O13. HYPERMOBILITY IS A RISK FACTOR FOR MUSCULOSKELETAL PAIN IN ADOLESCENCE: FINDINGS FROM A PROSPECTIVE COHORT STUDY
Jon Tobias1, Kevin Deere1, Shea Palmer4, Emma Clark1 and Jackie Clinch3

Musculoskeletal Research Unit, University of Bristol, Bristol, England and Paediatric Rheumatology, Bristol Royal Hospital for Children, Bristol, UK

Background: Cases series suggest joint hypermobility (JH) is a risk factor for musculoskeletal pain in childhood, but this has not been supported by epidemiological studies. However, the latter have largely comprised small samples, and prospective data based on large cohorts are lacking. We aimed to exploit the Avon Longitudinal Study of Parents and Children (ALSPAC), a unique birth cohort, to determine whether joint hypermobility (JH) in childhood is a risk factor for the subsequent development of musculoskeletal pain.

Methods: JH was determined by Beighton score at age 13.8 years in ALSPAC, using a cut-off of >6. Musculoskeletal pain was evaluated by questionnaire at age 17.8 years. Logistic regression analysis was performed in 2901 participants (1267 boys and 1634 girls) with complete data.

Results: 4.6% of participants were hypermobile at age 13.8 years. Moderately troublesome musculoskeletal pain at age 17.8 was reported most commonly at the lower back (16.1%), upper back (8.9%), neck (8.6%), shoulder (9.5%), knee (8.8%) and ankle/foot (6.8%). JH was associated with an increased risk of at least moderately troublesome musculoskeletal pain at the shoulder (1.68; 1.04, 2.72), knee (1.83; 1.10, 3.02) and ankle/foot (1.82; 1.05, 3.16) (OR with 95% CI, adjusted for gender, maternal education and BMI). An equivalent relationship was not observed at other sites including the spine, elbows, hands and hips. In analyses examining interactions with obesity, associations between JH and knee pain showed higher ORs in obese participants (1.6 and 11.0 in non-obese and obese participants, respectively, P = 0.04 for obesity interaction).

Conclusions: JH represents a risk factor for musculoskeletal pain in adolescence, comprising a specific distribution namely the shoulder, knee and ankle/foot. These relationships were strongest in the presence of obesity, consistent with a causal pathway whereby JH leads to pain at sites exposed to the greatest mechanical forces.

Disclosures: The authors have declared no conflicts of interest.

O14. THE ASSOCIATION BETWEEN GASTROINTESTINAL SYMPTOMS AND THE JOINT HYPERMOBILITY SYNDROME IN A POPULATION OF UNIVERSITY STUDENTS
Asma Fikree1, Rubina Akter1, Georgina Wellstead1, Charles Knowles1, Rodney Grahame4 and Qasim Aziz5

Faculty of Health and Life Sciences, University of the West of England, Bristol and The Bristol Gastrointestinal Research Unit, University of Bristol, England

Background: Joint hypermobility syndrome (JHS) is a non-inflammatory hereditary connective tissue disorder which is common. Recent data suggest JHS patients report gastrointestinal (GI) symptoms, particularly abdominal pain, reflux, dyspepsia, bloating, constipation and diarrhoea. JHS is also associated with autonomic dysfunction, psychopathology and fibromyalgia, all of which can cause GI symptoms. The association between GI symptoms and JHS in a ‘non-patient’ population and the effect of the above-mentioned factors has never been studied. This was our aim.

Methods: A cross sectional study in students at Queen Mary University, London. All 16,000 students were invited to complete a validated hypermobility screening questionnaire online. Those that screened negative (score 0/5) and positive (score >2/5) were invited to participate; those that agreed were then examined for JHS, fibromyalgia and skin stretchiness using the Brighton criteria. 190 Wolfe criteria, and corrected skin extensibility score respectively. Validated questionnaires were used to assess for GI symptoms, autonomic symptoms, anxiety, depression and somatization. GI symptoms and other factors were compared in the JHS and non-JHS students. A logistic regression analysis using variables which were significantly different in the 2 groups was used to determine whether the presence of GI symptoms was dependent on these factors.

Results: 220 students agreed to participate in the study. Of these 73 were screen positive and had confirmed JHS (JHS+); 89 were screen negative and had no JHS (JHS-). There were no significant age, gender or BMI differences. The JHS+ students had significantly more musculoskeletal problems, higher Beighton and skin extensibility scores and were more likely to have a Marfanoid habitus (all, P < 0.005). There was no significant difference in the presence of abdominal pain, reflux, bloating, constipation or diarrhoea in the 2 groups; however the JHS+ students had significantly more postprandial fullness and early satiety (P = 0.03), features of dyspepsia. There was no significant difference in anxiety, depression, or somatization. The JHS+ students had significantly more tender points on examination (P = 0.005), and higher autonomic scores (P = 0.03). With logistic regression analysis, the addition of autonomic scores reduced the association between JHS and postprandial symptoms, suggesting that the association was mediated by autonomic symptoms.

Conclusions: Studies in patients are limited because patients do not represent the general population, and are more likely to report symptoms, leading to a response bias. We studied healthy, previously undiagnosed, students thus overcoming these limitations. Only postprandial symptoms were significantly more prevalent in young JHS+ students, and these symptoms appear to be mediated by autonomic dysfunction.

Disclosures: The authors have declared no conflicts of interest.

O15. A COMPARISON OF THE OUTCOME OF ADOLESCENT- AND ADULT-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS
Beatriz Amaral1, Grainne Murphy1, Yiannis Ioannou1 and David A. Isenberg1

1Arthritis Research UK Centre for Adolescent Rheumatology, University College London, London, UK

Background: Previous reports have suggested that juvenile (usually <16 years at onset) SLE is associated with a worse prognosis than adult-onset disease. Many single-centre studies have however, been limited by small sample sizes and few have specifically addressed the outcome of patients with an adolescent onset of disease.

Methods: Patients with adolescent onset lupus (11–19 years) were identified from an established cohort of patients under active follow-up within the Department of Rheumatology in University College Hospital London from January 1978 to October 2012. All adult patients (onset >19 years) under active follow-up within the same department were used as a comparator group. Data were analysed by univariable and multivariable analysis for age, gender, ethnicity, clinical symptoms, serological profile and duration of follow-up assessing differences in outcome measures such as mortality, development of LN, cancer and cardiovascular disease.

Results: 124 patients with adolescent-onset and 484 patients with adult-onset disease were identified. There was a higher percentage of males (12.9% vs 7.2%, P = 0.036) and patients of Asian ethnicity within the adolescent group (P = 0.01). There were no differences in duration of follow-up [median (interquartile range) adult = 16 years (15), juvenile = 14 years (11)]. Adolescent-onset SLE was associated with a higher frequency of renal disease (42.7% vs 27.1%) (P = 0.001), haemolytic anaemia (7.3% vs 2.9%, P = 0.03) and a lower frequency of serositis (28.2% vs 41.4%, P = 0.007) and secondary Sjogren’s syndrome (2.4% vs 9.7%, P = 0.003). No serological differences
were observed apart from a greater prevalence of rheumatoid factor within the adult cohort. Ischaemic vascular events were observed in 6.6% of adult patients (32 per 4182 person-years of follow-up) with SLE (vs 2.4% of adolescent-onset cases per 1828 person years follow-up), \( P = 0.06 \). 33 adult-onset patients developed cancer (6.8%) in comparison with 6 cases within the adolescent group (4.8%). \( P = 0.54 \). The mortality rate in the adult cohort was 15% compared with 5.6% in the adolescent cohort, \( P = 0.007 \). By multivariate analysis, adolescent onset of disease retained a significant association with the occurrence of LN.

**Conclusions:** While adult patients had more frequent serositis and sicca syndrome, adolescent-onset disease in this cohort was significantly associated with the development of LN, a negative prognostic indicator. Moreover, adolescent patients were not protected from the development of vascular events or cancer despite their youth. These data suggest a more aggressive phenotype of disease in patients with onset of SLE in the adolescent years and supports the need for intensive follow-up and aggressive therapy in this population.

