Abstract Book

NOVEMBER 29 - DECEMBER 1, 2018

IOF REGIONAL SYDNEY'18

7TH ASIA-PACIFIC OSTEOPOROSIS CONFERENCE

ICC SYDNEY

www.iof-regional.org

Organizer
International Osteoporosis Foundation

Secretariat
www.humacom.com

IOF International Osteoporosis Foundation

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Our vision is a world without fragility fractures in which healthy mobility is a reality for all.
www.iofbonehealth.org

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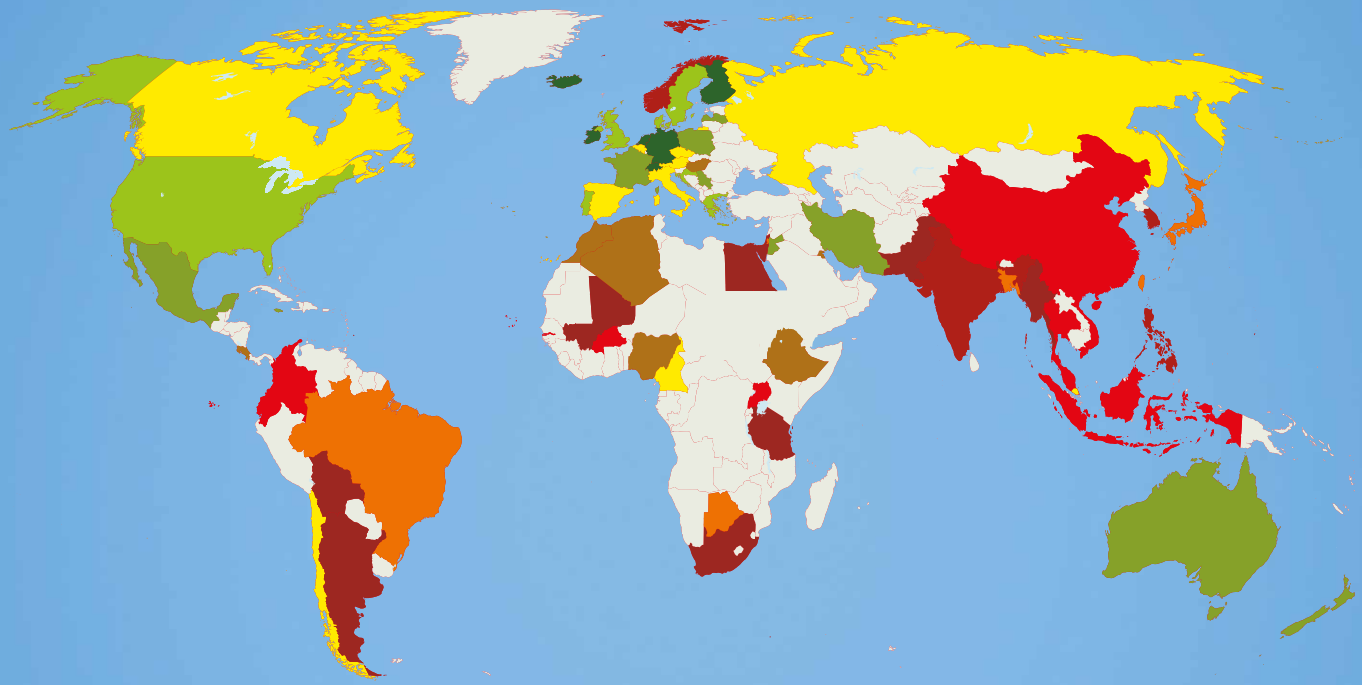
Global Map of Dietary **Calcium Intake**

IS YOUR COUNTRY GETTING ENOUGH ?



Resources and Outreach

Interactive map
Infographics
Factsheet
Webinar
Interviews
Symposium
Press releases
Digital dissemination

Interactive map available at

www.iofbonehealth.org/facts-and-statistics/calcium-map

IOF International Osteoporosis Foundation

Our vision is a world without fragility fractures, in which healthy mobility is a reality for all.

www.iofbonehealth.org

Welcome Message

Dear Colleagues,

it is with great pleasure that we welcome you to Sydney and the IOF Regional - 7th Asia Pacific Osteoporosis Conference.

The Conference's scientific programme has been developed by a team comprising members of the Committee of Scientific Advisors of the International Osteoporosis Foundation (IOF) and regional specialists. We would like to thank the Scientific Chairs, Professors Serge Ferrari and Joon Kiong Lee, for taking the lead in setting up an exciting and comprehensive programme that brings together the world's best in the field of musculoskeletal health and disease.

We are all meeting in Sydney with a common aim - to gather new knowledge, skills and tools in the prevention and treatment of osteoporosis and osteoarthritis, the two most disabling conditions in elderly people. An important addition is a focus on sarcopenia because of its intimate relation to bone and joint disease. It is our hope that this Conference will move the field one step forward on all fronts; from new understanding of bone metabolism and pathology, to new strategies and options in prevention, diagnosis and treatment.

The core scientific programme consists of 6 plenary sessions by renowned speakers, 1 CNS Roundtable and 10 oral communications selected from the very best of hundreds of submitted abstracts. In addition, participants can choose among 11 different Meet-The-Expert sessions and 3 special sessions on issues of clinical importance.

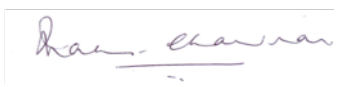
We also encourage you to attend the scheduled poster viewing sessions, 3 industry sponsored satellite symposia and to visit the large commercial exhibition presented by the leading companies in the bone field.

The city of Sydney offers a modern and most convenient and pleasant setting for international conferences. We hope that you will also take the opportunity to explore its many attractions!

Thank you for your participation. We will do our best to ensure that this meeting is a memorable, enriching experience for all.

John A. Kanis

Manju Chandran



About IOF

The **International Osteoporosis Foundation** (IOF) is the only worldwide organization dedicated to the prevention, diagnosis and treatment of osteoporosis and related musculoskeletal diseases. It is a Swiss not-for-profit Foundation acting as an umbrella organization bringing together all stakeholders; including, scientists, physicians, patient and medical societies as well as corporate partners interested in osteoporosis, osteoarthritis and bone health.

IOF International Osteoporosis Foundation

IOF has three membership committees including the Committee of National Societies representing 240 members in 99 countries or regions, the Committee of Scientific Advisors represented by 154 thought leaders from around the world and Committee of Corporate Advisors, comprised of 12 companies interested in bone health.

www.iofbonehealth.org

Vision

A world without fragility fractures, in which healthy mobility is a reality for all.

Mission

To promote bone and musculoskeletal health as a worldwide priority.

Event Information

IOF REGIONAL SYDNEY'18
7th Asia Pacific Osteoporosis Conference

November 29 - December 1, 2018

IOF Regional
ICC - International Convention Centre Sydney
14 Darling Drive
Sydney, NSW 2000
www.iccsydney.com.au

Contact Information

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(iofap@iofbonehealth.org)

Posters & abstracts
Sophie Leisten
(abstracts@iof-regional.org)

Committees

Congress Chairpersons
John A. KANIS
Manju CHANDRAN

Scientific Committee
Serge FERRARI (Chairperson)
Joon Kiong LEE (Chairperson)
Manju CHANDRAN
Cyrus COOPER
Bess DAWSON-HUGHES
Peter EBELING
John A. KANIS
Ambrish MITHAL
Toshitaka NAKAMURA
René RIZZOLI

Local Committee
Manju CHANDRAN (Chairperson)
Peter EBELING (Chairperson)
Gustavo DUQUE
Helena JOHANSSON
John A. KANIS
S. KUKREJA
Timothy KWOK
Joon Kiong LEE
Lyn MARCH
Paul MITCHELL
Ambrish MITHAL
Hajime ORIMO
Kerrie SANDERS
Ego SEEMAN
Yoshiya TANAKA
Vu Thi THANH THUY
Zhao YANLING

Conference Information

Opening Ceremony Venue
November 29
International Convention Centre Sydney
14 Darling Drive,
Sydney, NSW 2000
PO Box Q965, QVB, NSW 1230,
Australia

Conference Venue
November 30 - December 1
International Convention Centre Sydney
14 Darling Drive,
Sydney, NSW 2000
PO Box Q965, QVB, NSW 1230,
Australia

Operating Dates and Hours
Thursday, Nov. 29 . . . . . 17.30 - 20.30
Friday, Nov. 30 . . . . . 08.00 - 19.00
Saturday, Dec. 1. . . . . 08.00 - 17.00

Poster Viewing Sessions
Friday, Nov. 30 . . . . . 13.30 - 14.00
Saturday, Dec. 1. . . . . 13.30 - 14.00

Accreditation

RANZCR CPD

15 RANZCR CPD points can be claimed for attendance at the 7th Asia-Pacific Osteoporosis Conference that will be held in Sydney on November 30th and December 1st, 2018.

CPD points will be awarded as follow:

- 8.5 points may be claimed for attendance at the "7th Asia-Pacific Osteoporosis Conference" to be held on 30/11/2018
- 6.5 points may be claimed for attendance at the "7th Asia-Pacific Osteoporosis Conference" to be held on 01/12/2018

A total of 15 points may be claimed for attendance at the "7th Asia-Pacific Osteoporosis Conference" to be held on 30th Nov - 1st Dec 2018.

For anyone who attends only part of this session, points may be claimed pro rata at 1 point per hour per lecture

RACS CPD

17 RACS CPD points can be claimed for participation in the Conference.

The IOF-Regional 7th Asia-Pacific Osteoporosis Conference has been approved in the RACS CPD Program. Fellows who participate can claim one point per hour in Maintenance of Knowledge and Skills.

In order to receive the points, RACS Fellows must register their RACS ID during the event at the Accreditation Point in the exhibition area.

CME

Europe

The IOF-Regional 7th Asia-Pacific Osteoporosis Conference, Sydney, Australia, 29/11/2018-01/12/2018 has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with 14 European CME credits (ECMEC®s). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.

America

Through an agreement between the Union Européenne des Médecins Spécialistes and the American Medical Association, physicians may convert EACCME® credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the process to convert EACCME® credit to AMA credit can be found at www.ama-assn.org/education/earn-credit-participation-international-activities.

Canada

Live educational activities, occurring outside of Canada, recognised by the UEMS-EACCME® for ECMEC®s are deemed to be Accredited Group Learning Activities (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.

Badges
For registered participants, personalized badges will be requested for entry to all scientific programmes and to access the exhibition and posters areas. Blank badges are prohibited.

Lost badges: 40 USD fee/badge

Certificate of Attendance
A certificate of attendance will be sent by email after the conference. In order to receive it, make sure to have your badge scanned at the entrance of the exhibition area.

Cloakroom
A cloakroom service for clothing and reasonably sized items is available during the opening hours of the Conference. Items of value should not be left in the cloakroom. Please make sure to collect all belongings at the end of each day.

Internet Access
A free Wireless internet connexion is available in the Conference Center.

Lunches, Breaks and Refreshments
Coffee breaks will be served in the exhibition area. Lunch and snack boxes will be provided to participants attending Sponsored Symposia.

Media
The IOF Regional Conference will not provide any Media Center.

Tourist Information
www.sydney.com

General Emergency Number
Australian Telephone Number: 000

Language
English will be the official language of the Conference. No translation is provided.

PARTNERS

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EXHIBITORS

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Venue Map

5. Medi
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WORLD CONGRESS ON OSTEOPOROSIS,
OSTEOARTHRITIS AND MUSCULOSKELETAL DISEASES

WCO IOF-ESCEO

2019 PARIS

April 4-7, 2019

Palais des Congrès

www.WCO-IOF-ESCEO.org

IOF International Osteoporosis Foundation

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WORLD'S LEADING CLINICAL CONFERENCE ON BONE, JOINT AND MUSCLE HEALTH

Final Programme

Thu, November 29 | Fri, November 30 | Sat, December 1

17.30 **OPENING CEREMONY**

- *Welcome* — C. Cooper, J. A. Kanis & M. Chandran
- *Best clinical papers of 2018* — R. Rizzoli
- *Inclusion of diversity in science* — S. Lee Brennan
- *Hearing the Consumer voice* — G. Lyubomirsky
- *Osteoporosis, global challenge, local impacts* — L. March
- *Conclusion*

19.30 – 20.30 **WELCOME COCKTAIL**

Thu, November 29 | Fri, November 30 | Sat, December 1

08.00 – 19.00 **EXHIBITION AREA OPEN**

08.15 **PLENARY SESSION I**

Improving the identification of high risk patients
Chair: J. A. Kanis & E. Seeman

- *Can FRAX be improved* — J. A. Kanis
- *CtF/FLS: what have we achieved* — C. Cooper
- *New imaging modalities* — S. Ferrari

9.30 **ORAL COMMUNICATIONS SESSION I**

Chair: J. Eisman

- 9.30 — **OC1** — *T-SCORE AS AN INDICATOR OF FRACTURE RISK ON THERAPY: EVIDENCE FROM ROMOSOZUMAB VS ALENDRONATE TREATMENT IN THE ARCH TRIAL* — F. C. Cosman
- 9.40 — **OC2** — *DENOSUMAB COMPARED WITH RISEDRONATE IN GLUCOCORTICOID-TREATED SUBJECTS: RESULTS FROM THE FINAL 24-MONTH ANALYSIS OF A RANDOMIZED, DOUBLE-BLIND, DOUBLE-DUMMY STUDY* — K. S. Saag
- 9.50 — **OC3** — *VITAMIN D SUPPLEMENTATION IN PREGNANCY: A RANDOMIZED DOUBLE-BLIND CONTROLLED TRIAL* — R. Khadgawat

Thu, November 29 | **Fri, November 30** | Sat, December 1

10.00 **INDUSTRY-SPONSORED SATELLITE SYMPOSIUM** (Detailed programme on page 19)

11.00 **PLENARY SESSION II**

Similarities and differences in fracture risk and treatments response: Asia vs West (IOF-OA session)
Chair: C. Cooper (IOF) & G. Liubomirsky (OA)

- *BMD and other parameters of bone in Asia vs West* — K. Sanders
- *FRAX: intervention threshold in Asia vs West* — E. Lau
- *Response to osteoporosis treatment: is it the same in Asian and Caucasian (benefit/risk including AFF)* — P. Ebeling

12.30 **INDUSTRY-SPONSORED LUNCH SYMPOSIUM** (Detailed programme on page 19)

13.30 **BREAK AND POSTER VIEWING SESSION**

14.00 **MEET-THE-EXPERT SESSIONS**

- *Recent Fracture: when and how to treat osteoporosis* — J.-K. Lee
- *Chronic renal failure: how to assess and manage bone fragility?* — P. Ebeling
- *Vitamin D: which & how much?* — A. Mithal
- *Protein intake and supplement in fracture patient* — R. Rizzoli

14.45 **PLENARY SESSION III**

Quality of life in musculoskeletal diseases - ESCEO symposium
Chair: R. Rizzoli & E. Biver

- *Introduction* — O. Bruyère
- *Assessment of quality of life in osteoporosis* — J.-M. Kaufman
- *Assessment of quality of life in osteoarthritis* — N. Arden
- *Assessment of quality of life in sarcopenia* — F. Buckinx
- *Discussion* — J.-Y. Reginster
- *Conclusion* — J.-Y. Reginster

16.15 **INDUSTRY-SUPPORTED SESSION: IOF - APOA JOINT SESSION**
(more information on page 19)

Osteoporosis - Orthopedic Surgery in Asia Pacific, The Missing Link?

- *Introduction* — S. Ferrari
- *Osteoporosis in Asia Pacific* — P. Ebeling
- *Orthopedic Surgery in Asia Pacific* — D. Choon
- *IOF-APOA Collaboration - "The Link"* — J. K. Lee
- *Launch of the IOF-APOA collaboration and Promising Future* — C. Cooper

17.00 **ORAL COMMUNICATIONS SESSION II**

Chair: M. Chandran

- 17.00 — **OC4** — *ANTI-OSTEOPOROSIS MEDICATIONS ARE ASSOCIATED WITH DECREASED MORTALITY AFTER HIP FRACTURE* — Y. Li
- 17.10 — **OC5** — *ASIA-PACIFIC BONE ACADEMY FRACTURE LIAISON SERVICE EDUCATIONAL INITIATIVE* — P. E. Ebeling
- 17.20 — **OC6** — *INCREASED CORTICAL POROSITY AND REDUCED TRABECULAR DENSITY ARE NOT NECESSARILY SYNONYMOUS WITH BONE LOSS AND MICROSTRUCTURAL DETERIORATION* — E. Seeman

17.30 **CNS ROUNDTABLE**

Mapping calcium intake

Chair: B. Dawson-Hughes & A. Mithal

- *Dietary calcium intake worldwide (Ca map)* — B. Dawson-Hughes
- *Consequences of low calcium intake in the Asia Pacific region* — R. Rizzoli
- *Calcium supplements and fracture prevention* — A. Mithal
- *Calcium intake and its implication in China* — Wei-bo Xia
- *Roundtable: Potential strategies to improve calcium intake - What is feasible within the low intake countries*

19.00

Thu, November 29 | Fri, November 30 | **Sat, December 1**

08.00 – 17.00 **EXHIBITION AREA OPEN**

08.15 **MEET-THE-EXPERT SESSIONS**

- *Falls prevention: is it possible* – W. L. Hsu
- *Bone loss in early menopause: to treat or not?* – A. Vincent
- *Genetic markers of bone fragility: what have we learned* – E. Duncan
- *Can we trust bone turnover markers to improve fracture assessment* – H. Morris

09.00 **PLENARY SESSION IV**

Assessment and management of bone fragility beyond idiopathic osteoporosis (IOF-ANZBMS session)
Chair: S. Ferrari (IOF) & P. Croucher (ANZBMS)

- *Fracture prevention in cancer patients* – E. Biver
- *Fracture prevention in diabetes patients* – M. Chandran
- *When to suspect a genetic disorder?* – J. Eisman

10.15 **ORAL COMMUNICATIONS SESSIONS III**

Chair: J. Center

- 10.15 – **OC7** – *EFFECTS OF TERIPARATIDE ON HIP AND UPPER LIMB FRACTURES IN PATIENTS WITH OSTEOPOROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS* – M. Hassanzai
- 10.25 – **OC8** – *DIGITAL X-RADIOGRAMMETRY COMBINED WITH MAMMOGRAPHY TO SCREEN POSTMENOPAUSAL WOMEN FOR REDUCED BONE MINERAL DENSITY* – A. Rao
- 10.35 – **OC9** – *DO DEFINITIONS OF SARCOPENIA PREDICT FRACTURE RISK INDEPENDENT OF FRAX, FALLS AND BMD? (A META-ANALYSIS OF THE OSTEOPOROTIC FRACTURES IN MEN (MROS) STUDY)* – H. Johansson
- 10.45 – **OC10** – *ASSESSING CLINICAL UTILITY (IMPACT) OF GENETIC PROFILING IN FRACTURE RISK ASSESSMENT: A DECISION CURVE ANALYSIS APPROACH* – T. Ho-Le

Thu, November 29 | Fri, November 30 | **Sat, December 1**

11.00 **PLENARY SESSION V**

New insights in the management of knee osteoarthritis - ESCEO Symposium
Chair: C. Cooper & F. Cicuttini

- *Welcome* — C. Cooper
- *The 2014-2016 ESCEO algorithm for the management of knee osteoarthritis* — O. Bruyère
- *New insights on the safety of anti-osteoarthritis medications* — E. Dennison
- *New clinical evidence supporting the use of SYSADOAs as a first-line background treatment in knee osteoarthritis* — J.-Y. Reginster, G. Honvo, A. Geerinck, O. Bruyère
- *Update of the 2014-2016 ESCEO algorithm for the managment of knee osteoarthritis* — C. Cooper
- *Discussion* — C. Cooper
- *Conclusion* — J.-Y. Reginster

12.30 **INDUSTRY-SPONSORED SATELLITE SYMPOSIUM** (Detailed programme on page 19)

13.30 **BREAK AND POSTER VIEWING SESSION**

14.00 **IOF-OA-ANZBMS JOINT SESSION**

Chair: G. Lyubomirsky & B. Dawson-Hughes

- *Excercice and osteoporosis* — B. Beck
- *Monetary cost of osteoporosis* — J. A. Kanis
- *Morbidity and mortality of osteoporosis* — J. Center

14.45

IOF-AGNOVOS HEALTHCARE YOUNG INVESTIGATOR AWARDS

Chair: A. Mithal

- 14.51 – **P118** – *ORAL BISPHOSPHONATE USE AND ALL-CAUSE MORTALITY IN PATIENTS WITH ADVANCED (STAGE IIIB+) CHRONIC KIDNEY DISEASE: A POPULATION-BASED COHORT STUDY* – D. Alarkawi
- 15.00 – **P050** – *PREDICTION OF FRACTURES IN MEN WITH DYSGLYCAEMIA USING FRAX (AUS)* – K. Holloway-Kew
- 15.09 – **P137** – *ATYPICAL FEMUR FRACTURES IN AN AUSTRALIAN HOSPITAL SETTING: INCIDENCE, PATIENT RISK FACTORS AND DENSITOMETRIC CHARACTERISTICS* – H. Nguyen
- 15.18 – **P046** – *ASSOCIATIONS BETWEEN PAIN AT MULTIPLE SITES AND PREVALENT AND INCIDENT FRACTURES IN OLDER ADULTS* – F. Pan
- 15.27 – **P011** – *MID-CALF SKELETAL MUSCLE DENSITY AND ITS ASSOCIATIONS WITH ACCELEROMETER-DETERMINED PHYSICAL ACTIVITY, BONE HEALTH AND INCIDENT 12-MONTH FALLS IN OLDER ADULTS: THE HEALTHY AGEING INITIATIVE* – D. Scott
- 15.36 – **P083** – *PERSISTENT HIGH-IMPACT ACTIVITY AND FITNESS DURING ADOLESCENCE AND EARLY ADULTHOOD AND BONE DENSITY AND MICROARCHITECTURE IN EARLY ADULTHOOD* – Y. Yang

14.45

MEET-THE-EXPERT SESSIONS

- *Osteosarcopenia* – G. Duque
- *Glucocorticoid osteoporosis* – E. Dennison
- *Assessment of physical strength and performance* – F. Buckinx

15.45

PLENARY SESSION VI

Osteoporosis treatment: update

Chair: J.-Y. Reginster & A. Mithal

- *Benefit/Risk of long term treatment* – S. Ferrari
- *Fracture risk off therapy* – E. Dennison
- *Closing the gap in the treatment of patients at imminent risk of fracture: role of the new anabolic agents* – J.-Y. Reginster

17.00

Industry-Sponsored Sessions

Thu, November 29 | **Fri, November 30** | Sat, December 1

10.00 **MEDTRONIC SATELLITE SYMPOSIUM**

UNDERSTANDING MORTALITY RISK FOR PATIENTS WITH VCF
Chair: K. L. Ong

- *Understanding mortality risk for patients with VCF* – K. L. Ong

11.00

12.30 **AMGEN SATELLITE SYMPOSIUM**

ACHIEVING THE GOALS OF OSTEOPOROSIS THERAPY

- *Arrivals and welcome – P. Ebeling*
- *Presentation and Q & A – S. Ferrari*
- *Long term treatment – case study – K. M. Kim*
- *Panel discussion – All*

13.30

16.15 **IOF-APOA JOINT SESSION SUPPORTED BY AGNOVOS HEALTHCARE**

Osteoporosis - Orthopedic Surgery in Asia Pacific, The Missing Link?

- *Introduction* – S. Ferrari
- *Osteoporosis in Asia Pacific* – P. Ebeling
- *Orthopedic Surgery in Asia Pacific* – D. Choon
- *IOF-APOA Collaboration - "The Link"* – J. K. Lee
- *Launch of the IOF-APOA collaboration and Promising Future* – C. Cooper

17.00

Thu, November 29 | Fri, November 30 | **Sat, December 1**

12.30 **ELI LILLY SATELLITE SYMPOSIUM**

THE IMPORTANCE OF BONE FORMING AGENTS IN THE TREATMENT OF SEVERE OSTEOPOROSIS
Chairperson: D. Thiebaud

- *Welcome & Introduction* – D. Thiebaud
- *Differing Effects of Antiresorptive and Anabolic Therapies on Bone Structure* – E. Seeman
- *Differential Effects of Teriparatide VS Antiresorptives on Osteoporotic Fractures* – S. Ferrari
- *Audience Questions and Answers* – All Panel
- *Closing Remarks* – D. Thiebaud

13.30

Keep up with the latest research and advances in the field

LEADING JOURNALS with impact

IOF offers an extensive publication portfolio of leading scientific journals in the field of osteoporosis and bone health.

Osteoporosis International

Editors-in-Chief: John A. Kanis and Felicia Cosman

Highly cited, journal of choice for the latest clinical research in the musculoskeletal field

Archives of Osteoporosis

Editors-in-Chief: John A. Kanis and Felicia Cosman

With an impressive first impact factor, a key forum for regional research and guidelines

Calcified Tissue International & Musculoskeletal Research

Editors-in-Chief: Stuart H. Ralston and René Rizzoli

Cutting edge preclinical and translational research in the bone and muscle field

IOF International Osteoporosis Foundation

Our vision is a world without fragility fractures, in which healthy mobility is a reality for all.

www.iofbonehealth.org

IOF REGIONAL SYDNEY'18
7TH ASIA-PACIFIC OSTEOPOROSIS CONFERENCE

IOF Regional 7th Asia-Pacific Osteoporosis Conference
Sydney, Australia – 2018

Plenary Lecture Abstracts

PL1
CAN FRAX BE IMPROVED?

J. A. Kanis[1,2]

[1]Centre for Metabolic Bone Diseases, University of Sheffield Medical School, Sheffield, United Kingdom, [2]Mary McKillop Health Institute, Australian Catholic University, Melbourne, Australia

FRAX® is a computer-based algorithm (http://www.shef.ac.uk/FRAX) that calculates the 10-year probability of a major fracture (hip, clinical spine, humerus or wrist fracture) and the 10-year probability of hip. Fracture risk is calculated from age, body mass index and well validated dichotomized risk factors. Femoral neck bone mineral density can be optionally input to enhance fracture risk prediction. The first 8 models were launched in 2008 and there are currently 68 models in 63 countries covering more than 80% of the world population. With the increasing geographic representation of FRAX, uptake has risen progressively and there are upwards of 3 million calculations undertaken each year.

A probability calculation is of no use unless guidance is provided on its use. This demands the setting of intervention thresholds – namely the fracture probability above which treatment can be recommended. This depends critically on the development of country-specific assessment guidelines that incorporate FRAX and reimbursement policies that are attuned to the guideline. As expected, there is a lag between the availability of FRAX and its incorporation into assessment guidelines. In the countries of the European Union, approximately half now mention FRAX in the guideline and, of these, about half give explicit instructions on its use. As expected, the uptake of FRAX is heterogeneous in different countries and is higher in those with established assessment guidelines. The future development of FRAX thus depends in part on national rather than international initiatives.

The question arises whether future iterations of FRAX should include additional risk variables that will improve the sensitivity and specificity of the tool for fracture prediction. Of the several candidates proposed, the most frequently raised is falls as a risk variable. Its incorporation into FRAX is not straightforward for several reasons. First, falls risk is inherently considered in the algorithm, though not as an input variable. Thus, the fracture probability given for any combination of risk factors assumes that the falls risk is that observed (but not documented) in the cohorts used to construct FRAX. Second, the interrelationship of falls risk with the other FRAX variables has been inadequately explored on an international basis. Third, the relationship between the risk variable and mortality needs to be accounted for, but there are no data available. These technical gaps aside, FRAX is intended to identify a risk that is amenable to a therapeutic intervention. The evidence that fracture reduction is similar in individuals with or without recent multiple falls is inconsistent. A stronger case can be made for the inclusion of type 2 diabetes as a risk variable. Thus, improvements in FRAX depend on its judicious application and the inclusion of well validated risk variables.

PL2
CTF/FLS: WHAT HAVE WE ACHIEVED

C. Cooper[1,2]

[1]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom, [2]NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, United Kingdom

The case for Fracture Liaison Service (FLS) to prevent secondary fractures is clear. With an ageing population, the burden of osteoporosis is increasing. Despite evidence for the clinical effectiveness of secondary fracture prevention, translation in the real-world setting remains disappointing. Worldwide, eighty per cent of fragility fracture patients are neither assessed nor treated for osteoporosis.

To support the use of effective models of care, the International Osteoporosis Foundation (IOF) launched the Capture the Fracture® (CTF) programme in 2012. This expert-led and evidence-based programme aims to reduce secondary fractures by facilitating the implementation of FLS globally. A primary CTF resource is the Best Practice Framework, which sets standards for FLS, serves as a benchmark for existing FLS, and provides guidance for developing FLS.

In an effort to engage the global medical community, CTF offers a Best Practice Recognition programme where FLS can submit their service for evaluation against the BPF for gold, silver or bronze star recognition of achievements. The FLS is then plotted on the CTF Map of Best Practice, which displays participating FLS and their level of achievement. To influence change, the map is used as a visual representation of the international FLS network, their achievements, as well as an incentive for other facilities to join the programme.

Furthermore, IOF has developed numerous free resources including the FLS toolkit and holds webinars which provide essential knowledge on secondary fracture prevention to health care professionals. Since 2016, IOF has been running the mentorship programme that connects local and international FLS experts with institutions interested in establishing an FLS. A combination of both on-site training and workshops have been organised to provide guidance on FLS implementation. They have been conducted worldwide, with interest growing especially in the Middle East and Asia-Pacific.

Capture the Fracture® is an initiative of the IOF Fracture Working Group and a flagship programme of IOF. The programme has now grown to display 296 FLS on the map, across 39 countries. CTF shows that a single framework with set criteria is able to benchmark services across healthcare systems worldwide.

PL3
NEW IMAGING MODALITIES

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More than half of all fragility fractures occur in subjects with aBMD better than -2.5 T-scores, i.e. with osteopenia and sometimes even normal BMD. Notwithstanding the importance of falls and the highly variable energy that these falls may impact on the skeleton, this observation has pointed to the importance of alterations in bone quality, primarily bone microstructure, as a determinant of bone fragility above and beyond bone mineral mass. Of the few techniques allowing to evaluate bone microstructure non-invasively, peripheral high-resolution pQCT (HR-pQCT) has been the most commonly used. Many studies comparing women or men with / without prevalent fractures have shown that alterations in both the trabecular and cortical compartment at the distal radius and/or tibia are associated with fragility fractures. Ultimately, estimates of bone strength derived by FEA from the HR-pQCT parameters have proven to be better predictors of fracture risk than central aBMD. Very recently, some investigators have demonstrated that baseline assessment of radius vBMD and microstructure improves the prediction of incident fragility fractures beyond FN aBMD and FRAX. However, a study has also shown that aBMD measured at the distal radius captures most of the components of bone fragility measured by HR-pQCT at the same site.

Hence these studies have allowed the clinician to realize the importance of trabecular and cortical bone, particularly cortical porosity, as a main constituent of bone fragility and raised interest into understanding the differential effects of osteoporosis drugs on these parameters. Although the potential value of evaluating bone microstructure to predict fragility fractures has been demonstrated, the improvement over aBMD at the same site and/or FRAX is limited. Therefore, it remains unlikely that the evaluation of bone microstructure and/or strength by currently available tools will find a place in clinical practice.

PL4

BMD AND OTHER PARAMETERS OF BONE IN ASIA VS WEST

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A notable divide in fracture incidence exists between Asian and Caucasian Western populations which do not consistently parallel ethnic differences in areal BMD (aBMD). Asians have lower aBMD, but age-standardised non-vertebral fracture rates are lower compared to Western populations. In contrast, vertebral fracture risk appears higher among the Chinese, and age-standardised hip fracture rates are decreasing in the West and increasing in Asia. A systematic review was conducted to summarise differences in bone strength and its determinants between Asian and Caucasian populations that may help explain these paradoxes.

