saline. Pain relief observed with IA saline should prompt health care providers to consider the additional effectiveness of current IA treatments that use saline comparators in clinical studies, and challenges of identifying IA saline injection as a "placebo."

Database: Medline

Arthritis as a risk factor for carpal tunnel syndrome: a meta-analysis.

Source: Scandinavian journal of rheumatology; Oct 2016; vol. 45 (no. 5); p. 339-346

Publication Type(s): Journal Article

Author(s): Shiri, R

Abstract: The effects of inflammatory and degenerative arthritis on carpal tunnel syndrome (CTS) are not well known. This systematic review and meta-analysis aimed to assess whether rheumatoid arthritis (RA) and osteoarthritis (OA) increase the risk of CTS. Literature searches were conducted in PubMed, Embase, Web of Science, Scopus, Google Scholar, and ResearchGate until January 2015. Twenty-three (five cohort, 10 case control, and eight cross sectional) studies qualified for the meta-analyses. A random-effects meta-analysis was used and heterogeneity and publication bias were assessed. Both RA and OA were associated with CTS. Pooled unadjusted odds ratios (ORs) were 1.91 [95% confidence interval (CI) 1.33-2.75, I(2) = 55.2%, nine studies, n = 10 688] for arthritis (either inflammatory or degenerative), 2.91 (95% CI 2.33-3.62, I(2) = 22.3%, 11 studies, n = 74 730) for RA, and 2.13 (95% CI 1.65-2.76, I(2) = 39.2%, five studies, n = 20 574) for OA of any joint. Pooled confounder-adjusted ORs were 1.96 (95% CI 1.21-3.18, I(2) = 73.1%, six studies, n = 11 542) for arthritis, 1.96 (95% CI 1.57-2.44, I(2) = 32.2%, eight studies, n = 72 212) for RA, and 1.87 (95% CI 1.64-2.13, I(2) = 0%, two studies, n = 19 480) for OA. There was no evidence of publication bias, and excluding cross-sectional studies or studies appraised as having a high risk of selection bias did not change the magnitude of the associations. The findings of this systematic review and meta-analysis suggest that both RA and OA increase the risk of CTS. Further prospective studies on the effect of wrist OA on CTS are needed.

Improving the power of clinical trials of rheumatoid arthritis by using data on continuous scales when analysing response rates: an application of the augmented binary method.

Source: Rheumatology (Oxford, England); Oct 2016; vol. 55 (no. 10); p. 1796-1802

Publication Type(s): Journal Article

Author(s): Wason, James M S; Jenkins, Martin

Abstract: In clinical trials of RA, it is common to assess effectiveness using end points based upon dichotomized continuous measures of disease activity, which classify patients as responders or non-responders. Although dichotomization generally loses statistical power, there are good clinical reasons to use these end points; for example, to allow for patients receiving rescue therapy to be assigned as non-responders. We adopt a statistical technique called the augmented binary method to make better use of the information provided by these continuous measures and account for how close patients were to being responders. We adapted the augmented binary method for use in RA clinical trials. We used a previously published randomized controlled trial (Oral SyK Inhibition in Rheumatoid Arthritis-1) to assess its performance in comparison to a standard method treating patients purely as responders or non-responders. The power and error rate were investigated by sampling from this study. The augmented binary method reached similar conclusions to standard analysis methods but was able to estimate the difference in response rates to a higher degree of precision. Results suggested that CI widths for ACR responder end points could be reduced by at least 15%, which could equate to reducing the sample size of a study by 29% to achieve the same statistical power. For other end points, the gain was even higher. Type I error rates were not inflated. The augmented binary method shows considerable promise for RA trials, making more efficient use of patient data whilst still reporting outcomes in terms of recognized response end points.

Efficacy of progressive aquatic resistance training for tibiofemoral cartilage in postmenopausal women with mild knee osteoarthritis: a randomised controlled trial.

Source: Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society; Oct 2016; vol. 24 (no. 10); p. 1708-1717

Publication Type(s): Journal Article

Author(s): Munukka, M; Waller, B; Rantalainen, T; Häkkinen, A; Nieminen, M T; Lammentausta, E; Kujala, U M; Paloneva, J; Sipilä, S; Peuna, A; Kautiainen, H; Selänne, H; Kiviranta, I; Heinonen, A

Abstract: To study the efficacy of aquatic resistance training on biochemical composition of tibiofemoral cartilage in postmenopausal women with mild knee osteoarthritis (OA). Eighty seven volunteer postmenopausal women, aged 60-68 years, with mild knee OA (Kellgren-Lawrence grades I/II and knee pain) were recruited and randomly assigned to an intervention (n = 43) and control (n = 44) group. The intervention group participated in 48 supervised aquatic resistance training sessions over 16 weeks while the control group maintained usual level of physical activity. The biochemical composition of the medial and lateral tibiofemoral cartilage was estimated using single-slice transverse relaxation time (T2) mapping and delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC index). Secondary outcomes were cardiorespiratory fitness, isometric knee extension and flexion force and knee injury and OA outcome (KOOS) questionnaire. After 4-months aquatic training, there was a significant decrease in both T2 -1.2 ms (95% confidence interval (CI): -2.3 to -0.1, P = 0.021) and dGEMRIC index -23 ms (-43 to -3, P = 0.016) in the training group compared to controls in the full thickness posterior region of interest (ROI) of the medial femoral cartilage. Cardiorespiratory fitness significantly improved in the intervention group by 9.8% (P = 0.010). Our results suggest that, in postmenopausal women with mild knee OA, the integrity of the collagen-interstitial water environment (T2) of the tibiofemoral cartilage may be responsive to low shear and compressive forces during aquatic resistance training. More research is required to understand the exact nature of acute responses in dGEMRIC index to this type of loading. Further, aquatic resistance training improves cardiorespiratory fitness. ISRCTN65346593.

The prevalence of patellofemoral osteoarthritis: a systematic review and meta-analysis.

Source: Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society; Oct 2016; vol. 24 (no. 10); p. 1697-1707

Publication Type(s): Journal Article Review

Author(s): Kobayashi, S; Pappas, E; Fransen, M; Refshauge, K; Simic, M

Abstract: To determine the prevalence of radiographic patellofemoral osteoarthritis (OA) from population- and symptom-based cohorts and to evaluate if knee pain, physical function and quality of life (QOL) differ between people with isolated patellofemoral OA, isolated tibiofemoral OA and combined patellofemoral and tibiofemoral OA. Terms associated with "patellofemoral OA", "prevalence" and "clinical features" were used to search Medline, EMBASE, CINAHL, SCOPUS, AMED and Web of Science databases with no language restriction' from inception to August 2014. Two independent reviewers screened papers for eligibility. Studies were included if they reported prevalence of compartmental patterns of radiographic knee OA in population- or symptom-based cohorts. Studies were excluded if they evaluated a targeted sample (e.g., occupation-specific participants) or repeated already reported data from the same cohorts. Point prevalence estimates of patellofemoral OA were extracted from eligible studies, pooled and quantitatively analysed. A critical appraisal tool was used to evaluate methodological quality. The search yielded 1891 records. The inclusion criteria were met by 32 studies. The crude prevalence of patellofemoral OA was 25% in the population-based cohorts (aged >20 years) and 39% in the symptom-based cohorts (aged >30 years). Eight studies reported knee pain, physical function and QOL in people with different compartmental disease; however no significant differences were found. These findings confirm the substantial prevalence of patellofemoral OA, demonstrating the need to specifically consider the patellofemoral joint in knee OA research and clinical settings.