**Disclosures:** The authors have declared no conflicts of interest.

O16. **ANTI-NXP2 AUTOANTIBODY STATUS IS A PREDICTOR OF CALCINOSIS IN OLDER BUT NOT YOUNGER CHILDREN WHO DEVELOP JUVENILE DERMATOMYOSITIS**

Sarah L. Tansley, Zoe E. Betteridge, Harsha Gunawardena, Gavin Shaddick, Hemlata Varsani, Lucy Wedderburn and Neil McHugh

**Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, Research Institute of Rheumatic Diseases, Bath, Rheumatology, North Bristol NHS trust, Bristol, Mathematics, University of Bath, Bath and Rheumatology, Institute of Child Health, London, UK**

**Background:** JDM is characterized by a pathognomonic skin rash and skeletal muscle inflammation. It is a heterogeneous disorder with a range of additional disease features and complications. It is known that patient age at disease onset and the presence of myositis-specific autoantibodies (MSA) can influence the particular disease features seen in addition to overall prognosis. Children whose JDM starts before their 5th birthday have more ulceration and generalized oedema compared with those with onset after 5 years, both considered poor prognostic indicators. Anti-NXP2 antibodies are a common MSA found in JDM and can be identified in 13–23% of children. Our group have previously demonstrated that anti-NXP2 are strongly associated with the development of calcinosis, a major cause of morbidity in JDM. Here we report that the established association of anti-NXP2 antibodies with calcinosis is not apparent in younger children.

**Methods:** Serum samples were available from 203 JDM patients recruited to the UK Juvenile Dermatomyositis Research Repository and Cohort Study. Immunoprecipitation of radio-labelled KS62 cells was performed on all samples to determine the presence of autoantibodies. Those with a band in the 140kDa region were confirmed to be anti-NXP2 by development of an in-house ELISA using recombinant NXP2 (Origene). Clinical data were collected prospectively on standardized proformas. Children were divided into two groups; those aged 0–5 years and those aged 6–16 years at disease onset (91 aged 0–5 years and 112 aged 6–16 years). Statistical analysis was performed using SPSS and R software looking at Chi-squared test and logistic regression analysis.

**Results:** The frequency of anti-NXP2 antibodies (17% 0–5 years and 14% 6–16 years) and calcinosis (26% 0–5 years and 20% 6–16 years) was not significantly different between the two age-onset groups. Overall the presence of anti-NXP2 antibodies was strongly associated with the development of calcinosis (\( P < 0.001 \)). Calcinosis was significantly associated with the presence of anti-NXP2 antibodies in children aged 6–16 years at disease onset (65% with anti-NXP2 developed calcinosis vs 13% without, \( P < 0.001 \)) but not those aged 0–5 years. There was a trend for the development of calcinosis in younger children with anti-NXP2 antibodies (40% with anti-NXP2 developed calcinosis vs 23% without, \( P = 0.32 \)). The effect of anti-NXP2 antibody status on the development of calcinosis was not significantly different between the two age of onset groups (\( P = 0.3 \)).

**Conclusions:** Anti-NXP2 antibodies are only significantly associated with calcinosis in older children diagnosed with JDM, despite a similar trend in younger children. As the frequency of calcinosis is similar in both groups, factors other than anti-NXP2 antibody status must have an important role in the development of calcinosis in younger children.

**Disclosures:** The authors have declared no conflicts of interest.

O17. **CATCH-UP GROWTH DURING TOCILIZUMAB THERAPY FOR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: TENDER 2-YEAR DATA**

Fabrizio De Benedetti, Niccolino Ruperto, Graciela Espada, Valeria Gerbini, Berit Flato, Gerd Hornf, Barry L. Myones, Karen Onel, James Frane, Andrew Kenwright, Tere H. Lipman, Kamal N. Bharucha, Alberto Martini and Daniel J. Lovell

**1Rheumatology, Ospedale Pediatrico Bambino Gesù, Rome, 2Paediatric Rheumatology, Paediatric Rheumatology International Trials Organisation-IRCPCS [PRINTO], Genoa, Italy, 3Paediatric Rheumatology, Centre of Paediatric Rheumatology, Sankt Augustin, Germany, 4Paediatric Rheumatology, Pediatric Rheumatology Collaborative Study Group [PRCSG], Cincinnati, OH, 5Medical, Genentech, South San Francisco, CA, USA, 6Medical, Roche Products Ltd, Welwyn Garden City, UK and 7Nursing of Children, University of Pennsylvania School of Nursing, Philadelphia, PA, USA**

**Background:** Systemic JIA (sJIA), characterized by chronic arthritis associated with prominent systemic and laboratory features, has a significant impact on skeletal growth, resulting in impaired linear growth and systemic osteoporosis. A phase III trial (TENDER) demonstrated that the IL-6 receptor inhibitor tocilizumab (TCZ) is effective in the treatment of patients with sJIA. Long-term growth responses for children in the TENDER trial (up to week 104) are presented.

**Methods:** TENDER enrolled 112 patients (age 2–17 years) with active, refractory sJIA (>6-month duration with inadequate response to previous nonsteroidal anti-inflammatory drugs and oral corticosteroids). Following a 12-weeks randomized, placebo-controlled phase, patients received open-label TCZ in the long-term extension study. Height parameters, laboratory data and clinical assessments of disease activity were compared at baseline and through year 2 of the study.

**Results:** At entry to the TENDER trial, there was profound growth failure among patients with sJIA (mean height standard deviation score [SDS] of -2.1; \( n = 107 \)). During treatment, the majority of patients experienced greater than normal height velocities, with 76% of female patients and 73% of male patients demonstrating catch-up growth. The height SDS increased significantly from baseline to year 2 of the study, with a mean improvement of 0.61 (\( P = 0.0001 \), paired \( t \)-test). Despite higher mean corticosteroid doses in the first year (0.13 mg/kg/day vs 0.05 mg/kg/day in year 2), mean height velocities in years 1 and 2 were comparable at 5.8 and 6.3 cm/year respectively (\( P = 0.32 \), paired \( t \)-test). During TCZ treatment, a significant increase in insulin-like growth factor 1 (IGF-1) levels was observed, suggesting a normalization of growth hormone (GH) axis function (mean baseline IGF-1 SDS of -1.1; \( n = 95 \) compared with year 2 mean IGF-1 SDS of 0.0; \( n = 91 \); \( P < 0.0001 \), paired \( t \)-test). The osteocalcin/c-tepeptide of type 1 collagen (OC/CTX-1) ratio increased significantly (\( P = 0.0045 \), paired \( t \)-test) suggesting an increase in osteoblast activity relative to osteoclast activity. Improvement in JADAS-71 scores during the first year was associated with improved height velocities during that year (\( r = -0.35 \), \( P = 0.0002 \); mean decrease in JADAS-71 of 29.2 \( n = 107 \)).

**Conclusions:** In sJIA patients, TCZ therapy resulted in catch-up growth, TCZ therapy also resulted in increased IGF-1 levels and OC/CTX-1 ratios, suggesting beneficial effects on the GH axis and on bone metabolism. Improvement in JADAS scores correlated with increased height velocity. Continued data collection (for a total of 5 years) will allow a comprehensive analysis of growth outcomes in the TENDER study.

**Disclosures:** K.B., Genentech—Employment, P.D., Abbott, BMS, Pfizer, SOBI, Novimmune, Genentech, Novartis—Research Grants, BMS, Pfizer, Roche Pharmaceuticals—Consulting Fees or Other Remuneration, J.F., Genentech—Employment, G.H., Abbott, Pfizer—Research Grants, Abbott, Pfizer, Novartis, Roche Pharmaceuticals—Chugai—Speakers’ Bureau, A.K., Roche Pharmaceuticals—Employment, D.L., National Institutes of Health—Research Grants, AstraZeneca, Centocor, Wyeth, Amgen, BMS, Abbott, Pfizer, Regeneron, Hoffmann-La Roche, Novartis, UCSB, Xoma—Consulting Fees or Other Remuneration, Arthritis and Rheumatism, Genentech—Sponsors’ Bureau, Forest—Other, A.M., BMS, Abbott, Novartis, Roche Pharmaceuticals, Centocor, ACRAF, Pfizer, Xoma—Research Grants, Novartis, Roche Pharmaceuticals—Consulting Fees or Other Remuneration, BMS—Sponsors’ Bureau, K.O., Merck, Roche Pharmaceuticals—Research Grants, N.R., BMS, Abbott, Novartis, Roche Pharmaceuticals—Sponsors’ Bureau. All other authors have declared no conflicts of interest.
O18. EFFICACY AND SAFETY OF TOCILIZUMAB IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS: CHERISH RESULTS AT WEEK 40

Eileen Baldam1, Nicolino Ruperto2, Hermine Brunner3, Zbigniew Zuber1, Caroline Keane1, Olivier Harari4, Andrew Kenwright5, Ruben J. Cuttica6, Vladimir Kettlevev7, Ricardo Xavier7, Inmaculada C. Penades8, Ilona Nikishina9, Nadina Rubio-Perez10, Ekaterina Alekseeva11, Vyacheslav Chasnyny11, Jose Chavez12, Gerd Hornert13, Violetta Opoka-Winiarska11, Pierre Quartier14, Clovis A. Silva15, Earl D. Silverman16, Alberto Spindler17, Daniel J. Lovell18 and Fabrizio De Benedetti19

1Paediatric Rheumatology, Royal Liverpool Children’s Hospital, Liverpool, UK. 2Paediatric Rheumatology, Paediatric Rheumatology International Trials Organisation-IRCCS [PRINTO], Genoa, Italy. 3Paediatric Rheumatology, Pediatric Rheumatology Collaborative Study Group [PRCSG], Cincinnati, OH, USA. 4Medical, Roche Products Ltd, Welwyn Garden City, UK. 5Rheumatology, Scientific Research Institute of Rheumatology RAMS, Moscow, Russia. 6Rheumatology, International Investigator Consortium for MAS Diagnostic Criteria, Moscow, Russian Federation. 7Paediatric Rheumatology, Centre of Paediatric Rheumatology, Sankt Augustin, Germany. 8Rheumatology, Necker-Enfants Malades Hospital, Paris, France and 9Paediatric Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy

Background: Tocilizumab (TCZ) inhibits IL-6 mediated inflammatory pathways.