Non-interventional studies and baseline data from interventional and longitudinal projects on bone parameters and fracture risk in the Asian population were identified from 1985 to July 2018 by a PubMed, Scopus, Web of Science search. Evaluable studies were reviewed for quality by the relevant National Heart, Lung, and Blood Institute Quality Assessment Tool.

Overall 75 full-text studies were assessed for eligibility and inconsistent findings in the included studies made generalizing bone qualities within different Asian populations challenging. The Chinese appear to compensate for smaller bone size via changes in hip geometry and microstructure leading to stronger bone with more connectivity and less porosity. Cross-sectional data suggests that peri-menopausal Chinese women have dissimilar deterioration between cortical and trabecular bone than Caucasian women. This may contribute to the different trends in hip fracture rates between Asian and Western populations.

Artefactual aBMD differences exist between Asian and Western populations largely due to variations in bone size. Advances in imaging technologies have helped overcome this problem and improved our understanding of bone microstructure and biomechanical properties that contribute to ethnic differences in fracture rates. More prospective cohort studies with sophisticated imaging that can also identify changes attributable to urbanization are needed and may lead to targeted phenotypic interventions to reduce fracture risk in our ageing populations.

PL5

FRAX: INTERVENTION THRESHOLD IN ASIA VS THE WEST

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By the year 2050, half of all hip fractures in women >65 years of age will occur in Asia. In many Asian countries, measurement of bone mineral density by DEXA is not widely available. In these circumstances, the use of FRAX to document fracture risk in the clinical setting allows patients at high risk of fractures to be identified and treated.

The use of fix fracture thresholds versus country specific fracture thresholds has been reviewed by several organizations. In a recent review, more than one half of 58 publications identified applied a threshold probability of 20% for a major osteoporotic fracture, many of which also mention a hip fracture probability of 3%. This was based on the National Osteoporosis Foundation guidelines.

However, due to the difference in fracture thresholds in different ethnic groups, ethnic/country specific thresholds are preferable. Various approaches have been adopted to develop country specific thresholds in Asian countries. For instance, in Hong Kong, when the threshold probability was set to the age-specific fracture probability equal to that of a woman with a prior fracture (FRAX, with BMD), the sensitivity and specificity was 47% and 83% respectively. In China, intervention thresholds were set at 4% for the 10 year probability of major osteoporotic fracture and 1.3% for hip fracture. In Japan, thresholds of equivalence varied with age, ranging from 5% at an age of 50 years to more than 20% at the age of 80 years.

The collection of epidemiological data on fracture incidence, and the studies on applicability of FRAX in defining at risk subjects are essential in other Asian countries.

PL6

RESPONSE TO OSTEOPOROSIS TREATMENT: IS IT THE SAME IN ASIANS AND CAUCASIANS (BENEFIT/RISK INCLUDING AFF)?

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In considering differences in responses to anti-osteoporosis treatment between Asians and Caucasians, it is important first to examine differences in fracture risk and bone geometry and microarchitecture. In Asia, hip fracture rates are highest in Malaysia and South Korea and lowest in the Philippines (133/100,000) being less than one quarter the rates seen in Sandinavia. Paradoxically, Asians have smaller bones and lower areal bone mineral density (aBMD), but their rates of hip and wrist fractures are lower than Caucasians. Bone microarchitecture changes compensate for these differences which would favour reduced bone strength with higher cortical thickness, lower cortical porosity and higher cortical tissue mineral density leading to higher cortical BMD and total BMD due to smaller total and trabecular areas. Bone strength is therefore sustained in Asians and not different to that in Caucasians.

Although few head-to-head studies have been performed comparing responses to anti-osteoporosis drugs between Asians and Caucasians, responses are likely to be similar. For alendronate (5 mg/day), increases in spine and hip BMD and reductions in bone resorption were similar in Asians and Caucasians over two years. A meta-analysis of the Fracture Prevention Trial with teriparatide and smaller Japanese trials showed that was no significant heterogeneity for vertebral and non-vertebral fractures among included studies. Odds ratio estimates (95% CI) were 0.29 (0.20, 0.43) for vertebral fracture and 0.53 (0.32, 0.86) for non-vertebral fracture. In the FRAME study with romosozumab versus placebo, about 11.6% of the 7,180 included participants were from Japan, Hong Kong or India. The only ethnic difference in this study was a low baseline absolute fracture risk fracture in participants from Latin America, in whom non-vertebral fractures were not reduced, whereas vertebral, clinical and non-vertebral fractures were reduced in the rest of world population. Similarly, in the ARCH study of romosozumab versus alendronate, about 10.5% of the 4,093 included participants were from Hong Kong, South Africa, South Korea, and Taiwan. There were no ethnic differences in responses, and romosozumab reduced the risk of vertebral, clinical, non-vertebral and hip fractures compared with alendronate.

In terms of risks, the most relevant to consider in Asians are atypical femur fractures (AFF). The aetiology of these antiresorptive therapy-related fractures is uncertain, but they may be secondary to increased mineralisation, reduced bone remodeling or changes in bone geometry (lateral femoral bowing and varus hip geometry). Asians are more susceptible to AFF. In a large study with a median follow up of 7.7 years, the age-adjusted relative hazard for AFF was 8.5 (95% CI 4.9-14.9) comparing Asian to Caucasian women, and was only modestly reduced to 6.6 (3.7-11.5) after adjusting for bisphosphonate duration and current use. These data are in contrast to findings from a smaller retrospective cohort study from Korea that showed AFF incidence was similar to in western countries (100/100,000 after 8 years of bisphosphonates). There is also evidence that bone turnover markers are reduced more in Asian patients with AFF. It is interesting to speculate that the bone microarchitectural differences at baseline of lower cortical porosity and higher cortical tissue mineral density may predispose to the propagation of AFF. The increased lateral femoral bowing and varus hip geometry present in Asians may also contribute to their increased risk of AFF.

In conclusion, although absolute fracture risk in Asians is lower than in Caucasians increased population ageing and urbanisation mean Asia will be the epicentre of hip fractures by 2050. Both anti-resorptive and anabolic drugs for osteoporosis are effective at reducing fractures in Asians and benefits of treatment far outweigh any risks.

PL7
ASSESSMENT OF QUALITY OF LIFE IN OSTEOPOROSIS

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Health-related quality of life (HRQoL) is a subjective assessment of the impact of disease and its treatment. It involves all factors directly or indirectly relevant to health status and encompasses physical, mental and social domains of functioning and well-being. To measure HRQoL is to assess objectively subjective feelings. For this purpose, numerous questionnaire-based instruments have been developed and more or less well validated as to their psychometric properties and power to discriminate between diseased and control subjects.

Common low trauma fractures in osteoporosis, in particular hip-, vertebral- and wrist fractures, have been shown to adversely affect HRQoL. The purpose of HRQoL measurements in osteoporosis may be for assessment of the burden of the disease, for evaluation of treatment effects or to estimate cost-effectiveness of treatments. For assessment of HRQoL in osteoporosis both not disease-specific 'generic' QoL questionnaires and/or 'osteoporosis-specific' QoL questionnaires or even 'fracture-specific' QoL questionnaires may be used. Examples of generic tools are the Short Form 36 of the Medical Outcomes Study (SF-36), the Nottingham Health Profile (NHP), and the Euroqol five item questionnaire (EQ-5D).

Several osteoporosis-specific HRQoL instruments have been proposed. Probably most widely applied is the QoL questionnaire of the International Osteoporosis Foundation (formerly European Osteoporosis Foundation), the Qualeffo-41 with 41 questions related to the domains pain, physical function, social function, mental function and general health. An abridged version, the Qualeffo-31 has also been validated as well as an IOF-wrist questionnaire including 12 items. Other proposed osteoporosis-specific HRQoL instruments are the Osteoporosis-targeted Quality of Life Questionnaire (OPTQOL), the Osteoporosis Assessment Questionnaire (OPAQ), the Osteoporosis Quality of Life Questionnaire (OQLQ), and the Osteoporosis Functional Disability Questionnaire (OFDQ). The Questionnaire Quality of Life in Osteoporosis (QUALIOST) has been developed as a disease-specific module in addition to the generic SF-36. Osteoporosis-specific tools may have the advantage of being more user-friendly and more discriminative than generic tools. The latter, on the other hand, allow for comparisons between diseases. Moreover, some generic tools such as the EQ-5D permit to address utility, i.e. the value attached to specific health states, from which loss of quality-adjusted life years (QUALY) can be calculated as an important parameter for cost-effectiveness studies. Important variables to take into account in the interpretation of HRQoL assessments are type of fracture, time elapsed since fracture, and cross-regional / cross-cultural factors. As to the latter, there are several examples of translation, adaptation and validation of osteoporosis-specific tools for use in a particular region or country.

PL8

ASSESSMENT OF QUALITY OF LIFE IN OSTEOARTHRITIS

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Osteoarthritis (OA) is the most common joint disorder in the world with a global prevalence of hip and knee OA of approximately 5%. Obesity is one of the strongest risk factors for OA and its rates are rising globally, making it likely that the rates of hip, hand and spinal OA, will also increase in coming decades. Osteoarthritis is associated with considerable costs to health service providers and accounts for over 90% of lower limb joint replacements performed in western health care systems. More recently, OA has been demonstrated to be associated with an increased mortality, especially from cardiovascular causes.

Most people with OA suffer from pain, which is often reported as the key limiting factor to maintaining physical activity and social participation. The impairment in function and participation can vary in severity from mild, caus-ingintermittent pain and limiteddifficulty performing daily activities, to severe disabling chronic pain and loss of function, often with associated decline in quality of life. OA related disability can limit a person's major daily life activities such as walking, eating, communicating or self-care.

It is estimated that 242 million people in the world are living with symptomatic and activity limiting OA of the hip and/or knee, accounting for 13 million years lived with disability (YLD): 2.4% of all years live with disability. More importantly, it is the third most rapidly rising cause of YLD. It is therefore essential that we can accurately capture and describe the reduction in quality of life throughout the disease course in these people with OA.

PL9

ASSESSMENT OF QUALITY OF LIFE IN SARCOPENIA

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Musculoskeletal disorders affect morbidity, quality of life and mortality, and represent an increasing economic and societal burden in the context of population aging and increased life expectancy. Improvement of quality of life should be one of the priorities of any interventions to prevent and treat musculoskeletal disorders in the ageing population. Two main approaches, namely generic and disease-specific instruments, can be applied to measure health-related quality of life. Among the generic tools available in scientific literature, the short form 36 questionnaire (SF-36) and the Euroqol five item questionnaire (EQ-5D) are two of the most popular questionnaires used to quantify the health related quality of life in people with musculoskeletal disorders. However, because generic tools may not always be able to detect subtle effects of a specific condition on quality of life, a specific tool is highly valuable. Specific tools improve the ability to clinically characterize quality of life in subjects with a specific musculoskeletal disorder, as well as the capacity to assess changes over time in the QoL of these subjects. Therefore, a sarcopenia-specific QoL questionnaire, called SarQoL (Sarcopenia Quality of Life), designed for community-dwelling elderly subjects aged 65 years and older, has been developed. The psychometric properties of this new tool have been assessed. The recent development of this specific tool should help to validate preventive and therapeutic interventions in the field of sarcopenia.

PL10
FRACTURE PREVENTION IN CANCER PATIENTS

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Owing to early detection and major advances in cancer treatment, a majority of patients with breast or prostate cancer are long-term survivors. As cancer is a common diagnosis, prevention of osteoporosis and fracture risk in cancer patients is an important component of care. The majority of bone loss occurs during cancer treatment, especially during chemotherapy, androgen deprivation therapy in prostate cancer, and treatment with gonadotropin-releasing hormone agonists or tamoxifen in premenopausal women and aromatase inhibitors in postmenopausal women with breast cancer. Cancer treatment-induced bone loss (CTIBL) adds to age-dependent bone loss, prevalent classical risk factors of bone fragility and potentially additional transient factors associated with cancer (nutritional issues, decrease of physical activity). Fracture risk is significantly higher in women treated with aromatase inhibitors and men receiving androgen deprivation therapy. While tamoxifen preserves bone mass in postmenopausal women, it is not associated with lower fracture risk. Prevention and management of bone loss and fracture risk is therefore needed in these patients, during the treatment period but also for long-term preservation of bone health. Bisphosphonates and denosumab prevent breast and prostate CTIBL and randomised controlled trials with denosumab have been designed to demonstrate a reduction of fracture risk in these contexts. In addition, recent data support additional survival benefit from adjuvant bisphosphonate treatment in postmenopausal women with breast cancer, which might be of potential interest beyond bone health indications in postmenopausal women at high risk of disease recurrence. It remains unclear whether similar benefit regarding breast cancer outcomes is obtained with adjuvant denosumab. Management of non-metastatic bone disease in cancer patients receiving endocrine treatment known to accelerate bone loss includes maintenance of optimal calcium intakes and vitamin D status, promotion of exercise, and bisphosphonate or denosumab use in case of prior fragility fracture, low BMD (T-score ≤ -2.0/-2.5SD according to guidelines) or additional clinical risk factors or FRAX (although it underestimates fracture risk in this population). Compliance, change of bone turnover after discontinuation, long-term safety, and regional approval of the various drugs also need to be taken into account when advising on fracture prevention in these patients.

PL11

FRACTURE PREVENTION IN DIABETIC PATIENTS

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Both Type 1 and Type 2 Diabetes are associated with an increased fracture risk. Both BMD T-socre and FRAX may underestimate fracture risk in Type 2 DM. This raises challenges in identifying the diabetic patient at risk for fracturing. Longer duration of diabetes may be detrimental to bone health and the optimal level of blood sugar control needed for fracture prevention in DM is not defined. Treatments that are presribed for advanced stages of the disease including insulin may be associated with increased risk of fractures. It is not known however whether insulin by itself is deleterious to the bones or whether insulin use is just a marker for the severity and /or duration of the disease. It is alos not known whether the increased fracture risk associated with insulin use is secondary to insulin induced hypoglycemia and increased falls. Management of bone loss in DM requires special attention. A careful therapeutic approach that balances antihyperglycemic benefits of conventional anti-diabetic medications with minimization of risk to bone health should be employed. Lifestyle interevention with physical exercise as well as falls prevention recommendation should be an integral part of the management of the diabetic patient who is at increased risk for fractures. Medications with a neutral or beneficial effect on bone health such as metformin or incretin based therapies should be preferably chosen. Medications such as TZDs that have demonstrated deleterious effect on bone metabolism should be avoided. Further studies on agents such as certain SGLT2 inhibitors are needed before conclusively recommeding them to the diabetic patient at increased risk for fractures. Presently there are no guidelines that help in deciding at what stage and with which antiosteoporosis medication should treatment be intiated for the diabetic patient with osteoporosis. A pragmatic approach might be to consider a T-score of </=-2.5 as a threshold for intiating treatment. FRAX based fracture risk estimation may have to be adjusted in the presence of DM. Evidence based on subgroup studies of osteoporosis patients with DM enrolled in osteoporosis fracture trials suport the use of both antiresorptive agents and anabolic agents, with BMD responses to these agents being the same in both diabetic and non-diabetic patients. No evidence however exists to show that currently available anti-osteoporosis agents have anti fracture efficacy in diabetic patients with non- osteoporotic range or normal BMD. The development of newer agents such as anti-sclerostin antibodies that improve osteoyte function and cortical microarchitecture may hold promise in this regard with their potential to improve bone strength in addition to their beneficial effects on bone density.

The author has no conflicts of interest to disclose.

PL12

WHEN TO SUSPECT A GENETIC DISORDER?

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Osteoporosis is a common health disorder affecting roughly half of older women and about a third of older men with the clinically relevant outcome of fragility fractures. Bone density, usually measured at the spine and hip, is strong predictor of future fracture risk. It is affected by a number of secondary factors such as early menopause, fat malabsorption, corticosteroid exposure, poor protein and calcium nutrition and deteriorates in both men and women with advancing age. However bone density also has strong genetic determinants with 60-75% of its variance attributable to inherited factors. In this context, the search for specific genetic contributors has been ongoing for the past 25 years. Initially candidate genes were interrogated and then, when these proved of limited value, genome wider association studies (GWAS) were carried out in progressively larger cohorts and group of cohorts. These GWAS identified SNPs associated modestly with bone density and also with fracture risk. These SNPs identify rather non-specifically, large sections of the genome and, at present, they explain only a small proportion of bone density variance in these large cohorts.

On the other hand, a number of very specific genetic variants have been shown to cause very specific bone disorders of low or high bone density. In each case, these rare variants have identified specific genes and pathways involved in bone homoeostasis. Some of these have led to new therapeutic developments, either already in clinical use or late stage development.So what might suggest a genetic disorder? Often the patient and their family will identify the concern that a particular condition "runs in their family". Other times, without such history, the patient may have some unusual features such as early presentation with bone problems, such as fractures at birth or early childhood, without any recognised secondary cause. They may be associated with unusual facies or abnormalities of limb, digit or tooth development.These features can inform a search in the various genetic databases for possible genetic causation that could be sought via targeted exome, gene groups or whole genome sequencing. Identifying such causation may inform treatment as well as risk for further pregnancies for the parents or affected individuals. All of these help deliver optimal patient care and are reasonable outcomes. As the genetic tools become cheaper and more widely available, these hopes will become realities for more and more individuals.

PL13

THE 2014-2016 ESCEO ALGORITHM FOR THE MANAGEMENT OF KNEE OSTEOARTHRITIS

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The European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) published a treatment algorithm for the management of knee osteoarthritis (OA) in 2014, which provides practical guidance for the prioritization of interventions. Basic principles consist of the need for a combined pharmacological and non-pharmacological treatment with a core set of initial measures, including information access/education, weight loss if overweight, and an appropriate exercise program. Four multimodal steps are then established. Step 1 consists of background therapy, either non-pharmacological (referral to a physical therapist for re-alignment treatment if needed and sequential introduction of further physical interventions initially and at any time thereafter) or pharmacological. The latter consists of chronic Symptomatic Slow-Acting Drugs for OA (e.g., prescription glucosamine sulfate and/or chondroitin sulfate) with paracetamol at-need; topical NSAIDs are added in the still symptomatic patient. Step 2 consists of the advanced pharmacological management in the persistent symptomatic patient and is centred on the use of oral COX-2 selective or non-selective NSAIDs, chosen based on concomitant risk factors, with intra-articular corticosteroids or hyaluronate for further symptom relief if insufficient. In Step 3, the last pharmacological attempts before surgery are represented by weak opioids and other central analgesics. Finally, Step 4 consists of end-stage disease management and surgery, with classical opioids as a difficult-to-manage alternative when surgery is contraindicated. Further analysis of real-world data for OA, published in 2016, provided additional evidence in support of pharmacological interventions, in terms of management of OA pain and function, avoidance of adverse events, disease-modifying effects and long-term outcomes, e.g., delay of total joint replacement surgery, and pharmacoeconomic factors such as reduction in healthcare resource utilization. Since 2014, these guidance documents have received international endorsement, with translation, adaptation to the local context, and publication in China, Russia, and South-East Asia.

PL14

NEW INSIGHTS ON THE SAFETY OF ANTI-OSTEOARTHRITIS MEDICATIONS

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Osteoarthritis (OA) is the most common form of arthritis worldwide, and is commonly treated with cyclooxygenase-2 (COX-2) inhibitors and opioid therapies. The safety of these medications was recently assessed in a systematic review and meta-analysis undertaken by the International Osteoporosis Foundation. A comprehensive literature search was undertaken in the databases MEDLINE, Cochrane Central Register of Controlled Trials (Ovid CENTRAL), and Scopus. Randomized, double-blind, placebo-controlled, parallel-group trials that assessed adverse events (AEs) with COX-2 inhibitors and opioid drugs in patients with OA were eligible for inclusion. Database searches identified 40 trials included in the COX-2 meta-analysis.The use of COX-2 inhibitors in OA was associated with a significant increased risk of drug-related AEs compared with placebo (relative risk [RR] = 1.26, 95% CI 1.09, 1.46; I^2= 24%). The risk of upper gastrointestinal complications was significantly increased with COX-2 inhibitors versus placebo (RR = 1.19, 95% CI 1.03, 1.38; I^2= 0%). The risk of hypertension increased by 45% overall (RR = 1.45, 95% CI 1.01, 2.10; I^2= 25%); this became non-significant when rofecoxib was removed from the analysis (RR = 1.21, 95% CI 0.80, 1.83; I^2= 20%). The overall risk of heart failure and edema was increased by nearly 70% with COX-2 inhibitors versus placebo (RR = 1.68, 95% CI 1.22, 2.31). Seventeenpapers were included in the opioid meta-analysis. More disorders of thelower gastrointestinal (GI) tract were reported with both immediate-release (IR) and extended-release (ER) formulations of opioids versus placebo: IR opioids (relative risk [RR] = 5.20, 95% confidence interval [CI] 3.42, 7.89); ER opioids (RR = 4.58, 95% CI 3.57, 5.88). The risk of upper GI AEs increased 4-fold with ER opioids compared with placebo (RR = 4.03, 95% CI 0.87, 18.62); an increased risk of dermatologic AES (rash and pruritis) (IR opioids: RR = 3.60, 95% CI 1.74, 7.43; ER opioids: RR = 7.87, 95% CI, 5.20, 11.89) and central nervous system disorders (IR opioids: RR = 2.76, 95% CI 1.90, 4.02; ER opioids: RR = 2.76, 95% CI, 2.19, 3.47) was found with all opioid formulation versus placebo.

PL15

NEW CLINICAL EVIDENCE SUPPORTING THE USE OF SYSADOAS AS A FIRST-LINE BACKGROUND TREATMENT IN KNEE OSTEOARTHRITIS

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Symptomatic slow-acting drugs for osteoarthritis (SYSADOAs) are an important class in the pharmacological treatment armamentarium for osteoarthritis, that are demonstrated to alleviate the symptoms of pain and functional impairment, with additional evidence of a disease-modifying effect in the long-term. There are many different agents in the class of SYSADOAs including Glucosamine, Chondroitin, Diacerein and Avocado-Soybean Unsaponifiables (ASU) which are supported by varying degrees of clinical efficacy data. The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) recommends the use of SYSADOAs as step 1 pharmacological background therapy, with or without Paracetamol as add-on rescue analgesia when needed. However, the level of recommendation for the use of SYSADOAs by other international and national guidelines is sometimes less favourable, likely due to the multiple products available in various countries that contain the active ingredients included in this class, but for which the pharmaceutical quantity and strength of the supporting evidence base is considerably reduced. Among the SYSADOAs products available, ESCEO recommends specifically the use of prescription, pharmaceutical-grade Glucosamine and Chondroitin products, for which the evidence base is unequivocal.

PL16

UPDATE OF THE 2014-2016 ESCEO ALGORITHM FOR THE MANAGEMENT OF KNEE OSTEOARTHRITIS

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Knee osteoarthritis (OA) affects around 4% of people worldwide and accounts for 17.1 million years of life lived with disability. It is expected to become the fourth leading cause of functional impairment by 2020, placing a huge burden on health services. Recommendations for the management of knee OA have been issued by several international and national bodies, including the European League Against Rheumatism (EULAR); the American Society for Rheumatology (ACR); and the Osteoarthritis Research Society (OARSI). These have recently been systematically evaluated by the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO), to construct a treatment algorithm that might enhance OA management throughout Europe and worldwide. The initiative advanced existing practice guidelines, which typically evaluate interventions individually, by prioritising these into a well- ordered series of practical steps which can be undertaken by physicians. The algorithm was constructed by an international taskforce experienced in the performance, analysis and interpretation of clinical trial evidence in OA. The core set of measures, which are applicable to all patients with knee OA include: (a) Access to information about the disease and education about the disorder; (b) Weight loss if adipose; and provision of (c) an exercise programme. The consequent treatment algorithm consists of four multimodal steps. Step 1 consists of background therapy, either non-pharmacological (referral to a physical therapist for realignment treatment if needed and sequential introduction of further physical interventions) or pharmacological. The latter consists of chronic symptomatic slow-acting drugs for OA (eg prescription of glucosamine sulphate with chondroitin sulphate) with paracetamol if required; topical NSAIDs are added in the still symptomatic patient. Step 2 consists of the advanced pharmacological management in the persistently symptomatic patient. It centres on the use of oral COX-2 selective or non-selective NSAIDs, chosen based o concomitant risk factors, with intra-articular glucocorticoids or hyaluronic acid derivatives for further symptom relief. Step 3 incorporates the remaining pre-surgical pharmacological measures including weak opioids and other central analgesics such as duloxetine; Step 4 progresses to surgical intervention, or classical opioids where surgery is contraindicated. This treatment algorithm represents a new framework for the development of future guidelines for OA management, which are more easily accessible to primary and secondary care physicians.

PL17

BENEFITS/RISK OF LONG-TERM TREATMENT OF OSTEOPOROSIS

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As osteoporosis is a chronic condition, the optimal duration of treatment is an important decision that depends on the repeated evaluation of individual fracture risk and goal of therapy. For bisphosphonates, there is evidence to support continuous use for 3-5 years. The extension phase of the HORIZON trial found that patients on zoledronic acid (Zol) 5 mg annually for up to 6 years had a 51% lower risk of new morphometric vertebral fractures versus those who discontinued after 3 years. However the rate of non-vertebral fractures remained constant past the first three years, whether or not Zol was discontinued. Moreover aBMD at hip plateaued at +4% above baseline and didn't further increase with continuous therapy. The FLEX study showed that alendronate (ALN) therapy progressively increased bone mineral density (BMD) for up to 5 years, but continuation to 10 years was associated with a plateauing of BMD at hip. Similar to Zol, ALN discontinuation increased (clinical) vertebral fracture risk by about 2 fold, but no differences in non-vertebral fractures were observed whether or not ALN was discontinued for 5 yrs. However in those subjects with hip T-scores of -2.5 or lower, discontinuing ALN was associated with a high fracture rate whereas continuing ALN reduced this risk. Meanwhile observational studies indicate that the risk of skeletal complications increases with duration of BPS use: for instance the rate of AFF increases from 1-2/100'000 to 1/1'000 after 10 yrs. These observations have led to the first recommendations from the American Society of Bone and Mineral Research regarding the duration of use of BPs depending on the individualized risk after 3-5 yrs of therapy: when no fractures have occurred, the hip BMD is above -2.5T-score and the fracture probability is below the intervention threshold (20% by FRAX in the US), treatment could be suspended.

In the extension phase of the FREEDOM trial, BMD of the lumbar spine and hip continued to improve with continuous denosumab therapy and fracture incidence remained low. Of note, a further drop in the incidence of non-vertebral fractures at year 4 was noted with denosumab, which was maintained for 7 and 10 yrs, whereas the risk of AFF+ONJ remained < 0.1%. In contrast, the discontinuation of denosumab was associated with a rapid increase in vertebral fracture risk to placebo levels, with a slight excess (+1%) in multiple vertebral fractures, particularly in women with previous vertebral fractures. Altogether these data suggest a new target for long-term therapy, namely the absence of fragility fractures and a hip T-score as close as possible to normal (>-1.5) in order to minimize fracture risk.

PL18
FRACTURE RISK OFF THERAPY

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Prospective and retrospective analyses report that the risk of new clinical fractures and vertebral fracture increases when treatment with bisphosphonates or denosumab is stopped. Given the safety and efficacy of these interventions, the concept of recommending drug holidays may be inappropriate for many patients. The IOF has recently reviewed the available literature to assess what evidence exists to inform clinical decision making with regard to drug holidays following treatment with bisphosphonates or denosumab, performing a systematic review of thirty eight articles that reported the findings of clinical trials, and 142 papers that reported the results from observational studies This study found that prospective and retrospective analyses report that the risk of new clinical fractures was 20-40% higher in subjects who stopped treatment and vertebral fracture risk was approximately doubled.The risk of discontinuing denosumab therapy without follow on treatment was highlighted as of particular concern, given recent studies suggesting that this is associated with rapid bone loss and vertebral fractures. Studies have not identified risk factors for fracture after stopping treatment other than those that provide an indication for treatment (e.g. prior fracture and low bone mineral density).. The incidence of atypical fractures and osteonecrosis of the jaw was very rare. The findings of this latest IOF analysis suggest that the commonly held view that patients on long-term anti-osteoporosis treatment should be offered a drug holiday can no longer be supported as a default position.

PL19

CLOSING THE GAP IN THE TREATMENT OF PATIENTS AT IMMINENT RISK OF FRACTURE: ROLE OF THE NEW ANABOLIC AGENTS

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Osteoporosis represents a significant and increasing healthcare burden but most patients at increased risk of fracture do not receive medication, resulting in a large treatment gap. For patients at increased (or imminent) risk of osteoporotic fracture, the use of medications able to preferentially stimulate bone formation, hence increasing bone mass and strength and reducing fracture risk, is the treatment of choice. New bone forming agents have recently been made available in the armamentarium against osteoporosis. Abaloparatide (ABL) is an novel 34-aminoacid peptide created to be a patent and selective activator of the parathyroid hormone receptor type 1 signalling pathway. Abaloparatide provides protection against vertebral and non-vertebral fractures across a wide variety of ages and baseline risks including those with and without prior fractures. ABL has a faster onset of action compared to Teriparatide. Eighteen months of treatment with daily subcutaneous Abaloparatide followed by twenty-four months of treatment with Alendronate improves bone mineral density and reduces fracture risk throughout the skeleton. Romosozumab (Romo) is a monoclonal antibody that binds to and inhibits Sclerostin, increases bone formation and decreases bone resorption. In post-menopausal women with osteoporosis who were at high risk for fracture, Romo treatment for 12 months followed by Alendronate resulted in a significant lower risk of vertebral, non-vertebral and hip fracture than Alendronate alone. Romo was also associated with a lower risk of vertebral fracture than placebo at 12 months and, after the transition to Denosumab at 24 months. After a careful assessment of their risk/benefit ratio, ABL and Romo might be considered as first-line treatments for patients at increased risk of fracture.

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Opening Ceremony Abstracts

OP1
INCLUSION OF DIVERSITY IN SCIENCE

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Objective: Current efforts to promote diversity in science are predominantly focused on the undeniable importance of gender equity, but conscious efforts are necessary to remove unintentional bias that excludes of other forms of diversity. This session discusses how multicultural, ability and demographic diversity in conference representation, research teams, committees and working parties will enhance the radicalness of scientific innovation and have a higher absorptive capacity to exploit external knowledge.

Method: Based on a narrative review of published and grey literature, this discussion focuses on the barriers to achieving, and strategies to enhance, diversity in science.

Results: Barriers to inclusiveness of diversity include unconscious bias in vocabulary, policies and processes. Based on concrete efforts to achieve gender equity in science, strategies to achieve multicultural, ability and demographic diversity may fall into one or more categories of: 1) remove obstacles, 2) increase capacity, 3) change culture, and/or 4) advocate. Efforts to remove obstacles include the development and/or amendment of Speaker Policies that demonstrate commitment to diversity in speaker composition and thus quality in conversation. Improving diversity at management level, and initiatives that provide specific funding opportunities could increase capacity. Strategies aimed at changing culture focus on 'fixing workplaces' rather than attempts to 'fix individuals', whilst advocacy must swell across the world, similar as the current movement observed in terms of gender equity.

Conclusion: Diversity is consistent with high-quality conference programs, research teams, committees and working parties. Providing equity of opportunities for all scientists is achievable by conscious consideration of unconscious bias.

Disclosures: SLB-O is supported a NHMRC, Australia, Career Development Fellowship and received speaker fees from Amgen Australia and Pfizer Australia.

OP2

OSTEOPOROSIS: GLOBAL CHALLENGES, LOCAL IMPACTS

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Aim: The global and local challenges of osteoporosis are numerous. This paper will outline the key challenges and introduce some new concepts to dispel the myth that osteoporotic fractures only follow minimal trauma. Local solutions for preventing the next fracture will be described.

Methods: An overview of the epidemiological literature for fracture and osteoporosis prevalence, including analyses from the Global Burden of Diseases (GBD) and uptake of re-fracture prevention programs described.