Melanoma risk in patients with rheumatoid arthritis treated with tumour necrosis factor alpha inhibitors: a systematic review and meta-analysis.

Source: Melanoma research; Oct 2016; vol. 26 (no. 5); p. 517-523

Publication Type(s): Journal Article

Author(s): Olsen, Catherine M; Hyrich, Kimme L; Knight, Lani L; Green, Adèle C

Abstract: Clinicians are concerned that treatment of rheumatoid arthritis (RA) with tumour necrosis factor alpha antagonists (TNFα biologics) may increase patients' risk of melanoma compared with treatment with nonbiologic disease-modifying antirheumatic drugs (nbDMARDS). We aimed to assess the risk of melanoma in RA patients treated with TNFα biologics compared with RA patients treated with nbDMARDS. A secondary aim was to quantify the risk of melanoma in RA patients treated with TNFα biologics compared with the general population. We carried out a systematic review and meta-analysis searching Medline, Embase and the ISI Science Citation Index databases to January 2016. Cohort studies that enabled a quantitative assessment of the risk of melanoma in RA patients treated with TNFα biologics compared with either RA patients treated with nbDMARDS or the general population or both were included. Data were pooled using a random-effects model. From 812 articles, we identified six that fulfilled the inclusion criteria. Four studies reported on the risk of melanoma in RA patients treated with TNFα biologics compared with those treated with nbDMARDS, with a pooled effect estimate of 1.60 (95% confidence interval 1.16-2.19). Five reported on the risk of melanoma in RA patients treated with TNFα biologics compared with the general population, and the pooled effect estimate was 1.87 (95% confidence interval 1.53-2.30). There was no significant heterogeneity in either analysis. This systematic review and meta-analysis does not allay clinician's fears and, while awaiting further evidence from large collaborative studies, this patient population may benefit from regular skin checks and counselling to avoid excessive sun exposure.

33. Variation in Private Payer Coverage of Rheumatoid Arthritis Drugs.

Source: Journal of managed care & specialty pharmacy; Oct 2016; vol. 22 (no. 10); p. 1176-1181

Publication Type(s): Journal Article

Author(s): Chambers, James D; Wilkinson, Colby L; Anderson, Jordan E; Chenoweth, Matthew D

Abstract: Payers in the United States issue coverage determinations to guide how their enrolled beneficiaries use prescription drugs. Because payers create their own coverage policies, how they cover drugs can vary, which in turn can affect access to care by beneficiaries. To examine how the largest private payers based on membership cover drugs indicated for rheumatoid arthritis and to determine what evidence the payers reported reviewing when formulating their coverage policies. Coverage policies issued by the 10 largest private payers that make their policies publicly available were identified for rheumatoid arthritis drugs. Each coverage determination was compared with the drug's corresponding FDA label and categorized according to the following: (a) consistent with the label, (b) more restrictive than the label, (c) less restrictive than the label, or (d) mixed (i.e., more restrictive than the label in one way but less restrictive in another). Each coverage determination was also compared with the American College of Rheumatology (ACR) 2012 treatment recommendations and categorized using the same relative restrictiveness criteria. The policies were then reviewed to identify the evidence that the payers reported reviewing. The identified evidence was divided into the following 6 categories: randomized controlled trials; other clinical studies (e.g., observational studies); health technology assessments; clinical reviews; cost-effectiveness analyses; and clinical guidelines. Sixty-nine percent of coverage determinations were more restrictive than the corresponding FDA label; 15% were consistent; 3% were less restrictive; and 13% were mixed. Thirty-four percent of coverage determinations were consistent with the ACR recommendations, 33% were more restrictive; 17% were less restrictive; and 17% were mixed. Payers most often reported

reviewing randomized controlled trials for their coverage policies (an average of 2.3 per policy). The payers reported reviewing an average of 1.4 clinical guidelines, 1.1 clinical reviews, 0.8 other clinical studies, and 0.5 technology assessments per policy. Only 1 payer reported reviewing cost-effectiveness analyses. The evidence base that the payers reported reviewing varied in terms of volume and composition. Payers most often covered rheumatoid arthritis drugs more restrictively than the corresponding FDA label indication and the ACR treatment recommendations. Payers reported reviewing a varied evidence base in their coverage policies. Funding for this study was provided by Genentech. Chambers has participated in a Sanofi advisory board, unrelated to this study. The authors report no other potential conflicts of interest. Study concept and design were contributed by Chambers. Anderson, Wilkinson, and Chenoweth collected the data, assisted by Chambers, and data interpretation was primarily performed by Chambers, along with Anderson and with assistance from Wilkinson and Chenoweth. The manuscript was written primarily by Chambers, along with Wilkinson and with assistance from Anderson and Chenoweth. Chambers, Chenoweth, Wilkinson, and Anderson revised the manuscript.

PANLAR Consensus Recommendations for the Management in Osteoarthritis of Hand, Hip, and Knee.

Source: Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases; Oct 2016; vol. 22 (no. 7); p. 345-354

Publication Type(s): Journal Article

Author(s): Rillo, Oscar; Riera, Humberto; Acosta, Carlota; Liendo, Verónica; Bolaños, Joyce;

Abstract: The objective of this consensus is to update the recommendations for the treatment of hand, hip, and knee osteoarthritis (OA) by agreeing on key propositions relating to the management of hand, hip, and knee OA, by identifying and critically appraising research evidence for the effectiveness of the treatments and by generating recommendations based on a combination of the available evidence and expert opinion of 18 countries of America. Recommendations were developed by a group of 48 specialists of rheumatologists, members of other medical disciplines (orthopedics and physiatrists), and three patients, one for each location of OA. A systematic review of existing articles, meta-analyses, and guidelines for the management of hand, hip, and knee OA published between 2008 and January 2014 was undertaken. The scores for Level of Evidence and Grade of Recommendation were proposed and fully consented within the committee based on The American Heart Association Evidence-Based Scoring System. The level of agreement was established through a variation of Delphi technique. Both "strong" and "conditional" recommendations are given for management of hand, hip, and knee OA and nonpharmacological, pharmacological, and surgical modalities of treatment are presented according to the different levels of agreement. These recommendations are based on the consensus of clinical experts from a wide range of disciplines taking available evidence into account while balancing the benefits and risks of nonpharmacological, pharmacological, and surgical treatment modalities, and incorporating their preferences and values. Different backgrounds in terms of patient education or drug availability in different countries were not evaluated but will be important.

Pain beliefs and problems in functioning among people with arthritis: a meta-analytic review.