Methods: CHERISH is a 104-week double-blind placebo-controlled (PBO) study in patients age 2–17 years with active polyarticular-course JIA (pJIA) who failed MTX. All patients received TCZ during the 16-week open-label (OL) lead-in period every 4 weeks (if body weight [BW] <30 kg, 8 mg/kg; BW <30 kg, patients randomly assigned to 8 mg/kg or 10 mg/kg). At week 16, eligible patients (>JIA ACR30 response) entered a 24-week randomized, double-blind withdrawal period (DBWP) to evaluate the primary endpoint (JIA ACR30 flare relative to week 16). Patients who completed the DBWP entered an OL extension study.

Results: 188 patients were enrolled (79% on MTX and 46% on oral steroids); 166 patients entered the DBWP. The primary endpoint was met. JIA ACR30/50/70 responses were significantly higher with TCZ compared with PBO at week 40 (Table 1). Efficacy responses for initial lead-in period at week 16 are shown (Table 1). At safety data cut, there were 480 and 12.5; infections were the most common AEs (164/100PY) and SAEs (4.9/100PY). ALT and AST elevations were each reported in 3.7% and <1% of patients. Neutropenia, thrombocytopenia and LDL-cholesterol elevation occurred in 3.7%, 1.1% and 11.4% of patients.

Conclusions: TCZ is efficacious for the treatment of pJIA with a sustained clinically meaningful improvement using doses of 8 mg/kg if BW >30 kg and 10 mg/kg if BW <30 kg. The safety profile is consistent with that in other TCZ-treated patients.


Table 1. Efficacy endpoints

<table>
<thead>
<tr>
<th>Randomized DB period week 16–40; ITT population</th>
<th>P-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>All placebo n = 81</td>
<td>All TCZ n = 82</td>
</tr>
<tr>
<td>Primary endpoint JIA ACR30 flare (relative to week 16) n (%)</td>
<td></td>
</tr>
<tr>
<td>JIA ACR30</td>
<td>44 (54.3)</td>
</tr>
<tr>
<td>JIA ACR50</td>
<td>42 (51.9)</td>
</tr>
<tr>
<td>JIA ACR70</td>
<td>34 (42.0)</td>
</tr>
</tbody>
</table>

Initial lead-in period (at week 16; ITT population)

<table>
<thead>
<tr>
<th>TCZ 10 mg/kg</th>
<th>TCZ 8 mg/kg</th>
<th>TCZ 8 mg/kg</th>
<th>All TCZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW n = 35</td>
<td>BW n = 34</td>
<td>BW n = 119</td>
<td>n = 188</td>
</tr>
<tr>
<td>JIA ACR30 responses at week 16n, (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JIA ACR30</td>
<td>31 (88.6)</td>
<td>26 (76.5)</td>
<td>111 (93.3)</td>
</tr>
<tr>
<td>JIA ACR50</td>
<td>28 (80.0)</td>
<td>24 (70.6)</td>
<td>104 (87.4)</td>
</tr>
<tr>
<td>JIA ACR70</td>
<td>22 (62.9)</td>
<td>14 (41.2)</td>
<td>81 (68.1)</td>
</tr>
</tbody>
</table>

Δ: Change; BL: baseline. *Analysis adjusted for background therapy at week 16. ⅄Patients withdrawing/escaped classified as flared or non-responders. ⅆPatients withdrawing/withdstanding no endpoint classified as non-responders.
ARTHRITIS: AN EXPLORATORY TRIAL OF A MULTIDISCIPLINARY FOOT CARE PROGRAMME FOR CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: AN EXPLORATORY TRIAL

Gordon J. Hendry1,2, Gordon F. Watt,1, Mhairi Brandon3, Lorraine Friel1, Deborah Turner3, Paula K. Longley3, Janet Gardner-Medwin3, Roger D. Sterrock1 and James Woodburn1
1Institute for Applied Health Research, Glasgow Caledonian University, Glasgow, UK, 2School of Science and Health, University of Western Sydney, Penrith, NSW, Australia, 3Glasgow Royal Infirmary, NHS Greater Glasgow and Clyde, Glasgow, UK

Background: The need for optimum management of foot problems in JIA is an emerging issue in paediatric rheumatology practice. Foot-related impairments and disability persist in over 60% of children who have JIA despite modern day treatment paradigms. The aim of this study was to 1) evaluate the clinical and cost-effectiveness of a new, integrated multi-disciplinary foot care programme for patients with JIA, and 2) to evaluate the methodological considerations of a trial of multidisciplinary care in JIA.

Methods: An exploratory randomized controlled trial (RCT) compared an integrated multidisciplinary foot care programme developed according to current evidence of best practice and expert opinion, with current standard medical care for improving foot-related impairments and disability. This programme was centred on strict disease control through rigorous examination and interventions delivered by a team comprised of a paediatric rheumatologist, podiatrist, physiotherapist and musculoskeletal ultrasonographer. Patients were assessed on foot impairment and disability scores at 6 and 12 months from baseline using the juvenile arthritis foot disability index (JAFI). A full economic evaluation comprising cost-effectiveness, cost-utility and cost-benefit analyses were embedded within the trial.

Results: Forty-four patients, aged 3–17 years with a history of inflammatory joint disease affecting the foot/ankle were randomly assigned to receive the experimental (n = 21) or usual care (n = 23) intervention. There was an overall improvement in levels of foot related impairments in both groups over 12 months. Between-group differences in change scores for the JAFI were not statistically significant at 6 or 12 month follow-ups. Estimated mean annual costs of care per participant were significantly greater for those in the intervention arm.

Conclusions: Over a 12 months period, targeted intervention via an integrated multi-disciplinary foot care programme did not result in a significant improvement of disease-related foot impairments and disability despite increased care costs. This exploratory trial successfully identified several useful areas for the development of future definitive trials in this area by uniquely highlighting sources of bias, procedural problems, and limitations of the study design and primary outcome measure. This trial demonstrated that the inclusion of musculoskeletal ultrasound (MSUS) for the examination of the joints and soft tissues of the feet appeared to influence medical decision making with regards to ICIs. Moreover the use of MSUS for the examination of children and adolescents with JIA is feasible, timely and well-accepted in the clinical setting. The integrated multidisciplinary foot care interventions described in this RCT appears to be safe, with few minor adverse events recorded over the 12 months trial period.

Disclosures: G.H., Arthritis Research UK—Research Grant. D.T., Arthritis Research UK—Research Grant. All other authors have declared no conflicts of interest.
021. I'M BEING A BETTER DOCTOR: TRAINING FOR CLINICIANS TO SUPPORT SELF-MANAGEMENT
Emma Dures1, Sarah Hewlett2, Nicholas Ambler2, Joyce Clarke2, Rachael Gooberman-Hill1 and Remona Jenkins1
1Academic Rheumatology, University of the West of England, Bristol, 2Academic Rheumatology, University of Bristol, 3Academic Rheumatology, University of Bristol, 4Orthopaedic Surgery Research Group, University of Bristol, Bristol, UK

Background: Self-management (SM) requires informed, activated patients to manage the physical and psychosocial consequences of arthritis, yet formal staff training in theory and skills underpinning SM is not widely available. Understanding the challenges and benefits of putting SM theory into practice is key for developing such training. A qualitative study explored rheumatology clinicians' experiences of a range of brief SM training courses (e.g. holistic care, shared agenda setting, cognitive-behavioural approaches).

Methods: 16 health professionals participated in semi-structured interviews: 3 physicians, 3 physiotherapists, 4 nurses, 6 OTs. Transcripts were analysed (ID) using an inductive thematic approach, with a subset independently analysed (SH, RG-H, RJ). Initial codes were generated, depicting patterns across the dataset, and combined to form themes.