Results: A key challenge is that osteoporosis (OP) and related fractures are yet to be identified as a disease in their own right. This limits data collection in any national or global burden of diseases study – if a health condition isn't defined by an ICD code it doesn't exist. "No data- no disease". Osteoporosis has been defined by low bone mineral density, but also by the presence of a low or minimal trauma fracture in people over 50 years of age. While low BMD is a very strong predictor for having a fracture there are numerous other factors that contribute to fracture risk and many fractures will occur in the presence of normal or only mildly reduced BMD. Osteoporosis and risk of fracture increases significantly with age and as such often attracts low interest as an inevitable association with ageing for which nothing can be done. With the rise in the ageing population, the prevalence of people living in the community with low BMD, and thus at risk of having a fracture, is also rising. This is particularly evident in the Asian-Pacific region. Osteoporosis is a silent disease until a person sustains a fracture. That first fracture is a significant risk factor for a subsequent fracture. Medications are available that can significantly reduce the risk of subsequent fractures yet these are not being introduced to people who may benefit. For the past two decades we have been discussing this evidence-care-gap. Local, national and international audits lamenting the lack of identification, assessment and treatment of OP fracture to prevent the next fracture abound. Multiple barriers at all levels have been identified from the individual, to the full range of health professionals involved in the OP fracture care and to the health system and society as a whole. Qualitative research reveals that people with OP do not associate fractures with low bone density and do not perceive themselves to be at risk. Lifestyle interventions, while important, are insufficient alone for reducing the increased risk of secondary fractures. Medications, while effective, are not without risk of adverse events.

It is estimated that there are more than 200 million women globally with low BMD and that 1 in 2 to 3 women and 1 in 5 men over the age of 50 years will experience an osteoporotic fracture in their life time. Currently in Asia over 1 million hip fractures occur each year with an estimated 2.5 million in 30 years predominantly attributable to ageing and growing populations in China and India.By 2050 it is estimated that 50% of the world's hip fractures would come from Asia. In the Global Burden of Diseases (GBD) 2010 study low bone density (LBMD) was included as a risk factor in the comparative risk analyses for the first time. Low BMD accounted for 0.21% of the world's total deaths and disability (a doubling in 20 years). Recent analyses have highlighted that low BMD is associated with almost 15% of total DALYs related to falls; is associated with 35% of the increased mortality related to falls; at age 50 years low BMD is associated with ~7.5% of deaths related to road traffic accidents, increasing to 40% in the 80+ age group.

Discussion: Solutions include for this OP and fracture burden include:- creating an ICD code for osteoporosis and osteoporotic fractures; improving imaging and biomarkers to better define OP fracture risk; updating and improving validation of fracture risk algorithms; recognition that all fractures over the age of 50 years should be assessed for OP treatment; more widespread adoption of some of the numerous international campaigns such as Capture the Fracture, 2million2many National Bone Health Alliance, Break the Break, Break Free from Osteoporosis to raise awareness; more widespread implementation of Fracture Liaison Services (FLS) and Osteoporosis Re-fracture Prevention Programs (ORPP) at the local level to identify, investigate and initiate the right treatment for the right person and the right time ie BEFORE they sustain another fracture

Conclusion: Fractures in the elderly are associated with enormous burden to the individual and society globally; the numbers will rise due to the ageing population; a previously unrecognised proportion of mortality associated with road traffic accidents is related to low bone density in the older person; one fracture is a clear signal of increased risk for another fracture; interventions are available to reduce the risk of a re-fracture; barriers are multi-factorial but solutions including FLS, ORP programs which require more widespread coverage to make a difference.

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Meet-the-Expert Sessions Abstracts

MTE1

RECENT FRACTURE: WHEN AND HOW TO TREAT OSTEOPOROSIS

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The dilemma in clinical practice is when to initiate treatment following an osteoporosis related fracture. There are concerns whether early treatment with antiresorptive agents in particular bisphosphonates may impair fracture healing. This is one of the main reasons why patients with fragility fractures do not receive appropriate pharmacological treatments following their fractures. Low treatment rate, poor compliance and adherence lead on to increase incidence of subsequent fractures.

Bisphosphonates are commonly used to treat osteoporosis in clinical practice. The potent antiresorptive agents suppress bone turnover therefore improve bone density and bone quality. However, the concern of using such potent antiresorptive in clinical practice is over suppression of bone turnover leading on to hyper-mineralization. In animal models, both oral bisphosphonates and intravenous zoledronic acids are shown not to delay endochondral fracture healing or initiation of callus formation, but may delay callus remodeling. However, the callus volume, bone mineral content and callus strength increase with bisphosphonates treatment. Asingle bolus dose of intravenous zoledronic acid administered 2 weeks after fracture provides optimal outcome. Similar findings are seen in Denosumab treated animal models. Implant stability improved with improved periprosthetic bone volume, implant fixation strength and bone implant contact in bisphosphonates treated animal studies.

Parathyroid hormone, the anabolic agent, administered within one week of fractures in animal studies result in faster fracture healing with increase callus volume and density, callus mineralization and improved biomechanical properties. Similar results are seen in human cases treated with improved fractures healing and reduction of implant loosening in spinal fusion as well as functional outcome.

MTE2

CHRONIC RENAL FAILURE: HOW TO ASSESS AND MANAGE BONE FRAGILITY?

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Chronic kidney disease (CKD) is one of the commonest medical problems associated with ageing. The majority have stage 1, 2 or 3 CKD with estimated glomerular filtration rates (eGFR) of >90 mLs/min, 60-89 mLs/min, and 30-59 mLs/min, respectively. However, many have stage 4 CKD (15-29 mLs/min) and stage 5 CKD (<15 mLs/min) or are on dialysis. CKD is associated with excess morbidity, mortality and increased health care costs. CKD-Metabolic Bone Disorder (MBD) occurs in stage 4 and 5 CKD, and is characterized by bone (renal osteodystrophy), soft tissue (calcifications), and mineral (phosphate, calcium, fibroblast growth factor-23, calcitriol, sclerostin, Dikkopf-1) abnormalities. The pathological end-points of CKD-MBD are increased cardiovascular risk, mortality and fractures.

Hip fracture incidence increases with age in the general population, but is increased at every age for patients with Stage 3b, 4 and 5 CKD. Mortality after any fracture is also increased in patients with CKD, being highest in patients with Stage 5 CKD. Physicians are unsure on whether conventional anti-osteoporosis drugs are either appropriate or effective in patients with CKD. There has been reluctance to measure bone mineral density (BMD) using dual energy absorptiometry (DXA) as there is concern it may not be as predictive of fractures in patients with CKD as in the general population. There is also a reluctance to use anti-resorptive drugs, as patients may have low turnover renal osteodystrophy, so they could theoretically worsen skeletal fragility. The TMV classification system exists for CKD and is based on bone Turnover, Mineralization and Volume; each can be low/absent, normal or high. The combination of each component can be used to classify the disease – for example, in adynamic bone disease, turnover is low, mineralization is normal, and volume is low, while in hyperparathyroidism, turnover is high, mineralization is normal, and volume is low. By contrast, in osteomalacia, turnover is low, mineralization is low, and volume is normal.

New 2017 KDIGO guidelines state that the optimal PTH level is not known. Instead, they emphasise a renewed focus on assessment of both fracture risk and bone turnover in the individual patient with CKD. In patients with CKD G3a–G5D with evidence of CKD-MBD and/or risk factors for osteoporosis, BMD testing by DXA is suggested to assess fracture risk, if these results will impact treatment decisions. In patients with high turnover bone disease, an anti-resorptive drug +/- vitamin D should be used, while in patients with low turnover bone disease, an anabolic drug +/- vitamin D should be used instead. The use of calcitriol or vitamin D analogs is reserved for patients with CKD stages 4–5 with severe and progressive hyperparathyroidism. Both risedronate and denosumab have been shown to reduce vertebral fractures in patients with mild CKD (stage 2-4 CKD for risedronate, and stage 2-3 CKD for denosumab). However, it should be noted that the use of denosumab can be associated with hypocalcaemia in patients with stage 4 CKD and it is probably best avoided in stage 5D CKD.

Alternative 2017 European guidelines from European Calcified Tissue Society (ECTS) and European Renal Association of Nephrology Dialysis and Transplantation (ERANDT) recommend the combination of PTH levels with the bone formation marker, bone specific alkaline phosphatase (BSAP) which is not affected by renal function, remain the best non-invasive way to divide patients into high or low bone turnover. However, in cases with either low PTH or low or intermediate levels of BSAP, a bone biopsy may be required to exclude causes of low turnover renal osteodystropy (adynamic bone disease and osteomalacia).

In conclusion, there is evidence that anti-resorptive drugs reduce fractures in patients with CKD stage 2-4 and it is critical that an individual and tailored approach to managing bone disease is taken in patients with CKD.

MTE3
VITAMIN D: WHICH & HOW MUCH?

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Vitamin D is essential for bone health. Deficiency of vitamin D can lead to clinical conditions like osteomalacia and rickets, especially when accompanied by poor calcium intake. More subtle forms of deficiency can have a "long latency' effect on bone health and contribute to osteoporosis and increased risk of fractures. Although the criteria for defining vitamin D deficiency continue to be widely debated and controversial, studies have revealed a high prevalence of vitamin D deficiency globally. Among the most severely affected regions are South Asia and the Middle East.

The main source of vitamin D is sunlight. Dietary sources play a limited role except in populations exposed to or having access to fortified food products. Sunny countries suffer from vitamin D deficiency because of avoidance of sunlight exposure, clothing, skin pigmentation, use of sun block creams and atmospheric pollution. Although typically RDIs are in the 600-800 IU range, intakes of up to 2000 IU/day have been recommended for achieving optimum levels and preserving bone health.

Numerous dose schedules have been used to correct vitamin D deficiency, depending on the clinical symptoms, baseline 25(OH)D levels, and the presence of secondary hyperparathyroidism. A broad guidance proposed for populations where deficiency is common is as follows:

1. 60,000IU of Vitamin D3, once a week for 8 weeks, followed by a maintenance dose of 1500-2000IU daily or 50,000-60,000IU once a month. This regimen is for patients with metabolic bone disease like rickets/ osteomalacia and can be also be used in those mildly symptomatic patients who have very low levels (25(OH)D <10 ng/mL).

2. 60,000 IU to 120,000 IU per month. This option is for apparently healthy people who have vitamin D deficiency, and can be given as monthly doses of 60,000 IU in summer and 120,000 IU in winter.

3. Daily supplementation of 1000-2000 IU. This option is typically for those who need simultaneous calcium and vitamin D (elderly, low calcium intake) and have mild vitamin D deficiency.

4. Parenteral mega doses of 300,000 to 600,000 IU. Intramuscular vitamin D can be used in special conditions, such as those who have absorption problems or where compliance is a challenge. Risk of vitamin toxicity due to overuse remains a concern.

Vitamin D supplementation: D2 vs D3 debate

Vitamin D exists in two different forms: Ergocalciferol (vitamin D_2), which occurs in plants; and cholecalciferol (vitamin D_3), which occurs in animals. It has long been debated as to which of the two is more suitable for use as a supplement. Recent studies suggest that D3 is superior to D2 in raising 25(OH)D levels, and in particular 25 (OH)D3 levels. In general the pendulum is shifting toward the use of vitamin D3 over vitamin D2.

MTE4

CONSEQUENCES OF A LOW CALCIUM INTAKE

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With ageing there is a decrease in calcium intakes, particularly by a reduction in dairy products consumption, in intestinal absorption of calcium efficacy, in absorptive capacity of the intestinal epithelium to adapt to a low calcium intake, and in the exposure to sunlight and the capacity of the skin to produce vitamin D. A state of chronic secondary hyperparathyroidism results from calcium and vitamin D deficiencies and increases bone turnover with a negative bone balance, hence osteoporosis. Low calcium intakes and vitamin D levels are associated with higher mortality. Calcium and vitamin D repletion decreases secondary hyperparathyroidism and reduces the risk of proximal femur fracture, particularly in the elderly living in nursing homes, in whom calcium and vitamin D insufficiency may be more prevalent.From reviewing the numerous trials and meta-analysis with respect to the evidence supporting calcium repletion, with or without vitamin D, in the management of patients with osteoporosis, the following conclusions can be drawn.1) calcium and vitamin D repletion are associated with some reduction in fracture risk; 2) supplementation with calcium alone for fracture reduction is not supported by the literature; 3) side effects of calcium supplementation include renal stones and gastrointestinal symptoms; 4) vitamin D supplementation, rather than calcium supplementation, reduces falls risk; and 5) assertions of increased cardiovascular risk consequent on calcium repletion are not convincingly supported by current evidence. Though a meta-analysis has concluded that calcium supplements without co-administered vitamin D were associated with an increased risk of myocardial infarction, large long-term observational studies have not confirmed this hypothesis.All trials on anti-osteoporosis agents have been conducted in vitamin D and calcium replete individuals. Patients with calcium and vitamin D insufficiency have increased risk of various negative outcomes, justifying calcium and vitamin D repletion.

MTE5
FALLS PREVENTION: IS IT POSSIBLE?

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Objectives: People with low bone mineral density (BMD) often have thoracic kyphotic posture, decreased trunk muscle strength, and poor gait and balance performance, and they are thus at an increased risk of falls. Trunk muscle stabilization exercise can improve their kyphotic posture, trunk muscle strength, and quality of life. However, compensatory strategies during training can lead to low back pain and compression fractures. Electromyography biofeedback training can enhance the effects of training. Therefore, this study investigated whether trunk muscle biofeedback training can improve posture and balance control in people with low BMD.

Material and Methods: We recruited 18 women with low BMD; they received trunk muscle biofeedback training two times a week for 6 weeks. Pretraining and posttraining clinical and biomechanical assessments, including spinal curvature, spinal mobility, muscle strength, static balance performance (quiet standing), and dynamic balance performance (functional forward reach), were performed.

Results: The results demonstrated that the 6-week training improved the spinal curvature and mobility in trunk extension. The muscle strength of the rectus abdominis and back extensors also increased. The 95% confidence ellipse area decreased after training during quiet standing with eyes closed. The functional forward reach peak velocity and trunk muscle activity pattern also improved.

Conclusions: In conclusion, 6-week trunk muscle biofeedback training can improve spinal curvature, mobility, trunk muscle strength, and balance performance in women with low BMD. This training precisely targets the training muscles and can increase balance control in people with low BMD.

Acknoledgements: This study was supported by the National Health Research Institutes (NHRI-EX105-10218EC) and the Ministry of Science and Technology awarded to Dr. Hsu. The authors would be like to thank the members of the Movement Science Lab, as well as study participants.

Disclosure: I declare that the authors have no competing interests as defined by Nature Research, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

MTE6

BONE LOSS IN EARLY MENOPAUSE: TO TREAT OR NOT?

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Early menopause (EM) is defined as menopause occurring prior to age 45 years and Premature Ovarian Insufficiency (POI) is defined as loss of ovarian function prior to age 40 years[1]. Spontaneous POI/EM affects up to 10% of women. The consequences of iatrogenic POI is of increasing importance with higher rates of cancer survivorship. POI/EM is associated with increased bone loss and decreased peak bone mass, with a reported osteoporosis prevalence of 8-14%[1]. Osteoporosis was reported by women with POI/EM as their most feared long term consequence[2]. Age of onset, diagnostic delay, non-compliance with hormone replacement therapy (HRT) and the specific cause of POI (eg. Turner syndrome or chemotherapy) contribute to risk in addition to conventional osteoporosis risk factors. Although published guidelines recommend treatment with HRT, unless contraindicated, until the usual age of natural menopause[1,3], uncertainties exist regarding screening, diagnosis and optimal management. Fracture prediction tools, such as FRAX®, are not validated for women <40 years. The presence of fragility fractures and/or a T-score below −2.5 at spine or hip is proposed as diagnostic of osteoporosis unless the individual is still growing and peak bone mass not yet achieved[1,4]. Limited bone mineral density data from randomised controlled trials indicate that oestradiol HRT preparations may be preferable to ethinyl-oestradiol oral contraceptive pills but fracture outcomes are lacking. There is limited data regarding bisphosphonates, denosumab and teriparatide in this population and the use of these agents may be problematic where future pregnancy may be desired. These challenges will be discussed in a case-based format during this session.

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MTE7

GENETIC MARKERS OF BONE FRAGILITY: WHAT HAVE WE LEARNED

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The study of osteoporosis genetics has provided a goldmine of information about this commonest of all metabolic bone diseases. GWAS have already provided enormous insight into the disease; and alternative approaches and technologies will identify many of the remaining heritable factors determining BMD. Further dialogue is needed between the genetics and functional biology communities to ensure translation of these many genetic findings into treatment outcomes for patients.

In this Meet-The-Professor session, I will cover the following learning objectives:

- To understand common genetic terms and how they apply to gene mapping in osteoporosis
  - What is heritability? What is the heritability of BMD? How is this assessed?
  - What is linkage?
  - What is association? What is the difference between candidate gene and whole genome association studies?
  - What the principles underlying GWAS?
  - What have GWAS actually found?
    - The "big hits"
    - Pathways in bone
- What is the future for gene mapping in osteoporosis?
  - What is 'missing heritability'?
  - Massive parallel sequencing
    - What are the principles of whole exome vs. whole genome sequencing?
    - Rare and low-frequency variants
      - Use in rare disease mapping
      - Use in common disease mapping
- What are the implications for patients and clinicians?
  - Predictive algorithms for osteoporosis and/or fracture
  - Therapeutic implications
    - pharmacogenomics
  - Ethical and legal considerations

MTE8

CAN WE TRUST BONE TURNOVER MARKERS TO IMPROVE THE ASSESSMENT OF FRACTURE RISK?

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The incidence of metabolic bone disease is highest amongst the elderly and so with the ageing of the population, clinical interest in diagnosis and prognosis of osteoporosis and estimation of fracture risk has increased. Biochemical markers of bone turnover (BTM) have the theoretical potential for assessing two major clinical questions. Can baseline levels of BTM predict the rate of bone loss or future fracture risk? Can BTMs be used to monitor the response to treatments for osteoporosis? While assays for numerous BTMs are readily available on automated clinical analysers, there is no strong consensus on their clinical utility. There are significant associations between bone turnover markers and incident fracture risk, though these are modest.

Studies on the use of BTMs for the monitoring of treatment have shown, in general, that the larger the decrease in BTM, the larger the reduction in fracture risk. The 'treatment effect explained' was calculated for two of these trials indicating that the change in a number of BTMs accounted for some 28% to 77% of the reduction in fracture risk with anti-resorptive therapies. The clinical value of BTMs is limited by inadequate appreciation of the sources of variability, by limited data for comparison of treatments using the same bone marker and inadequate quality control. Considerable progress is being made towards defining sources of variability for two BTMs, CTX and P1NP through comparability studies of the two major automated clinical assays across European laboratories as well as effects of whole-body energy status on CTX levels. It is expected that this new knowledge will assist the clinical utility of these BTMs.

MTE9
MEET-THE-EXPERT SESSION: OSTEOSARCOPENIA

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In older persons, the combination of osteopenia/osteoporosis and sarcopenia - known as osteosarcopenia - has been proposed as a subset of frailer individuals at higher risk of institutionalization, falls, and fractures. Osteosarcopenic patients have very particular clinical, biochemical, diagnostic, and functional characteristics that could be identified in clinical practice. In addition, new therapies targeting both muscle and bone are being developed. In this session, a clinical definition of osteosarcopenia aiming to describe the clinical, functional, and biochemical features that are unique to these patients will be discussed. The use of imaging combined with functional assessments for the diagnosis of osteosarcopenia will be also presented. In addition, we will analyze preventive measures and therapeutic interventions that can benefit both muscle and bone simultaneously. We intend to go over the translational aspects of sarcopenia and osteoporosis research, and highlight expected outcomes from different interventions for both conditions.

MTE10

GLUCOCORTICOID INDUCED OSTEOPOROSIS

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This session will focus on two key questions of clinical relevance; (1) what do we know about fracture risk during and after steroid therapy? and (2) how can we reduce risk?

It is well recognised that steroid use is associated with an excess fracture risk. In this workshop I will present recent data from a study of the clinical practice research datalink (CPRD) an electronic medical records dataset from the United Kingdom of over 10million patients. Patients from the CPRD were identified as suitable for inclusion in the study if they were adults, had a diagnosis of rheumatoid arthritis and had at least one year "up to standard" follow up. Patients were classified as exposed or unexposed to GCs upon entry and exposed patients were matched to up to two unexposed patients. The study sample comprised 16,507 patients of which 8,357 were exposed to oral GCs. Risk of fracture increased with current daily dose; in addition the risk of fracture increased with cumulative dose, and with duration of use: HR (95%CI) 1.09 (1.13, 1.05) to 1.25 (1.16, 1.35) to 1.42 (1.30, 1.55) for 5mg/day for 1, 3 and 6 months respectively. Dosing route to a given cumulative dose was also important. After discontinuation risk of fracture returned to baseline between 6 months and 1 year.

The second part of this workshop will focus on the evidence base for prevention of GIOP, and how these data are incorporated into current management algorithms.

MTE11

ASSESSMENT OF PHYSICAL STRENGTH AND PERFORMANCE

F. Buckinx[1,2]

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Several tools have been recommended to assess muscle strength and physical performance in clinical trials. Whilst these tools have proven to be accurate and reliable in investigational settings, many are not easily applied to daily practice.

Handgrip strength appears to be the most widely used method for the measurement of muscle strength. The measurement is easy to perform, inexpensive and does not require a specialist trained staff. Lower limb muscle strength, most frequently of the quadriceps, can also be measured. Commercial dynamometers can enable isometric and/or isokinetic measurements of strength. Even if these measurements are feasible in frail people, they are often limited in clinical practice by their relative expense, the need to purchase dedicated equipment, the lack of trained staff and limited data in older populations. However, the repeated chair stand test, has been shown to be able to provide a reasonably reliable and valid indication of lower body strength.

The most widely used tool in clinical practice for the assessment of physical performance is the gait speed measurement. The test is highly acceptable for participants and health professionals in clinical settings. No special equipment is required as it only needs a flat floor devoid of obstacles. Gait speed can be performed alone or as part of a test battery, the most popular of which is the Short Physical Performance Battery (SPPB). Other standalone tests can be performed to assess physical performance: Timed Up and go test, 6 min walk distance, 400 m walk, stair climb power test.

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IOF Regional 7th Asia-Pacific Osteoporosis Conference
Sydney, Australia – 2018

IOF-APOA Joint Session Abstracts

IOF-APOA1

OSTEOPOROSIS IN THE ASIA-PACIFIC

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Hard-won gains in health and well-being throughout Asia, which have increased longevity, could be undermined by a rise in musculoskeletal disoders and an epidemic of fragility fractures. Musculoskeletal disorders have increased by 45% from 1990 to 2010 and more than all other chronic non-communicable diseases, being the second greatest cause of disability worldwide. The four most important trends contributing to this burden are the ageing of the population, urbanization, widespread vitamin D deficiency and low dietary calcium intakes.

Demographic changes alone can be expected to increase hip fracture numbers dramatically. In Asia, a 7.6-fold increase in elderly people is predicted between the years 2000 and 2050, with 60% and 59% of men and women, respectively, aged 80 years and older worldwide being from Asia in 2050. Despite hip fracture incidence attaining a plateau in Hong Kong, Japan, Chinese Taipei, and Australia, this trend will be offset by population ageing. Largely as a result of this population ageing, it has been projected that over half of all hip fractures in the world will occur in Asia by 2050, with the majority occurring in China.

Urbanisation is rapidly increasing from 50% in China to 66% in Japan and the Philippines. Urbanisation leads to a more sedentary lifestyle, lower BMD and a greater risk of vitamin D deficiency due to both sun avoidance behaviour and an increase in pollution diminishing available UVB radiation. Widespread lactase deficiency in Asia also limits access to dairy foods rich in calcium and other calcium rich foods are low in the Asian diet as demonstrated by the recent IOF Global Calcium Map. These factors contributed to 50 million people from India having either osteoporosis or osteopenia in 2013.Osteoporosis remains a neglected chronic disease, despite its serious human, social and economic burden. Only a minority of countries have osteoporosis as a national health priority. Osteoporosis remains greatly under-diagnosed and under-treated in the region, even in the case of high-risk patients who have already fractured. With the exception of Singapore and Chinese Tapei, Fracture Liaison Services (FLS), coordinated, post-fracture models of care for secondary fracture prevention, are uncommon in the Asia-Pacific. Less than 10-25% of hospitals in each country have implemented FLS, except Singapore and Chinese Tapei. FRAX algorithms to assess individual 10-year risk of fracture are now available for the majority of countries in the Asia-Pacific. However, access to dual-energy X-ray absorptiometry (DXA) is limited in many countries or unavailable in rural areas. Reimbursement of medication is not available in all countries, and even when available may be only partial, limited to private health care, or subject to various restrictions including age, BMD T-score, or prior fracture.

In conclusion, the major public health problem of fractures due to osteoporosis needs to be urgently addressed in the Asia-Pacific. Fracture liaison services in clinics and hospitals should be established to systematically identify and treat fracture patients and prevent secondary fractures. Health authorities should improve reimbursement levels and reduce restrictive criteria which may prevent access to approved treatment. DXA availability and accessibility should be raised to adequate levels to meet both existing and projected needs, and disparities in rural versus urban areas must be addressed. Low vitamin D and calcium intakes need to be addressed as a public health intervention, including consideration of food fortification with vitamin D and establishment of nutritional guidelines to address low calcium intakes.

IOF-APOA2

ORTHOPEDIC SURGERY IN ASIA PACIFIC

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As the Asian population ages the incidence of osteoporosis and its concomitant complications has risen. The enormity of the problem varies throughout Asia as it is home to a spectrum of countries that have older populations such as Japan to young countries such as the Philippines. The interest to provide a holistic response the burden of disease varies according to political and economic priorities.Prioritisation of resources in each Asian country will of course depend on what its citizens demand. At this moment it is clear that the countries with the oldest voting populations have allocated the largest resources to identify populations at risk and provide appropriate solutions.Rather than approach the problem from different directions such as medical, surgical and socio-economic viewpoints a more coordinated effort would be likely to be more lasting and satisfying.

IOF-APOA3
THE MISSING LINK

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Osteoporosis awareness among medical practitioners and publics in Asia Pacific countries has increased in the recent years. This increased awareness is mainly due to the efforts of various professional organizations and health care providers in this region in which scientific meetings, bone health programs, clinical practice guidelines, governmental policy change and publics campaigns on bone health are being organized regularly in various countries. The awareness on osteoporosis forms the basis and the first crucial step in initiating the cascade of risk assessment, early and appropriate diagnosis, treatment intervention, primary and secondary fracture prevention as well as post fracture care.

Advances in surgical treatment of osteoporosis fractures has also been seen in implants design, surgical approaches and fracture fixation techniques. Complicated osteoporosis fractures can be fixed effectively to allow early mobilization and ambulation to prevent complications.

Post fracture care is crucial to prevent secondary fractures which include appropriate pharmacological treatment after fracture fixations. However, this becomes the most challenging point in which many patients who have their fractures fixed are not assessed for future fracture risk, they are not treated medically with appropriate pharmacological agents, worse still patients disappear from further follow up after fracture fixations. This increases the risks of subsequent fractures which carry much higher morbidity and mortality. This "missing link" between the physicians or osteoporosis experts and the orthopedic surgeons need to be addressed in order to correct the gap through more pro-active attitude to initiate the above measures for every patient presenting with fragility fractures. The collaboration between International Osteoporosis Foundation (IOF) and Asia Pacific Orthopedics Association (APOA) is meant to "link" physicians and surgeons through the IOF-APOA Document, various programs as well as to exchange knowledge and experience between members of both organizations. This will change the attitude and practice of both physicians and surgeons towards a much better patient care.

IOF-APOA4

LAUNCH OF THE IOF-APOA COLLABORATION FOR A PROMISING FUTURE

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The case for Fracture Liaison Service (FLS) for the prevention of secondary fractures is clear. With an ageing population, the burden of osteoporosis is set to increase. Despite evidence for the clinical effectiveness of secondary fracture prevention, translation in the real world setting remains disappointing: worldwide, eighty per cent of fragility fracture patients are neither assessed nor treated for osteoporosis or falls risk to reduce future fracture incidence. Where implemented at all, a wide variety of service models are used to deliver effective secondary fracture prevention. To support and promote the use of effective models of care across the globe, the International Osteoporosis Foundation (IOF) launched the Capture the Fracture® (CTF) programme in 2013. This expert-led and evidence based programme aims to reduce secondary fractures by facilitating the implementation of FLS on a global level. A primary resource developed by CTF is the Best Practice Framework (BPF) which sets standards for FLS, serves as a benchmark for existing FLS and serves as a guidance tool for developing FLS. In an effort to engage the global medical community, CTF offers a Best Practice Recognition programme where FLS can submit their service to IOF for evaluation against the BPF for a gold, silver or bronze star in recognition of achievements. The FLS is then included in the showcase of best practice and plotted on the CTF Map of Best Practice that displays participating FLS and their respective achievement level. To influence change, the map can be used as a visual representation of FLS available worldwide, their achievements, as well as the areas for opportunity and development in secondary fracture prevention. The integration of these efforts with those of other AP agencies in the region will facilitate IOF in its global mission to reduce the fracture burden worldwide.

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IOF-OA-ANZBMS Joint Session Abstracts

IOF-OA-ANZBMS1
EXERCISE AND OSTEOPOROSIS

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Exercise has traditionally been considered, at best, an ancillary strategy for the management of osteoporosis, largely due to a preconception that it is a less effective therapy than medications. Furthermore, the paradox that bone requires the application of large magnitude strains to initiate positive adaptive changes, but that osteoporotic bone is at high risk of fracture under high load conditions, has been a deterrent to empirical testing in this demographic. Recently however, the landscape has changed. Novel RCT evidence has shown that not only can brief, high load exercise notably improve bone mass in postmenopausal women with osteoporosis and osteopenia, it can be achieved without injury under supervised conditions. Bearing in mind the simultaneous benefit for sarcopenia and falls, neither of which are enhanced by bone medications, exercise can in fact be described as providing a more 'broad spectrum' management strategy for osteoporosis than pharmaceuticals. Moreover, exercise has few deleterious side effects; something which cannot always be said for medications. The requirement for supervision is often argued to be a fatal hindrance to widespread rollout of exercise therapy for osteoporosis; however, findings from translational research in the clinical setting reveals this is not the case. Coupled with the arrival of exercise physiologists on the Allied Health scene, bone-targeted exercise can now be considered a safe, effective and feasible intervention for many patients with osteoporosis. Growing evidence thus suggests that exercise should be moved from an ancillary strategy in the management of osteoporosis, to a front-line therapy central to patient care.

IOF-OA-ANZBMS2

MONETARY COST OF OSTEOPOROSIS

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Fragility fractures incur long-term consequences both in terms of costs and morbidity. However, the costs related to fracture is at its peak the period immediately following a fracture. The fracture costs in the first year following a fracture differ between fracture types, and to some extent reflect the severity of fracture. Hip fractures are the most severe fracture type, and almost always lead to hospitalization.

There have been several national and international estimates of the monetary cost of osteoporosis. The most recent is a report of the International Osteoporosis Foundationwhichprovides an overview and comparison of the burden and management of fragility fractures in six European countries (France, Germany, Italy, Spain, Sweden, and the UK), referred to as the EU6.In 2017, it was estimated that there were 20 million individuals with osteoporosis in the EU6 using the diagnostic criterion of the WHO. Of those, 15.8 million were women and 4.2 million were men. Country-specific prevalence estimates for women aged 50 years and older ranged from 21.8% to 23.1% (EU6 mean 22.5%) and for men ranged from 6.7% to 7.0% (EU6 mean 6.8%). The number of new fragility fractures in 2017 in the EU6 was estimated at 2.7 million, comprising approximately 526,000 hip fractures, 415,000 clinical vertebral fractures and 1,734,000 other fractures (i.e. forearm, pelvis, rib, humerus, tibia, fibula, clavicle, scapula, sternum, and other femoral fractures).The unit costs of fracture varied by site and country. The cost of hip fracture in the first year ranged from €10,000 (Spain) to €21,000 (Germany, Italy and UK) in part related to the length of hospital stay. The cost of clinical vertebral fracture and forearm fracture was more heterogeneous with a greater than 7-fold and 4-fold difference, respectively, between countries (Table).