Source: Journal of behavioral medicine; Oct 2016; vol. 39 (no. 5); p. 735-756

Publication Type(s): Journal Article Review

Author(s): Jia, Xiaojun; Jackson, Todd

Abstract: In this meta-analysis, we evaluated overall strengths of relation between beliefs about pain, health, or illness and problems in functioning (i.e., functional impairment, affective distress,

pain severity) in osteoarthritis and rheumatoid arthritis samples as well as moderators of these associations. In sum, 111 samples (N = 17,365 patients) met inclusion criteria. On average, highly significant, medium effect sizes were observed for associations between beliefs and problems in functioning but heterogeneity was also inflated. Effect sizes were not affected by arthritis subtype, gender, or age. However, pain belief content emerged as a significant moderator, with larger effect sizes for studies in which personal incapacity or ineffectiveness in controlling pain was a content theme of belief indices (i.e., pain catastrophizing, helplessness, self-efficacy) compared to those examining locus of control and fear/threat/harm beliefs. Furthermore, analyses of longitudinal study subsets supported the status of pain beliefs risk factors for later problems in functioning in these groups.

A Critical Review of Biosimilars in IBD: The Confluence of Biologic Drug Development, Regulatory Requirements, Clinical Outcomes, and Big Business.

Source: Inflammatory bowel diseases; Oct 2016; vol. 22 (no. 10); p. 2513-2526

Publication Type(s): Journal Article

Author(s): Ha, Christina Y; Kornbluth, Asher

Abstract: On February 9, 2016, the Food and Drug Administration Arthritis Advisory Committee recommended by a vote of 21 to 3, that the biosimilar to infliximab, CT-P13, be approved for rheumatoid arthritis and ankylosing spondylitis and, by extrapolation, for all the indications for which infliximab is currently approved, including adult and pediatric ulcerative colitis and Crohn's disease. On April 5, 2016, the Food and Drug Administration concurred with this recommendation and approved CT-P13 (Inflectra; Pfizer Inc.) for all diseases for which infliximab had previously been approved, including adult and pediatric moderate to severe ulcerative colitis and pediatric and adult moderate to severe and fistulizing Crohn's disease. This was despite the absence of any randomized controlled trials studying the infliximab biosimilar in any inflammatory bowel disease. This highly controversial approach has been criticized by various rheumatology and gastroenterology professional societies around the world. This review will cover the stepwise approach to biosimilar development, issues of extrapolation and interchangeability, and conclude with a discussion of the regulatory, intellectual property issues, and financial implications, which will all intersect in the decision and ability to prescribe a biosimilar or reference anti-tumor necrosis factor drug.

The Effect of TNF Inhibitors on Cardiovascular Events in Psoriasis and Psoriatic Arthritis: an Updated Meta-Analysis.

Source: Clinical reviews in allergy & immunology; Oct 2016; vol. 51 (no. 2); p. 240-247

Publication Type(s): Journal Article

Author(s): Yang, Zheng-Sheng; Lin, Ning-Ning; Li, Li; Li, Yang

Abstract:TNF inhibitors have been used in psoriasis (Pso) and psoriatic arthritis (PsA), which were associated with increased risk of cardiac and cerebrovascular events. However, whether TNF inhibitors reduce cardiovascular event is still unclear. Therefore, we aimed to evaluate the effect of TNF inhibitors on adverse cardiovascular events (CVEs) in Pso with or without PsA. We undertook a meta-analysis of clinical trials identified in systematic searches of MEDLINE, EMBASE, Wanfang database, Cochrane Database, and Google scholar through December 31, 2015. Five studies (49,795 patients) were included. Overall, compared with topical/photo treatment, TNF inhibitors were associated with a significant lower risk of CVE (RR, 0.58; 95 % CI, 0.43 to 0.77; P < 0.001; I (2) = 66.2 %). Additionally, compared with methotrexate (MTX) treatment, risk of CVE was also markedly decreased in the TNF inhibitor group (RR, 0.67; 95 % CI, 0.52 to 0.88; P = 0.003; I (2) = 9.3 %). Meanwhile, TNF inhibitors were linked to reduced incidence of myocardial infarction

compared with topical/photo or MTX treatment (RR, 0.73; 95 % CI, 0.59 to 0.90; P = 0.003; I (2) = 56.2 % and RR, 0.65; 95 % CI, 0.48 to 0.89; P = 0.007; I (2) = 0.0 %, respectively). Furthermore, there was a trend of decreased rate of mortality in the TNF inhibitor group compared with other therapy (RR, 0.90; 95 % CI, 0.54 to 1.50; P = 0.68; I (2) = 70.9 %). TNF inhibitors appear to have net clinical benefits with regard to adverse cardiovascular events in Pso and/or PsA. Rigorous randomized controlled trials will need to evaluate whether TNF inhibitors truly result in reduction of cardiovascular diseases.

Biologic Therapies and Risk of Infection and Malignancy in Patients With Inflammatory Bowel Disease: A Systematic Review and Network Meta-analysis.

Source: Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association; Oct 2016; vol. 14 (no. 10); p. 1385

Publication Type(s): Journal Article

Author(s): Bonovas, Stefanos; Fiorino, Gionata; Allocca, Mariangela; Lytras, Theodore; Nikolopoulos, Georgios K; Peyrin-Biroulet, Laurent; Danese, Silvio

Abstract: Safety issues are a major concern for patients considering treatments for inflammatory bowel disease (IBD). We performed a systematic review and meta-analysis to determine whether biologic agents affect the risk of infection or malignancy in adults with IBD. We searched PubMed, Embase, Scopus, Cochrane IBD Group Specialized Trials Register, World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov through March 2016 for randomized placebo-controlled or head-to-head trials of biologic agents approved for treatment of adults with IBD (ie, adalimumab, certolizumab, golimumab, infliximab, natalizumab, or vedolizumab). Two reviewers independently extracted study data and outcomes (serious infections, opportunistic infections, tuberculosis, any infection, and malignancies) and rated each trial's risk of bias. We used conventional meta-analysis to synthesize direct evidence and a network meta-analysis for adjusted indirect treatment comparisons. We identified 49 randomized placebo-controlled studies comprising 14,590 participants. Synthesis of the evidence indicated that patients treated with biologics had a moderate increase in risk of any infection (odds ratio [OR], 1.19; 95% confidence interval [CI], 1.10-1.29) and a significant increase in risk of opportunistic infections (OR, 1.90; 95% CI, 1.21-3.01). Risk of serious infections was not increased in patients treated with biologics (OR, 0.89; 95% CI, 0.71-1.12). On the contrary, biologics appeared to significantly reduce risk of serious infections in studies with low risk of bias (OR, 0.56; 95% CI, 0.35-0.90). We did not find an increased risk of malignancy with use of biologic agents (OR, 0.90; 95% CI, 0.54-1.50), but data were insufficient in terms of exposure and follow-up times. None of the indirect comparisons, either among the individual agents or between the anti-tumor necrosis factor and anti-integrin classes, reached significance for any of the outcomes analyzed. On the basis of a systematic review and meta-analysis, biologic agents increase the risk of opportunistic infections in patients with IBD, but not the risk of serious infections. It is necessary to continue to monitor the comparative and long-term safety profiles of these drugs.

Generalizability of Patients With Rheumatoid Arthritis in Biologic Agent Clinical Trials.