Results: 4 main themes were identified: Challenging Professional Identity (‘it does question some of your fundamental beliefs about yourself and your role’), Training shaped ideas of responsibility (‘from medical school there is a strong emphasis to concentrate on the physical, pathological’, ‘remit [your mindset shifts in terms of what is a treatment]’, and ways of helping patients (‘as nurses we like to fix people’). However for some, it formalized existing approaches (‘it sits very nicely with the OT role’).

Conclusion: ‘Training is about building that bridge from the academic research to the clinical practice’: Training was valued by its evidence-base, evoking examples (‘case studies are really useful’), usefulness in practice (‘you can make use of even though you’ve maybe only got 10 minutes’, and acknowledging concerns (‘the fear that you get into a hole that you can’t get out of’).

Clinical Supervision (‘you do a course and then it’s quite hard to practice it’s about having some kind of support system’), Ongoing support influenced implementation in care (‘had I not been encouraged through mentoring I wonder whether I would have kept using it, it takes a lot of effort to change’), and development (‘I moved from being a novice in terms of using skills gleaned from that course, and became more confident in clinic’); while lack of support meant skills could decline (‘it just fades from the front of your mind’).

Conclusion: Ongoing Consultations (‘I am being a better doctor’): Ongoing support influenced implementation in care (‘had I not been encouraged through mentoring I wonder whether I would have kept using it, it takes a lot of effort to change’), and development (‘I moved from being a novice in terms of using skills gleaned from that course, and became more confident in clinic’); while lack of support meant skills could decline (‘it just fades from the front of your mind’).

Conclusion: ‘Training is about building that bridge from the academic research to the clinical practice’: Training was valued by its evidence-base, evoking examples (‘case studies are really useful’), usefulness in practice (‘you can make use of even though you’ve maybe only got 10 minutes’, and acknowledging concerns (‘the fear that you get into a hole that you can’t get out of’).

Clinical Supervision (‘you do a course and then it’s quite hard to practice it’s about having some kind of support system’), Ongoing support influenced implementation in care (‘had I not been encouraged through mentoring I wonder whether I would have kept using it, it takes a lot of effort to change’), and development (‘I moved from being a novice in terms of using skills gleaned from that course, and became more confident in clinic’); while lack of support meant skills could decline (‘it just fades from the front of your mind’).

Conclusion: Ongoing Consultations (‘I am being a better doctor’): Training altered clinicians’ approaches by encouraging them to address patients’ agendas (I always say ‘What do you want to get out of seeing me today?’) and supporting SM by enhancing self-efficacy and problem solving skills (you can sort of facilitate that in a way that the patient can actually work it out for themselves).

Conclusions: To optimize SM support in routine care, brief training could be provided, with ongoing clinical supervision. Further research will examine the patient perspective, different models of SM support and develop a rheumatology-specific training module.

Disclosures: The authors have declared no conflicts of interest.

022. WIDESPREAD AND REGIONAL PAIN PREDICT SOCIAL PARTICIPATION RESTRICTION IN OLDER ADULTS: A PROSPECTIVE COHORT STUDY
Ross Wilkie1, Millia Bucknall2, Kelvin Jordan1 and John McBeth1
1Research Institute for Primary Care and Health Sciences, Keele University, Keele, UK

Background: In older people maintaining social participation (a measure of social function and social roles, such as being a worker, carer or community member), is associated with reduced morbidity and mortality. Social participation restriction results from complex interactions between health, physical capacity, psychological, socio-demographic and environmental factors. Musculoskeletal pain is associated with participation restriction although due to the cross-sectional nature of previous studies the temporal relationship is unclear. This longitudinal study tested the hypotheses that musculoskeletal pain would predict social participation restriction and that the strength of that relationship would be stronger in those with more extensive pain.

Methods: The study was set within the North Staffordshire Osteoarthritis Project (NorSTOp), a population-based prospective cohort study of adults aged 50 years and over. Participants were those who completed baseline, 3- and 6-year follow-ups (n = 4826). Participants were classified into those reporting no, regional or widespread pain (WP) (ACR criteria) at baseline. The Keele Assessment of Participation (KAP), an assessment tool validated for use in older people, measures 11 aspects of participation. Zero-inflated poisson regression models tested the association between baseline pain status and number of participation restrictions (range from 0 to 11) at 3 and 6 years. Unadjusted analyses were initially performed and then adjusted for putative confounders: demographics (age, gender, education, occupational class); time-dependent measures of BMI, cognitive impairment, anxiety and depression, comorbidity (count of self-reported morbidities), financial strain, social network; and baseline KAP score. Results were expressed as an incidence rate ratio (IRR) with 95% CI.

Results: The median age of subjects was 59 (inter-quartile range: 54 to 67) and 2751 (57%) were female. At baseline, 1378 (29%) had no pain, 2188 (45%) had regional pain, 1296 (26%) had WP. Of those 31%, 40% and 55% had restriction in at least one aspect of participation respectively. Baseline regional and widespread pain were associated with increasing participation restriction at 3 and 6 years; unadjusted IRR (95% CI) at 3 years was 1.38 (1.25, 1.54) for regional pain and 1.81 (1.63, 2.00) for WP; 6 years regional pain 1.22 (1.12, 1.34) and WP 1.53 (1.40, 1.68). While attenuated these associations persisted and were significant following adjustment for covariates: 3 years 1.19 (1.06, 1.31), 1.21 (1.08, 1.35); 6 years 1.12 (1.02, 1.23) and 1.15 (1.04, 1.27), respectively.

Conclusion: Independent of known risk factors, having musculoskeletal pain, and the extent of that pain, were important predictors of social participation restriction. Future studies should seek to determine the mechanisms of this relationship that may be targeted to increase social participation.

Disclosures: The authors have declared no conflicts of interest.

023. QUALITY OF LIFE OVER THE FIRST 5 YEARS OF RA: FINDINGS FROM THE EARLY RHEUMATOID ARTHRITIS NETWORK
Sam Norton1, David Walsh2, Patrick Kiey2, Richard Williams3 and Adam Young2
1Psychology Department, King’s College London, London, 2Arthritis Research UK Pain Centre, University of Nottingham, Nottingham, 3Rheumatology, St George's Healthcare NHS Trust, London, 4Rheumatology, Hereford Hospitals NHS Trust, Hereford and 5Rheumatology, West Hertfordshire Hospitals NHS Trust, St Albans, UK

Background: Quality of life (QoL) in RA is known to be reduced compared with the general population. The aim of this study is to examine QoL longitudinally in a large sample of patients with early RA, and identify correlates of change in QoL over time.

Methods: Data are from the Early Rheumatoid Arthritis Network (ERAN), a prospective observational cohort recruiting DMARD naïve patients at presentation from 21 centres in the UK and Ireland. In total, 1036 patients were recruited between 2002 and October 2012. Patients were re-assessed after 3-6 months, 12 months and then yearly. QoL was assessed using the SF36, which measures QoL across four mental subscales (mental health, vitality, emotional role functioning, social role functioning) and four physical subscales (physical functioning, bodily pain, general health, physical role functioning). Scores were normed against the UK general population (mean = 50, S.D. = 10), to enable indirect comparison. Piecewise mixed effects models were used to examine changes in QoL over the first 5 years of follow-up.

Results: Mean age at onset was 57.1 years and 68% were female. At presentation to the rheumatologist, all SF36 subscales were significantly reduced compared with the general population—physical subscales were reduced to a greater extent than mental subscales. Over the first year of follow-up, significant improvements were observed in all mental subscales and all physical subscales, except general health. Greater improvement over the first year in mental subscales was related to lower baseline assessments of HAQ and comorbidity (count of self-reported morbidities), financial strain, social network; and baseline KAP score. Results were expressed as an incidence rate ratio (IRR) with 95% CI.

Disclosures: The authors have declared no conflicts of interest.
subscapes were related to younger age only, and in physical subscapes to younger age, male sex and lower baseline DAS.

**Conclusions:** Compared with the general population, both mental and physical QoL are significantly reduced in early RA. Improvements in mental and physical QoL occur over the first year and are maintained up to 5 years. However, levels remain substantially lower than general population over this period for all except the mental health subscale. There may be a ‘window of opportunity’ for interventions targeted at improving QoL early in the RA disease course.

**Disclosures:** The authors have declared no conflicts of interest.

**024. SCOTTISH SOCIETY OF RHEUMATOLOGY OCCUPATIONAL THERAPY RHEUMATOID ARTHRITIS WORK AUDIT**

Janet E. Harke$$1$$ and Katie McAlarey$$2$$

$$1$$Occupational Therapy Department, Fife Rheumatic Diseases Unit, Kirkcaldy and $$2$$Occupational Therapy Department, New Victoria Hospital, Glasgow, UK

**Background:** Work disability rates remain a problem and particularly in Scotland. Patients with RA often have problems at work (work instability) and therefore work screening is important. Screening involves asking the patient ‘the work question’ (how are you getting on at work?) and using tools such as the Rheumatoid Arthritis Work Instability Scale (RA-WIS). Specialist Occupational Therapy (OT) improves work outcomes in RA and early intervention is therefore required. The aim of the audit was to establish current screening practices for work instability, referral onto OT and levels of OT service provision in Scotland.