Table. Unit cost (€) of fractures by country

	France	Germany	Italy	Spain	Sweden	UK
Hip	12,856	20,884	21,307	9,724	16,409	20,650
Vertebral	3,205	11,805	4,713	1,928	14,474	4,028
Wrist	1,468	1,275	1,301	533	2,477	2,568

The total monetary cost for the EU6 was €37.5 billion in 2017. Hip fracture represented 56.4% of the total fracture related costs whilst vertebral fractures and other osteoporotic fractures accounted for 8.2% and 35.4%, respectively. Whereas hip fractures accounted for 20% of all fragility fractures, they accounted for 56.4 % of costs.

By 2030, the total number of fractures in the EU6 was estimated at 3.3 million, an increase of 23.3%. The largest percentage increase was projected for Spain (28.8%) and the lowest in Germany (18.5%). The fracture related costs in EU6 are projected to increase from €37.5 billion in the year 2017 to €47.4 billion in 2030, an increase of 27% based on changes in population demography alone.

IOF-OA-ANZBMS3

MORBIDITY AND MORTALITY OF OSTEOPOROSIS

J. Center[1]

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Osteoporosis and its major outcome of osteoporotic fracture are associated with significant morbidity and premature mortality. This talk will focus particularly on non-hip non-vertebral fractures which encompass over 50% of all low trauma fractures. Recent research suggests that these fractures are not as benign as commonly believed.

All fracture types are associated with a 2-4-fold increased risk of subsequent fracture with the greatest risk of re-fracture occurring within the first few years of the initial fracture. The risk is higher in men than women with a significant proportion of subsequent fractures being hip or vertebral fractures. As well as increased risk of subsequent fracture, all proximal and not just hip or vertebral fractures are associated with an increased mortality risk. In the older population, this even extends to some distal fractures. Again, the risk is highest close to the fracture event and persists for about 5 years for non-hip non-vertebral fractures and up to 10 years for hip and vertebral fractures before declining to the background population mortality rate. A subsequent fracture further increases this risk.

Importantly, several cohort and RCTs suggest that potent anti-resorptive medication may be associated with improved survival in those at fracture risk.Thus osteoporotic fracture is associated with poor outcomes and early intervention is essential to reduce subsequent fracture and possibly also mortality risk.

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Committee of National Societies (CNS) Roundtable Abstracts

CNS1
DIETARY CALCIUM INTAKE WORLDWIDE

B. Dawson-Hughes[1]

[1]Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, United States

Low calcium intake can adversely affect bone health in adults. Recognizing the presence of low calcium intake is a necessary first step in the process of optimizing intake for bone health. The IOF, in collaboration with a professional search team led by Dr. E. Balk at Brown University in Providence, RI, USA conducted a systematic review of the literature from the year 2000 on to identify the most representative national dietary calcium intake data in adults from the general population in countries around the globe. The search of over 13 electronic databases yielded 9780 abstracts. Of the current 195 countries, data were found for only 74, and survey data for three quarters of the 74 available countries were not nationally representative. Among the 74 countries with data, average national dietary calcium intake ranged from 175 to 1,233 mg per day. Many countries in Asia have average dietary calcium intake less than 500 mg per day. Countries in Africa and South America mostly have low calcium intake between about 400 and 700 mg/day. From the search results, the IOF developed an interactive color-coded map to illustrate the calcium intake of the different countries. The interactive component provides the data source for each of the countries with available data. This symposium will focus on calcium intake in the Asia-Pacific region, on its implications for bone health, and on regionally and culturally appropriate strategies to increase calcium intake to locally recommended levels, where needed.

Reference:

Balk EM, Adam GP, Langberg VN, Earley A, Clark P, Ebeling PR, Mithal A, Rizzoli R, Zerbini CAF, Pierroz DD, Dawson-Hughes B. Global Dietary Calcium Intake Among Adults: A Systematic Review. Osteoporosis Int 2017;28:3315–3324.

CNS2

PROTEINS INTAKES AND SUPPLEMENTS IN PATIENTS WITH FRACTURE

R. Rizzoli[1]

[1]Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

A common denominator of various musculoskeletal functions decline with ageing is malnutrition. Several nutritional insufficiencies contribute to a negative calcium balance, and to bone mass and bone structure alterations, together with a loss in muscle mass and function. Inthe elderly, protein undernutrition can favour the occurrence of hip fracture by increasing the propensity to fall as a result of muscle weakness, by affecting protective mechanisms, such as reaction time, and/or by decreasing bone mass. Bone mineral density (BMD) is positively correlated to dietary protein intakes. Regarding bone microstructure, which is another important determinant of bone strength not captured by BMD, estimated from microstructure bone strength, trabecular and cortical microstructure are positively correlated with total protein intakes. When analyzing the associations according to the various sources of proteins, mainly animal proteins, especially dairy proteins, are correlated with bone strength. In a balanced western diet, dairy products are responsible for about 50 to 70% of total dietary calcium intakes and 20-28% of total protein intakes in adults. Protein supplements in patients with a recent hip fracture have been shown to lower the rate of medical complications and to reduce the length of stay in rehabilitation wards.

CNS3
CALCIUM SUPPLEMENTS AND FRACTURE PREVENTION

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Currently it is estimated that over 200 million people worldwide suffer from osteoporosis. The number of hip fractures is rapidly rising in Asian countries due to an increase in the aging populations within this region. It has been estimated that in 2050 more than half of all hip fractures worldwide will occur in Asia. Among the various risk factors for osteoporosis, low lifetime calcium intake is one of the modifiable risk factors. Calcium is an important component of bone, accounting for about 30 to 35% of its mass and much of its strength. However, there is continuing debate regarding the optimal level of calcium intake for preserving bone health. Recommended daily calcium allowances differ between countries. The global map revealed thatcountries with very low calcium intake are clustered in the Asia-Pacific region and include countries with large populations such as China, India, Indonesia, and Vietnam, among others (1). Inadequate calcium intake was found throughout Asia with daily intake well below the World Health Organization (WHO) general recommended levels of 1000–1300 mg/day. Asia-Pacific countries with very low calcium intakes also have suboptimal vitamin D status.

Effects of calcium supplementation on bone mineral density have been variable depending on the study population. Daily supplementation with as little as 500 mg of calcium slows lumbar spine bone loss in perimenopausal Japanese females with low calcium intake and similar effects have been observed in postmenopausal females from Hong KongChina, Chile, Argentina, and Nigeria. In contrast, calcium supplementation had no consistent effects on bone mineral density in studies of calcium-sufficient populations

The data on fracture rates are even more variable. The variable results are likely due to differences in patient populations and study design. The Women's Health Initiative(WHI) trial did not show a significant reduction in hip fractures or other fractures in women randomly assigned to 1000 mg of elemental calcium plus 400 IU of vitamin D per day as compared with women assigned to placebo, perhaps because the mean calcium intake in the placebo group was 1154 mg per day. A systematic review of RCTs and cohort studies of dietary calcium, milk or dairy intake or calcium supplements (with or without vitamin D) with fracture as an outcome and subjects aged>50, showed that that dietary calcium intake is not associated with risk of fracture, and there is no evidence currently that increasing dietary calcium intake prevents fractures. Calcium supplements had small inconsistent benefits on fracture reduction (2). Similarly, another meta-analysis of RCTs, revealed that the use of supplements that included calcium, vitamin D, or both compared with placebo or no treatment was not associated with a lower risk of fractures among community-dwelling older adults (3). Of note, lack of beneficial effect of increase dietary calcium intake or calcium supplements on fracture prevention in various trials could be explained by the fact that many trials did not preferentially recruit persons with low dietary calcium intake. It seems calcium supplementation has greater benefits for people in regions with low dietary calcium intake while the benefits may be marginal or absent for people with enough calcium in their diet.

More data from countries with low calcium intakes are needed to elucidate the role of calcium supplementation in fracture prevention. The evidence suggesting adverse cardiovascular effects of calcium supplementation is inconsistent. Future research is needed to establish calcium requirements for premenopausal women, men, and nonwhite populations.

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CNS4

CALCIUM INTAKE AND ITS IMPLICATION IN CHINA

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The aging population in China is growing rapidly and by the middle of this century will peak. As a result, both the prevalence of osteoporosis and the incidence of osteoporotic fracture are rapidly rising in Chinese population. In this context, bone health draws common concern of the whole society. Sufficient intake of calcium and vitamin D is important in maintaining the healthy status of bone. Currently there is a high prevalence of calcium and vitamin D insufficiency in China. According to China Nationwide Nutrition and Health Surveys 2012, the mean Ca intake is 366 mg/day/reference man, which is much below the recommended intake of 800-1000 mg/d. Calcium intake also show regional difference within China. Urban areas have average calcium intake of 412 mg/d, while rural areas have calcium intake of 321 mg/d. The low calcium intake in China may be due to plant-based diets and low milk and dairy products cosunmption. In recent years, many studies have investigated the effect of calcium and vitamin D supplementation but get divergent results. This review will discuss the studies in China and other Pacific Rim countries that address the role of calcium and vitamin D in bone health, the overall calcium intake in China as well as its regional difference. We will also evaluate the potential benefits and risks of increasing calcium intake in China, and discuss the appropriate strategies to increase calcium intake based on the current evidence.

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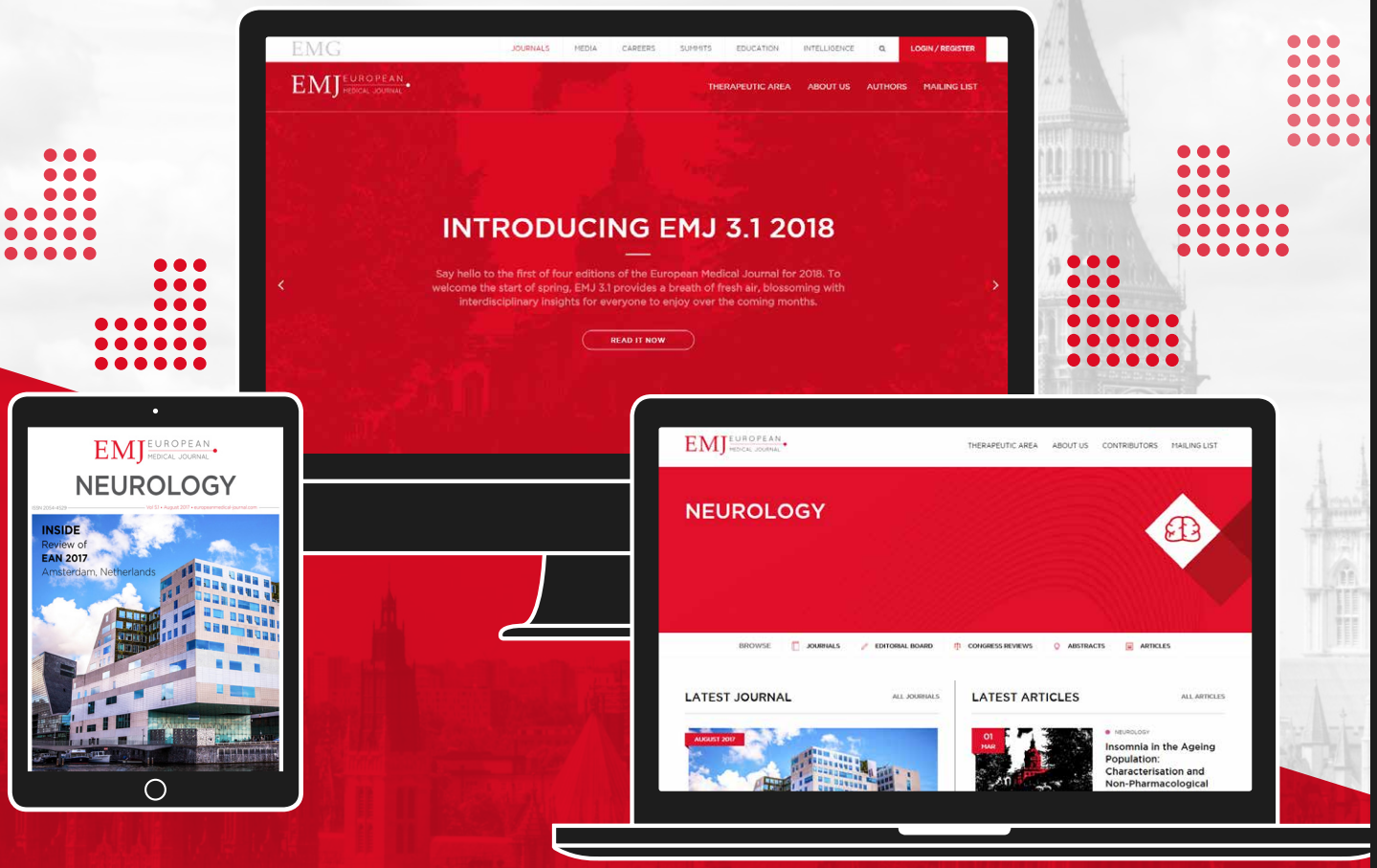

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Sponsored Symposia Abstracts

SY1
UNDERSTANDING MORTALITY RISK FOR PATIENTS WITH VCF

K. L. Ong[1,2]

[1]Exponent Inc., Philadelphia, United States, [2]School of Biomedical Engineering, Science and Health Systems, Drexel University, Philadelphia, United States

Were vertebral compression fracture (VCF) patients at higher risk of mortality following the 2009 publication of the vertebroplasty "sham" trials? – Osteoporosis Int 2017

Vertebral compression fractures are the most common osteoporotic fractures. The onset of a VCF can lead to a downward spiral of morbidity including mortality. Treatment options for a VCF patient include non-surgical management, such as back braces and opioids. Alternatively, surgical interventions include vertebroplasty (VP) or balloon kyphoplasty (BKP).

This presentation will discuss the differences in mortality risks for VCF patients who undergo non-surgical management, VP, and BKP. The presentation will further describe the treatment pattern changes and associated mortality risks after 2009, when controversy was raised over the VP versus sham trials.

SY2
ACHIEVING THE GOALS OF OSTEOPOROSIS THERAPY

S. Ferrari[1]

[1]Service of Bone Diseases, Geneva University Hospital, Geneva, Switzerland

There are two main goals of osteoporosis therapy. First an early and sustained reduction of fracture risk, particularly in patients at imminent risk. Second a long-term improvement of bone mass and structure so that treatment can eventually be interrupted once subjects have achieved a level of bone strength capable to definitely sustain a fall with a minimal risk of fracture.

Although all osteoporosis drugs reduce vertebral fracture risk significantly within one year, evidence for clinical and particularly non-vertebral fracture reduction early in the course of therapy is still limited. Zoledronate post-hip fracture reduces clinical fracture by 32% within 2-3 yrs, whereas denosumab reduces hip fractures 48-62% within 3 years in high risk patients. A recent study comparing TPT and risedronate in patients with prevalent vertebral fractures, 30% of which were recent, provides new evidence that a bone forming agent could be used first in patients at high fracture risk. An observational study in Medicare subjects aged 65+ also indicates that osteoporosis drugs reduce fracture rate early in the course of therapy (i.e. within 15 months), but more so with denosumab and teriparatide.

Regarding the long-term benefits on bone mass, bisphosphonates achieve limited gains in hip BMD within 3 yrs, whereas denosumab has provided continuous gains for up to ten years, with further reductions in non-vertebral fracture rates from year 4 and a benefits/risk ratio (i.e. number of fractures avoided / skeletal adverse events of ONJ and AFF) > 100 long-term. Interrupting therapy on another side has proven deleterious with all drugs in patients remaining at high risk, such as those with vertebral fractures and/or not achieving a hip BMD at least > -2.5 (ideally >-2), and with denosumab in particular because of the transient rebound in bone turnover. In this case, the rate of vertebral fractures rapidly increases back to untreated levels, with a slightly higher rate (+1%) of multiple vertebral fractures. Patients in whom discontinuation of denosumab is considered, transition to other therapies must be considered. to consolidate the bone mass gained on that therapy.

SY3

THE IMPORTANCE OF BONE FORMING AGENTS IN THE TREATMENT OF SEVERE OSTEOPOROSIS

E. Seeman[1], S. Ferrari[2]

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Bone remodelling maintains bone's material and structural strength until menopause whenremodeling becomes unbalanced and rapid. Less bone is deposited than resorbed during each of the many more remodeling events causing a reduction in total bone matrix volume, microstructural deterioration and bone fragility. Antiresorptives slow unbalanced remodelling, they do not abolish it and so they do not reverse or abolish worsening of microstructural deterioration. The less often remodeled matrix continues to deteriorate albeit more slowly and becomes more glycated, mineralized and so, more brittle. The relative risk for vertebral and hip fractures is reduced by ~50%, but by only 20-30% for non-vertebral fractures. The challenge is to restore bone matrix volume, microstructure, material composition and strength. Teriparatide produce mainly remodelling-based net bone formation by acting on cells of existing remodelling units and by initiating new remodeling events. There is a transitory phase of increased numbers of resorption sites as treatment stimulates RANKL production by osteoblast precursors and osteocytes. Existing and newly generated remodeling events excavate older more mineralized and glycosylated bone upon trabecular, endocortical and intracortical surfaces. These cavities refill or overfill with younger matrix, producing increased numbers of new osteons with their cement lines, lamellae, and osteocytic network. Vertebral and non-vertebral fracture risk is reduced. Studies are needed to evaluate anti-hip fracture efficacy. Recent studies demonstrate that teriparatide has better antifracture efficacy than the bisphosphonate, risedronate. Kendleret al. (2018) compared anti-fracture efficacy of 20 µg of teriparatide once daily versus 35 mg oforal risedronate in postmenopausal women with severe osteoporosis in a double-blind trial (VERO). During 24 months new vertebral fractures occurred in 28/680 (5·4%) of patients in the teriparatide group and 64/680 (12·0%) patients in the risedronate group (risk ratio 0·44, 95% CI 0·29–0·68; p<0·0001). Clinical fractures occurred in 4·8% in the teriparatide group and 9·8% in the risedronate group (hazard ratio 0·48, 95% CI 0·32–0·74; p=0·0009). Non-vertebral fragility fractures occurred in 4·0% patients in the teriparatide group and 6·1% in the risedronate group (hazard ratio 0·66; 95% CI 0·39–1·10; p = 0·10). In a preplanned subgroup analysis of fracture data across subgroups (age, number and severity of prevalent vertebral fractures, prevalent non- vertebral fractures, glucocorticoid use, prior osteoporosis drugs, recent bisphosphonate use), the risk reduction of teriparatide versus risedronate did not significantly differ in any of the subgroup analyzed (Geusens et al).

In conclusion, in postmenopausal women with established osteoporosis, who are at high risk of fracture, treatment with teriparatide was associated with a significant reduction in the incidence of vertebral and clinical fractures compared with risedronate, consistent across most clinical subgroups. These results indicate additional fracture benefit of using an anabolic as compared to an anti-resorptive drug.

Kendler DL, et al. Effects of teriparatide and risedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy, randomised controlled trial. Lancet. (2018); 391:230-240.

Geusens P. et al. J Bone Miner Res. (2018);33(5):783-794.

IOF REGIONAL SYDNEY'18
7TH ASIA-PACIFIC OSTEOPOROSIS CONFERENCE

IOF Regional 7th Asia-Pacific Osteoporosis Conference
Sydney, Australia – 2018

Oral Communications Abstracts

OC1

T-SCORE AS AN INDICATOR OF FRACTURE RISK ON THERAPY: EVIDENCE FROM ROMOSOZUMAB VS. ALENDRONATE TREATMENT IN THE ARCH TRIAL

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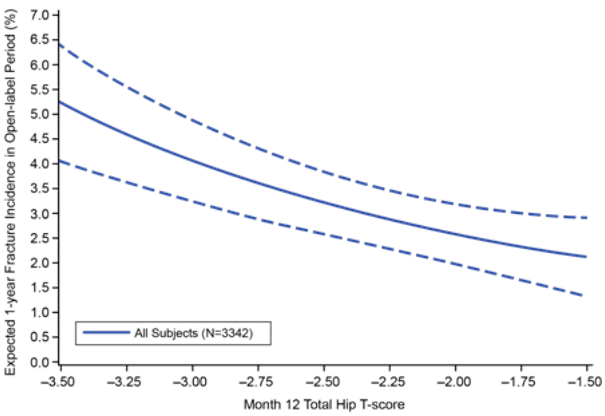
Postmenopausal women with osteoporosis and prior fragility fracture were randomized 1:1 to receive Romo 210mg SC QM or ALN 70mg PO QW for 12 months, followed by open-label (OL) ALN 70mg PO QW for ≥12 months. We examined change from baseline in BMD and T-scores at 12 months and the relationship between total hip (TH) T-scores at month 12 and subsequent nonvertebral (NVT) fx rates. We also compared fractures in the OL period, including new vertebral (VT) fractures in year 2 (based on month 24 spine radiographs) and clinical, NVT, and hip fractures between arms in the full OL period.

Mean baseline T-scores were −2.96 at the lumbar spine and −2.80 at the TH. 3465 patients (1739 Romo, 1726 ALN) received ≥1 OL ALN dose in the OL period (median 1.9 years follow-up). Mean TH BMD increased by 6.2% for Romo and 2.8% for ALN in the first year, with increases in T-score of 0.31 and 0.15, respectively. At month 12, the achieved TH T-score was associated with the 1-year NVT fracture rate observed in the OL period (Figure) and the relationship was independent of the drug received in the first year. During the OL period, when all patients were on ALN, patients who received Romo first had a 75% lower relative risk of new VT fracture (P<0.001), and had reductions in clinical (32%, P=0.001), NVT (19%, P=0.120), and hip (40%, P=0.041) fractures vs. patients who received ALN first.

Higher absolute TH T-scores achieved on therapy at month 12 resulted in subsequent lower fracture risk regardless of the treatment received, with ongoing benefits from building a BMD foundation. These data support the concept of a T-score target to improve outcomes in osteoporosis treatment.

Figure: Month 12 total hip T-score and nonvertebral fracture rate during the open-label period



The dashed lines indicate upper and lower 95% confidence intervals. Likelihood ratio test P<0.001.

OC2

DENOSUMAB COMPARED WITH RISEDRONATE IN GLUCOCORTICOID-TREATED SUBJECTS: RESULTS FROM THE FINAL 24-MONTH ANALYSIS OF A RANDOMIZED, DOUBLE-BLIND, DOUBLE-DUMMY STUDY

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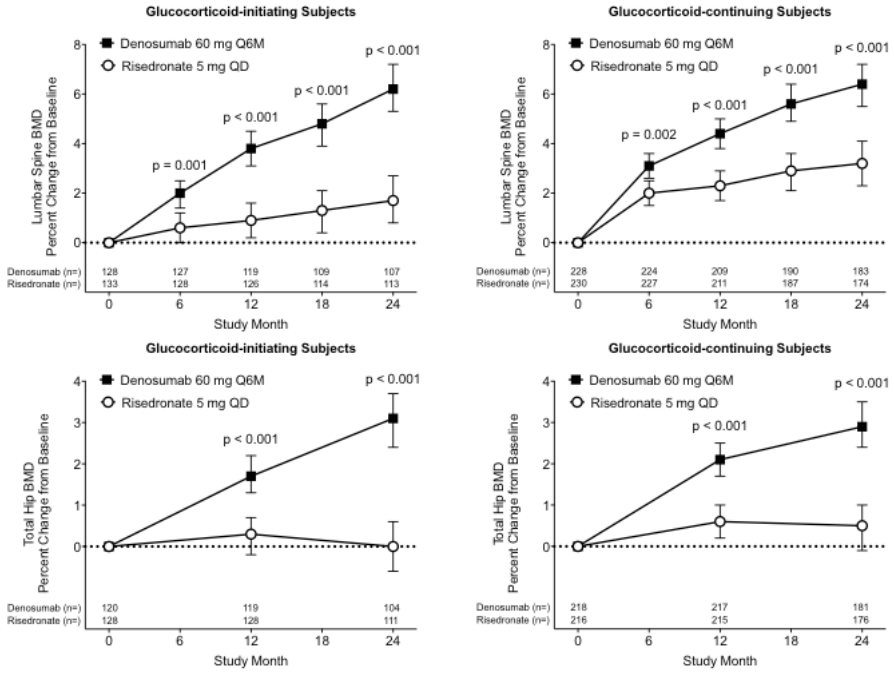
Denosumab 60 mg subcutaneously Q6M increased spine and hip BMD significantly more than risedronate 5 mg orally QD at 12 months in glucocorticoid-treated subjects (as previously reported). This analysis compared the BMD effects of denosumab vs. risedronate and further characterized denosumab safety in this population at 24 months.

This phase 3, randomized, double-blind, double-dummy study enrolled adults ≥18 y receiving ≥7.5 mg daily prednisone (or equivalent) for <3 months (glucocorticoid-initiating subpopulation) or ≥3 months (glucocorticoid-continuing subpopulation). All subjects <50 y had history of osteoporotic fracture. Glucocorticoid-continuing subjects ≥50 years had lumbar spine (LS), total hip (TH), or femoral neck BMD T-scores ≤-2.0, or ≤-1.0 and history of fracture. Subjects were randomized 1:1 to denosumab 60 mg subcutaneously Q6M or risedronate 5 mg orally QD for 24 months. This analysis assessed denosumab superiority over risedronate for percentage change from baseline in LS and TH BMD at 24 months.

Of 795 randomized subjects, 590 (74.2%) completed the 24-month study (glucocorticoid-initiating: 109/145 denosumab, 117/145 risedronate; glucocorticoid-continuing: 186/253 denosumab, 178/252 risedronate). Denosumab was superior to risedronate for increases from baseline in LS and TH BMD at all timepoints assessed through 24 months in each subpopulation (Figure). Adverse events, serious adverse events (including infection), and fractures were similar between groups.

Figure. BMD Percentage Change (95% CI) From Baseline Through Month 24



BMD: bone mineral density; CI: confidence interval; Q6M: every 6 months; QD: once daily.
Based on ANCOVA model adjusting for treatment, baseline BMD value, gender, machine type, and baseline BMD value-by-machine type interaction. For glucocorticoid-continuing subpopulation, duration of prior glucocorticoid use (< 12 vs ≥ 12 months) was included as an additional covariate.

In conclusion, denosumab was superior to risedronate for increases in spine and hip BMD through 24 months. The overall safety profile was similar between groups. Denosumab may offer a valuable osteoporosis treatment option for patients receiving glucocorticoids.

OC3

VITAMIN D SUPPLEMENTATION IN PREGNANCY: A RANDOMIZED DOUBLE-BLIND CONTROLLED TRIAL

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Objective: To investigate the efficacy and safety of vitamin D supplementation, in the doses of 600, 1000, 2000, and 4000 IU/d, started early in pregnancy (<16 weeks), on maternal (pregnancy weight gain, pre-eclampsia, gestational diabetes), fetal (fetal growth as assessed by ultrasonography at 18-24 weeks and 26-30 weeks) and newborn (newborn anthropometry namely head circumference, birth weight, length and cord blood vitamin D level) parameters.

Methods: This randomized double blind active controlled clinical trial was carried out in pregnant subjects, aged 18-40 y with gestational age between 12-16 weeks. Subject with high risk pregnancy were excluded. Subjects randomized into four groups in ratio of 1:1:1:1(Group 1 - active control group received 600 units of vitamin D per day; Group 2 – 1000 units/d; Group 3 – 2000 units/d; Group 4 - 4000 units/d). All groups received 1000 mg of elemental calcium. The primary outcome of the study was changes in vitamin D status of mother and newborn. Safety of intervention was assessed by regular monitoring.

Results: Total 243 subjects who completed the study were analyzed. High prevalence of vitamin D deficiency was seen in study population (93.6%). S.VitD level improved significantly in all four groups except group 1. Cord blood S.VitD levels were significantly higher in Gr 2, 3 and 4 in comparison to Gr 1. The highest cord blood S.VitD level was seen in Gr 4 (41.38±14.71 ng/ml) while lowest was in Gr 1 (12.49±12.95 ng/ml). No significant difference was observed among all four groups in any other maternal, fetal and newborn parameters including insulin resistance in mother as well as in cord blood. No adverse effect observed.

Conclusions: Our study shows that supplementation of vitamin D in mother started at 16 weeks, improves vitamin D status of newborn. However, vitamin D supplementation during pregnancy did not show effect on any other maternal, fetal and newborn parameter (maternal wt gain, pre-eclampsia, gestational diabetes, fetal growth, newborn head circumference, length, and weight and insulin resistance in mother at the time of delivery). Supplementation of vitamin D at this dose is found to be safe without any hypercalcemia or hypercalciuria. Dose of 2000 IU/d was found to be most appropriate for improving cord vitamin D status.

OC4

ANTI-OSTEOPOROSIS MEDICATIONS ARE ASSOCIATED WITH DECREASED MORTALITY AFTER HIP FRACTURE

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Objective: Hip fragility fractures in the old population are associated with high morbidity and mortality. The increased mortality is significant within first year after the fracture and extends beyond 10 years. Zoledronate has proved significantly to reduce new clinical fractures and mortality in the patients with hip fracture. In this retrospective study, we enrolled 690 patients with hip fracture and studied the effect of anti-osteoporosis therapies on the mortality after hip fracture.

Methods: This research was carried out in the Second Affiliated Hospital of Fujian Medical University and enrolled 690 patients 50 y of age and older who were admitted with hip fragility fractures between 2010-2015.The patients were followed in 2017. 690 patients' age was from 50-103 y, with the average of 78.08±9.7 y. There were 456 females and 234 males. The anti-osteoporosis medications were classified into no anti-osteoporosis medication, calcium + vitamin D supplementations, nonbisphosphonate medication and bisphosphonate medication. The physicians followed the patients or family members who lived with the patients before death by personal visit and telephone. Multivariable Cox regression analyses were done with known risk factors for mortality of hip fracture such as gender, age, number of combined internal diseases, fracture type, place of residence, Charlson comorbidity index to show which of anti-osteoporosis medications had significant effect on mortality after adjustment for these variables.

Results: 690 patients with hip fracture were followed between 7-52 months, with the average of 28.53±9.75 months. 166 patients died during follow-up period. The cumulative mortality was 36.24% in the patients receiving no anti-osteoporosis medication. Calcium + vitamin D supplementations had no association with the cumulative mortality post hip fracture (p=0.097, HR=0.606, 95%CI 0.335-1.095). Nonbisphosphonate medication for osteoporosis were significantly associated with reduction of cumulative mortality (p=0.000, HR=0.477, 95%CI 0.335-0.678), and bisphosphonate medication (zoledronic acid) had the most effective impact on reduction of cumulative mortality (p=0.000, HR=0.339, 95%CI 0.186-0.621).

Conclusions: Nonbisphosphonate and bisphosphonate medications for osteoporosis were significantly associated with decreased mortality after fragility hip fracture and zoledronic acid has the most effective impact on the reduction of mortality.

OC5

ASIA-PACIFIC BONE ACADEMY FRACTURE LIAISON SERVICE EDUCATIONAL INITIATIVE

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Objectives: To provide healthcare professionals and health administrators with a suite of tools to support the development of new Fracture Liaison Services (FLS) across the Asia-Pacific region using a multifaceted educational initiative.

Methods: A FLS Toolbox for Asia-Pacific was developed which included the following sections:

1. The burden of fragility fractures in the Asia-Pacific region.
2. A summary of evidence for FLS in the Asia-Pacific according to the Ganda Classification System[1].
3. A generic, fully referenced FLS business plan template.
4. Potential cost savings accrued by each country, based on a country-specific FLS Benefits Calculator.
5. How to start and expand FLS programmes in the Asia-Pacific context.
6. A step-by-step guide to setting up FLS in countries in the Asia-Pacific region.
7. Other practical tools to support FLS establishment.
8. FLS online resources and publications.