Source: Arthritis care & research; Oct 2016; vol. 68 (no. 10); p. 1478-1488

Publication Type(s): Journal Article

Author(s): Vashisht, Priyanka; Sayles, Harlan; Cannella, Amy C; Mikuls, Ted R; Michaud, Kaleb

Abstract: Randomized controlled trials (RCTs) have consistently demonstrated the efficacy of biologic agents in treating patients with rheumatoid arthritis (RA) who satisfy strict eligibility criteria, yet studies report that a majority of RA patients in the US have had biologic treatment exposure. We identified the proportion of RA patients in clinical practice satisfying entry criteria for biologic agent

RCTs. Eligibility criteria of 30 RCTs of 10 Food and Drug Administration-approved biologic agents to treat RA were reviewed, summarized, and applied to 2 observational clinical cohorts: the Veterans Affairs Rheumatoid Arthritis registry (VARA; n = 1,523) and the Rheumatology and Arthritis Investigational Network Database (RAIN-DB; n = 1,548). Patients at a single clinical encounter were assessed for overall trial eligibility as well as eligibility across 3 domains: demographics, disease activity, and medication exposure. The mean percentage of patients that satisfied eligibility criteria was 3.7% (interquartile range [IQR] 1.5-3.1) in VARA and 7.1% (IQR 4.4-7.7) in RAIN-DB. Ineligibility was most often due to low disease activity, specifically low joint counts. The mean Disease Activity Score in 28 joints at enrollment was 6.59 (range 6.1-7.1) across RCTs versus 3.87 (0.07-8.69) in VARA and 3.65 (0.49-7.21) in RAIN-DB. RCTs for non-tumor necrosis factor (TNF) inhibitor biologic agents were more restrictive than RCTs for TNF inhibitors. There was no trend in eligibility by RCT study publication or drug approval date. The vast majority of RA patients from our clinical cohorts did not satisfy criteria for participation in biologic agent RCTs. These findings underscore the need for caution in extrapolating trial results to day-to-day management of RA patients and may provide insight into the differential responses to biologic agents reported in prior observational studies.

Is Tibiofemoral or Patellofemoral Alignment or Trochlear Morphology Associated With Patellofemoral Osteoarthritis? A Systematic Review.

Source: Arthritis care & research; Oct 2016; vol. 68 (no. 10); p. 1453-1470

Publication Type(s): Journal Article

Author(s): Macri, Erin M; Stefanik, Joshua J; Khan, Karim K; Crossley, Kay M

Abstract: We conducted a systematic review to evaluate the associations of knee alignment or trochlear morphology (measured on imaging) with presence, severity, onset, and/or progression of patellofemoral osteoarthritis (PFOA). We prospectively registered our protocol with PROSPERO (International prospective register of systematic reviews) and followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to report this review. We searched 10 electronic databases, screened citing articles, and reviewed reference lists. We extracted data and evaluated methodologic quality. Due to study design heterogeneity, we used a best-evidence synthesis to summarize the evidence. We included 16 publications (2,892 participants, 66% women) after removing 4 papers that did not meet our threshold for methodologic quality. There were 11 cross-sectional and 5 longitudinal papers. The target population was knee OA in 11 studies, PFOA in 2 studies, and other knee conditions in 3 studies. Alignment or morphology was measured using radiographs in 8 studies, magnetic resonance imaging in 7 studies, and computed tomography in 2 papers. Limitations include substantial heterogeneity in samples and methods, short followup times in longitudinal studies, and a small number of studies that specifically recruited participants with PFOA. There is strong evidence that PFOA is associated with both trochlear morphology and frontal plane knee alignment, while evidence is limited but consistent in the sagittal and axial planes. These findings suggest that alignment should be evaluated clinically in individuals with PFOA. Clinical interventions targeting knee alignment warrant further investigation.

Quality of Community-Based Osteoarthritis Care: A Systematic Review and Meta-Analysis.

Source: Arthritis care & research; Oct 2016; vol. 68 (no. 10); p. 1443-1452

Publication Type(s): Journal Article

Author(s): Hagen, Kåre B; Smedslund, Geir; Østerås, Nina; Jamtvedt, Gro

Abstract: To evaluate the state of quality of care for osteoarthritis (OA) by summarizing studies that have assessed the care provided to patients. A systematic review of community-based observational studies of actual clinical practice treating people with OA compared with quality indicators (QIs) was performed. Four databases were searched from January 2000 to November 2015. Two reviewers independently determined study eligibility, assessed risk of bias, and extracted study data. The outcome was adherence to the QIs (pass rate). The overall pass rate (the total number of indicators passed divided by the total number of indicators for which the patients were eligible) was extracted from each study. When at least 50% of the studies had comparable individual QIs, the data were pooled with proportion meta-analyses. Fifteen studies comprising 16,103 patients were included, and the median overall pass rate across studies was 41% (range 22-65%). The pooled pass rates for individual QIs were "referral to orthopedic surgeon if no response to other therapy": 59.4% (95% confidence interval [95% CI] 47.5-70.3); "paracetamol or acetaminophen first drug used": 46.0% (95% CI 26.6-66.7); "assessed for pain and/or function": 45.5% (95% CI 33.9-57.6); "referral or recommendation to exercise": 38.7% (28.9-49.5); "offered education and self-management": 35.4% (95% CI 27.8-44.0); and "informed about potential risks if NSAIDs prescribed": 34.1% (95% CI 24.7-44.9). There is room for improvement in community-based OA care. © 2016, American College of Rheumatology.

Can rheumatoid arthritis (RA) registries provide contextual safety data for modern RA clinical trials? The case for mortality and cardiovascular disease.

Source: Annals of the rheumatic diseases; Oct 2016; vol. 75 (no. 10); p. 1797-1805

Publication Type(s): Journal Article

Author(s): Michaud, Kaleb; Berglind, Niklas; Franzén, Stefan; Frisell, Thomas; Garwood, Christopher;

Abstract: We implemented a novel method for providing contextual adverse event rates for a randomised controlled trial (RCT) programme through coordinated analyses of five RA registries, focusing here on cardiovascular disease (CVD) and mortality. Each participating registry (Consortium of Rheumatology Researchers of North America (CORRONA) (USA), Swedish Rheumatology Quality of Care Register (SRR) (Sweden), Norfolk Arthritis Register (NOAR) (UK), CORRONA International (East Europe, Latin America, India) and Institute of Rheumatology, Rheumatoid Arthritis (IORRA) (Japan)) defined a main cohort from January 2000 onwards. To address comparability and potential bias, we harmonised event definitions and defined several subcohorts for sensitivity analyses based on disease activity, treatment, calendar time, duration of follow-up and RCT exclusions. Rates were standardised for age, sex and, in one sensitivity analysis, also HAQ. The combined registry cohorts included 57 251 patients with RA (234 089 person-years)-24.5% men, mean (SD) baseline age 58.2 (13.8) and RA duration 8.2 (11.7) years. Standardised registry mortality rates (per 100 person-years) varied from 0.42 (CORRONA) to 0.80 (NOAR), with 0.60 for RCT patients. Myocardial infarction and major adverse cardiovascular events (MACE) rates ranged from 0.09 and 0.31 (IORRA) to 0.39 and 0.77 (SRR), with RCT rates intermediate (0.18 and 0.42), respectively. Additional subcohort analyses showed small and mostly consistent changes across registries, retaining reasonable consistency in rates across the Western registries. Additional standardisation for HAQ returned higher mortality and MACE registry rates. This coordinated approach to contextualising RA RCT safety data demonstrated reasonable differences and consistency in rates for mortality and CVD across registries, and comparable RCT rates, and may serve as a model method to supplement clinical trial analyses for drug development programmes. 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/

Database: Medline

Increased pretreatment serum IFN-β/α ratio predicts non-response to tumour necrosis factor α inhibition in rheumatoid arthritis.