**Methods:** All rheumatology OT centres in Scotland were invited to participate. Consecutive RA probable patients referred to OT from September 2011 to March 2012 were entered onto the Scottish Society of Rheumatology (SSR) web based audit tool. Anonymized demographic, work screening, work instability (measured by the Rheumatoid Arthritis Work Instability Scale (RA-WIS) and OT service provision information was collated.

**Results:** Data were collected on 431 patients from 13 Scottish OT centres. 27% of patients were employed (mean age 49years, 79% female, mean disease duration 3.5 years and 11% were currently off sick), Referral rates to OT varied across Scotland with only 6% of referrals reporting work problems.100% of Occupational Therapists however, carried out work screening and found that 63% of patients had work problems with 57% of patients reporting medium-high levels of work instability (RA-WIS score = 10–23). There were regional variations in RA-WIS scores. Patients received 6 work interventions on average and most patients received standard OT work interventions as opposed to more complex interventions. 51% of OT’s patients had their work problems fully addressed, 39% partially addressed and 9% of OT patients did not have their work problems addressed at all. Reasons for lack of provision remain unclear.

**Conclusions:** There appears to be limited work screening occurring in the rheumatology clinics despite high work instability rates in Scotland. Occupational Therapy referral ensures work instability is being measured by the Rheumatoid Arthritis Work Instability Scale (RA-WIS) and OT service provision information was collated.

**Disclosures:** The authors have declared no conflicts of interest.

**ORAL ABSTRACTS 5: PRIMARY CARE**

**025. TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION FOR THE MANAGEMENT OF TENNIS ELBOW: A PRAGMATIC RANDOMIZED CONTROLLED TRIAL**

Linda Chesterton$$1$$, Danièle A. van der Windt$$1$$, Julius Sim$$2$$, Martin Ley$$1$$, Christian D. Mallen$$1$$, Elizabeth Mason$$1$$ and Elaine Hay$$2$$

$$1$$Arthritis Research UK Primary Care Centre, Keele University, Keele, UK

**Background:** Tennis elbow (TE) is a common condition which is considered to be self-limiting over 6–18 months yet often causes considerable pain in normal daily activities. This study investigated the effectiveness of transcutaneous electrical nerve stimulation (TENS) as a non-pharmacological form of analgesia to reduce pain intensity in patients with tennis elbow.

**Methods:** A pragmatic randomized controlled trial of adults with a first or new clinical diagnosis of tennis elbow recruited from 38 General Practices and one physio-direct Centre in Staffordshire, UK. Randomization was on a 1:1 basis to receive either primary care management (GP consultation plus education and advice on exercise) or primary care management with the addition of self-applied TENS (one 45-min session per day when pain occurred, over 6 weeks). The primary outcome measure was mean change in intensity of elbow pain in the past 24h (0–10 numerical rating scale), at 6 weeks. Other clinical outcomes included: Patient-Rated Tennis Elbow Evaluation Questionnaire; global assessment of change; pain medication use; days of sick leave; health status (SF12). Outcomes were measured at 6 weeks and at 6 and 12 months by postal questionnaire. Participants’ satisfaction with overall care was elicited at 6-week follow-up. The following are preliminary results based on observed data (the final results will be published in a full intention-to-treat approach). The difference in the primary outcome measure was adjusted for baseline pain score, age and gender.

**Results:** 241 patients were recruited: 131 (54%) males and mean age 48 years. 103 (43%) reported duration of symptoms exceeding 3 months. 121 were randomized to primary care management plus TENS and 120 to primary care management alone. Reasons for lack of service provision in Scotland.

**Conclusions:** Both groups showed meaningful clinical improvements in reported pain. However TENS conferred no additional clinical benefit over GP consultation plus education and advice on exercise, in the management of tennis elbow.

**Disclosures:** The authors have declared no conflicts of interest.

**026. GOUT IS AN INDEPENDENT RISK FACTOR FOR ALL TYPES OF VASCULAR DISEASE: A RETROSPECTIVE COHORT STUDY IN THE UK GENERAL PRACTICE RESEARCH DATABASE**

Lorna E. Clasen$$1$$, Samantha L. Hider$$2$$, John Belcher$$2$$, Carl Heneghan$$1$$, Edward Roddy$$1$$ and Christian D. Mallen$$1$$

$$1$$Research Institute for Primary Care and Health Sciences, Keele University, and $$2$$Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

**Background:** Gout is the most prevalent inflammatory arthritis in the UK and is largely managed in primary care. Epidemiological studies have demonstrated an association between gout and cardiovascular disease (CHD), although the role played by traditional vascular risk factors such as hypertension and obesity is unclear. The associations between gout and cerebrovascular (CVD) and peripheral vascular disease (PVD) are poorly studied. The aim of this study was to examine the risk of incident cardiovascular, cerebrovascular and peripheral vascular disease in a primary care gout population.

**Methods:** Data from the UK General Practice Research Database (GPRD) were examined for 8396 gout patients, and 39,765 age, gender and practice-matched controls with no previous history of vascular disease. Time to incident CHD, CVD and PVD was identified in the following years using the baseline consultation date for gout, or an equivalent matched index date for controls. Multivariate analysis using Cox Proportional Hazard Modelling adjusted for traditional vascular risk factors including BMI, smoking, alcohol consumption, Charlson comorbidity index, history of hypertension, hyperlipidaemia, chronic kidney disease, statin use and aspirin use.

**Results:** After adjustment for BMI, smoking, alcohol consumption and Charlson comorbidity index, gout was associated with an increased risk of any vascular disease [hazard ratio (HR) 1.28, 95% CI 1.23, 1.34], any CHD (HR 1.27, 95% CI 1.25, 1.35), any CVD (HR 1.24, 95% CI 1.15, 1.34), and PVD (HR 1.53, 95% CI 1.32, 1.77). Following
adjustment for the wider range of variables, risk was attenuated but remained significant for any vascular disease (HR 1.09, 95% CI 1.04, 1.14), any CHD (HR 1.08, 95% CI 1.02, 1.15) and PVD (HR 1.37, 95% CI 1.31, 1.43). These relationships were particularly strong in women for any vascular disease (HR 1.23, 95% CI 1.14, 1.34), any CHD (HR 1.43, 95% CI 1.16, 1.76) and PVD (HR 1.53, 95% CI 1.16, 2.01).

Conclusions: Gout patients, especially women, are at increased risk of any vascular disease, any CHD and PVD. This study highlights the excess gout burden in women, and the potential burden on both individuals and the health economy. Further research is required to establish the effect of optimal management of both vascular and gout risk factors and gout itself on the long term health of gout patients.

Disclosures: The authors have declared no conflicts of interest.

Q27. CASE-FINDING FOR OSTEOPOROSIS AND FRACTURE IN PRIMARY CARE

Jane Gibson1, Susan Whiteford1, Elizabeth Williamson1, Shona Beatty2 and Norma Hamilton-Dyer1
1Fife Osteoporosis Service, NHS Fife, Kirkcaldy and 2Department of Nursing, NHS Fife, Dunfermline, UK

Background: Fragility fractures occur as a result of a combination of factors leading to reduced bone micro architecture and fracture. Many such fragility fractures are well recognized e.g. easily fractured long bone due to glucocorticoid therapy. Morbidities and medication are now coded in Primary Care and are part of the electronic patient record. It is therefore possible to scan the GP database for recognized risk factors for fragility fracture. Patients can then be selected for further investigation or treatment.

This approach has been recommended in NICE Guideline 146, published in August 2012.

Methods: Since 2009, GP practices in Fife have been offered an electronic search of their patient database to detect patients with risk factors for osteoporosis or those > age 50 years with a prevalent fragility fracture. 50% of practices have taken up this offer and have had at least one search. Follow-up searches have been provided for some practices. A list of patients is provided to the Practice which indicate those who require further investigation (e.g. DXA) or those who need treatment without DXA. Practices can opt to follow-up patients on the list themselves or have a pharmacist provide some of the interventions.

Prescribing rates for bone active treatments were subsequently analysed.

Results: 28,834 patients >65 years old were in the intervention screening group (IG) and 35,780 in the non-intervention group (NIG). 56% female in both groups. Groups were well matched for demographics.