The FLS Toolbox was provided as a resource to support FLS workshops immediately following the 5th Scientific Meeting of the Asian Federation of Osteoporosis Societies (AFOS) held in Kuala Lumpur in October 2017. The FLS workshops addressed three key themes:

- The FLS business case
- Planning the FLS patient path
- The role of the FLS coordinator in fragility fracture care management

Results: A follow-up survey of 142 workshop participants conducted in August-September 2018 will be presented at the IOF Regional 7th Asia-Pacific Osteoporosis Conference to demonstrate the impact of the educational initiative. The survey includes questions regarding how FLS were developed, funded, the scope of service provision and the support provided by the educational initiative.

Conclusions: The Asia-Pacific Bone Academy FLS Focus Group educational initiative has stimulated activity across the Asia-Pacific region with the intention of supporting widespread implementation of new FLS.

Disclosures: The Asia Pacific Bone Academy FLS Focus Group and development of the multifaceted educational initiative relating to FLS implementation has been supported by unrestricted educational grants from Amgen Asia.

Reference: Ganda K et al. *Osteoporos Int* 2013;24:393.

OC6

INCREASED CORTICAL POROSITY AND REDUCED TRABECULAR DENSITY ARE NOT NECESSARILY SYNONYMOUS WITH BONE LOSS AND MICROSTRUCTURAL DETERIORATION

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Absolute values of cortical porosity and trabecular density are used to estimate fracture risk, but these values are the net result of their growth-related assembly and age-related deterioration. Because bone loss affects both cortical and trabecular bone, we hypothesized that a surrogate measure of bone fragility should capture the age-related deterioration of both traits independent of their peak values. We developed a Structural Fragility Score (SFS) which quantifies the increment in distal radial cortical porosity and decrement in trabecular density relative to their premenopausal mean values in 99 postmenopausal women with forearm fractures and 105 controls using high resolution peripheral computed tomography. We expressed the results as odds ratios (95%CI). Cortical porosity was associated with fractures in the presence of deteriorated trabecular density (2.30, 1.30 – 4.05, p=0.004), but its absence (0.96, 0.50 – 1.86; p=0.91). Trabecular density was associated with fractures in the presence of high cortical porosity (3.35, 1.85 – 6.07, p<0.0001), but its absence (1.60, 0.78 – 3.28, p=0.20). The SFS was associated with fractures (4.52, 2.17 – 9.45, p<0.0001). BMD was associated with fracture before accounting for the SFS (5.79, 1.24 – 27.1, p=0.026), not after (4.38, 0.48 – 39.9, p=0.19). The SFS was associated with fracture before (4.67, 2.21 – 9.88) and after (3.94, 1.80 – 8.6) accounting for BMD (both p<0.0001). The disease of bone fragility is captured by the coexistence of cortical and trabecular deterioration the measurement of is likely to identify women at risk for fracture more robustly than absolute values.

OC7

EFFECTS OF TERIPARATIDE ON HIP AND UPPER LIMB FRACTURES IN PATIENTS WITH OSTEOPOROSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives: In randomized clinical trials (RCTs) with teriparatide, the number of patients with incident hip fractures was small. We conducted a meta-analysis to evaluate the effects of teriparatide on hip and upper limb fractures compared to placebo or osteoporosis drugs in patients with osteoporosis.

Methods: A literature search was conducted for RCTs of teriparatide of at least 6-month duration, with the approved treatment indications and dose, and that reported non-spine fractures (hip, humerus, forearm, wrist). Study selection and data extraction were performed by two independent reviewers. Statistical procedures included Peto's method and Mantel-Haenszel with empirical correction, as most of the RCTs reported zero events in at least one of the treatment arms. The results are expressed as odds ratios (OR) with 95%CI. Publication bias and heterogeneity were assessed with standard statistical tests.

Results: Twenty-three RCTs were included, 19 with an active-controlled arm, 11 double-blind, representing data on 8591 subjects (3888 treated with teriparatide). Mean age was 67.0 y, median treatment duration 18 months (range: 6-24 months). Thirty-four incident hip, 28 humerus, 31 forearm, and 73 wrist fractures were reported. Meta-analysis results showed an OR (95%CI) for hip fractures of 0.44 (0.22-0.87; p=0.019) in patients treated with teriparatide compared with controls. The effects on the risk of humerus [0.82 (0.38-1.74)], forearm [0.53 (0.26-1.08)] and wrist [1.14 (0.71-1.83)] fractures were not statistically significant.

Conclusions: This meta-analysis provides evidence of efficacy of teriparatide in reducing osteoporotic hip fractures by 56%. No significant effects were demonstrable for upper limb fractures.

OC8

DIGITAL X-RADIOGRAMMETRY COMBINED WITH MAMMOGRAPHY TO SCREEN POSTMENOPAUSAL WOMEN FOR REDUCED BONE MINERAL DENSITY

A. Rao[1], E. Elder[2], J. Center[3], N. Pocock[3], G. Elder[2]

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Objectives: To assess whether BMD, determined by digital X-radiogrammetry (DXR) in women who attend for a follow-up mammography, might be a useful screening tool for fracture risk.

Methods: 200 participants were recruited from the diagnostic clinic at the Breast Cancer Institute (BCI), Westmead Hospital (Sydney), between August 2014 and February 2016. Participants were aged over 50 y, postmenopausal and provided informed consent. Participants completed a questionnaire and underwent DXR on their nondominant hand immediately after, and on the same equipment as mammography, followed by DXA. Lin's concordance coefficient and Receiver Operator Characteristic (ROC) area under the curve (AUC) were used to assess agreement between DXA and DXR values.

Results: Participants were aged 64±7 y, 82% had a diagnosis of breast cancer, 37% had a prior fracture and 18% had a diagnosis of osteoporosis. By DXA, 77.5% had a T-score ≤ -1 at any spine, hip or forearm site, For DXR and DXA at the1/3 radius, Lin's concordance Rho c was 0.635 ($p<0.001$) with similar concordance at other DXA forearm sites. For the diagnosis of osteopenia or osteoporosis by DXR and DXA at any site, T-Scores ≤ -1 and >-1 were concordant for 77% of patients; Using ROC AUC, for DXR prediction of DXA derived T-scores ≤ -2.5 at the 1/3 radius, the AUC was 0.87 (95%CI: 0.81-0.94), total radius 0.82 (95%CI: 0.75-0.89) and ultradistal radius 0.77 (95%CI: 0.70-0.84). For T-scores ≤ -2.5 by DXR or DXA at any site, the AUC was 0.79 (95%CI: 0.73-0.86).

Conclusions: DXR correlates closely to DXA particularly at forearm sites, and may be useful to screen for low BMD at the time of mammography.

OC9

DO DEFINITIONS OF SARCOPENIA PREDICT FRACTURE RISK INDEPENDENT OF FRAX, FALLS AND BMD? A META-ANALYSIS OF THE OSTEOPOROTIC FRACTURES IN MEN (MROS) STUDY

H. Johansson[1], C. Harvey[2], A. Odén[3], E. Orwoll[4], T. Kwok[5], M. Karlsson[6], B. Rosengren[6], E. Ribom[7], P. Cawthon[8], K. Ensrud[9], C. Cooper[2], J. Kanis[10], C. Ohlsson[11], D. Mellström[11], E. Mccloskey[3]

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Objectives: Recently we have demonstrated that the relationship between appendicular lean mass/height2 (ALM/ht2) and incident fracture is markedly attenuated by femoral neck BMD (fnBMD). Most sarcopenia definitions use ALM/ht2, and so our aim was to investigate the value of sarcopenia definitions for predicting incident fracture, independent of fnBMD, FRAX probability and prior falls.

Methods: In US, Sweden and Hong Kong MrOS cohorts, we used an extension of Poisson regression to investigate associations between definitions of sarcopenia and incident major osteoporotic fracture (MOF: clinical vertebral, hip, wrist, proximal humerus). Sarcopenia definitions tested were those published by Baumgartner, Fielding, Cruz-Jentoft, Morley, Chen, Delmonico, Studenski (1 & 2). Associations were adjusted for age and time since baseline, and reported as hazard ratio (HR) for first incident MOF. Further analyses adjusted additionally for FRAX MOF probability (available in 7531 men and calculated with and without fnBMD), prior falls or fnBMD T-score.

Results: Data were available for 5660 men in USA, 2764 in Sweden and 1987 in Hong Kong with mean ages 73.5, 75.4 and 72.4 y, respectively. Mean follow-up time was 8.7-10.9 y. Prevalence of sarcopenia ranged from 0.9% (Studenski 2) to 21% (Baumgartner) in US; corresponding figures were 0.4% to 22% in Sweden and 4% to 35% in Hong Kong. Sarcopenia status, by all definitions except those of Studenski, was associated with incident MOF (HR: 1.40 to 1.92), e.g., Delmonico (HR:1.40; 95%CI:1.23, 1.59) and Chen (HR:1.92; 95%CI:1.43, 2.57). Relationships were robust to adjustment for prior falls or FRAX probability (with and without fnBMD). Adjustment for fnBMD T-score alone led to marked attenuation of HR:s, e.g., Delmonico (HR:1.06 95%CI:0.93, 1.22) and Chen (HR:1.54; 95%CI:1.15, 2.07).

Conclusion: The value of sarcopenia definitions based on ALM in predicting incident fractures is reduced by inclusion of fnBMD T-score. Given that both ALM and BMD are derived from DXA, these findings might suggest that alternative muscle indices, such as from pQCT, might helpfully be investigated in the characterisation of sarcopenia status.

OC10

ASSESSING CLINICAL UTILITY (IMPACT) OF GENETIC PROFILING IN FRACTURE RISK ASSESSMENT: A DECISION CURVE ANALYSIS APPROACH

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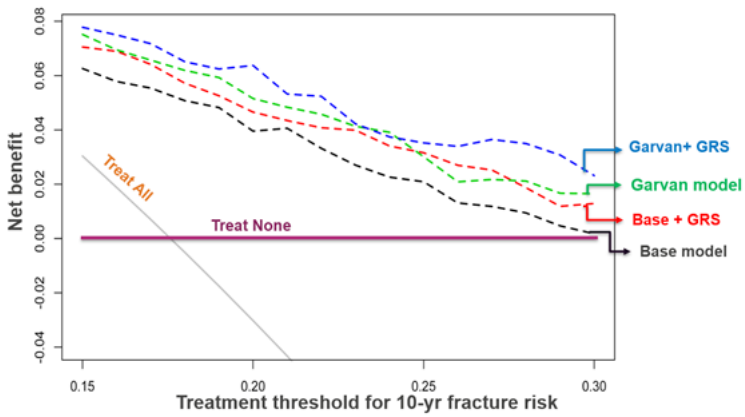
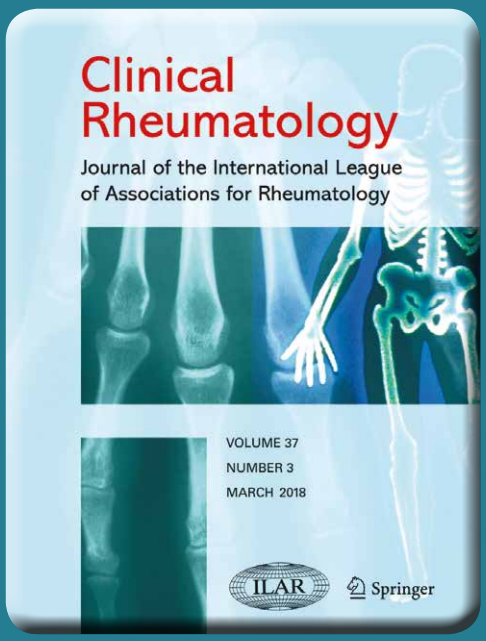
Objective: Genetic profiling is emerged as a promising tool for assessing the risk fracture in asymptomatic individuals. Decision curve analysis (DCA) is a novel approach to evaluate the contribution of a new predictive marker or model. This study sought to use the DCA to determine the utility of genetic profiling in prediction of fracture.

Methods: The study involved 2188 women and 1324 men aged 60 y and above who have been followed up to 20 y. BMD and clinical risk factors were obtained at baseline. The incidence of fracture and mortality was recorded during the period. A weighted genetic risk score (GRS) was constructed for each individual from 62 BMD-associated genetic variants. Four models were considered: Model I (Base model) included only clinical risk factors (CRF); Model II (Garvan model) included CRF and femoral neck BMD; Model III (Garvan+GRS) included CRF, femoral neck BMD and GRS; and Model IV (Base+GRS) included CRF and GRS. Decision curve analysis was used to evaluate the clinical net benefit in terms of true positives and false positives of predictive models.

Results: In women, for risk threshold above 0.15, the Base+GRS model had a significantly higher net benefit than the Base model; however, for threshold below 0.15, there was no significant difference in net benefit between the two models. The Garvan model yielded the highest net benefit; adding GRS into the Garvan model did not substantially improve the net benefit. In men with fracture risk greater than 0.15, the Base+GRS model resulted in a better net benefit than the Base model. Interestingly, the Garvan+GRS model did improve the net benefit over and above the Garvan model.

Conclusion: Genetic profiling can provide additional prognostic information to that obtained from clinical risk factors, particularly in women at higher risk of fractures. However, in the presence of BMD in a predictive model, GRS does not further improve net clinical benefit.





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Posters Abstracts

P001

FRACTURE RISK IN HOSPITALIZED PATIENTS DEPEND ON EACH SPECIFIC DISEASE AREA IN ACUTE CARE HOSPITAL

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Objective: The purpose of OLS (Osteoporosis Liaison service) in Japan is both primary and secondary preventions of fragility fractures. Nowadays, many Japanese hospitals including acute care hospitals have started OLS to reduce osteoporotic fractures. When the patients are admitted to the hospital for their first fragility fracture, it is easy to start OLS for secondary prevention. On the other hand, with patients admitted to the hospital with other reasons, we need some effort to find high risk patients of fragility fractures. FRAX® is well known fracture risk assessment tool for osteoporotic fracture and its process to predict fracture probability is adapted to each country including Japan. The aim of this study was to compare the number of high risk patients among each clinical department to establish more effective screening program in acute care hospitals in Japan.

Methods: Patients (age: 40-90 y) who were hospitalized at either of 24 clinical departments except pediatrics at Fujita Health University Hospital between September 2017 and March 2018. The following patient data were collected: age, height, weight, BMI (kg/m^2) and the risk factors included in FRAX. The value was expressed as mean±SD. Differences and associations with $P<0.05$ were considered statistically significant.

Results: The study included 1565 Japanese patients. Mean age was 66.98±12.20 y, and BMI was 22.74±4.05. Major osteoporotic fracture and hip fracture risks in 10 y assessed by FRAX was 11.59±10.37% and 4.85±7.04%, respectively. Several clinical departments showed higher existence ratio of high risk patients for major osteoporotic fracture assessed by FRAX: rheumatology (18.55±16.81%), emergency and critical medicine (17.74±12.93%), liver, biliary tract and pancreas diseases (15.87±11.48%), orthopedic surgery (15.72±14.83%), psychiatry (13.51±14.97%) and gastroenterology (13.49±10.50%).

Conclusions: Our results suggest that there is higher existence of high risk patients for fragility fracture in clinical departments that carry out glucocorticoid therapy and/or treat the diseases which can cause secondary osteoporosis. Active early intervention for primary and/or secondary prevention by OLS is seemed to be necessary in these departments as well as in the department of orthopedic surgery.

P002

INCIDENCE AND RISK FACTORS FOR HIP FRACTURE IN ELDERLY PATIENTS UNDERGOING LUMBAR SPINE SURGERY: A NATIONWIDE DATABASE STUDY WITH 11-YEAR FOLLOW-UP

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Background: Spinal surgeries are currently performed frequently to treat various diseases. Impaired balance mechanisms and functional movement may occur after spinal surgery. Fall episodes may cause hip fractures, which further deteriorate quality of life and increase mortality. The incidence of hip fracture after spinal surgery is still unknown.

Methods: We used the National Health Insurance Research Database (NHIRD) to identify 3345 patients undergoing spinal surgery and a random dataset to identify 6690 age-, sex- and Charlson Comorbidity Index (CCI)-matched controls to compare the incidence of hip fractures in an 11-year follow-up period. We also enrolled 82,730 patients with spinal surgeries from the inpatient dataset to investigate the impact of different types of spinal surgeries.

Results: Patients who received spinal surgeries had higher risks of hip fractures (adjusted HR: 1.63, 95% CI: 1.20 - 2.21), especially patients aged 60-79 y and female patients. The patients with long-segment thoracolumbar spinal fusions had a significantly higher risk of hip fracture than those with only decompression (HR: 1.61, 95%CI: 1.36-1.91). Short segmental lumbar spine fusions also slightly increased the risk of hip fracture (HR: 1.14) compared with discectomies.

Conclusions: The incidence of hip fracture increased after spinal surgery, especially after fusion procedures and among female patients. Fall prevention for the elderly undergoing lumbar spinal surgery is necessary due to the high increase in hip fracture incidence after spinal surgery.

P003

COMPARISON OF 25-HYDROXYVITAMIN D3 SERUM LEVELS IN PATIENTS WITH PSORIATIC ARTHRITIS WITH OR WITHOUT PSORIASIS SKIN INVOLVEMENT

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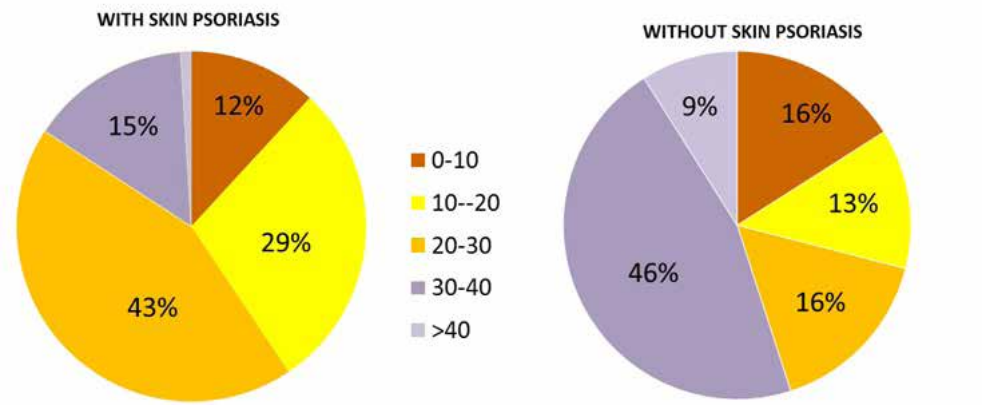
Objective: To determine 25-hydroxyvitamin D3 (25OH-D3) serum levels in patients with psoriatic arthritis (PA) and to assess differences according to the presence or absence of psoriasis skin involvement.

Methods: Observational retrospective study including patients with diagnosis of PA according to the CASPAR criteria who had at least one serum determination of 25OH-D3 in the last 36 months. Clinical and epidemiological data were collected, including treatment received and serum 25OH-D3 levels at baseline and within the subsequent 3 months if oral supplements had been initiated. Patients already receiving oral vitamin D supplements at baseline were excluded.

Results: Sixty patients met the inclusion criteria. 42 were female (70%), with a mean age of 47.6 y (range: 30-82). Psoriasis skin involvement was present in 40 patients and preceded onset of arthritis in 80% of them. Regarding 25OH-D3 levels, mean value was 17.99±13.23 ng/dL. In the global analysis, 7 patients (11.6%) had levels between 0-10 ng/dL, 22 patients (36.6%) between 10-20 ng/dL, 23 patients (38.3%) between 20-30 ng/dL, 6 patients (10%) between 30-40 ng/dL and 2 patients had ≥40 ng/dL. In our sample, 58.53% of patients with psoriasis skin involvement had 25OH-D3 levels higher than 20 ng/dL in contrast to the group without skin involvement, with only 37.5% reaching sufficiency levels. In the comparative analysis, patients with skin psoriasis had a mean 25OH-D3 serum level of 20.88 ng/dL, whereas patients without skin involvement had lower levels (mean value 19.42 ng/dL). Similarly, patients with skin psoriasis had more frequently 25OH-D3 levels between 20-30 ng/dL (insufficiency) compared to those without this manifestation, who presented lower levels (44% vs. 16%) without statistically significant difference. Results are shown in Figure 1.

Figure 1. 25-Hidroxyvitamin D3 levels in patients with Psoriatic arthritis with and without psoriasis skin involvement (ng/dL)



Conclusions: In patients with PA, the presence of skin psoriasis correlates with higher 25OH-D3 serum levels. This finding could be explained by the treatment received in these patients for moderate-severe skin involvement, which includes topical vitamin D analogs and phototherapy that could increase 25OH-D3 serum levels.

P004

SEASONAL VARIATIONS OF 25-HYDROXYVITAMIN D3 LEVELS AND ITS RELATION TO PTH LEVELS

M. A. Teran-Tinedo[1], C. Pijoan-Moratalla[1], W. A. Sifuentes-Giraldo[1], M. Vázquez-Díaz[1]

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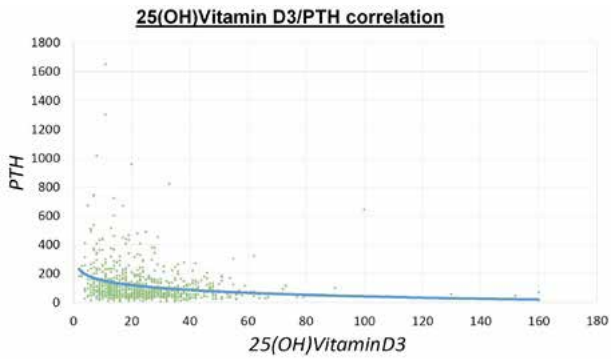
Objective: To analyze the relationship between 25-hydroxyvitamin-D3 (25OH-D3) and PTH levels and to determine its variation between the different seasons of the year.

Methods: We conducted an observational descriptive study collecting and analyzing 25OH-D3 and PTH serum levels of patients seen in our center between January-August 2017. The distribution of the frequencies of both variables was compared and Pearson´s correlation coefficient was used to analyze if linear relationship between them existed. The results were classified by date into three seasons: winter, spring or summer, assessing the mean seasonal oscillations of each variable and calculating correlation in each case. Different levels of 25OH-D3 were evaluated in order to identify differences in the grade of correlation.

Results: Serum samples from 847 patients were recollected. In the frequency distribution analysis, 58.84% of the patients had 25OHD3 levels lower than 25 ng/ml and 79% had PTH levels lower than 156 pg/ml. Correlation between both groups was analyzed, resulting in a negative correlation of -0.207 ($p<0.01$) (Figure 1). The mean values of 25OH-D3 were calculated for each seasonal period, establishing a mean level of 22 ng/mL for winter, 25 ng/ mL for spring and 29 ng/mL for summer. Regarding PTH levels, the mean values for each season were 118 pg/ml, 101 pg/ml and 72 pg/ml for each season (winter, spring and summer, respectively). PTH/vitamin D correlation was also assessed for each period: The result of Pearson´s correlation coefficient during the winter was -0.169 ($p<0.01$), in spring -0.249 ($p<0.01$), and in summer 0.069 ($p=0.52$). Correlation calculated with deficiency levels of 25OH-D3 (<30 ng/ml) was -0.18 ($p<0.01$), and with levels inferior than 10 ng/ml was -0.108 ($p<0.24$).



Conclusions: Linear correlation between levels of 25OH-D3 and PTH could not be established in our study, not even using levels classified as vitamin D deficiency. 25OH-D3 levels were found to increase from winter to summer; whereas PTH levels decreased inversely during these time periods without any linear correlation.

P005

VALUE OF FOREARM BONE MINERAL DENSITY IN SCREENING OSTEOPOROSIS IN FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To compare the forearm BMD between lumbar spine and left hip BMD by DXA and explore the diagnostic value of the forearm BMD in rheumatoid arthritis (RA) patients.

Methods: In the study, 200 postmenopausal female patients with established RA underwent DXA of the lumbar, left hip and nonsuperior forearm DXA at the same time. We compared BMD at different sites, and the diagnostic cutoff value and risk factors of abnormal axial BMD by forearm BMD was explored. Sensitivity and specificity were calculated to determine the correlation between cases of osteoporosis detected by the axial DXA scan and forearm. Multiple linear regression was used to find the risk factors of forearm BMD.

Results: (1) The mean age of the 200 postmenopausal female patients was 55.9±13.8 y. Based on their axial DXA data and fracture history, 170 (85.0%) patients had abnormal BMD (T-score<-1.0). (2) Compared to abnormal axial BMD group, forearm BMD in normal axial group was significantly decreased 0.33±0.13 g/cm^2 vs. 0.44±0.06 g/cm^2, t=4.29, P<0.01). (3) Forearm BMD was significantly lower in patients whose disease duration was more than 1 and positive anti-CCP antibody group. (4) The sensitivity and specificity for identifying osteoporosis in lumber were 70.2% and 77.4%, respectively, when the T-score threshold of forearm was defined as -2.65; however, the sensitivity and the specificity for identifying osteoporosis at left hip were 74.1% and 70.6% when T-score threshold of forearm was defined as -2.5. (5) Multiple regression analysis showed that higher age, long disease duration and positive anti-CCP antibody are risk factors of forearm BMD in RA patients.

Conclusion: Our study confirmed that DXA measurement performed of forearm BMD is capable of screening osteoporosis defined by axial BMD in female RA patients. Forearm BMD is lower in patients who had higher age, longer disease duration and positive anti-CCP antibody.

P006

SELECTIVE SEROTONIN RE-UPTAKE INHIBITORS REDUCES BONE FORMATION MARKERS IN INDIAN POPULATION: A CROSS-SECTIONAL STUDY

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[1]Pharmaceutical Medicine, School of Pharmaceutical Education and Research, Jamia Hamdard, [2]Department of Psychiatry, Hamdard Institute of Medical Science & Research, Jamia Hamdard [3]Department of Psychiatry, Lady Hardinge Medical College, [4]Department of Pharmacology, School of Pharmaceutical Education and Research, Jamia Hamdard, New Delhi, India

Objectives: Several preclinical and clinical studies show that selective serotonin reuptake inhibitors (SSRI) are associated with bone loss and increase in fracture risk but few studies also demonstrate that it does not any impact on the bone, hence we enlightened the effect of the use of SSRI's on bone turnover markers in the population. Our aims were (1) to investigate the association between selective serotonin reuptake inhibitors treatment and bone turnover markers in North Indian population; (2) to investigate the possible mechanisms involved in the observed effects.

Methods: Each consecutive patient on SSRI treatment fulfilling the eligibility criteria were included in the treatment group. Serum procollagen type 1 N-terminal propeptide (P1NP), C-terminal telopeptide (CTX), phosphorylation of cyclic AMP response element binding (pCREB) and RANKL level was measured in the patients on SSRI treatment and compared with a healthy individual.

Results: A total of 85 subjects recruited in the study 44 in treatment and 41 in control group. Serum P1NP (P-0.015) level decreased in patients on SSRI treatment whereas no changes were observed in the CTX level showing the reduction in bone formation and no effect on bone resorption. Patients on SSRI treatment also shows that serum pCREB level was also significantly reduced (P<0.000) and no significant (P=0.947) changes were observed in the serum levels of RANKL in SSRI treated individuals as matched to control group. After logistic regression analysis, the significance was seen pCREB, CTX, sun exposure, and BMI.

Conclusions: SSRI shown to affect bone formation that may lead to bone orders. Hence further, more RCT required to validate our results.

P007

INADEQUATE VITAMIN D LEVEL: ASSOCIATION WITH LOW ENERGY FRACTURES OF DISTAL RADIUS IN YOUNG PATIENTS AND ITS PREDICTORS IN KARACHI PAKISTAN

M. Muzzammil[1]

[1]Jinnah Postgraduate Medical Center, Karachi, Pakistan

Objectives: To determine association of inadequacy of vitamin D level with low energy fractures of distal radius and its predictors in young patients in Karachi, Pakistan.

Methods: This cross-sectional study conducted in Accident and Emergency Department of Jinnah Postgraduate Medical Center Karachi, Pakistan between January-June 2016. Patients visited hospital with low energy fracture of distal radius and fulfilled the inclusion and exclusion criteria. A questionnaire was designed and filled after taking consent includes details regarding age, gender, occupation, area of skin and sun exposure duration, dietary habits, type of clothing and residence used. Serum vitamin D3 levels were determined and compared with serum calcium levels, serum phosphorus and alkaline phosphatase levels. Serum vitamin D level <20 µg/ml defined as deficiency.

Results: Among 220 patients ranging from 12-45 y, mean 28±23.33. Females were 172(78.18%). Patients were predominantly married (68%). All patients had low energy distal radius fracture. Most had history of fall (58%), RTA (29) and assault (8%). Exposure of face and hands while outdoor by most of them was (52.2%). Sun exposure duration in majority of participant was 1-2 h/d (60%). Most were residents of apartments (46.6%). Variable coloured clothes used by majority participant (61%) and variable fabric (46%). 202(91.8%) patients had deficiency of vitamin D and correlated with duration of sunlight exposure significantly, also with exposure of large skin area, dietary consumption of vitamin D rich food and worn variable clothing colours. Serum phosphorus level and serum alkaline phosphatase level were negatively correlated with vitamin D significantly, whereas positively correlated with serum calcium.

Conclusion: Prevalence of vitamin D deficiency is very high in low energy fracture of distal radius in young population and sun exposure duration found to be most common predictor of inadequate vitamin D levels. To combat this epidemic government support and commitment are needed. A national food fortification program of vitamin D and campaign of public awareness to increase sunlight exposure and increase intake of vitamin D rich food are urgently needed.

P008

LEVEL OF OSTEOPOROSIS AWARENESS AND ITS RELATED FACTORS IN LOW DENSITY DISTAL RADIUS FRACTURES PATIENTS AGED 50 YEARS AND OLDER IN ASIAN COUNTRY

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Objective: Because of rapid increase in ageing population in Asia, osteoporosis has become one of the most prevalent and costly health problems. Distal radius fracture which is considered as one of the most frequent fractures seen is now shown to be associated with an increased risk of further fractures. Not much is known about the level of awareness of the condition among these patients of distal radius fracture in Asian country. Awareness and treatment of osteoporosis is significant to prevent further fractures in patients with osteoporosis. The aim of this study was to evaluate the awareness of osteoporosis and related factors in distal radius fracture patients.

Method: Cross-sectional study was conducted on low energy distal radius fracture patients aged 50 years and over who presented in Emergency Department of tertiary care hospital Karachi, Pakistan between January-December 2016. The questionnaire designed had three sections: demographic information, knowledge about osteoporosis and the risk factors for osteoporosis which was applied to all patients after receiving consent. Data were analyzed on SPSS 21 for statistical significance.

Results: Total number of patients with distal radius fracture were 480, 352(73.33%) female and 128(26.66%) male. The average age was 72.5 y, with a minimum of 50 and a maximum of 95 SD± 31.81. Only 98(20.41%) had awareness about osteoporosis, and 382(79.58%) did not know what it was. Considering the educational levels 210(43.75%) of patients were not able to read and write or ever went to school, 52.5%, 158(32.91%) did not get primary education and 112(23.33%) were secondary or high school graduates. Awareness of osteoporosis was directly related to the level of education. Regarding sources of information, 312(65%) of patients reported physicians/doctors as the main source of information, followed by television (15%), newspaper (10%). Other sources of information included: books (2%), family members (3%), friends (2%), radio (1%), pharmacists (1%) and internet (1%). 382(79.58%) indicated they did not know anything about osteoporosis and could not answer the remaining questionnaire. Lifestyle practices varied considerably. Nearly 15% reported smoking (observed mainly in male patients), 20% indicated they exercised for at least 30 min daily, and 1% reported drinking alcoholic beverages occasionally. Only small number of patients reported that they take calcium and vitamin D supplements on regular basis (25% and 15%, respectively). 382(79.58%) patients did not know what were the risk factors leading to the development of osteoporosis. More than three quarters of patients could not identify risk factors such as vitamin D deficiency, family history of osteoporosis, poor eating habits, smoking, alcohol consumption, increasing age, some medications and menopause. There appeared to be a relationship between education and awareness of risk factors. When compared to respondents with a lower educational level (high school or less), a greater proportion of respondents with higher educational level (college or postgraduate education) were able to identify risk factors such as lack of exercise (32% vs. 11%), vitamin D deficiency (22% vs. 8%), family history (18% vs. 8%), smoking (12% vs. 6%), alcohol consumption (6% vs. 2%), and certain medicines (5% vs. 1.5%).