Source: Annals of the rheumatic diseases; Oct 2016; vol. 75 (no. 10); p. 1757-1762

Publication Type(s): Journal Article

Author(s): Wampler Muskardin, Theresa; Vashisht, Priyanka; Dorschner, Jessica M; Jensen, Mark A;

Available in full text at EULAR Meeting Abstracts - from Highwire Press

Available in full text at Annals of the Rheumatic Diseases - from Highwire Press

Abstract: Studies suggest that circulating type I interferon (IFN) may predict response to biological agents in rheumatoid arthritis (RA). Prediction of response prior to initiating therapy would represent a major advancement. We studied sera from a test set of 32 patients with RA from the Auto-immune Biomarkers Collaborative Network Consortium and a validation set of 92 patients with RA from the Treatment Efficacy and Toxicity in Rheumatoid Arthritis Database and Repository registry. The test set included those with good response or no response to tumour necrosis factor (TNF) inhibitors at 14 weeks by European League Against Rheumatism criteria. The validation set included subjects with good, moderate or no response at 12 weeks. Total serum type I IFN activity, IFN-α and IFN-β activity were measured using a functional reporter cell assay. In the test set, an increased ratio of IFN-β to IFN-α (IFN-β/α activity ratio) in pretreatment serum associated with lack of response to TNF inhibition (p=0.013). Anti-cyclic citrullinated peptide antibody titre and class of TNF inhibitor did not influence this relationship. A receiver-operator curve supported a ratio of 1.3 as the optimal cut-off. In the validation set, subjects with an IFN-β/α activity ratio >1.3 were significantly more likely to have non-response than good response (OR=6.67, p=0.018). The test had 77% specificity and 45% sensitivity for prediction of non-response compared with moderate or good response. Meta-analysis of test and validation sets confirmed strong predictive capacity of IFN-β/α activity ratio (p=0.005). Increased pretreatment serum IFN-β/α ratio strongly associated with non-response to TNF inhibition. This study supports further investigation of serum type I IFN in predicting outcome of TNF inhibition in RA. 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/

44. PANLAR Consensus Recommendations for the Management in Osteoarthritis of Hand, Hip, and Knee

Source: Journal of Clinical Rheumatology; Oct 2016; vol. 22 (no. 7); p. 345-354

Publication Type(s): Journal: Article

Author(s): Rillo O.; Riera H.; Quintero M.; Acosta C.; Liendo V.; Bolanos J.; Monterola L.; Nieto E.;

Abstract: Objective The objective of this consensus is to update the recommendations for the treatment of hand, hip, and knee osteoarthritis (OA) by agreeing on key propositions relating to the management of hand, hip, and knee OA, by identifying and critically appraising research evidence for the effectiveness of the treatments and by generating recommendations based on a combination of the available evidence and expert opinion of 18 countries of America. Methods Recommendations were developed by a group of 48 specialists of rheumatologists, members of other medical disciplines (orthopedics and physiatrists), and three patients, one for each location of OA. A systematic review of existing articles, meta-analyses, and guidelines for the management of hand, hip, and knee OA published between 2008 and January 2014 was undertaken. The scores for Level of Evidence and Grade of Recommendation were proposed and fully consented within the committee

based on The American Heart Association Evidence-Based Scoring System. The level of agreement was established through a variation of Delphi technique. Results Both "strong" and "conditional" recommendations are given for management of hand, hip, and knee OA and nonpharmacological, pharmacological, and surgical modalities of treatment are presented according to the different levels of agreement. Conclusions These recommendations are based on the consensus of clinical experts from a wide range of disciplines taking available evidence into account while balancing the benefits and risks of nonpharmacological, pharmacological, and surgical treatment modalities, and incorporating their preferences and values. Different backgrounds in terms of patient education or drug availability in different countries were not evaluated but will be important.

A case of acute recurrent pancreatitis and juvenile idiopathic arthritis: An association or chance occurrence

Source: American Journal of Gastroenterology; Oct 2016; vol. 111

Publication Type(s): Journal: Conference Abstract

Author(s): Qamar K.; Tiwari A.; Khan Z.; Nawras A.

Abstract: Introduction: Around 20-30% of cases of acute recurrent pancreatitis (ARP) are idiopathic. It is well known that variety of rheumatic syndromes have an association with visceral lesions; however there are only few case reports of autoimmune diseases involving pancreatitis and arthritis. No case report of Juvenile idiopathic Arthritis (JIA) and pancreatitis exist in English literature. We report the first case of JIA that presented with ARP without any obvious etiology for the same. Case Description: A 36-year-old Caucasian male with 33 years history of polyarticular JIA was evaluated in office for ARP. Even post-cholecystectomy he had multiple hospitalizations for acute pancreatitis over many years. The patient reported worsening of his joint pain with each episode of pancreatitis. There was no history of cigarette smoking, ethanol use, hypertriglyceridemia or hypercalcemia. Family history was unremarkable. He was on chronic steroid therapy along with pancreatic enzymes. Pertinent labs revealed mildly elevated ESR, CRP and RF. ANA and IgG4 levels were normal. Abdominal CT scan revealed calcification of pancreas consistent with chronic pancreatitis (CP). Endoscopic ultrasound with ERCP revealed atrophic and calcific pancreas with pancreatic duct stones but no evidence of choledocholithiasis. He was referred for intra-thecal pain pump placement for better pain control. Discussion: After extensive diagnostic work up, no etiology could be attributed to our patient's CP. No causal relationship was found between JIA and ARP after performing systematic review of literature. Autoimmune pancreatitis is responsible for 5 - 6 % cases of ARP. It is associated with other autoimmune disorders such as Rheumatoid arthritis, inflammatory bowel disease and primary biliary cirrhosis. However in our case IgG4 level was normal. Recent studies have shown that certain alleles confer increased risk of CP as well as JIA. HLADRB1*04:01 is one such allele that increases the risk of both CP and JIA. This could be an alternative explanation for ARP leading to CP in our patient with JIA. Our case report suggests that ARP could be a rare visceral complication of JIA as described in other chronic inflammatory rheumatism. Conclusion Association between JIA and ARP could have immunological basis or altered genetics that increases the risk of developing both these illnesses. This putative association requires other observations to definitely establish a link between ARP and JIA.