Prescribing rates were significantly higher in the IG than NIG for calcium and vitamin D supplements: OR 1.34 (Confidence intervals 1.28, 2.85, P < 0.001) for women and OR 1.31 (1.20, 1.44, P = 0.001) for men. The greatest difference was in the 80–85 year old age group, OR 1.67 (1.45, 3.13, P < 0.001) and for men in the 75–79 year olds, OR 1.69 (1.39, 2.05, P < 0.001).

Prescribing rates for bone active agents (British National Formulary 6.6.2) were significantly higher in the IG than NIG for women; overall OR 1.16 (1.10, 1.23, P < 0.001) but not in men; OR 1.09 (0.96,1.23, P = 0.18). The greatest difference was in the >90-year-old female group: OR 1.39 (1.12, 1.72, P = 0.003).

Conclusions: Prescribing rates for calcium and vitamin D supplements for older men and women are higher in practices that screen for patients at risk of osteoporosis. Prescribing rates for osteoporosis treatments are also higher in women but not men. This difference in prescribing rates may be due to a pre-existing awareness of osteoporosis in those practices or may be due to the research intervention. Further research will establish whether prescribing patterns have changed with the intervention and whether fracture rates are lower in the IG than in the NIG.

Disclosures: J.G., Prostrakan—Research Grant, Amana—Speaker’s Fees, Pfizer—Support to Attend Conference. All other authors have declared no conflicts of interest.

Q09. ROCKER SOLE SHOES ARE NO MORE BENEFICIAL THAN FLAT SOLE SHOES IN THE MANAGEMENT OF CHRONIC LOW BACK PAIN

Catharine S. MacRae1,2, Adam Shortland3,4, Jeremy Lewis5,6, Matthew Morrissey7 and Duncan Crutchley8
1Health and Social Care Research, King’s College London, London, 2Therapy Services, Chelsea and Westminster NHS Foundation Trust, London, 3Biomedical Engineering, King’s College London, London, 4One Small Step Gait Laboratory, Guy’s and St Thomas’ NHS Foundation Trust, London, 5Musculoskeletal Services, Central London Community Healthcare, London, 6Physiotherapy Department, St George’s Healthcare NHS Trust, London, UK and 7Faculty of Health Sciences, University of Ljubljana, Slovenia

Background: Over the past decade, persistent advertising has claimed that footwear constructed with a rocker sole will reduce low back pain (LBP). However, there is no robust evidence to support these claims. This investigation compared rocker sole shoes to traditional flat sole shoes as part of the management for people with chronic LBP.

Methods: 115 people with chronic LBP (mean age 43.1 (s.d. 12.1) years, 66.1% females) were randomized to wear a rocker sole shoe or...
O30. THE RISK OF A SUBSEQUENT CANCER DIAGNOSIS AFTER PMR: A PRIMARY CARE DATABASE STUDY

Sara Muller1, Christian D. Mallen1, John Belcher1, Toby Helliwell1 and Samantha L. Hider1

1Research Institute for Primary Care and Health Sciences, Keele University, Keele, UK

Background: PMR is the commonest inflammatory rheumatological disorder managed in primary care. Other inflammatory conditions such as RA and psoriasis have been associated with an increased incidence of cancer, specifically haematological malignancies and lymphoma. Small PMR studies have not shown consistent associations [1,2]. The aim of this study was to investigate whether there is an association between PMR and cancer in a primary care population.

Methods: All individuals in the General Practice Research Database (GPRD) aged >50 years and with a Read-coded diagnosis of PMR who were treated with corticosteroids between 01/01/1987 and 31/12/1999 were matched by age, gender, practice and consultation year to up to five patients without PMR. Those with a prior history of vascular disease or cancer were excluded.

The outcome of interest was a diagnosis of cancer following PMR diagnosis. This was defined as having received a Read code in Chapter B (neoplasms), excluding subchapter B7 (non-malignant neoplasms). Individuals were followed-up until first cancer diagnosis, death or May 2011, whichever was earliest. Event times were compared using a Cox regression model with robust standard errors to allow for matching. The model was adjusted for age group and having ever smoked. An interaction term was fitted to investigate changes in the association between PMR and cancer with time from diagnosis. The types of cancer occurring in the first 6 months were compared in those with and without PMR.

Results: 2877 PMR patients were matched with 9942 non-PMR patients. 9329 (73%) were female and mean age was 72 (SD: 9) years. Median (inter-quartile range) time under observation was 7.8 (3.4, 12.31) years. 23.2% of PMR patients (n = 667) and 19.5% of non-PMR patients (n = 1938) received a diagnosis of cancer in the study period. After adjusting for age group and ever smoking, PMR was significantly associated with a cancer diagnosis within 6 months [HR 1.96 (1.18, 2.42)], but after this time, there was no association (Table 1). No statistically significant difference was seen in the types of cancer between the two groups.

Conclusions: Analysis from a large cohort of general practice consulters suggests that there is no long-term association between PMR and malignancy. Whilst cancer diagnosis was twice as likely in the first 6 months after original PMR diagnosis, this may reflect an incorrect original PMR diagnosis, rather than a true association with malignancy. This highlights that clinicians should strongly consider malignancies as part of the differential diagnosis for PMR.

<table>
<thead>
<tr>
<th>Time since PMR diagnosis</th>
<th>Hazard ratio (95% CI) for cancer in those with PMR vs those without</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–6 months</td>
<td>1.96 (1.18, 2.42)</td>
</tr>
<tr>
<td>6–12 months</td>
<td>1.03 (0.70, 1.51)</td>
</tr>
<tr>
<td>1–2 years</td>
<td>1.04 (0.77, 1.40)</td>
</tr>
<tr>
<td>2–5 years</td>
<td>1.05 (0.87, 1.26)</td>
</tr>
<tr>
<td>5–10 years</td>
<td>1.11 (0.95, 1.30)</td>
</tr>
<tr>
<td>10+ years</td>
<td>1.00 (0.8, 1.23)</td>
</tr>
</tbody>
</table>

Disclosures: The authors have declared no conflicts of interest.
ORAL ABSTRACTS 6: OA AND METABOLIC BONE DISEASE

O31. MATERNAL MILK INTAKE IS ASSOCIATED WITH INCREASED OFFSPRING BONE MINERAL CONTENT
Zoe Cole1, Camille Parsons1, Sarah Crozier1, Sian Robinson1, Patricia Taylor2, Hazel Inskip1, Keith Godfrey1, Elaine Dennison1, Nicholas C. Harvey1 and Cyrus Cooper1
1MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton and 2Medical Physics and Bioengineering, University Hospital Southampton, Southampton, UK

Background: We have previously shown that maternal diet and vitamin D stores in pregnancy are associated with skeletal development of the offspring. Trials of milk or calcium products have shown benefits for bone health in children, but there are few studies relating to typical milk intake in children at a young age. The aim of this study was, in a large prospective population-based cohort, to investigate associations between maternal calcium intake and offspring bone mass at 6 years.

Methods: 1045 mother-child pairs were recruited from the Southampton’s Survey. The mothers had been characterized in terms of diet, body build and lifestyle before and during pregnancy by validated food frequency questionnaires. At 6 years old, the children’s diet (including milk intake) was assessed by questionnaire and whole body (minus head) bone size, mineralization and density by DXA (Hologic Discovery instrument using paediatric mode). Pearson correlation and linear/multivariable regression was used to explore associations between maternal calcium intake or child’s milk intake, and bone size and density of the child at age 6 years.

Results: There were statistically significant positive relationships between pre pregnancy maternal calcium intake and bone area (whole body: r = 0.08, P = 0.006; spine: r = 0.11, P = 0.0002) and bone mineral content (whole body: r = 0.06, P = 0.03; spine: r = 0.7, P = 0.02) at age 6 years. These associations remained for whole body and spine after inclusion of 6 year childhood milk intake.

Conclusions: Pre-pregnancy maternal calcium intake is positively associated with offspring bone mass at age 6 years, independent of maternal height, weight, current smoking, exercise, prudent diet score and the child’s birthweight and current milk intake. These findings suggest that whilst increasing childhood milk intake may be beneficial for skeletal growth, optimization of maternal calcium intake prior to conception may also lead to improved offspring skeletal development.

Disclosures: The authors have declared no conflicts of interest.

O32. BISPHOSPHONATE USE AND IMPROVED IMPLANT SURVIVAL: A NATIONWIDE COHORT STUDY
Daniel Prieto-Alhambra1,2, Ariel Lalomhamed3, Bo Abrahamsson4,5, Nigel Arden2,6,7, Anthonis de Boer4, Peter Vestergard4 and Frank de Vet4,8
1NIHR Musculoskeletal Biomedical Research Unit; 2Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK; 3MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK; 4Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, Netherlands; 5Department of Medicine, Gentofte Hospital, Hillerød, Denmark; 6OPEN, Institute of Clinical Research, University of Southern Denmark, Odense and 7Aalborg Hospital, Aalborg University, Aalborg, Denmark

Background: Osteodystasis and aseptic loosening are the most common causes of revision arthroplasty worldwide. Bisphosphonates might improve implant survival through their anti-osteoclast effects. We aimed to study the association between bisphosphonate use and implant survival.