Conclusion: With this study we were able to demonstrate that the level of awareness of osteoporosis in patients with distal radius fracture is very low and related to the educational level of the patients. The recognition of osteoporosis and thus starting its treatment earlier is necessary to prevent the osteoporotic fractures. Public education campaigns must address risk factors and the strategies to overcome those that are modifiable in order to prevent the development of osteoporosis and its complications.

P009

LEVEL OF PROTEIN CONCENTRATION ON PLATELET RICH PLASMA-1 INDUCED BY THE CALCIUM CHLORIDE

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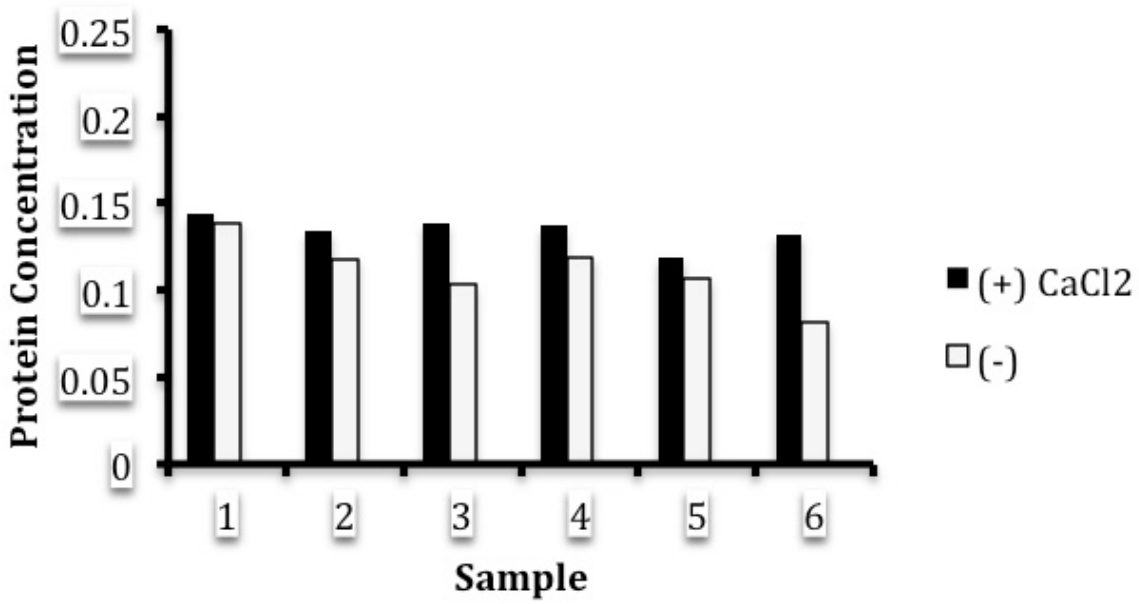
Objective: Platelet-rich plasma (PRP) is currently developed to obtain a more optimal healing therapy in improving the regenerative function of tissue, specifically for orthopedics. Activation by calcium is required to activate prothrombin into thrombin enzyme which is then changed into fibrinogen as one of the blood proteins for tissue-healing process.

Methods: This research was conducted experimentally to understand the concentration level of PRP-1 induced by $CaCl_2$ in Biochemistry Laboratory in Faculty of Medicine of Syarif Hidayatullah State Islamic University of Jakarta. PRP preparation: Venous blood from all the sample were centrifuged at speed and temperature that has been determined. After the first centrifugation, the top layer of buffy coat was collected, separating platelet from red blood cells (PRP-1). Other tubes added with $CaCl_2$ to be a positive control, and the other tubes to be a negative control. They were then incubated for 1 h. Determination of protein concentration: In order to determine its protein concentration, every sample was analyzed alternately using spectrophotometer tool.

Results: The result shows that the average value of protein concentration on PRP-1 induced by $CaCl_2$ increases (1.17915) compared with the average protein concentration of its negative control (0.46549). The increase of protein concentration is one of the indications that there is an increasing level of growth factors in the process of cell recovery. Based on the graphic, the average difference in protein concentration level between PRP-1 induced by $CaCl_2$ and its control is 0.02283. However, after statistical test with SPSS, the result of p-value from the concentration difference between positive and negative controls is 0.001 which indicates that the value is quite meaningful ($p<0.005$).



Conclusions: The result of this research is a protocol for making PRP-1 which is induced by $CaCl_2$ and optimized. It shows that there is an increase of protein concentration on PRP-1 induced by $CaCl_2$. The protein concentration level of PRP-1 induced by $CaCl_2$ has a higher value (1.17915) compared with its negative control (0.46549).

P010

HOW MANY VCF PATIENTS WERE EXPOSED TO ELEVATED MORTALITY RISK FROM THE 2009 DIMINUTION IN VERTEBRAL AUGMENTATION REFERRALS?

K. Ong[1], D. Beall[2], M. Frohbergh[1], E. Lau[3], J. Hirsch[4]

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Objectives: Following publication of the 2009 NEJM vertebroplasty (VP) studies, diminished balloon kyphoplasty (BKP) and VP volume ensued (Lindsey 2013). We evaluated the post-2009 decrease in BKP/VP volumes and estimated how many patients were exposed to elevated mortality risk.

Methods: The 100% U.S. Medicare dataset (2005-2014) was evaluated for the annual VCF prevalence and augmentation volume. A logarithmic rate was derived for the augmentation rate and BKP to VP ratio from 2005-2009 to project the corresponding levels in 2010-2014. A second method (uniform rate; average of 2007-2009) was also used. Differences in projected and actual rates/ratios were estimated. The absolute mortality risk of non-surgically managed (NSM) patients and their relative risk compared to BKP/VP patients from 2010-2014 were used to estimate the extra lives lost due to the BKP/VP volume reduction.

Results: 2,129,769 VCF patients were identified between 2005-2014. BKP/VP utilization was 20% in 2005, peaked at 24% in 2007-2008, and declined to 14% in 2014. Projected BKP/VP utilization was estimated at 25.7% (logarithmic rate) and 23.6% (uniform rate) in 2014, with a corresponding BKP/VP ratio of 2.6. Compared to projections, estimated diminution in augmentation volume in 2010-2014 was 59,389 to 75,452 patients. Because NSM patients had a higher mortality risk of 28% (5 y) to 52% (1 y) and 19% (5 y) to 34% (1 y) compared to BKP and VP patients, respectively ($p<0.001$), it was estimated that 5287 to 6814 extra lives may have been lost due to the reduction in augmentation volume in 2010-2014.

Conclusions: The 2009 NEJM VP trials may have changed referral/treatment pattern changes of VCF. In terms of the Medicare patients in the 100% dataset, this may have led to higher mortality risk for NSM patients and an estimated 5,287 to 6,814 extra lives may have been lost between 2010-2014 when extrapolated from referral pattern rates prior to publication of the trials.

Acknowledgements: Funding was received from Medtronic.

Disclosures: KO, EL, MF: employees of Exponent, Inc., a scientific and engineering consulting firm. Exponent received funding from Medtronic from this study. KO: Exponent has been paid fees by companies and suppliers for my consulting services on behalf of such companies and suppliers (Medtronic, Stryker Orthopaedics, Sanofi, Ferring Pharmaceuticals, Paradigm Spine, Pacira Pharmaceuticals, St. Jude Medical, Zimmer Biomet, Joerns Healthcare, SpineFrontier, Ethicon, DJO, Ossur, Karl Storz Endoscopy-America). EL: Exponent has been paid fees by companies and suppliers for my consulting services on behalf of such companies and suppliers (Medtronic, Stryker Orthopaedics, Sanofi, Ferring Pharmaceuticals, Paradigm Spine, Pacira Pharmaceuticals, Alcon Corp, Boston Scientific, CeramTec). MF: Exponent has been paid fees by companies and suppliers for my consulting services on behalf of such companies and suppliers (Medtronic) DB: Paid consultant (Benvenue, Lilly, Amendia, Medtronic, Stryker, Vertiflex); Paid presenter/speaker (Benvenue, Lilly, Medtronic, Stryker, Merit, Vertiflex); Stock/stock Options (Benvenue, Lilly, Amendia, Medtronic, Vexim); Board/committee member (Lilly, Amendia, Medtronic, SIR, Vexim); Research support (Lilly, Amendia, Medtronic).

P011

MID-CALF SKELETAL MUSCLE DENSITY AND ITS ASSOCIATIONS WITH ACCELEROMETER- DETERMINED PHYSICAL ACTIVITY, BONE HEALTH AND INCIDENT 12-MONTH FALLS IN OLDER ADULTS: THE HEALTHY AGEING INITIATIVE

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[1]Monash University, Clayton, Australia, [2]Umeå University, Umeå, Sweden

Objectives: To determine associations of mid-calf muscle density, an indicator of intramuscular fat infiltration, with objectively-determined physical activity, bone health and 12-month falls risk in community-dwelling older adults.

Methods: 2167 community-dwelling Swedish men and women who participated in the Healthy Ageing Initiative study at age 70 were included in this analysis. Mid-calf muscle density (mg/cm^3; higher values indicate lower intramuscular fat content) at the proximal tibia, and bone parameters at the distal and proximal tibia and radius, were assessed by peripheral quantitative computed tomography. Whole-body lean and fat mass, lumbar spine and total hip BMD were assessed by DXA. Participants completed the timed up-and-go (TUG) test, 7-day accelerometer measurements of physical activity intensity, and self-reported falls data were collected 6 and 12 months later.

Results: Only moderate/vigorous intensity physical activity, not sedentary or light activity, was positively associated with mid-calf muscle density (B=0.002 mg/cm^3 per minute; P<0.001). 258 (12%) participants experienced a fall within 12 months. After adjustment for confounders including sex, fasting glucose, average daily moderate/vigorous intensity physical activity, and total lean mass at baseline, each mg/cm^3 increase in mid-calf muscle density was associated with 4% and 11% reduced likelihood of experiencing a fall or multiple falls, respectively (both P<0.05). The association with multiple falls remained significant after further adjustment for TUG time (OR: 0.91 95%CI: 0.83, 0.99). In multivariable models, mid-calf muscle density was not associated with total hip BMD, was negatively associated with lumbar spine BMD (B=-0.003, 95%CI -0.005, -0.003 g/cm^2), and at the radius, was positively associated only with proximal cortical density (B=0.784, 95%CI 0.246, 1.323 mg/cm^3). However, at the tibia, muscle density was positively associated with distal total and trabecular BMD, and also proximal total and cortical BMD, cortical thickness and stress-strain index (all P<0.05).

Conclusions: Higher mid-calf muscle density is independently associated with decreased likelihood for multiple incident falls and appears to have localised positive effects on bone structure. Improvements in lower-limb muscle density may be achievable through increasing participation in moderate/vigorous intensity activity and could potentially reduce fracture risk in older adults.

P012

USEFULNESS OF SERUM CARDIAC BIOMARKERS FOR PREDICTING IN-HOSPITAL CARDIAC COMPLICATIONS IN ACUTE HIP FRACTURE: A PROSPECTIVE COHORT IN 20 HIGH SURGICAL RISK PATIENTS WITH AGE OVER 55 YEARS

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Background: Serum cardiac biomarkers have recently been demonstrated to be useful for predicting perioperative complication after hip fracture (HF). However, no previous study has revealed the comparative efficacy of different cardiac biomarkers in high surgical risk HF patients.

Methods: A prospective study was conducted, from June to December 2016, in 20 acute HF patients with American Society of Anesthesiologists (ASA) grade 3 or 4. All patients received blood test for high sensitivity troponin-I (hsTnI) and N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP) at the time of admission and 24-h postoperatively. Perioperative data, in-hospital, 3-month and 6-month postoperative complications were collected. The complications were classified as cardiac and non-cardiac HF-related complications.

Results: The average patients' age was 79±8 y. Six patients (30%) were male. The incidence of PCI was 30% (n=6). None of the patients (0%) died during the 6-month postoperative follow-up period. In-hospital overall, cardiac, and non-cardiac complications were found in 12(60%), 5(30%), and 7(45%), respectively. The mean serum hsTnI levels in the patients with cardiac complication were significantly greater than those in the patients without cardiac complication at both time of admission (99.5 ng/mL vs. 5.5 ng/mL, p=0.006) and 24-h postoperatively (28.6 ng/mL vs. 9.4 ng/mL, p=0.013). The mean serum NT-proBNP levels in patients with cardiac complication were also greater, but nonsignificant, compared to those in the patients without cardiac complication at both time of admission (2299 pg/mL vs. 281 pg/mL, p=0.239) and 24-h postoperatively (2266 pg/mL vs. 586 pg/mL, p=0.061). The other significant preoperative predictors for cardiac complication were low hemoglobin level (p=0.014) low glomerular filtration rate level (p=0.039), and ASA grade 4 (p=0.005).

Conclusion: In-hospital cardiac complication in high-risk HF patients was significantly associated with the abnormal rise of serum hsTnI level. Therefore, we recommended using the hsTnI test in the perioperative evaluation in high-risk HF patients.

P013

MULTIVARIATE ANALYSIS OF PERIOPERATIVE RISK FACTORS FOR PREDICTING NONUNION AFTER ATYPICAL FEMORAL FRACTURES TREATMENT

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Objective: To correlate the perioperative surgical factors and nonunion after treatment of atypical femoral fractures (AFFs).

Methods: Forty-four surgically treated displaced AFFs, between 2010-2016, were retrospectively reviewed. All patients had been followed for at least 12 months postoperatively. Perioperative data related to fracture and treatment were collected, and predictive factors for nonunion were analyzed using logistic regression analysis.

Results: Incidences of nonunion was 27.3% (n=12). All patients underwent plate fixation (n=4) were all resulted in nonunion (100%). On multivariate analysis, significant predictive factors for nonunion after AFF treatment were demineralized bone matrix (DBM) augmentation (OR 0.05, 95%CI 0.00-0.81, p=0.04) and diabetes (OR 14.50, 95%CI 1.08-194.45, p=0.04).

Conclusions: Regarding AFF treatment, if possible, an anatomical reduction with intramedullary nail, with or without biological enhancement such as DBM augmentation, should be considered to avoid the risk of nonunion, especially in the diabetes patients.

P014

REFRACTURE: AN EPIDEMIOLOGIC STUDY OF THE OSTEOPOROTIC FRACTURES PRODUCED IN ANDALUSIA BETWEEN 2000-2010

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Objectives: To evaluate the incidence of secondary osteoporotic fractures in Andalusia between the years 2000-2010 and its distribution according to gender, age range, location, comorbidity, seasonality, evolutive tendency and mortality.

Methods: It was an observational, longitudinal, retrospective study. The general hospitals of the Andalusia Community were included with a total result of 518 beds.

Results: In the 11 years studied, 5551 patients presented a total number of 5815 osteoporotic refractures, representing a 6% of the total number (95%CI: 5.88-6.18%). 82.8% occurred in women and 17.2% in men. The average age was higher in women than in men (79±9 vs. 76±11 y) and the gender (female/male) proportion was 4.8/1. From the 5815 refractures, 5300 were a second fracture (5.5% of the total [95%CI: 5.35-5.64%]), of which 82.7% occurred in women and 17.3% in men. The rest of refractures were distributed in 481 third fractures, 33 fourth fractures and finally one patient suffered a fifth fracture. Regarding the second fractures, most of them were produced in patients older than 70 years old, in particular older than 85, where 1.551 fractures occurred, accounting 28% of the total (95%CI: 26.75-29.13%). It was in 2008, when a major incidence was found (612 fractures, accounting a 11% of the total [95%CI: 10.19-11.86%]). The location of the majority of the second fractures was the contra lateral hip (4.408). That corresponds to 82.3% of the total refractures (95%CI: 82.6-84.57%) and 4.6% of total fractures (95%CI: 4.43-4.7%). On the other hand, it was in winter when the most part of the fractures were produced, being the results statistically significant.

Conclusions: Our results are within the international average of refractures (2-11%), being very similar to the ones of other Mediterranean countries and below the USA and Nordic countries results. The high refracture incidence, in particular the second one, must be studied with attention, in order to improve the prevention of secondary fractures, especially in winter.

P015

EPIDURAL ANALGESIC INJECTIONS AND THE RISK OF OSTEOPOROSIS IN SPONDYLOSIS PATIENTS: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Objective: Epidural analgesic injections (EAI) involve local anesthetic, steroids, or both into the spinal epidural space between ligamentum flavum and dura. The procedures are considered a reasonable approach for lumbosacral radiculopathy. The refractory period to analgesic medications may prolong over six weeks, which makes an option of nonsurgical management. However, recent studies have revealed the negative effect of epidural steroid injection on BMD. We aimed to study the association between EAIs and the risk of osteoporosis based on the nationwide population database.

Methods: In this study, 5253 patients diagnosed with spondylosis and have received EAIs were identified from National Health Insurance Research Database (2000-2013). Each patient was randomly selected and frequency-matched with an individual without epidural analgesic injections by age, sex, and the index year.

Results: The incidence rates of osteoporosis in EAIs group and non-EAIs group were 8.42 and 7.30 per 1000 person-years, respectively, in the spondylosis cohort. The EAIs group had a higher risk of osteoporosis [adjusted subhazard ratio (aSHR)=1.21, 95%CI=1.03-1.42]. The other correlated risk factors included male (aSHR=1.33, 95%CI=1.00-1.77), lowest urbanization level (aSHR=1.42, 95%CI=1.07-1.89), primarily retired, unemployed, or low income populations (aSHR=1.86, 95%CI=1.14-3.06).

Conclusion: EAIs in spondylosis are related to higher risks of osteoporosis. The therapy should be recommended with caution, especially in patients with correlated risk factors, such as osteoporotic fracture, lower social economic status and retired or unemployed status.

P016

LONGITUDINAL ASSOCIATION BETWEEN OBJECTIVELY MEASURED SEDENTARY TIME AND PHYSICAL ACTIVITY WITH MUSCLE STRENGTH, BALANCE AND FALLS IN A COHORT OF AUSTRALIAN MIDDLE-AGED WOMEN

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Objectives: The potential long-term effects of sedentary time and physical activity on muscle strength, balance and falls in middle-aged women are yet to be examined. This analysis aimed to describe longitudinal associations between sedentary time, physical activity and these outcomes in middle-aged women.

Methods: 308 women aged 36-57 y were followed for 5.3 y. Linear mixed-effects was used to examine associations of sedentary time and time spent in light and moderate to vigorous physical activity (MVPA) (by Actigraph GT1M accelerometer) with changes in lower limb muscle strength (LMS) and balance (timed up and go [TUG], functional reach [FRT], lateral reach [LRT], and step tests [ST]). Log-binomial regressions was used to examine the association of sedentary time and these activities with one-year retrospective incidence of falls at follow-up (n=239).

Results: After adjusting for confounders and MVPA, sedentary time was detrimentally associated with falls incidence (relative risk=1.28/unit, 95%CI: 1.01, 1.63) but was not associated with LMS or balance measures. One standard deviation increase in MVPA (28 min) was detrimentally associated with FRT (β=-0.69 cm/SD, 95%CI: -1.37, -0.01) but no other outcomes. This association was attenuated and no longer statistically significant after further adjustment for sedentary time. Light physical activity was not associated with any outcomes.

Conclusions: This the first study to show that shorter sedentary time in middle-age is associated with reduced risk of falls, independent of MVPA. This supports providing advice to reduce sedentary time as part of health promotion messages for maintaining musculoskeletal health in younger women.

P017

RHEUMATOID ARTHRITIS (RA) PATIENTS ON VEGAN DIETS, HARMFUL OR BENEFICIAL? A REGISTRY STUDY OF RA WITH OSTEOPOROSIS/FRACTURE

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Objectives: To explore the impact of long-term vegan diet on disease activity, BMD or prevalent fracture in RA patients.

Methods: This is an interim analysis of an RA registry, conducted at CGMHK for RA-related osteoporosis/fracture. Consecutive RA patients who visited the rheumatology clinic at CGMHK since September 1, 2014 and fulfilled the 1987 American College of Rheumatology (ACR) revised criteria (14) or the 2010 ACR/European League Against Rheumatism classification criteria for RA were enrolled. Clinical and biological assessments included demographic data (age, height, weight, BMI, presence and/or levels of anti-CCP, and RF). Disease duration was defined as the time that elapsed between the onset of first disease-related symptoms and enrollment. RA disease activity was assessed using the DAS28-ESR. Medication history was collected. In addition, lifestyle, evidence of previous fragility fracture (history or radiographic), and risk factors of fragility fracture in FRAX® tool were recorded. The 10-y probability of major and hip fracture (FRAX score, major and hip), calculated by the FRAX tool (Taiwan version), of each patient was collected as well. The participants were categorized into two groups according to participants on vegan diet ≥3 y (Group A) or not (Group B).

Results: The demographic and clinical characteristics of the 653 participants is illustrated in Table. There were 37(5.7%) and 616(94.3%) participants in Group A and B, respectively. The study population consisted of women mainly (n=559, 85.6%). The age, gender, BMI, DAS28 (ESR), ESR, disease duration, BMD (vertebral, hip, FN), prevalence of osteoporosis/previous fracture, fracture risk factors in FRAX tool, and FRAX score were comparable between groups. While the median (IQR) levels of 25(OH) Vit D (ng/ml) and iPTH (pg/ml) were 15.9 (11) vs. 22.0 (9.7) (p=0.0006) and 49.3(37.4) vs.39.3(26.4) (p=0.0102) in Group A and B, respectively.

Conclusions: RA patients on long-term vegan diet had similar disease activity, BMD levels, rate of osteoporosis and prevalent fracture as those on nonvegan diet but had lower 25(OH) Vit D and higher iPTH levels. The effects of long-term vegan diet on RA patients, either disease activity or BMD/fracture, needs further investigation.

Table. The demographics and clinical characteristics of participants

Variables	Group A (n=37)	Group B (n=616)	P
Age	59(12.0)	59(14.5)	0.6218
Gender			
Female (n, %)	35(94.6)	524(85.1)	0.1088
BMI (kg/m^2)	22.6 (3.3)	23. 2 (5.2)	0.2280
Anti-CCP			
+ (n, %)	20 (57.1)	420 (70.2)	0.1020
RF			
+ (n, %)	19 (54.3)	417 (68.4)	0.0836
ESR (mm/h)	16 (19)	16 (21)	0.8957
CRP (mg/L)	4.1 (8.4)	2.6 (7.1)	0.8012
DAS28 (ESR)	3.2 (1.1)	3.2 (1.7)	0.8778
25(OH) Vit D (ng/mL)	15.9 (11)	22.0 (9.7)	0.0006
iPTH (pg/mL)	49.3 (37.4)	39.3 (26.4)	0.0102
BMD (g/cm^2)			
FN	0.600 (0.161)	0.620 (0.144)	0.2466
Hip (total)	0.772 (0.239)	0.776 (0.178)	0.4599
Spine (L1-4)	0.811 (0.293)	0.862 (0.208)	0.1121
Prevalent fracture (n, %)	14(37.8)	178(28.90)	0.2463

BMI, body mass index; RF, rheumatoid factor; iPTH, intact parathyroid hormone; BMD, bone mineral density; FN, femoral neck, Data expressed as median (IQR)

P018

COMPLICATED TIBIAL PLATEAU FRACTURES IN YOUNG PATIENTS: FUNCTIONAL OUTCOME WITH DUAL PLATING VIA 2 INCISION TECHNIQUE EXPERIENCE OF TWO PUBLIC SECTOR HOSPITALS OF KARACHI PAKISTAN

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Objective: Motorbike accidents contribute one of the most important factors of tibial plateau fracture among young populations. This prospective study was designed to evaluate the functional outcomes of dual plating via a 2incisions technique for the fixation of complicated bicondylar fractures in young patients in Pakistan.

Methods: This prospective study include 94 cases of type V and VI tibial plateau fractures of young patients age range from 15-45 y, operated between January 2014 and Dec 2016 conducted in two public sector hospitals of Karachi, Pakistan. Exclusion criteria include patients with multiple fracture on same side or same bone, age more than 45 y, open contaminated fracture, open fracture and patients with head injuries. All cases were operated by anterio-lateral and posterior-medial approach and dual plating through these double incisions. These all cases were followed for a minimum of 24 months.

Results: A total of 94 patients (45 single plating and 49 dual plating) were operated during the study period of two. Both groups were somewhat similar in age, mechanism of injury, fracture pattern. Bone graft was used in majority of cases.74 (78.7%) applied graft. It took approximately 4-5 months for the fractures to get united. There was no malunion, nonunion or implant failure.10 cases with superficial infection in wounds of dual plating group which were treated with culture sensitive antibiotics for average two weeks, healed subsequently. A total of 38 (77%) patients in a double plating group regained full flexion (135°) and full extension (0°) with a good alignment and no pain and instability as compared to single plating group, seen in 30 (66%) patients at follow-up.

Conclusion: Dual plating by two incision method resulted in better functional outcome regarding limb alignment and range of movements at knee joint.

P019

ROLE OF ALENDRONATE/TERIPARATIDE IN STEROID INDUCED OSTEOPOROSIS IN DEVELOPING COUNTRIES

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Background: Bisphosphonate therapy is the standard of care for the prevention and treatment of steroid-induced osteoporosis. Studies of anabolic therapy in patients who are taking long-term steroids and are at high risk for fracture are lacking.

Methods: This is double-blinded randomized controlled trial that was conducted in Civil Hospital Karachi from January 2015 to June 2017. In this study comparison of alendronate with teriparatide in 214 women and men with osteoporosis (ages, 22-65 y) who had received glucocorticoids for at least 3 months (prednisone equivalent, 5 mg daily or more). A total of 107 patients received 20 µg of teriparatide once daily, and 107 received 10 mg of alendronate once daily. The primary result was the change in BMD at the lumbar region. Secondary outcomes included changes in bone mineral density at the total hip and in markers of bone turnover, the time to changes in BMD, the incidence of fractures, and safety.

Results: Conclusively, the mean (±SE) BMD at the lumbar spine had increased more in the teriparatide group than in the alendronate group (3.2±0.5% vs. 6.9±0.6%, P<0.001). A significant difference between the groups was reached by 6 months (P<0.001). At 12 months, BMD at the total hip had increased more in the teriparatide group. Fewer new vertebral fractures occurred in the teriparatide group than in the alendronate group (6.0% vs. 0.4%, P=0.004); the incidence of nonvertebral fractures was similar in the two groups (3.5% vs. 5.4%, P=0.36). Significantly more patients in the teriparatide group had at least one elevated measure of serum calcium.

Conclusions: Patients with osteoporosis who were at high risk for fracture, BMD increased more in patients receiving teriparatide than in those receiving alendronates.

P020

A STATISTICAL METHOD TO PREDICT TIME TO RECURRENT FRACTURES AND LIFE EXPECTANCY IN FRACTURE PATIENTS

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Studies showed that previous fractures could greatly increase the risk of subsequent fractures and patients who suffered multiple fractures had much higher mortality rate than that of patient without a previous fracture. Accurate predict when a subsequent fracture can happen, and the life expectancy is important for clinicians, care providers and patients.

Predict mean time to failure (MTTF) or mean time between failures (MTBF) and median survival time are quite common in Engineering reliability researches. In medical literature most prediction models are used to predict probability of an event during a certain period. However, provide a probability or a risk (another name of the probability) seems difficult to be understand by general population. In practice, the time axis remains the most natural measure for both clinicians and patients. It is much easier to understand a survival time rather than a subjective assessment of probability of survival to a certain time point. In this paper we introduce a statistical method to predict different survival times and assessed the accuracy of the point predictions. The method to construct confidence interval for the predicted survival time was also discussed.

P021

A RANDOMIZED DOUBLE-BLINDED PLACEBO CONTROLLED TRIAL OF ERGOCALCIFEROL 40,000 VS. 100,000 IU PER WEEK FOR VITAMIN D INADEQUACY IN INSTITUTIONALIZED POSTMENOPAUSAL WOMEN

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Objective: Vitamin D inadequacy is common in institutionalized postmenopausal women. The objective was to evaluate efficacy and safety of ergocalciferol 40,000 vs. 100,000 IU per week for 12 weeks for vitamin D inadequacy in institutionalized postmenopausal women.

Methods: A randomized double-blinded placebo-controlled trial was conducted in 94 institutionalized subjects with baseline 25(OH)D levels <30 ng/mL. Subjects were randomized to receive ergocalciferol 40,000 (standard dose) or ergocalciferol 100,000 IU (high dose) per week. Serum 25(OH)D levels, calcium, phosphate, handgrip strength, time up and go (TUG) test and quality of life by EQ-5D-5L were measured at baseline and 12 weeks after randomization.

Results: Of the 94 subjects enrolled, 85 subjects completed the study. Subjects in the high dose group had higher mean 25(OH)D levels than subjects in the standard group (51.73±19.35 and 34.5±9.12, p<0.001). More subjects in the high dose group (90.9%) achieved optimal 25(OH)D levels (>30 ng/mL) than in the standard group (65.9%), p=0.007. In a subgroup analysis of subjects with vitamin D deficiency (<20 mg/mL, n=44) and severe vitamin D deficiency (<10 ng/mL, n=9), more subjects in the high dose group achieved optimal 25(OH)D levels than those in the standard group (88% and 100% vs. 47.4% and 16.7% with p of 0.007 and 0.018, respectively). There were no differences in handgrip strength, TUG, EQ-5D-5L and adverse events between groups.

Conclusions: More subjects received high dose ergocalciferol achieved optimal 25(OH)D levels than those received standard dose. High dose ergocalciferol is preferred to optimize 25(OH)D levels in subjects with severe vitamin D deficiency.

P022

OSTEOPOROSIS AND HORMONE TREATMENT IN AN OUTPATIENT GYNECOLOGY CLINIC

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Background: A favorable BMD response to hormone replacement treatment can be expected in most postmenopausal women. This applies, in particular, if the women do not smoke and have a moderate/low alcohol intake, a high body mass and a low initial hip BMD. We evaluated which treatment regimens were used for bone loss prevention when women came to our gynecology clinic.

Methods: Retrospective follow-up on women with osteoporosis referred to the outpatient gynecology clinic. Hospital chart data from all regional hospitals were collected from the electronic journals together with paraclinical data, DXA results, medications and prescriptions in current or previous use. The national prescriptions registry was searched for each patient's historical use of any anti-osteoporotic and hormonal drugs.

Results: Seventy-five women were referred for gynecologic examination with a mean age of 68±16 y, BMI of 25±5 kg/m^2 and a T-score of -2.5±0.7. They were followed up for 4 y (range: 1-7 y). In total 42 women (56%) had fractures and half of them had experienced two or more. These multiple fractures nearly all involved vertebral compression fractures; yet, 17 and 11% had experienced radial and hip fractures, respectively. Only eight (11%) women were premenopausal but 38% of these had fractures already. Fractures seemed neither associated with ASA grouping, hormone treatment, former secondary hyperparathyroidism nor thyroid disorders. Hormone replacement treatment had only ever been used in 13% of the women. Surprisingly, 25% of all women were *not* on bisphosphonates, 20% did *not* take vitamin D/Calcium and 9% did *not* take either and none were associated with fracture status. The use of bisphosphonates and supplementation was, however, associated with T-scores ($p<0.05$). Eighteen women (24%) had a T-score indicating only osteopenia; but even so, seven (38%) of these women had experienced fractures and three (17%) two or more fractures. Age, BMI and T-scores showed no association with numbers of fractures (ANOVA). ASA score showed an association with age and the women presented considerable comorbidity beside osteoporosis and gynecology issues.

Conclusion: Despite the diagnosis of osteoporosis bone loss prevention by means of hormone replacement treatment was surprisingly rare. The observed high fracture risk and prevalence in the women with osteopenia is in concordance with several interventional, randomized studies.