The prevalence of patellofemoral osteoarthritis: a systematic review and meta-analysis

Source: Osteoarthritis and Cartilage; Oct 2016; vol. 24 (no. 10); p. 1697-1707

Publication Type(s): Journal: Review

Author(s): Kobayashi S.; Pappas E.; Fransen M.; Refshauge K.; Simic M.

Abstract: Objective To determine the prevalence of radiographic patellofemoral osteoarthritis (OA) from population- and symptom-based cohorts and to evaluate if knee pain, physical function and quality of life (QOL) differ between people with isolated patellofemoral OA, isolated tibiofemoral OA and combined patellofemoral and tibiofemoral OA. Method Terms associated with "patellofemoral OA", "prevalence" and "clinical features" were used to search Medline, EMBASE, CINAHL, SCOPUS, AMED and Web of Science databases with no language restriction' from inception to August 2014. Two independent reviewers screened papers for eligibility. Studies were included if they reported prevalence of compartmental patterns of radiographic knee OA in population- or symptom-based cohorts. Studies were excluded if they evaluated a targeted sample (e.g., occupation-specific participants) or repeated already reported data from the same cohorts. Point prevalence estimates of patellofemoral OA were extracted from eligible studies, pooled and quantitatively analysed. A critical appraisal tool was used to evaluate methodological quality. Results The search yielded 1891 records. The inclusion criteria were met by 32 studies. The crude prevalence of patellofemoral OA was 25% in the population-based cohorts (aged >20 years) and 39% in the symptom-based cohorts (aged >30 years). Eight studies reported knee pain, physical function and QOL in people with different compartmental disease; however no significant differences were found. Conclusion These findings confirm the substantial prevalence of patellofemoral OA, demonstrating the need to specifically consider the patellofemoral joint in knee OA research and clinical settings. Copyright © 2016

48. Efficacy of progressive aquatic resistance training for tibiofemoral cartilage in postmenopausal women with mild knee osteoarthritis: a randomised controlled trial

Source: Osteoarthritis and Cartilage; Oct 2016; vol. 24 (no. 10); p. 1708-1717

Publication Type(s): Journal: Article

Author(s): Munukka M.; Waller B.; Hakkinen A.; Kujala U.M.; Sipila S.; Heinonen A.; Rantalainen T.; Nieminen M.T.; Lammentausta E.; Peuna A.; Paloneva J.; Kautiainen H.; Selanne H.; Kiviranta I.

Abstract: Objective To study the efficacy of aquatic resistance training on biochemical composition of tibiofemoral cartilage in postmenopausal women with mild knee osteoarthritis (OA). Design Eighty seven volunteer postmenopausal women, aged 60-68 years, with mild knee OA (Kellgren-Lawrence grades I/II and knee pain) were recruited and randomly assigned to an intervention (n = 43) and control (n = 44) group. The intervention group participated in 48 supervised aquatic resistance training sessions over 16 weeks while the control group maintained usual level of physical activity. The biochemical composition of the medial and lateral tibiofemoral cartilage was estimated using single-slice transverse relaxation time (T2) mapping and delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC index). Secondary outcomes were cardiorespiratory fitness, isometric knee extension and flexion force and knee injury and OA outcome (KOOS) questionnaire. Results After 4-months aquatic training, there was a significant decrease in both T2 -1.2 ms (95% confidence interval (CI): -2.3 to -0.1, P = 0.021) and dGEMRIC index -23 ms (-43 to -3, P = 0.016) in the training group compared to controls in the full thickness posterior region of interest (ROI) of the medial femoral cartilage. Cardiorespiratory fitness significantly improved in the intervention group by 9.8% (P = 0.010). Conclusions Our results suggest that, in postmenopausal women with mild knee OA, the integrity of the collagen-interstitial water environment (T2) of the tibiofemoral

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Renal dosing of allopurinol results in suboptimal gout care
09 December 2016, 12:47:27 | Neogi, T., Dalbeth, N., Stamp, L., Castelar, G., Fitzgerald, J., Gaffo, A.,

Response: Renal dosing of allopurinol results in suboptimal gout care by T Neogi et al
09 December 2016, 12:47:27 | Richette, P., Doherty, M., Pascual, E., Bardin, T.

High frequency of antidrug antibodies and association of random drug levels with efficacy in certolizumab pegol-treated patients with rheumatoid arthritis: results from the BRAGGSS cohort
09 December 2016, 12:47:27 | Jani, M., Isaacs, J. D., Morgan, A. W., Wilson, A. G., Plant, D., Hyrich, K. L., Chinoy, H., Barton, A., on behalf of BRAGGSS

Bone marrow lesions and synovitis on MRI associate with radiographic progression after 2 years in hand osteoarthritis
09 December 2016, 12:47:27 | Damman, W., Liu, R., Bloem, J., Rosendaal, F., Reijnierse, M.,

WNT16 antagonises excessive canonical WNT activation and protects cartilage in osteoarthritis
09 December 2016, 12:47:27 | Nalesso, G., Thomas, B. L., Sherwood, J. C., Yu, J., Addimanda, O.,

Autologous tolerogenic dendritic cells for rheumatoid and inflammatory arthritis
09 December 2016, 12:47:27 | Bell, G. M., Anderson, A. E., Diboll, J., Reece, R., Eltherington, O.,

Ectopic expression of CXCL13, BAFF, APRIL and LT-{beta} is associated with artery tertiary lymphoid organs in giant cell arteritis
09 December 2016, 12:47:27 | Ciccia, F., Rizzo, A., Maugeri, R., Alessandro, R., Croci, S., Guggino, G., Cavazza, A., Raimondo, S., Cannizzaro, A., Iacopino, D. G., Salvarani, C., Triolo, G.

Composition of TWIST1 dimers regulates fibroblast activation and tissue fibrosis
09 December 2016, 12:47:27 | Palumbo-Zerr, K., Soare, A., Zerr, P., Liebl, A., Mancuso, R., Tomcik,

Transient receptor potential canonical 5 (TRPC5) protects against pain and vascular inflammation in arthritis and joint inflammation
09 December 2016, 12:47:27 | Alawi, K. M., Russell, F. A., Aubdool, A. A., Srivastava, S., Riffo-V

Genetic association of ankylosing spondylitis with TBX21 influences T-bet and pro-inflammatory cytokine expression in humans and SKG mice as a model of spondyloarthritis
09 December 2016, 12:47:27 | Lau, M. C., Keith, P., Costello, M.-E., Bradbury, L. A., Hollis, K. A.,

The European Scleroderma Trials and Research group (EUSTAR) task force for the development of revised activity criteria for systemic sclerosis: derivation and validation of a preliminarily revised EUSTAR activity index
09 December 2016, 12:47:27 | Valentini, G., Iudici, M., Walker, U. A., Jaeger, V. K., Baron, M.,

Histone deacetylase 3 regulates the inflammatory gene expression programme of rheumatoid arthritis fibroblast-like synoviocytes
09 December 2016, 12:47:27 | Angiolilli, C., Kabala, P. A., Grabiec, A. M., Van Baarsen, I. M.,

A combined large-scale meta-analysis identifies COG6 as a novel shared risk locus for rheumatoid arthritis and systemic lupus erythematosus
09 December 2016, 12:47:27 | Marquez, A., Vidal-Bralo, L., Rodriguez-Rodriguez, L., Gonzalez-Gay,
Nerve growth factor inhibition with tanezumab influences weight-bearing and subsequent cartilage damage in the rat medial meniscal tear model
09 December 2016, 12:47:27 | LaBranche, T. P., Bendele, A. M., Omura, B. C., Gropp, K. E., Hurst, S. I., Bagi, C. M., Cummings, T. R., Grantham, L. E., Shelton, D. L., Zorbas, M. A.