Methods: A retrospective cohort study was conducted within the Danish nationwide registries (5.5 million residents). We identified patients aged ≥ 40 years undergoing total joint replacement (TJR) during the study period (1998–2007) using ICD10 codes. Patients with inflammatory arthropathies, Paget disease of bone, hip fracture and use of DMARDs were excluded. Each participant was followed up until end of study, date of emigration, revision surgery, or patient’s death, whichever came first. Participants were classified as bisphosphonate users (BPU) if they had been on treatment for at least 6 months. A time-varying exposure was used to avoid immortal-time bias. Up to six BP non-users (BPNU) undergoing arthroplasty were matched to each BPU using propensity scores. Stratified Cox regression was used to model implant survival according to bisphosphonate use. Further, we studied the association between duration of use, adherence (medication possession ratio = MPRI), and timing of therapy initiation (pre-op vs post-op) and implant survival.

Results: 80,342/95,392 (84.2%) subjects were eligible. We identified 1,950 (2.4%) BPU and 1,911 (98.0%) of them were matched to 10,755 BPNU. In total, 226,12,666 (1.78%) of the participants (22,111 BPU and 204,10,755 matched BPNU) underwent revision surgery during study follow-up (median 11.1 years, inter-quartile range 0.43–2.29).

Cox regression models showed reduced revision risk in BPU (HR 0.59, 95% CI 0.37, 0.94). This protective effect was highest in patients with longest duration of treatment and highest adherence (Table 1).

Conclusions: BPU are at 40% reduced risk of revision compared with matched BPNU. These results are similar to previous findings using similar retrospective data from the UK [Prieto-Alhambra D et al. BMJ 2011]. Confirmation of causality in randomized controlled experiments is required.

Table 1. BP exposure and implant survival

<table>
<thead>
<tr>
<th>BP Exposure</th>
<th>Participants</th>
<th>Crude failure</th>
<th>HR (95% CI)</th>
<th>Adjusted HR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No BP use</td>
<td>10,755</td>
<td>755 (1.90)</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>BP use</td>
<td>1,911</td>
<td>226 (1.78)</td>
<td>0.36 (0.15, 0.84)</td>
<td>0.36 (0.15, 0.84)</td>
</tr>
<tr>
<td>Treatment 6–12 months</td>
<td>553</td>
<td>9 (1.63)</td>
<td>1.27 (0.79, 2.05)</td>
<td>1.29 (0.80, 2.08)</td>
</tr>
<tr>
<td>1–2 years</td>
<td>1,006</td>
<td>10 (0.99)</td>
<td>0.51 (0.28, 1.01)</td>
<td>0.50 (0.27, 1.02)</td>
</tr>
<tr>
<td>&gt;2 years</td>
<td>352</td>
<td>3 (0.85)</td>
<td>0.52 (0.21, 2.01)</td>
<td>0.51 (0.27, 2.00)</td>
</tr>
<tr>
<td>MPRI &gt;0.5</td>
<td>261</td>
<td>5 (1.92)</td>
<td>0.91 (0.33, 2.49)</td>
<td>0.96 (0.35, 2.67)</td>
</tr>
<tr>
<td>0.5–0.79</td>
<td>171</td>
<td>3 (1.75)</td>
<td>0.48 (0.14, 1.68)</td>
<td>0.50 (0.14, 1.74)</td>
</tr>
<tr>
<td>≤0.5</td>
<td>14 (0.93)</td>
<td>0.55 (0.31, 0.98)</td>
<td>0.53 (0.30, 0.95)</td>
<td></td>
</tr>
</tbody>
</table>

Timing of therapy initiation
| Post-op     | 800         | 6 (0.75)     | 0.36 (0.15, 0.84) | 0.36 (0.15, 0.84) |
| Pre-op      | 1,111       | 16 (1.44)    | 0.79 (0.45, 1.37) | 0.77 (0.44, 1.36) |

Disclosures: The authors have declared no conflicts of interest.

O33. MORTALITY FOLLOWING ELECTIVE TOTAL HIP REPLACEMENT AND HIP RESURFACING
Adrian Kendal1, Andrew Carr1, Daniel Prieto-Alhambra1,2 and Andrew Judge1
1NIHR Musculoskeletal Biomedical Research Unit, University of Oxford, Oxford and 2MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

Background: Although hip replacement is a highly successful surgical treatment for symptomatic hip OA, the operation has inherent risks including death. Severe hip pain can be so debilitating that people balance their expectations of improved lifestyle against this risk. Information is lacking on the long-term mortality risks of different types of hip replacement surgery performed in the UK. The aim of this study was to compare 10-year mortality rates amongst patients undergoing hip resurfacing to those undergoing total hip replacement in England.

Methods: Data were obtained from the English Hospital Episode Statistics (HES) database linked to Office for National Statistics (ONS) mortality records provided information on date and cause of death in all adults receiving elective primary hip replacement for OA in NHS hospitals in England between 1999 and 2012. The exposure of interest

TABLE 1. BP exposure and implant survival

<table>
<thead>
<tr>
<th>BP Exposure</th>
<th>Participants</th>
<th>Crude failure</th>
<th>HR (95% CI)</th>
<th>Adjusted HR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No BP use</td>
<td>10,755</td>
<td>755 (1.90)</td>
<td>REF</td>
<td>REF</td>
</tr>
<tr>
<td>BP use</td>
<td>1,911</td>
<td>226 (1.78)</td>
<td>0.36 (0.15, 0.84)</td>
<td>0.36 (0.15, 0.84)</td>
</tr>
<tr>
<td>Treatment 6–12 months</td>
<td>553</td>
<td>9 (1.63)</td>
<td>1.27 (0.79, 2.05)</td>
<td>1.29 (0.80, 2.08)</td>
</tr>
<tr>
<td>1–2 years</td>
<td>1,006</td>
<td>10 (0.99)</td>
<td>0.51 (0.28, 1.01)</td>
<td>0.50 (0.27, 1.02)</td>
</tr>
<tr>
<td>&gt;2 years</td>
<td>352</td>
<td>3 (0.85)</td>
<td>0.52 (0.21, 2.01)</td>
<td>0.51 (0.27, 2.00)</td>
</tr>
<tr>
<td>MPRI &gt;0.5</td>
<td>261</td>
<td>5 (1.92)</td>
<td>0.91 (0.33, 2.49)</td>
<td>0.96 (0.35, 2.67)</td>
</tr>
<tr>
<td>0.5–0.79</td>
<td>171</td>
<td>3 (1.75)</td>
<td>0.48 (0.14, 1.68)</td>
<td>0.50 (0.14, 1.74)</td>
</tr>
<tr>
<td>≤0.5</td>
<td>14 (0.93)</td>
<td>0.55 (0.31, 0.98)</td>
<td>0.53 (0.30, 0.95)</td>
<td></td>
</tr>
</tbody>
</table>

Timing of therapy initiation
| Post-op     | 800         | 6 (0.75)     | 0.36 (0.15, 0.84) | 0.36 (0.15, 0.84) |
| Pre-op      | 1,111       | 16 (1.44)    | 0.79 (0.45, 1.37) | 0.77 (0.44, 1.36) |

Disclosures: The authors have declared no conflicts of interest.
was prosthesis type classified as: total hip cemented, total hip uncemented, total hip unspecified fixation, and hip resurfacing. Confounding variables included age, gender, Charlson comorbidity index, and Index of Multiple Deprivation. The outcome was time from surgery to death (all cause mortality). Kaplan–Meier plots estimated the probability of survival up to 10 years following surgery. Cox regression modelling described the association of prosthesis type on death, adjusting for confounders. Propensity score matching was used to minimize the potential for confounding by indication. Results: Data were available on 429,806 patients receiving hip replacement, 383,916 (85.4%) were total hip cemented, 121,144 (28.2%) were total hip uncemented, 26,147 (6.1%) unspecified and 18,599 (4.3%) hip resurfacing. Hip resurfacing was more common in younger patients and in men compared with other prosthesis types. Compared with cemented hip replacements, Cox regression models demonstrated a survival advantage in uncemented [hazard ratio (HR) 0.86, 95% CI (0.84, 0.88) and hip resurfacing (HR 0.52, 95% CI 0.47, 0.57) operations, after adjustment for confounders. There was no evidence of interaction between prosthesis type and age. To address the issue of confounding by indication, 12,576 hip resurfacing patients were propensity score matched to 3 comparable cemented hip replacement patients (37,728 patients). Kaplan Meier survival curves demonstrated that matched hip resurfacing patients had a much higher survival probability. Cox regression models on matched patients confirmed a lower risk of death in hip resurfacing patients vs cemented (HR 0.49, 95% CI 0.43, 0.55).