P023

TUMOR-INDUCED OSTEOMALACIA: EXPERIENCE FROM THREE TERTIARY CARE INSTITUTES IN INDIA

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Tumour-induced osteomalacia (TIO) is a rare para-neoplastic syndrome characterized by recalcitrant hypophosphatemia. In most cases, fibroblast growth factor 23 (FGF23) produced by small, benign, mesenchymal tumors causes phosphaturia, leading to hypophosphatemia. TIO is rare and reports from the Indian subcontinent are scarce, with most being single center experiences involving few patients. Herein, we present the clinical, biochemical, radiological and treatment details of 30 patients of TIO diagnosed at three tertiary care hospitals in India.

Patients with persistent hypophosphatemia (despite correction of hypovitaminosis D), normocalcemia, elevated alkaline phosphatase, low TmP GFR and elevated or inappropriately normal FGF 23 levels were labeled as having TIO. They were sequentially subjected to functional followed by anatomical imaging. Patients with a well-localized tumor underwent excision; others were put on phosphorous and calcitriol supplementation.

The mean age at presentation was 39.6 y with a female preponderance (F:M=3:2). Bone pain (83.3%) and proximal myopathy (70%) were the chief complaints followed by fractures in 40% of cases. The mean delay in diagnosis was 3.8 y. Tumors were clinically detectable in 4 patients (13.3%). The mean serum phosphate was 1.5 mg/dl with a median serum FGF23 level of 518.1 RU/ml. Somatostatin-receptor based scintigraphy was found to be superior to FDG-PET in tumor localization. Lower extremities were the most common site of the tumor (72%). Tumor size was positively correlated with serum FGF23 levels. Twenty-two patients underwent tumor resection and 16 of them had phosphaturic mesenchymal tumors. Surgical excision led to cure in 72.7% of patients whereas disease persistence and disease recurrence were seen in 18.2% and 9.1% of cases, respectively. At the last follow-up, serum phosphate in the surgically treated group was significantly higher than in the medically managed group.

P024

THE OPTIMAL DOSE OF VITAMIN D MAINTENANCE IN ELDERLY WOMEN: A 6-MONTH FOLLOW-UP, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL

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Objective: Supplementation of vitamin D 800 unit daily as recommended by Thai endocrine society, appears to be insufficient to maintain vitamin D level (25-hydroxy (OH) vitamin D level ≥30 ng/mL) in elderly woman. Our aim was to compare vitamin D levels in elderly women between a group received standard recommended dose and a group received high dose vitamin D supplementation (recommended dose plus vitamin D_2 20,000 unit weekly).

Methods: Vitamin D-insufficient women (25(OH)D level <30 ng/mL), age 61-89 y were treated with vitamin D_2 60,000 unit weekly at least 12 weeks until achieved targeted adequate 25(OH)D level (≥30 ng/mL). All subjects received recommended dose vitamin D_3 800 unit daily. Patients were randomized to receive placebo or vitamin D_2 20,000 unit weekly (treatment group) for 24 weeks. Blood samples, handgrip strength, falls, time-up and go test and EuroQOL 5 dimensions questionnaire (EQ-5D) were collected at randomization (R), 12 weeks(V1) and 24 weeks(V2) after randomization.

Results: Among 69 subjects, 34 subjects received placebo and 35 received vitamin D_2 20,000 unit weekly. There were significant differences in mean±SD of 25(OH)D levels between placebo and treatment groups at 12 weeks and 24 weeks (31.36 vs. 40.86, p<0.001) and (27.69 vs. 38.10, p<0.001), respectively. There were no differences between handgrip strength, falls, time-up and go test and EQ5D between placebo and treatment group in all visits. There was no serious adverse event during the study.

Conclusion: More subjects in treatment group were able to maintain adequate vitamin D at 6 months follow-up than those in placebo group. After adequate vitamin D supplementation, subjects should receive higher maintenance dose of vitamin D than recommended dose.

P025

CONSTITUTIVE MELANIN DENSITY IS ASSOCIATED WITH HIGHER 25-HYDROXYVITAMIN D, TOTAL BODY BMD AND FRACTURE RISK IN OLDER CAUCASIAN ADULTS

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Objective: Higher cutaneous melanin reduces vitamin D3 production. This may impact lifetime vitamin D status and increase fracture risk. We examined the relationship between spectrophotometrically determined constitutive melanin density, fracture risk factors and outcomes in a cohort of older Caucasian adults.

Methods: 1072 community-dwelling adults aged 50-80 y had constitutive melanin density quantified using spectrophotometry. Sun exposure, skin phenotype, nonmelanoma skin cancer (NMSC) prevalence, smoking status and symptomatic fractures were assessed by questionnaire. BMD, falls risk, physical activity and 25-hydroxyvitamin D (25OHD) were measured using DXA, the short form Physiological Profile Assessment, pedometer and radioimmunoassay, respectively.

Results: Higher melanin density was independently associated with greater ability to tan (RR=1.27, $p<0.001$), less propensity to sunburn (RR=0.92, $p<0.001$), fewer lifetime sunburns (RR=0.94, $p=0.01$), current smoking (RR=1.41, $p<0.001$), female sex (RR=1.24, $p<0.001$) and less photodamage (RR=0.98, $p=0.01$). The associations between melanin density and sun exposure, sun protection behaviours and NMSC prevalence were not significant after accounting for skin phenotype and sun exposure, respectively. 25OHD was associated with higher melanin density ($\beta=2.05$, $p=0.001$). The association between melanin density and total body BMD ($\beta=0.007$, $p=0.04$) became nonsignificant after adjustment for 25OHD. There was no association between melanin density and physical activity, falls risk or BMD at other sites. Higher melanin density was associated with increased risk of prevalent fractures (RR=1.09, $p=0.01$), including vertebral (RR=1.49, $p=0.015$), nonvertebral (RR=1.07, $p=0.048$) and major osteoporotic fracture (RR=1.13, $p=0.03$).

Conclusions: Higher constitutive melanin density underpins a less photosensitive skin phenotype, permitting greater sun exposure with fewer sequelae and yielding higher 25OHD and, potentially, total body BMD. Paradoxically, prevalent fracture risk was increased with higher melanin density independent of its other associations.

P026

DISTAL RADIUS BONE MICROARCHITECTURE: WHAT HAPPENS BETWEEN AGE 25 AND OLD AGE?

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Objective: To describe differences in bone geometry, volumetric BMD (vBMD) and microarchitecture parameters at the distal radius between older and young adults.

Methods: Bone geometry, trabecular and cortical parameters and vBMD at distal radius were collected using HR-pQCT and analysed using StrAx in 201 participants from the prospective Tasmanian Older Adult Cohort study (mean age 72.2 y, range 61.9-89.4 y, female 47%) and 196 participants from the T-bone study (mean age 25.5 y, range 24.1-27.6 y, female 38%). Unpaired t-tests were used to compare means.

Results: Older adults had larger cross-sectional area of the transitional zone (outer 30.96 mm^2 vs. 28.38 mm^2, inner 36.34 mm^2 vs. 32.93 mm^2) and thicker transitional zone bone area (outer 0.57 mm vs. 0.54 mm, inner 0.71 mm vs. 0.65 mm) compared to young adults. In addition, the prevalence of cortical porosity (54% vs. 49%) and porosity of the transitional zone (outer 42% vs. 37%, inner 82% vs. 81%) were higher in older adults than in young adults. vBMD of total bone area (370.73 mg hydroxyapatite (HA)/cm^3 vs. 424.57 mg HA/cm^3), vBMD of transitional zone (outer 899.29 mg HA/cm^3 vs. 959.52 mg HA/cm^3, inner 385.47 mg HA/cm^3 vs. 408.34 mg HA/cm^3), cortical and trabecular vBMD (734.51 mg HA/cm^3 vs. 801.04 mg HA/cm^3, 144.19 mg HA/cm^3 vs. 178.02 mg HA/cm3) were all significantly lower in older adults. There were no significant differences between older and young adults in total, cortical, and trabecular cross-sectional area or cortical and trabecular thickness.

Conclusion: Compared to young adults at the time of peak bone mass, older adults have an increase in transitional zone bone size, decreased vBMD measures and increased prevalence of porosity, with the most significant differences in the compact cortex.

P027

2,3,5,4'-TETRAHYDROXYSTILBENE-2-O-B-D-GLUCOSIDE EXERTED OSTEOPRESERVE EFFECTS IN MICE WITH HYPERGLYCEMIA INDUCED BY STREPTOZOTOCIN

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Objective: 2,3,5,4'-tetrahydroxystilbene-2-O-β-D-glucoside, also named as tetrahydroxystilbene glucoside (TSG), is an active component from medicinal herb *Polygonum multiflorum* Thunb and is able to block the activity of the tissue renin-angiotensin system (RAS), which is involved in development of hyperglycemia-induced osteoporosis. This study aimed to determine if therapy with TSG could alleviate bone deteriorations in diabetic mice model induced by streptozotocin.

Methods: Diabetic mice were treated with TSG for 6 weeks. HE staining, TRAP staining and micro-CT were performed on the distal metaphysis of femur. Calcium content in serum, urine and femur was measured. The mRNA and protein expressions of regulators and RAS components in bone and MC3T3-E1 cell were determined by PCR and immunoblotting, respectively.

Results: The diabetic mice showed the loss of trabecular bone mass and the changes of trabecular bone micro-architectural parameters as well as increase in number of TRAP-positive osteoclasts at the distal metaphysis of femur when compared to those of nondiabetic mice. Treatment with TSG significantly elevated calcium content in serum and bone and improved biological parameters of trabecular bone, accompanied by increasing mRNA expression of RUNX-2, COL-I and OCN and protein expression of β-catenin as well as downregulating protein expression of RAS components including renin and AT1R. In addition, TSG repressed diabetes-induced decrease in ratio of OPG/RANKL expression and increase in sclerostin expression in bone. The similar effects of TSG on osteoblasts-specific genes were found in MC3T3-E1 cells.

Conclusions: The present study demonstrated the osteopreserve effects of TSG in diabetic mice and the underlying mechanism might be attributed to its regulation on osteogenesis and osteoclastogenesis.

Acknowledgments: This work was supported in part by Essential Drug Research and Development (2018ZX09201008-003-032) from Ministry of Science and Technology, Hundred Talents Program from Shanghai Municipal Commission of Health and Family Planning (2018BR03), and Longhua Medical Innovation Team Program (LYCX-01).

P028

SKELETAL BENEFIT/RISK OF LONG-TERM DENOSUMAB THERAPY: A VIRTUAL TWIN ANALYSIS OF FRACTURES PREVENTED TO SKELETAL SAFETY EVENTS OBSERVED

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Osteoporosis (OP) is a chronic disease, yet skeletal safety events — atypical femoral fracture (AFF) and osteonecrosis of the jaw (ONJ) — remain a concern with long-term treatment. Ten years of denosumab (DMAb) therapy in postmenopausal women with OP has demonstrated sustained and low vertebral and nonvertebral fracture rates, with low adverse event rates (Bone *Lancet Diabetes Endocrinol* 2017). Here, we generated a DMAb skeletal benefit/risk ratio derived from observed data and model-based estimates from the FREEDOM trial and its Extension.

Exposure-adjusted subject incidence per 100,000 subject-years of clinical, major osteoporotic, vertebral, nonvertebral, and hip fractures was calculated for long-term (LT) subjects randomized to DMAb in the 3-year FREEDOM trial and enrolled in the 7-year Extension (follow-up time on DMAb 3 to 10 years). Due to the lack of a long-term placebo group, fracture rates in a hypothetical cohort of 10-year placebo controls (virtual twins [VT]) were estimated: A regression model was generated using data from subjects randomized to PBO during FREEDOM and then enrolled in the Extension; a VT with identical baseline characteristics to each LT subject was derived; and fracture rates were then predicted for the untreated VT group using the regression model. The number of fractures prevented per 100,000 subject-years was calculated as (VT rate – LT rate). AFF and ONJ incidences on DMAb were based on observed cases in the LT group during the Extension; the VT group was assumed to have no AFF or ONJ in the absence of treatment. A skeletal benefit/risk ratio was calculated from fractures prevented per AFF or ONJ observed.

This analysis included 2343 subjects. The estimated number of clinical fractures prevented was 1403 per 100,000 subject-years (Table). There was 1 case of AFF and 7 ONJ (mild and moderate), corresponding to rates of 5 (AFF) and 35 (ONJ) per 100,000 subject-years. Hence, there were 281 and 40 clinical fractures prevented per AFF and ONJ observed, respectively. The skeletal benefit/risk ratio for other fracture endpoints is shown below (Table).

As long-term placebo-controlled fracture outcome studies in postmenopausal OP are not ethical, the virtual twin model provides a reasonable estimate of untreated fracture rates. Using this model, long-term DMAb therapy has a highly favorable benefit/risk profile when comparing fractures prevented per skeletal adverse event observed.

Table. Ratio of Fractures Prevented per Bone Safety Event Observed in Long-term FREEDOM Extension Subjects Using the Virtual Twin Method

		Exposure-adjusted subject incidence per 100,000 subject-years				
		Clinical fractures N=2343 Exp=18295	Major osteoporotic fractures[a] N=2343 Exp=18772	Vertebral fractures N=2116[b] Exp=18385	Nonvertebral fractures N=2343 Exp=18451	Hip fractures N=2343 Exp=19742
Long-term		1777	1525	901	1528	149
Twin		3180	2699	1879	2924	297
Ratio[c]		0.56	0.57	0.48	0.53	0.54
Fractures prevented		1403	1174	978	1396	148
Ratio of fractures prevented per AE observed[d]	AFF (5)[e]	280.6	234.8	195.6	279.2	29.6
	ONJ (35)[e, f]	40.1	33.5	27.9	39.9	4.2

Based on LT denosumab subjects. All results are based on 5000 bootstrap samples.

N=number of LT subjects who had fracture outcome data; Exp=exposure time in subject years indicating the time from FREEDOM baseline to the onset of first event (for subjects who had a fracture event) or end of study or last assessment date, whichever was greater (for subjects who did not have a fracture event)

[a] Major osteoporotic fractures were defined as clinical spine, forearm, hip, or shoulder fracture

[b] 227 LT subjects had missing vertebral fracture outcome data during FREEDOM and/or its Extension

[c] Calculated as (LT rate) / (VT rate)

[d] Calculated as (VT rate – LT rate) / AE rate

[e] The number in parentheses indicates the AE subject incidence rate per 100,000 subject-years in LT subjects

[f] There were 2 mild, 5 moderate, and no severe cases of ONJ in the LT group

AE: Adverse event; AFF: atypical femoral fracture; ONJ: osteonecrosis of the jaw

P029

YESTERDAY AND TODAY IN THE STUDY OF OSTEOPOROSIS MOLECULAR BIOLOGY

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The pathogenesis of osteoporosis was affected by genetics and environment, and was closely related to genes, receptors and cytokines. Genes, receptors, and cytokines associated with osteoporosis were a hot topic in osteoporosis research in recent years. This paper sorted out new major candidate genes in the field of osteoporosis research in recent years, provided molecular biology reference for early prevention, early treatment and anti-osteoporosis drug development of osteoporosis. This article discussed the application of calcium and phosphorus metabolism regulating hormone and its receptor genes, sex hormones and their receptor genes, cytokines and their receptor genes, and type I collagen genes in basic research and clinical research. There were more than 20 polymorphic sites of vitamin D3 receptor (VDR) gene, among which BsmI and ApaI cleavage sites on the 8th intron are closely involved, and the 9th exon is closely related to bone metabolism. TaqI and a Fok I restriction site located at the 5' end of the gene. Vitamin D3 mediated the physiological regulation of calcium and phosphorus metabolism by binding to VDR and promoted bone formation. Calcitonin acted to regulate calcium and phosphorus metabolism and maintain bone metabolism balance by binding to calcitonin receptor (CTR) on the cell membrane of osteoclasts and their precursors distributed in bone. Parathyroid hormone gene polymorphism was closely related to BMD and was an important genetic marker for susceptibility to osteoporosis. Estrogen played a biological role mainly by binding to estrogen nuclear specific receptors (estrogen receptor, ER) of osteoblasts and osteoclasts. The study of the relationship between ER gene and BMD had become osteoporosis. The main research direction. The cytokines closely related to osteoporosis include: tumor necrosis factor (TNF), interleukin (IL-1, IL-6, IL-17), insulin-like growth factor (IGF-1), transforming growth factor β (TGF-β) and the like. Molecular biology technology was the science of studying the structure and function of biological macromolecules at the molecular level to elucidate the nature of life phenomena such as heredity, reproduction, growth and development. Its main research areas include protein systems, protein-nucleic acid systems, and protein-lipid systems. The rise of molecular biology was a new phase in life science research. In summary, the condensing of the literature broadened the thinking for the molecular biology research of osteoporosis. The researcher should select the research object, design the research plan and technical route according to the research direction and research purpose, and selected the experimental method in a targeted manner. The statistical data of meaning makes the research results more advanced and innovative.

P030

DENOSUMAB AND OSTEOCLAST RANKL/RANK PATHWAY

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This review summarized the physiological mechanism of denosumab inhibition of bone resorption, and the research progress of denosumab in the treatment of osteoporosis and malignant tumor bone metastasis, providing better evidence-based medicine for the clinical application of denosumab. Denosumab was a synthetic, fully humanized monoclonal antibody (IgG2 antibody) that binded to RANKL. It had high affinity and specificity for human RANKL and had good Inhibition of bone resorption. It was a targeted therapy for osteoporosis based on the RANKL/RANK signaling pathway of osteoclasts and could reduce the occurrence of bone-related events (SRE) in patients with malignant bone metastases and delay the progression of bone pain. Denosumab was the first drug to prevent local osteolysis and bone erosion by anti-bone resorption, and it was the only approved antagonist against RANKL. Denosumab could compete with RANK for the DE-loop structure on human RANKL protein, and on the other hand, activated NF-κB, which entered the nuclear-affected genes and expresses osteoclasts. Cell activation, differentiation, proliferation, multinucleation and survival played a key role; on the other hand, inhibition of RANKL binding to RANK on the surface of osteoclasts and their precursors effectively blocks the interaction between ligands and receptors. Thereby, inhibited the formation, function and survival of activated osteoclasts, reduced osteoclast activity, inhibited osteoclast differentiation, inhibited bone resorption, reduced bone dissolving, increased bone density, increased bone strength, and inhibited tumor growth. Denosumab was a potent and effective bone resorption inhibitor and was a targeted therapy for osteoporosis that targets the osteoclast regulatory pathway. It was a cytokine essential for the formation, function and survival of osteoclasts. The specific binding of denosumab and RANKL, blocking the binding of RANKL to the RANK receptor located on osteoclasts and their precursor cells, can significantly inhibited the reduction of the number of osteoclasts, inhibited the differentiation of osteoclasts, and reduced bone turnover. The level of bone turnover was lower than the premenopausal reference interval and can significantly increase the bone density of the lumbar spine and hip, increased bone strength, and reduce the incidence of fracture. Denosumab was an important selective drug for the treatment of postmenopausal women with osteoporosis, and it could reduce the risk of fracture.

P031

RISK OF OSTEOPOROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A NATIONWIDE POPULATION-BASED COHORT STUDY

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Objectives: Patient with Systemic Lupus Erythematosus (SLE) treated with steroid may get lower bone density. There are few population-based studies which discuss the direct relationship between osteoporosis and SLE. The purpose of this study is to investigate the relationship between osteoporosis and SLE by a Nationwide Population-based Cohort Study, and other risk factors about osteoporosis in SLE patients.

Methods: According to the data in the Longitudinal Health Insurance Database (LHID 2000) of Taiwan, we enrolled 6485 patients in both the SLE and non-SLE cohort between January 1, 2000, and December 31, 2003 and the age and sex were matched. The incidence rate and the risk ratios (RRs) of subsequent newly onset osteoporosis were calculated for both cohorts. We used Cox proportional hazards models to access the influence of SLE. The Kaplan-Meier method was applied to estimate the cumulative osteoporosis incidence curves. The incidence rate and the hazard ratios (HRs) of SLE were calculated for both cohorts.

Results: The SLE cohort consisted of 1497 patients, and the comparison group comprised 5988 matched control patients without SLE. The risk factors that contributed to osteoporosis were mentioned below, such as above 65 years old (HR=4.48, 95%CI=3.07-6.55), female (HR=3.10, 95%CI=2.11-4.56), hypertension (HR=2.047, 95%CI=1.46-2.84), above factors were higher in the SLE cohort than in the comparison cohort. In addition, the incidence rate of osteoporosis is statistically significantly higher in newly diagnosed SLE group and remained higher in the follow-up durations (0-1, 1-5, 5-10 y, but not in >10 y group).

Conclusions: SLE may be a risk factor of osteoporosis. Patients have higher incidence of osteoporosis when they were diagnosed with SLE. Clinicians should pay more attention to SLE patients to prevent and treat osteoporosis. Other risk factors such as female, above 65 years old are also contributed to osteoporosis, which compatible with previous literatures.

P032

THE BIOLOGY STUDY REVIEW OF VITAMIN K2 REGULATING ON BONE METABOLISM

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Vitamin K was a class of 2-methyl-1,4- naphthoquinone derivative, vitamin K_2 was one kind of essential natural nutrients, mainly distributed in the kidney, bone, and blood vessel walls and other genital organizations. In addition to coagulation functions, vitamin K_2 was related to many physiological functions in the body, and it was an important role in many areas of bone metabolism, which complexed in the bone metabolism regulation. In this paper, we retrospective reviewed the physiological role of vitamin K_2 on regulating bone metabolism, animal experiments and clinical trials research, and the important role of vitamin K_2 in the prevention and treatment of osteoporosis.

During the regulation of bone metabolism, vitamin K_2 had two-way action regulate bone metabolism, it could increase osteoblast activity through multiple pathways, promote osteoblast production, increase osteoblast activity, inhibit osteoclastogenesis, downregulate osteoclast activity, and promote osteoclast apoptosis. The balance of bone metabolism was maintained by multiple levels of regulation of cells, molecules, and genes. Thereby, achieving BMD, increasing bone strength, promoting bone mineralization, maintaining bone health, and playing an important role in the treatment of osteoporosis and reducing fracture risk. More and more scholars were paying attention to vitamin K2 to regulate bone metabolism and prevent osteoporosis and had carried out a large number of animal experiments and clinical trials. In recent years, a number of animal experiments and clinical trials at home and abroad had shown that vitamin K2 could increase bone density and reduce the incidence of fractures. In clinical applications, vitamin K_2 had the advantages of good biosafety, less adverse reactions, and less toxic side effects. Animal experiments and clinical trials had affirmed the synergistic effect of vitamin K_2 combined with vitamin D3 and bisphosphonates. It prevented bone loss and improves the mechanical properties of bone. The effect was better than single drug. It had important clinical significance for the prevention and treatment of osteoporosis.

P033

THE CORRELATION BETWEEN BONE MINERAL DENSITY, MENOPAUSAL YEARS AND BODY MASS INDEX OF 2043 CASES IN 35- to 79-YEAR-OLD HAN NATIONALITY FEMALES

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Objective: To investigate L1-L4 TOTAL lumbar spine BMD of 2043 cases of 35-to 79-year-old Han nationality females, to analyze the incidence of osteoporosis, and study the correlation between lumbar spine BMD, menopausal years, and BMI.

Methods: Used the BMD detector (Hologic Discovery-WA, USA) to detect L1-L4 TOTAL lumbar spine BMD. The 2043 cases of subjects lumbar BMD test results were grouped according to a 5-y segment of age, used SPSS 19.0 software for statistical analysis. Used linear correlation to analysis the correlation between age, menopause age, BMI with BMD and osteoporosis incidence.

Results: With age and menopausal years prolonged, lumbar spine BMD values decreased, and the incidence of osteoporosis increased. Age was negatively correlated with lumbar spine BMD, and positively correlated with the incidence of OP. Menopausal years were negatively correlated with lumbar spine BMD and positively correlated with the incidence of OP. In the low BMI group, the lumbar spine BMD value was lowest, and the incidence of osteoporosis was highest; with BMI increased, the lumbar spine BMD increased, and the incidence of osteoporosis reduced, BMI was positively correlated with the lumbar spine BMD and was negatively correlated with incidence of osteoporosis.

Conclusion: Aging, menopausal years prolonged and lower BMI were the risk factors for osteoporosis.

P034

THE RELEVANCE OF VITAMIN D RECEPTOR GENE BSM I AND FOK I POLYMORPHISM WITH BONE MINERAL DENSITY IN HAN FEMALE IN CHANGCHUN CITY

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Objective: To study the polymorphisms of VDR gene Bsm I and Fok I in Han female aged 35-85 years old in Changchun City and to analyze the relationship with BMD.

Methods: Polymorphisms of Bsm I and Fok I were analyzed by PCR-RFLP, and lumbar spine (L1-4) BMD were detected by Hologic Discovery-WA-type BMD detector. 230 objects were divided into menopausal group and premenopausal group, then we observed the distribution characteristics of each genotype. SPSS 19.0 software was used to analyze the experimental results.

Results: In the present study, the genotype distributions of Bsm I were bb (83.9%), Bb (12.6%) and BB (3.5%). The b allele frequency was as high as 90.2% and the B allele frequency was 9.8%. The genotype distributions of Fok I were ff (18.3%), Ff (43.9%) and FF (37.8%). The frequency of f allele was 40.2% and the frequency of F allele was 59.8%. The distribution of genotypes of two sites both were in accordance with Hardy-Weinberg law ($\chi 2=1.283$, $P=0.125$; $\chi 2=0.96$, $p=0.342$); There was no significant difference in the genotype distribution between the premenopausal group and the menopausal group ($P>0.05$). BMD for each genotype of Bsm I was not significantly different between premenopausal group and menopausal group ($P>0.05$). BMD of Fok I ff type was lower than FF type and Ff type, but there was no significant difference in premenopausal group ($P>0.05$), and there was significant difference in BMD between ff type and FF type in menopause group ($P<0.05$).

Conclusion: In this study about 230 cases Han women aged 35-85 years, the distribution of Bsm I genotype is mainly bb, B allele frequency is as high as 90.2%, and there is no difference in BMD of each genotype; Fok I ff type have lower BMD, but there is no significant difference in premenopausal group, ff type is associated with lower BMD in postmenopausal women.

P035

1,25(OH)D3 ABROGATES PALMITIC ACID-INDUCED LIPOTOXICITY IN NORMAL HUMAN OSTEOBLASTS IN VITRO

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Objective: Bone loss begins in the third decade of life and involves decreased bone formation associated with a progressive reduction in osteoblasts (Ob) survival, function and number. In ageing, MSC number and differentiation potential decrease due to reduced capacity to transform into Ob, leading instead to increased adipogenesis and lipid accumulation in the bone marrow of osteoporotic bones. Adipocytes produce palmitic acid (PA), a fatty acid (FA) known to be toxic to Ob *in vitro*. Potential mechanisms include induction dysfunctional autophagy and reduced differentiation. Vitamin D (1,25(OH)2D_3) induces osteoblastogenesis and has an anti-apoptotic effect on Obs. We therefore hypothesised that 1,25(OH)2D_3 might rescue Obs from PA-induced lipotoxicity in vitro.

Methods: Initially we compared the capacity of human Obs (Lonza, CC2538) to differentiate and form bone nodules in the presence of PA or 1,25(OH)2D_3 or in combination. Cell survival was assessed using a 3-(-2,5-diphenylterazolium bromide (MTT) assay. Autophagy was also assessed via LC3-II expression, confocal microscopy, and monitoring life autophagosomes at different time points. Changes in nuclear activity of β-catenin and runt-related transcription factor 2 (Runx2) were assessed to determine the osteogenic activity.

Results: Co-addition of 1,25(OH)2D_3 with PA exposure increased Ob survival (P<0.01). 1,25(OH)2D3 also increased mineralization and differentiation of Obs in these cultures in the presence of PA. In addition, a significant increase in the transcription of β-catenin that is associated with Runx2 signalling.

Conclusion: This study identified potential mechanisms to explain how 1,25(OH)2D3 might abrogate PA-induced lipotoxicity; including facilitation of mineralization and significant activation of the β-catenin signalling pathways in Ob exposed a strong lipotoxic milieu, mimicking human bone marrow. Further evidence of the relationship between elevated lipid levels in tissues and the deleterious impacts on bone was provided. future work should characterise the mechanisms of this effect to develop novel therapies to overcome lipotoxicity in the bone setting.

P036

OSTEOPOROTIC FRACTURE GUIDELINE AND MEDICAL EDUCATION RELATED TO CLINICAL PRACTICES: A NATIONWIDE SURVEY IN CHINA

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Objectives: To investigate the knowledge and practices of Chinese doctors on management of osteoporotic fractures (OFs) after the Chinese osteoporotic fractures guideline update and serial medical educations in 2017.

Methods: Doctors were surveyed with questionnaire after scientific meetings during 2017.2-2018.1 by WeChat, paper form or conference digital platforms. Based on 2017 Chinese guideline for the diagnosis and treatment of osteoporotic fractures, the questionnaire was designed and pretested for reliability and validity.

Results: The questionnaire was reliable and valid. Overall 314 valid questionnaires were confirmed. Regarding diagnosis, 77% agreed osteoporosis could be diagnosed once OF occurred; 83% believed that the BMD criteria for osteoporosis diagnosis would be T≤-2.5 SD. For treatment, almost all (99.7%) agreed anti-osteoporosis treatment as one of the basic principles of treatment; 71.6% considered bisphosphonates (BPs) as the most commonly used anti-osteoporosis drug; 97% believed that patients who have used anti-osteoporosis drugs should reassess osteoporosis after OF instead of discontinue; 95% thought that the patients who did not use anti-osteoporosis medications before OF should be treated with anti-osteoporosis drugs after fracture treatment as early as possible; 89% agreed that the standard use of BPs after OF wouldn't affect bone healing adversely; 59% believed the course of BPs treatment for osteoporosis would be 3-5 y, and 27% considered to be 1-3 y. The patient follow-up rate was poor: 46% selected follow-up rate <30%, only 20% selected follow-up rate >50%. Only 31% of the hospitals had long-term management program for OF. Compared with survey data in 2016, the awareness of osteoporosis is improved in diagnosis, BPs and bone healing, long term treatment and patient compliance. Furthermore, the frequency of attending medical education and doctor's title are related to the improvement.

Conclusions: Doctors generally adhered to the updated Chinese guidelines for osteoporotic fractures. High frequency medical education can help doctors to increase the awareness of osteoporosis as well as the acceptance and practice of guideline.

P037

LONG-TERM EFFICACY AND SAFETY OF ZOLEDRONIC ACID IN THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS

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Objectives: The follow-up and evaluation of efficacy and safety of zoledronic acid after treatment of postmenopausal osteoporosis for 3 y.

Methods: 255 postmenopausal women were collected in Changchun, observation period is 3 y. Giving zoledronic acid 5 mg intravenous infusion annually, while taking calcitriol capsule 0.25 μg and calcium carbonate D3 tablets 600 mg a day. Before the initial infusion of zoledronic acid and after 1 y, 2 y, 3 y, record the BMD values and VAS pain scores, and observe the adverse reactions.

Results: After 1, 2, and 3 y of treatment, the BMD of the patients was significantly higher than that before treatment. After 3 y of initial treatment, the BMD of the lumbar spine 1-4, the left femoral neck, and the Ward's triangle was increased most notably, the percentage change of lumbar spine 1-4 BMD was as high as 15.82% ($P<0.05$). The VAS pain scores of patients after the first treatment of 1, 2, and 3 y were significantly lower, and the difference was statistically significant ($P<0.05$). Of the 255 patients, 114 had a short-term adverse reaction after the first instillation of zoledronic acid, including fever, headache, myalgia, joint pain and other symptoms, and no serious adverse reactions occurred.