Canakinumab reverses overexpression of inflammatory response genes in tumour necrosis factor receptor-associated periodic syndrome
09 December 2016, 12:47:27 | Torene, R., Nirmala, N., Obici, L., Cattalini, M., Tormey, V., Caorsi, R.,

A family-based genome-wide association study reveals an association of spondyloarthritis with MAPK14
09 December 2016, 12:47:27 | Costantino, F., Talpin, A., Said-Nahal, R., Leboime, A., Zinovieva,

Erratum: Differences and similarities in rheumatology speciality training programmes across European countries
09 December 2016, 12:47:27

Checkpoint immunotherapy: good for cancer therapy, bad for rheumatic diseases
09 December 2016, 12:47:26 | Calabrese, L., Velcheti, V.

Clinical trials of biosimilars should become more similar
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Is it time to revisit the role of ultrasound in rheumatoid arthritis management?
09 December 2016, 12:47:26 | D'Agostino, M., Boers, M., Wakefield, R. J., Emery, P., Conaghan, P. G.

2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary Sjögren's syndrome: A consensus and data-driven methodology involving three international patient cohorts
09 December 2016, 12:47:26 | Shiboski, C. H., Shiboski, S. C., Seror, R., Criswell, L. A., Labetoulle, M.,

EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update
09 December 2016, 12:47:26 | Agca, R., Heslinga, S. C., Rollefstad, S., Heslinga, M., McInnes, I. B.,

2016 updated EULAR evidence-based recommendations for the management of gout
09 December 2016, 12:47:26 | Richette, P., Doherty, M., Pascual, E., Barskova, V., Becce, F.,

Inflammatory arthritis and sicca syndrome induced by nivolumab and ipilimumab
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A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy
09 December 2016, 12:47:26 | Emery, P., Vencovsky, J., Sylwestrzak, A., Leszczynski, P., Porawska,

A randomised, double-blind, phase III study comparing SB2, an infliximab biosimilar, to the infliximab reference product Remicade in patients with moderate to severe rheumatoid arthritis despite methotrexate therapy
09 December 2016, 12:47:26 | Choe, J.-Y., Prodanovic, N., Niebrzydowski, J., Staykov, I.,

A phase III, multicentre, randomised, double-blind, active-controlled, parallel-group trial comparing safety and efficacy of HD203, with innovator etanercept, in combination with methotrexate, in patients with rheumatoid arthritis: the HERA study
09 December 2016, 12:47:26 | Bae, S.-C., Kim, J., Choe, J.-Y., Park, W., Lee, S.-H., Park, Y.-B., Shim,
Allopurinol and the risk of atrial fibrillation in the elderly: a study using Medicare data
09 December 2016, 12:47:26 | Singh, J. A., Yu, S.

Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1
09 December 2016, 12:47:26 | Mease, P. J., van der Heijde, D., Ritchlin, C. T., Okada, M.,

Baricitinib in patients with inadequate response or intolerance to conventional synthetic DMARDs: results from the RA-BUILD study
09 December 2016, 12:47:26 | Dougados, M., van der Heijde, D., Chen, Y.-C., Greenwald, M.,

Certolizumab pegol in combination with dose-optimised methotrexate in DMARD-naïve patients with early, active rheumatoid arthritis with poor prognostic factors: 1-year results from C-EARLY, a randomised, double-blind, placebo-controlled phase III study
09 December 2016, 12:47:26 | Emery, P., Bingham, C. O., Burmester, G. R., Bykerk, V. P., Furst, D. E.,

Cancer risk in patients with spondyloarthritis treated with TNF inhibitors: a collaborative study from the ARTIS and DANBIO registers
09 December 2016, 12:47:26 | Hellgren, K., Dreyer, L., Arkema, E. V., Glintborg, B., Jacobsson, L. T.

The association between anti-carbamylated protein (anti-CarP) antibodies and radiographic progression in early rheumatoid arthritis: a study exploring replication and the added value to ACPA and rheumatoid factor
09 December 2016, 12:47:26 | Ajeganova, S., van Steenbergen, H. W., Verheul, M. K., Forslind, K.,

How well do ACPA discriminate and predict RA in the general population: a study based on 12 590 population-representative Swedish twins
09 December 2016, 12:47:26 | Hensvold, A. H., Frisell, T., Magnusson, P. K. E., Holmdahl, R., Askling,

Economic considerations and patients' preferences affect treatment selection for patients with rheumatoid arthritis: a discrete choice experiment among European rheumatologists
09 December 2016, 12:47:26 | Hifinger, M., Hiligsmann, M., Ramiro, S., Watson, V., Severens, J. L.,

Are allopurinol dose and duration of use nephroprotective in the elderly? A Medicare claims study of allopurinol use and incident renal failure
09 December 2016, 12:47:26 | Singh, J. A., Yu, S.

Does knee replacement surgery for osteoarthritis improve survival? The jury is still out
09 December 2016, 12:47:26 | Misra, D., Lu, N., Felson, D., Choi, H. K., Seeger, J., Einhorn, T., Neogi,

Omega-3 fatty acids are associated with a lower prevalence of autoantibodies in shared epitope-positive subjects at risk for rheumatoid arthritis
09 December 2016, 12:47:26 | Gan, R. W., Demoruelle, M. K., Deane, K. D., Weisman, M. H.,

Combined role of vitamin D status and CYP24A1 in the transition to systemic lupus erythematosus
09 December 2016, 12:47:26 | Young, K. A., Munroe, M. E., Guthridge, J. M., Kamen, D. L., Niewold,

Long-term outcome in juvenile-onset mixed connective tissue disease: a nationwide Norwegian study
09 December 2016, 12:47:26 | Hetlevik, S. O., Flato, B., Rygg, M., Nordal, E. B., Brunborg, C.,
Elevated circulating levels of interferon-{gamma} and interferon-{gamma}-induced chemokines characterise patients with macrophage activation syndrome complicating systemic juvenile idiopathic arthritis
09 December 2016, 12:47:26 | Bracaglia, C., de Graaf, K., Pires Marafon, D., Guilhot, F., Ferlin, W.,

Canakinumab treatment for patients with active recurrent or chronic TNF receptor-associated periodic syndrome (TRAPS): an open-label, phase II study
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Establishment of reference intervals for osteoarthritis-related soluble biomarkers: the FNIH/OARSI OA Biomarkers Consortium
09 December 2016, 12:47:26 | Kraus, V. B., Hargrove, D. E., Hunter, D. J., Renner, J. B., Jordan, J.

Predictive validity of biochemical biomarkers in knee osteoarthritis: data from the FNIH OA Biomarkers Consortium
09 December 2016, 12:47:26 | Kraus, V. B., Collins, J. E., Hargrove, D., Losina, E., Nevitt, M., Katz, J.