Conclusion: Patients receiving hip resurfacing have reduced long-term mortality compared with patients receiving other types of hip replacement. This persisted after adjustment for confounding factors but the potential for residual confounding remains. Although patients receiving hip resurfacing are younger, there was no evidence of interaction with age. These findings require validation in external cohorts.

Disclosures: The authors have declared no conflicts of interest.

O34. EFFECT OF STRONTIUM RANELATE ON KNEE PAIN IN OSTEARTHRITIS: A RESPONDER ANALYSIS
Cyris Cooper1, Roland Chapurlat2, Nicholas Bellamy3, Edward Czerwinski4, Jean Pierre Devogelaer5, Lynn March6, Karel Pavelka7 and Jean-Yves Reginster8
1University of Southampton, MRC Lifecourse Epidemiology Unit, Southampton, UK, 2INSERM UMR 1033, Université de Lyon, Lyon, France, 3CONRCD, University of Queensland, Herston, QLD, Australia, 4Královské Military Centre, University of Krakow, Krakow, Poland, 5Cliniques Universitaires St Luc Service de Rhumatologie, University of Brussels, Brussels, Belgium, 6Institute of Bone and Joint Research, University of Sydney, Sydney, NSW, Australia, 7Department of Rheumatology, University of Prague, Prague, Czech Republic and 8Department of Public Health Epidemiology, University of Liege, Liege, Belgium

Background: In a large, randomized, placebo-controlled, double-blind phase-III 3-year study (SEKOIA), strontium ranelate 2 g/day (SrRan) has demonstrated a structure-modifying activity associated with symptomatic and radiographic improvement in patients with knee OA. In clinical trials, results are usually reported as mean of change in score which is not directly clinically meaningful. The objective of this analysis was to describe, at individual level, the effects of strontium ranelate on pain in patients with knee OA compared with placebo.

Methods: Main objective of the SEKOIA study was to demonstrate the effects of strontium ranelate on the radiographic progression of knee OA. Included patients were to be male or female over 50 years old, with symptomatic (at least 40) on a 100 mm visual analog scale (VAS) on most days of the previous month i.e. 1/2 days primary knee OA (Kellgren and Lawrence [KL] grade 2 or 3, joint space width [JSW] 2.5–5 mm). Clinical symptoms were assessed every 6 months over 3 years by the WOMAC questionnaire and a 100 mm VAS (How would you rate your knee pain and function but not patient’s global assessment not assessed in OMERACT-OARSI-like responders [1] (calculated taking into account the pain you have felt in the studied knee within the last 48 h?). The WOMAC questionnaire and a 100 mm VAS (How would you rate your knee pain and function but not patient’s global assessment not assessed in OMERACT-OARSI-like responders [1] (calculated taking into account the pain you have felt in the studied knee within the last 48 h?). Results are usually reported as mean of change in score which is not directly clinically meaningful. The objective of this analysis was to describe, at individual level, the effects of strontium ranelate on pain in patients with knee OA compared with placebo. These results were confirmed on the VAS, with a greater number of patients having an improvement in global knee pain of at least 20% (76% vs 70%, P = 0.034) or at least 50% (42% vs 36%, P = 0.010) and responders 50% (51% vs 45%) on the WOMAC pain subscore were observed in the strontium ranelate 2 g group compared with placebo. When combining improvement in pain with improvement in function (OMERACT-OARSI-like responders) the number of responders was more important in the strontium ranelate 2 g group (54% vs 44%, P = 0.039) than in the placebo group.

Conclusions: Strontium ranelate 2 g/day is associated with a greater number of patients having a clinically relevant decrease of their pain level over 3 years compared with placebo-treated patients. A higher number of OMERACT-OARSI responders was also associated with strontium ranelate treatment.

Disclosures: N.B., Servier—Consulting Fees, R.C., Merck, Amgen, Servier, Lilly, Roche, Novartis—Research Funding and/or Honoraria. O.C.C., Servier, MSD, Amgen, GSK, Roche, Alliance, Novartis, Eli Lily, Medtronic—Consulting/Lecture Fees. J.R., Servier, Novartis, Lilly, Wyeth, Amgen, GlaxoSmithKline, Roche, Merck, Nycomed, NPS, Theramex, UCB—Consulting Fees/Advisory Boards. All other authors have declared no conflicts of interest.

Reference
O36. PEGLOTICASE FOR REFRACTORY GOUT: EFFICACY AND SAFETY SUMMARY OF THE GOUT1 AND GOUT2 PHASE III TRIALS

John S. Sundy1, Herbert S. Baraf2, Michael Becker3, Edward L. Treadwell4, Robert Yood5 and Faith D. Ottery6

1Duke Clinical Research Unit, Duke University Medical Centre, Durham, NC, 2Rheumatology and Bone Research, Centre for Rheumatology and Bone Research, Wheaton, MD, 3Department of Medicine, University of Chicago, Chicago, IL, 4Medicine-Rheumatology/Immunology, Brody School of Medicine-East Carolina University, Greenville, NC, 5Rheumatology, Reliant Medical Group, Worcester, MA and 6Global Medical Affairs, Savient Pharmaceuticals, Inc, Bridgewater, NJ, USA

Background: Pegloticase, a recombinant modified mammalian uricase, is approved in the USA for chronic gout refractory to conventional therapy. The drug development programme for pegloticase included 2 replicate randomized trials and an open-label extension (OLE) study (total treatment duration up to 3 years). Here we summarize key data from the placebo-controlled phase III trials.

Methods: Patients (212) were randomized to pegloticase 8 mg q2weeks or q4weeks or placebo in a 2:2:1 ratio in 6-month, concurrent randomized, double-masked phase III trials: Gout Outcomes and Urate-lowering Therapy 1 (GOUT1) and GOUT2. Patients were >18 years of age, had baseline uric acid (UA) ≥218 mg/dl and at least one of the following: ≥3 self-reported gout flares during the prior 18 mos, ≥1 tophi or gouty arthropathy, and contraindication to allopurinol or failure to normalize UA during ≥3 mos of treatment at the maximum medically appropriate dose. The primary efficacy end point was defined as plasma uric acid (PUA) response (<6 mg/dl for ≥80% of the time during mos 3 and 6). Any patient who withdrew before study completion was considered a nonresponder. Patients who completed the randomized trials were given the option to enroll in a 30-month OLE study.

Results: The mean age of patients from the pooled population was 55 years; 82% were male. Comorbidities included hypertension (72%), dyslipidaemia (49%), chronic kidney disease (28%), diabetes (24%) and coronary artery disease (18%). Table 1 shows that PUA response after 6 mos of treatment was significantly higher with pegloticase vs placebo in both trials. Complete resolution of at least 1 tophus was seen in 40% (q2week dose; P = 0.002 vs placebo) and 21% (q4week dose; P = 0.20) of patients with evaluable tophi at baseline (last observation carried forward). Gout flares and infusion reactions (IRs) were the 2 most common adverse events across the active treatment arms. Post-hoc analyses revealed a direct relationship between loss of UA-lowering response, IR risk and development of high titre antibodies to pegloticase. Among the 56 pegloticase-treated patients with ≥1 IRs during these trials, loss of urate-lowering efficacy (UA >6 mg/dl) preceded the first IR in 44 (79%) patients.

Conclusions: 42% of patients treated with pegloticase reached the primary end point and achieved sustained urate-lowering response to therapy. A similar proportion of patients had complete resolution of at least 1 tophus; in some instances as early as 13 weeks. Nonresponders showing loss of their initial UA response should be discontinued from therapy. Thus, routine UA monitoring prior to pegloticase infusions is key to safe and successful patient management.

Table 1. Proportion of patients achieving primary end point of PUA response by treatment arm

<table>
<thead>
<tr>
<th></th>
<th>Pegloticase</th>
<th>P</th>
<th>Pegloticase</th>
<th>P</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOUT1</td>
<td>20/43 (47)</td>
<td>&lt;0.001</td>
<td>8/41 (21)</td>
<td>0.044</td>
<td>0/20 (0)</td>
</tr>
<tr>
<td>GOUT2</td>
<td>16/42 (38)</td>
<td>&lt;0.001</td>
<td>21/43 (48)</td>
<td>&lt;0.001</td>
<td>0/23 (0)</td>
</tr>
</tbody>
</table>

Results are given as n/N (%). *Pegloticase vs placebo.