Intravenous administration of expanded allogeneic adipose-derived mesenchymal stem cells in refractory rheumatoid arthritis (Cx611): results of a multicentre, dose escalation, randomised, single-blind, placebo-controlled phase Ib/IIa clinical trial
09 December 2016, 12:47:26 | Alvaro-Gracia, J. M., Jover, J. A., Garcia-Vicuna, R., Carreno, L.,

Secukinumab improves patient-reported outcomes in subjects with active psoriatic arthritis: results from a randomised phase III trial (FUTURE 1)
09 December 2016, 12:47:26 | Strand, V., Mease, P., Gossec, L., Elkayam, O., van den Bosch, F.,

Arthritis & Rheumatology

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Clinical Connections

Special Articles

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Daniel H. Solomon and Richard J. Bucala

Editorial: Inflammatory Osteoclasts: A Different Breed of Bone Eaters? (pages 2834–2836)
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Review: Novel Insights Into Tumor Necrosis Factor Receptor, Death Receptor 3, and Progranulin Pathways in Arthritis and Bone Remodeling (pages 2845–2856)
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Rheumatoid Arthritis

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Toward Electronic Health Recording: Evaluation of Electronic Patient-reported Outcome Measures System for Remote Monitoring of Early Rheumatoid Arthritis
Yasser El Miedany,
J Rheumatol December 2016 43(12):2106-2112 Abstract

Success Rate and Utility of Ultrasound-guided Synovial Biopsies in Clinical Practice
Aurélie Najm,
*J Rheumatol December 2016 43(12):2113-2119;*Abstract

Five-year Safety Data from 5 Clinical Trials of Subcutaneous Golimumab in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis
Jonathan Kay,
J Rheumatol December 2016 43(12):2120-2130; Abstract

Quantification of Bone Marrow Edema by Magnetic Resonance Imaging Only Marginally Reflects Clinical Neck Pain Evaluation in Rheumatoid Arthritis and Ankylosing Spondylitis
Xenofon Baraliakos,
J Rheumatol December 2016 43(12):2131-2135; Abstract

Developing a Risk-scoring Model for Ankylosing Spondylitis Based on a Combination of HLA-B27, Single-nucleotide Polymorphism, and Copy Number Variant Markers
Seung-Hyun Jung,
*J Rheumatol December 2016 43(12):2136-2141; p*Abstract

Physical Function and Spinal Mobility Remain Stable Despite Radiographic Spinal Progression in Patients with Ankylosing Spondylitis Treated with TNF-α Inhibitors for Up to 10 Years
Denis Poddubnyy,
*J Rheumatol December 2016 43(12):2142-2148;*Abstract

Incidence of Malignancies in a Cohort of Psoriatic Arthritis Patients Taking Traditional Disease Modifying Antirheumatic Drug and Tumor Necrosis Factor Inhibitor Therapy: An Observational Study
uisa Costa,
*J Rheumatol December 2016 43(12):2149-2154;*Abstract

Disease Activity and Increased Risk of Cardiovascular Death among Patients with Psoriatic Arthritis
Kristina Juneblad,
J Rheumatol December 2016 43(12):2155-2161; Abstract

Predictors of Cardiovascular Hospitalization in Giant Cell Arteritis: Effect of Statin Exposure. A French Population-based Study
Grégory Pugnet,
J Rheumatol December 2016 43(12):2162-2170; Abstract

Interobserver and Intraobserver Reliability of Clinical Assessments in Knee Osteoarthritis
Nasimah Maricar,
J Rheumatol December 2016 43(12):2171-2178; Abstract

Bone Area Provides a Responsive Outcome Measure for Bone Changes in Short-term Knee Osteoarthritis Studies
Michael A. Bowes,

J Rheumatol December 2016 43(12):2179-2182; Abstract

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Evidence for Tocilizumab as a Treatment Option in Refractory Uveitis Associated with Juvenile Idiopathic Arthritis
Christoph Tappeiner,
*J Rheumatol December 2016 43(12):2183-2188;*Abstract

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*J Rheumatol December 2016 43(12):2199;*Excerpt
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*J Rheumatol December 2016 43(12):2199;*Excerpt
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Osteoporosis International

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Thalassemia-associated osteoporosis: a systematic review on treatment and brief overview of the disease
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Health-related quality of life in older people with osteoporotic vertebral fractures: response to comments by Sani et al.
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Exercise: Relative Risk

The relative risk is the ratio of probability of an event (a specified outcome) occurring in one group (i.e. those exposed to a particular intervention) compared to those in another group (i.e. those not exposed – a control group).

The relative risk can be interpreted using the following chart. First, you must determine whether the event (the outcome measure) is adverse or beneficial.

Relative Risk	Adverse outcome (e.g. death)	Beneficial outcome (e.g. recovery of limb function)
<1	Intervention better than control	Intervention worse than control
1	Intervention no better or worse than control	Intervention no better or worse than control
>1	Intervention worse than control	Intervention better than control

Have a go at interpreting the relative risks for these three studies using the chart above. Is the intervention better or worse than the control?

	Intervention	Population	Outcome measure (think: adverse or beneficial?)	Relative Risk
Study 1	Drug X	Adults at risk of a heart attack	Heart attack	1.2
Study 2	Therapy programme Y	Smokers	Smoking cessation	0.8
Study 3	Probiotic Z	Children on antibiotics	Diarrhoea	0.3

*Find out more about relative risk in one of our **Statistics** training sessions.*
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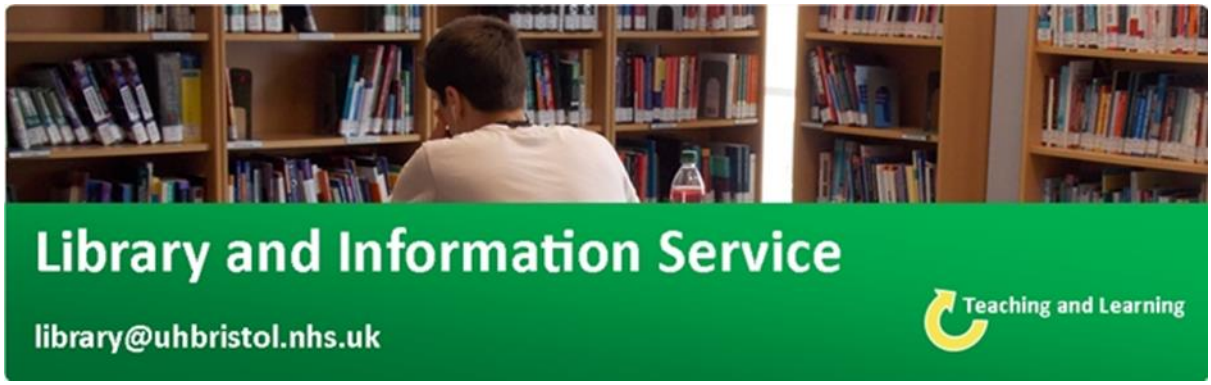
Answers: Study 1: worse; Study 2: worse; Study 3: better



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