Conclusions: Zoledronic acid is a third-generation bisphosphonate that has been infused intravenously and has a high affinity for certain structures on the surface of the bone. It can accumulate on the surface of the trabecular bone after absorption, by inhibiting osteoclast pyrophosphate synthase (PPF synthase) to inhibit the destruction of bone by osteoclasts, which is taken up by osteoclasts, inhibits osteoclast activity and induces osteoclast apoptosis, and reactivates inhibited osteoblasts, producing positive bone balance, thereby increasing the bone mass. During the 3-y follow-up, continuous application of 5 mg of zoledronic acid increased lumbar spine 1-4 BMD 15.82%, femoral neck BMD 5.31%, Ward's triangle 5.00%, greater trochanter 4.32%, and intertrochanteric 3.01%. And reduce the risk of fractures in postmenopausal women. After the application of zoledronic acid, the symptoms of pain can be improved year by year. Increased bone resorption and reduced bone mineral content are the main causes of pain. Therefore, the treatment of osteoporosis pain should focus on inhibiting bone resorption and increasing bone density. In the study, 255 patients had no fever after the second and third instillation of zoledronic acid, which may be related to the body's tolerance to the production of febrile substances.

P038

PROSPECTIVE ASSOCIATIONS BETWEEN MULTI-SITE PAIN AND FALLS IN COMMUNITY-DWELLING OLDER ADULTS: FINDINGS FROM THE TASMANIAN STUDY OF COGNITION AND GAIT (TASCOG) STUDY

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Objectives: Pain at multiple sites is prevalent among older people. Yet, studies investigating the relationship between pain and falls focus largely on single site pain. This study aims to examine whether the number and distribution of painful sites increases the risk of falls in older people.

Methods: Participants aged >60 y were randomly selected from electoral roll. Falls were recorded prospectively over 12 months. Pain at multiple anatomical sites was assessed using a questionnaire. Depending on the presence and distribution pain, participants were classified as having no pain, localised pain and widespread pain. Widespread pain was defined as pain in the axial skeletal region and in the upper and lower limbs. Participants with pain in one or two of upper limbs, lower limbs and axial skeleton region were classified as having localised pain. Log multinomial regression, with adjustment for confounders, was used to estimate the relative risk (RR) of single (1 fall) and multiple falls (≥2 falls) associated with widespread pain or number of painful sites.

Results: There were 431 participants (57% women; mean age 73±7.0 y). The frequencies of single and multiple falls were 22% and 17%, respectively. Increasing number of painful sites was associated with a higher risk of single (RR=1.18, 95%CI: 1.01, 1.37) but not multiple falls (RR=1.17, 95%CI: 0.97, 1.40). Compared to those without pain, older adults with widespread pain, but not those with localised pain, had a higher risk of single (RR=2.57, 95%CI: 1.02, 6.45) but not multiple falls (RR=1.49, 95%CI: 0.53, 4.17).

Conclusions: Older adults with widespread pain are a high-risk group who may benefit from strategies aimed at falls prevention.

P039

HEART FAILURE INCREASE FRACTURE RISK: A META-ANALYSIS

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Objectives: Recent studies have suggested that heart failure may be associated with factors contributing to accelerated bone loss and subsequent fractures, but whether heart failure is a risk factor for fracture is unknown. This meta-analysis was conducted to investigate whether heart failure is associated with an increased risk of fractures by summarizing all available evidence.

Methods: The search of eligible literature was performed using PubMed, Cochrane Library and EMBASE database from inception to April 2018. Studies that investigated the effect of heart failure on fractures compared with controls and reported relative risks, odd ratios, or hazard ratios were included.

Results: Five cohort studies and three case-control studies were finally identified among 4678 studies initially yielded. All studies included were evaluated as high quality using the Newcastle-Ottawa Scale. In five cohort studies, risk for fracture was higher for patients with heart failure than for patients without heart failure (RR 2.84, 95%CI 1.26-2.70, I^2=96%, P=0.002), and a more significant increase of risk of hip fracture was also found (RR 2.32, 95%CI 1.53-3.52, I^2=93%, P<0.001). Moreover, significant increasement was also observed in humeral fracture (RR 1.91, CI 1.07-3.40, I^2=39%, P=0.03)

Conclusion: This study is the first meta-analysis to evaluate the risk of fracture among patients with heart failure. We have found that a significantly increased risk of fracture among heart failure patients compared with those without history of heart failure, especially for hip and humerus fracture. It indicates the necessity of intervention to treat osteoporosis and prevent fracture in clinical practices among patients with heart failure.

P040

A META-ANALYSIS OF EFFECT OF GLYCEMIC CONTROL ON FRACTURE DIABETES

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Objective: Diabetes and fractures are common diseases with increasing popularity in the aging population. Although several studies have reported cases of fractures after glycemic control for diabetes patients, data from large clinical studies are inconsistent regarding the fracture risk following glycemic control. The aim of this meta-analysis was to investigate the fracture risk associated with glycemic control in diabetes subjects.

Methods: Relevant studies published from database inception to March 2018 were identified in PubMed, Embase, MEDLINE and Cochrane Library. The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of the observational studies, and the Jadad score evaluated randomized controlled trails. Among the 1392 studies initially identified, eight observational trails and on randomized controlled trails were eligible for inclusion. All studies included in the meta-analysis were considered high quality. We conducted separate meta-analyses for different levels of HbA1c. We distinguished 5 categories of glycemic control: (1) HbA1c<6.5% (the reference category); (2) 6.5%< HbA1c< 7.5%; (3)7.5%< HbA1c< 8.5%; (4) 8.5%< HbA1c <9.5%; and (5) HbA1c≥9.5%.

Results: The pooled HRs (95%CI) of fractures were significantly higher in the >6.5% category than in the <6.5% reference category (HR 1.15, 95%CI 1.02-1.30). The HR for any fractures was 0.82(0.72-0.94), 0.98(0.86-1.11), 1.27(1.00-1.62) and 1.39(1.24-1.56) for the 6.5%-7.5%, 7.5%-8.5%, 8.5%-9.5%, >9.5% categories of HbA1c compared with the reference category (HbA1c<6.5%). Compared with T1DM subjects (pooled HR 1.08, 95%CI 0.86-1.35), T2DM subjects who underwent inadequate glycemic control tended to have an increased fracture risk (pooled HR 1.28, 95%CI 1.05-1.56).

Conclusion: This meta-analysis found that both too tight or poor glycemic control is associated with an increased risk for fracture in T2DM subjects. Patients with diabetes may benefit from a HbA1c range of 6.5-7.5% to prevent excess risk for fractures.

P041

ACCURACY OF THE OSTEOPOROSIS SELF ASSESSMENT TOOL FOR ASIANS (OSTA) AND THE FRACTURE RISK ASSESSMENT TOOL - FRAX® TO IDENTIFY DENSITOMETRIC DEFINED OSTEOPOROSIS: A DISCRIMINATORY VALUE ANALYSIS IN SINGAPOREAN CHINESE WOMEN

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Objectives: Early identification of patients at risk of osteoporosis is key to address increasing fragility fracture rates associated with ageing populations. Though individuals who were screened using FRAX®; a tool developed to estimate fracture probabilities, have demonstrated fracture risk reduction with treatment and organizations such as the USPTF recommend BMD testing in women <65 y if they have a major osteoporotic fracture (MOF) score higher than that of a 65-y old woman without major risk factors, its accuracy as a screening tool and how it compares with tools such as OSTA (Osteoporosis Self-Assessment tool for Asians) in Chinese women has so far been unexplored. We aimed to determine the FRAX thresholds that would accurately identify axial DXA defined osteoporosis and to compare its performance with that of OSTA for this purpose.

Methods: 1500 Singaporean Chinese postmenopausal women between 50-90 y who had DXA scans done during routine work-up for osteoporosis, health screening, or as part of the protocol for inclusion into a prospective post-menopausal well women cohort were evaluated. Subjects with secondary osteoporosis and those on medications affecting bone metabolism were excluded. with a resultant final study population of 841. Their FRAX scores without BMD and OSTA (weight-age x 0.2) indices were calculated. ROC curves were constructed to identify via the Youden index, the cutoff point of the above with balanced sensitivity and specificity.

Results: 230 (27.3%) of the study population had osteoporosis. The FRAX MOFP with the highest Youden index was 7.2% (AUC:76.5% [95%CI:72.8-80.3%]). It had a sensitivity, specificity, PPV and NPV of 55, 83, 55 and 83%, respectively, in identifying osteoporosis. The above characteristics for a FRAX HFP of ≥2.5% (AUC: 79% [75.6%-82.4%]) were 53, 87,62 and 83%. An OSTA cutoff of ≤-1.2 (AUC:82% [78.9%-85.1%]), had sensitivity, specificity, PPV and NPV of 79,69, 49 and 90%, respectively.

Conclusion: FRAX and OSTA have comparable AUCs on ROC curves. However, OSTA which has only 2 parameters and is thus simpler to use may be an easier screening tool to identify the Chinese woman at high risk for osteoporosis on DXA scanning.

P042

EFFECT OF ORAL BISPHOSPHONATE ON URINARY ALBUMIN EXCRETION IN TYPE 2 DIABETES PATIENTS

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Objective: Fragility fractures are nowadays recognized as a complication of diabetes. However, there is few reports about the effect of anti-osteoporotic drugs on diabetic complications. In the present study, we aimed to explore the effect of oral bisphosphonates (BPs) on urinary albumin excretion, which is a surrogate marker of early diabetic nephropathy, in type 2 diabetes patients.

Methods: This retrospective study was performed in the 40 diabetes patients (male/female=10/30, mean age was 67.1±13.9 y) who were treated with oral BPs. Estimated glomerular filtration rate of the study subject was above 30 ml/min/1.73m^2. Urinary albumin/creatinine ratio (UACR, mg albumin/g creatinine) was examined before and after BP treatment. The increment of UACR/duration of treatment (d) was defined as delta-UACR. Median duration of BP treatment was 151.5 (91-331, 25th-75th) days.

Results: Median UACR of before and after BP treatment was 19.6 (9.23-76.7, 25th-75th) and 24.2 (9.03-52.0, 25th-75th), respectively. The breakdown of oral BPs was 17 alendronate, 11 risedronate, 11 minodronic acid and 1 ibandronate. The usage of oral BP was not associated with the increase of UACR. At the same time, the duration of BP treatment did not affect delta-UACR.

Conclusions: Our results suggest that oral BPs do not affect the progress of early diabetic nephropathy.

P043

CLINICAL FACTORS ASSOCIATED WITH OSTEOPOROSIS IN FEMALE LUPUS PATIENTS

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Objective: To determine clinical factors associated with osteoporosis in female lupus patients of Chinese origin

Methods: 172 Chinese female lupus patients were studied. Lupus patients fulfilled the 1982 ACR criteria for classification of SLE. Osteoporosis was diagnosed by DXA scan and WHO classification for osteoporosis. Diabetes was identified by either (a) symptoms of polyuria and polydipsia with a random blood glucose level >11 mmol/l or a fasting blood glucose level of >7 mmol/l, or (b) asymptomatic with 2 blood glucose levels of greater than the values stated. Hypertensive patients have readings of >160/90 mmHg on 3 separate occasions. A cumulative prednisolone dose of >10 g is equivalent to an average daily dose of 10 mg for 3 y. Clinical data obtained through chart reviews were entered into a database. The following data were analysed: age, disease duration, chronic renal failure, diabetes mellitus, hypertension, cumulative corticosteroid dosage, anti-epileptic and/or anticoagulant treatment for more than 6 months. Univariate analyses with p-value <0.05 was considered significant.

Results: 15 patients had osteoporosis. Age, cumulative corticosteroid dosage, presence of diabetes mellitus or hypertension were significant factors associated with osteoporosis. A fragility fracture was noted in the osteoporosis group. No significant correlations were found with the rest of the factors analysed.

	No osteoporosis	Osteoporosis present	p-value
Number (%)	157 (91%)	15 (9%)	
Mean age (y) [range]	41.5 [17-66]	55.1 [26 - 84]	
Age >50 y	40 (25%)	9 (60%)	0.05
Mean disease duration (y) [range]	8.09 [1-31]	11.4 [2-30]	
Chronic renal failure (GFR <50%)	8 (5.0%)	1 (7%)	n.s.
Anti-epileptic treatment >6/12	3 (2%)	1 (7%)	n.s.
Anticoagulant treatment > 6/12	17 (11%)	1 (7%)	n.s.
Cumulative prednisolone dose (>10 g)	11 (7%)	6 (40%)	0.02
Diabetes mellitus	8 (5.0%)	3 (20%)	0.04
Hypertension	36 (23%)	9 (60%)	0.03

n.s.: not significant

Conclusions: Postmenopausal lupus patients with more than 10 g cumulative prednisolone ingestion or diabetic or hypertensive are at higher risk of developing osteoporosis. They need early identification and treatment to prevent fragility fractures.

P044

EFFECTIVENESS OF A TWO-STEP POPULATION-BASED OSTEOPOROSIS SCREENING PROGRAM USING FRAX: THE RANDOMIZED RISK-STRATIFIED OSTEOPOROSIS STRATEGY EVALUATION (ROSE) STUDY

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Objective: The Risk-stratified Osteoporosis Strategy Evaluation (ROSE) study investigated the effectiveness of a two-step screening program for osteoporosis in women. We found no overall reduction in fractures from systematic screening compared to the current case-finding strategy. The group of moderate- to high-risk women, who accepted the invitation to DXA, seemed to benefit from the program. The purpose of the ROSE study was to investigate the effectiveness of a two-step population-based osteoporosis screening program using the fracture risk assessment tool (FRAX) derived from a self-administered questionnaire to select women for DXA scan. After the scanning, standard osteoporosis management was followed according to Danish national guidelines.

Methods: Participants were randomized to either a screening or control group and stratified according to age and area of residence. Inclusion took place from February 2010 to November 2011. Participants received a self-administered questionnaire and women in the screening group with a FRAX score ≥15% (major osteoporotic fractures) were invited to a DXA scan. Primary outcome was incident clinical fractures. Intention-to-treat analysis and two per-protocol analyses were performed.

Results: A total of 3416 fractures were observed during a median follow-up of 5 y. No significant differences were found in the intention-to-treat analyses with 34,229 women included aged 65-80 y. The per-protocol analyses showed a risk reduction in the group that underwent DXA scanning compared to women in the control group with a FRAX ≥15%, in regard to major osteoporotic fractures, hip fractures, and all fractures combined. The risk reduction was most pronounced for hip fractures (standardized hip-fracture reduction ratio 0.741, p=0.007).

Conclusions: Compared to an office-based case-finding strategy, the two-step systematic screening strategy had no overall effect on fracture incidence. The two-step strategy seemed, however, to be beneficial in the group of women who were identified by FRAX as moderate- or high-risk patients and complied with DXA.

P045

THE FREQUENCY OF INFECTIOUS COMPLICATIONS AND PRESCRIBING ANTIBIOTICS IN PATIENTS WITH JIA WITHOUT SYSTEMIC MANIFESTATIONS IMMUNIZED WITH 13 PKV ON THE BACKGROUND AND PRIOR TO THE INITIATION OF ANTIRHEUMATIC THERAPY

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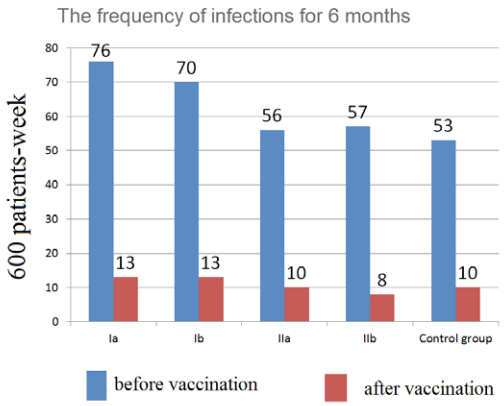
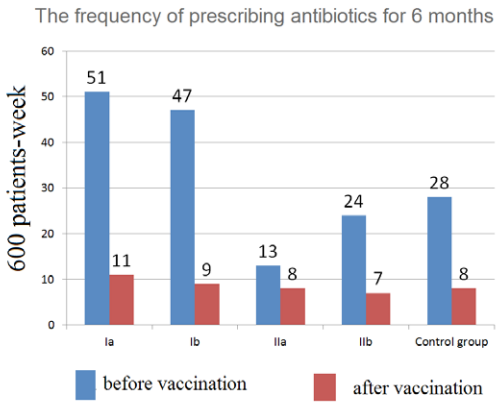
Objective: Juvenile idiopathic arthritis (JIA) is a chronic immunoaggressive inflammatory disease that, in the absence of treatment, leads to irreversible damage to the joints. Patients with JIA have an increased risk of developing infections due to immunological dysfunction, the impact of powerful immunosuppressants and disease activity. The results of the studies demonstrate that antirheumatic drugs used for the treatment of JIA increase the risk of developing infectious diseases. When using methotrexate and other immunosuppressants, the risk of developing not only hepatotoxicity, neutron and / or lymphopenia, but also pneumonia, especially during the first year of treatment, increases. Tumor necrosis factor (TNF) inhibitors increase the risk of developing bacterial, fungal and opportunistic infections. Approximately half of all infectious adverse events in patients with JIA are associated with airway disease. Our aim was to analyze the incidence of infectious complications, prescribing antibacterial drugs and adherence to antirheumatic therapy in patients with JIA without systemic manifestations before and after immunization of 13 PCV.

Methods: During the prospective cohort study, five groups were formed: children with JIA in remission phase with methotrexate (group 1) or etanercept (group 2), with JIA in the active phase prior to the appointment of methotrexate (group 3) or etanercept (group 4), control group (conditionally healthy children). 13-valent PCV was injected once in 0.5 ml subcutaneously against therapy in patients in the remission phase, or 3 weeks before the appointment of methotrexate or etanercept in patients in the active phase. In the course of the study, the frequency of acute infectious complications, the frequency of prescribing antibacterial drugs in patients with JIA, as well as adverse events against vaccination was assessed. The study compared the incidence of infectious complications and the prescription of antibiotics for 6 months before and after vaccination in patients with JIA immunized against methotrexate and etanercept, and patients with JIA vaccinated prior to antirheumatic drugs.

Results: In patients with JIA, immunized with 13 PCV before the appointment of methotrexate and etanercept, for the next 6 months carrying out immunosuppressive and biological therapy significantly less than in patients with JIA, vaccinated against long-term treatment with methotrexate and etanercept, infectious complications developed, and antibacterial drugs were prescribed. The frequency of infectious complications for 6 months. The pre-vaccination observations in Ia (MT) and Ib (ETA) group were 76 and 70/600 patient-weeks, for 6 months. after vaccination in IIa (MT) and IIb (ETA) group - 13 and 23/600 patient-weeks. The frequency of prescribing antibiotics for 6 months. The pre-vaccination observations in Ia (MT) and Ib (ETA) group were 51 and 47/600 patient weeks, respectively, for 6 months; after vaccination in IIa (MT) and IIb (ETA) group - 8 and 7/600 patient-weeks. Before the vaccination, 13 PKV showed that in patients with Ia and Ib of the group, methotrexate and etanercept in the event of an infectious event were canceled at a frequency of 52 and 49/600 patient-weeks. Within 6 months after immunization with 13 PCV, the adherence of patients with JIA of antirheumatic therapy was significantly improved, as evidenced by a significant decrease in the incidence of methotrexate withdrawal events (52/600 and 12/600 patient weeks, p=0.001 before and after vaccination, respectively) and etanercept (49/600 and 10/600 patient weeks, p=0.001 before and after vaccination).





Conclusions: Immunization of 13 PCV patients with JIA without systemic manifestations provides a significant reduction in the incidence of infectious complications, the incidence rate, the frequency of prescribing antibiotics in conditions of immunosuppressive and genetic engineering biological therapy, and increased adherence to treatment, which is manifested by a significant reduction in the frequency of methotrexate and etanercept.

P046

ASSOCIATIONS BETWEEN PAIN AT MULTIPLE SITES AND PREVALENT AND INCIDENT FRACTURES IN OLDER ADULTS

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Objective: Musculoskeletal pain is common in the elderly typically involving multiple sites. Pain at multiple sites has an adverse impact on health outcomes; however, whether multi-site pain is associated with fractures, and whether this association is dependent on falls risk and/or BMD is unknown. This study aimed to examine the association between multi-site pain and fractures and to explore whether multi-site pain is an independent marker for fractures.

Methods: Data from a longitudinal population-based study of older adults (mean age 63 y, 51% female) were utilized with measurements at baseline (n=1086), 2.6 (n=875) and 5.1 y (n=768). Presence/absence of pain at the neck, back, hands, shoulders, hips, knees and feet were assessed by questionnaire. Fractures were self-reported at each time-point. BMD was measured by DXA. Baseline demographic, lifestyle, and falls risk assessment were collected.

Results: A total of 385 fractures were reported at the three time-points and 86 incident fractures were observed over 5.1 y. Greater number of painful sites was associated with higher fracture prevalence at any site, and fractures occurring at the vertebral, nonvertebral and major sites (including the femur, radius, ulnar, vertebrae, rib and humerus) in univariate and multivariable analyses with adjustment for age, sex, BMI, smoking history, physical activity, pain medication, BMD and falls risk. There was a dose-response relationship between number of painful sites and fracture prevalence at these sites (P for trend <0.05). In addition, there was a dose-response relationship between number of painful sites and the risk of incident fractures occurring at any sites [relative risk (RR) 1.4, 95%CI 1.1-1.8] and major sites (RR 1.9, 95%CI 1.2-2.9) over 5.1 y after adjustment for confounders. No significant association between number of painful sites and prevalent and incident hip fractures was observed possibly due to the small sample size (7 prevalent and 3 incident hip fractures).

Conclusions: Pain at multiple sites is associated with a higher risk of prevalent and incident fractures, which is independent of falls risk and BMD, suggesting that widespread pain may be an independent marker of higher fracture risk.

P047

BALANCE ABILITY AND ITS RELATIONSHIP WITH FALL, BONE MASS AND FRACTURE AMONG WOMEN IN SICHUAN, CHINA

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Objective: The impaired balance ability is an important risk factor for falling, and the aged are more prone to fall, thus understanding the age-related decline of balance ability is of great importance. As muscle and bone are closely related in motor function, both of which declined can increase the incidence of low traumatic fracture. Therefore, the relationship between balance ability and bone mass should be studied, as well the association between impaired balance ability and fall, low traumatic fracture. Our aims were the following: 1) To describe the age-related decline in balance ability and search for the main factors influencing balance ability; 2) To analyse the relationship between balance ability and bone mass; 3) To analyse the association between impaired balance ability and fall, low traumatic fracture.

Methods: The data came from a cross-sectional study, which was "Vitamin D status and its correlation to bone density, bone turnover markers and muscle strength in community-dwelling people in Sichuan Province, P.R. China (MISP-40407)". 1508 female residents in Sichuan Province were investigated, during the period from November 2012 to February 2013. Questionnaire survey was conducted to collect information about daily diet and exercise, chronic diseases, falls and low traumatic fractures. Physical performance was scored using short physical performance battery (SPPB). Serum 25(OH)D, $1,25(OH)_2D$ and PTH were measured by ELISA. BMD of lumbar spine, femoral neck and hip were measured by DXA. Our study included a representative sample of 1101 women aged 29-95. SPSS software was used for statistical analysis. The CART analysis of decision tree was used to determine the cut point of age with declined balance ability. The age-related decline in balance ability was described. Logistic regression analysis was used to analyze the main factors affecting balance ability and the relationship of fall, low traumatic fracture with balance ability. Spearman correlation test was used to analyze the relationship between balance ability and BMD.

Results: The average age of all subjects was 58.1 y old, ranging from 29-95 y old, postmenopausal women accounted for 69.1%, and the incidence of impaired balance ability (SPPB score <10) was 19.5%. 1) The balance ability was strong and stable before 45 y old, with a mean SPPB score of 11.8±0.6. The balance ability declined slowly with age during 46-75 y old, with a mean SPPB score of 10.9±1.7, while the balance ability declined sharply after 76 y old, with a mean SPPB score of 8.3±2.5. The most important factors affecting the decline of balance were aging (OR=1.11, P<0.001), chronic obstructive pulmonary disease (OR=1.98, P<0.001), protein intake (OR 0.53, P=0.001), and daily exercise (OR=0.82, P<0.001). There was no correlation between the balance ability and vitamin D, PTH. 2) There was no correlation between SPPB score and BMD (P>0.05) in premenopausal women. SPPB score was related to the BMD of lumbar spine, femoral neck and hip in postmenopausal women, r_s of which were 0.146, 0.294, and 0.146, respectively (P<0.001). 3) The incidence of falls was 14.7% in the recent 6 months. Without adjusting confounding factors, participants with impaired balance ability (SPPB score <10) had increased incidence of fall (OR=2.02, P<0.001). However, after adjusting confounding factors, impaired balance ability did not affect the incidence of fall. 4) The prevalence of low traumatic fractures in postmenopausal women was 21.1%. Without adjusting confounding factors, participants with impaired balance ability (SPPB score <10) had increased prevalence of low traumatic fractures (OR=2.03, P<0.001), however, after adjusting confounding factors, impaired balance ability did not affect prevalence of low-traumatic fracture in postmenopausal women.

Conclusions: The balance ability began to decrease since the age of 45 and declined dramatically after 75 y old among the adult women. Increasing dietary protein intake and daily exercise may help to slow down the age-related declined balance ability of the elderly. Significant positive correlations were observed between SPPB score and BMD in postmenopausal women. The balance ability measured by SPPB test has no relationship with the fall or low traumatic fracture, and the relationship between the severity of declined balance ability with the occurrence of fall and low traumatic fracture remains to be discussed further.

P048

ATYPICAL FEMORAL FRACTURES IN ASSOCIATION WITH ANTIRESORPTIVE THERAPY: A CASE SERIES

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Objectives: Recent evidence has suggested that bisphosphonates and denosumab are associated with atypical femoral fractures (AFFs) and the risk appears to increase with duration of therapy. We present herein a case series of patients with AFFs.

Methods: We describe the two cases of atypical femoral fractures in association with antiresorptive therapy, highlighting the characteristic radiological findings of these fractures.

Results: Our first patient was a 78-y-old woman with a history of polymyalgia rheumatica requiring long term prednisolone. She was on alendronate for 5 y and this was believed to have been started for the prevention of osteoporosis as her previous bone densitometry was normal. Radiograph revealed cortical thickening of the right proximal femoral shaft (Figure 1), with bone scan showing focally increased activity at the lateral aspect of her femora, highly suggestive of AFFs. Alendronate was discontinued and bilateral proximal femoral nail insertion was performed. The second patient, a 60-y-old woman who presented with a left hip pain following a fall from a standing height. She had a history of steroid-dependent systemic lupus erythematous and osteoporosis. She had received alendronate for 12 y before switching to denosumab a year prior. Radiographs confirmed a subtrochanteric fracture of the left femoral shaft (Figure 2) in keeping with AFF and a contralateral intercondylar distal femoral fracture. She underwent femoral nail insertion of both hips and screw insertion of the right distal femur. Teriparatide was substituted for denosumab.

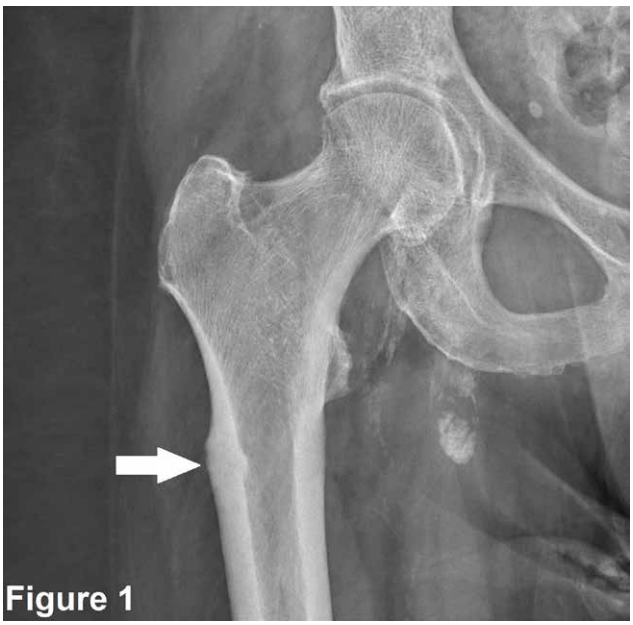

Figure 1

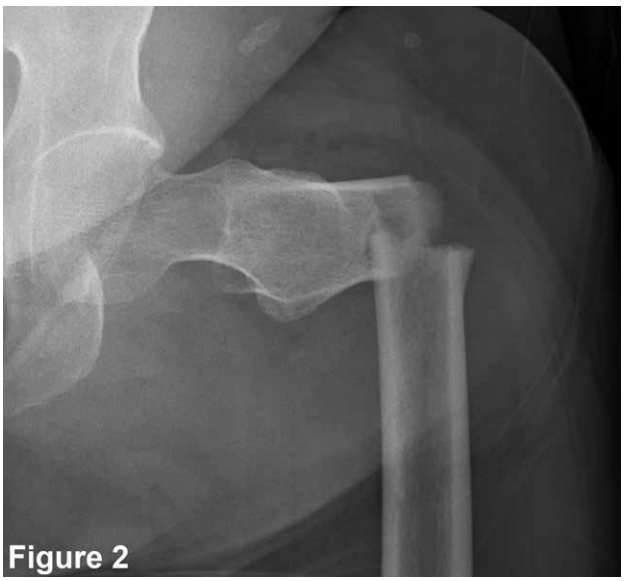

Figure 2

Conclusions: The radiological findings of AFFs differ from osteoporotic femoral fractures and the defining features of these fractures have been established by The American Society of Bone and Mineral Research. The major characteristics include noncomminuted fracture with a medial cortical spike, subtrochanteric location, mild or no inciting trauma and a transversely oriented fracture plane. Minor features include prodromal pain, delayed

fracture healing, generalized lateral cortical thickening and bilaterality. Our case series highlight the association of AFFs with denosumab or bisphosphonate therapy and emphasize the need for awareness of this rare complication.

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P049

BETTER EFFICACY OF MINODRONIC ACID THAN RALOXIFENE CHLORIDE OBSERVED IN POSTMENOPAUSAL WOMEN WITH MULTICENTER, OPEN-LABEL RANDOMIZED CONTROLLED HEAD-TO-HEAD TRIAL, JAPANESE OSTEOPOROSIS INTERVENTION TRIAL (JOINT-04)

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Objective: To obtain clinical evidence supporting the efficacy and safety of bisphosphonate and SERM as a treatment of osteoporosis in clinical practice, we conducted a head-to-head randomized trial of minodronic acid (MIN) and raloxifene chloride (RLX).

Methods: The subjects were postmenopausal women of over 60 y who had one or more risk factors of the fracture (over 70 y old, one or more previous vertebral fractures, low BMD; T-score <-3.0 SD). The observation period was 2 y and the incidence of vertebral fractures or major osteoporotic fractures (clinical vertebral fracture, femur, radius and humerus) were observed. Among them whose BMD of proximal femurs were measured, we compared the effects of both drugs on the proximal femoral bone structure by hip structure analysis with Hologic DXA.

Results: 3247 subjects who provided the informed consent were capable of analyzing the effectiveness, 1623 in the MIN group and 1624 in the RLX group. Osteoporotic fractures occurred in 211 cases in the MIN group and 226 cases in the RLX group during the observation period, but there was no significant difference between the 2 groups. On the other hand, the increase in BMD (T-score) during the 2-y observation period was 0.279 (95%CI=0.250-0.309) in the MIN group and 0.150 (95%CI=0.120-0.180) in the RLX group. The BMD significantly increased in MIN group than RLX group ($p<0.0001$). The 818 subjects who received hip structure analysis in both the groups, the cortical bone thickness, bone sectional area and section modulus increased and buckling ratio decreased. In the MIN group, the cortical bone thickness (all three sites), the cross-sectional area (femoral neck and trochanter), the section modulus (trochanter), and the buckling ratio (trochanter) showed significant changes than those in the RLX group.

Conclusion: In this study, although no significant difference was found in the fracture prevention in both groups, MIN improves the BMD and the structure of the proximal femur compared with RLX, and may show some advantage in terms of fracture prevention.

P050

PREDICTION OF FRACTURES IN MEN WITH DYSGLYCAEMIA USING FRAX (AUS)

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Objectives: To determine how well (i) FRAX(Aus) without BMD ($FRAX_{noBMD}$) and (ii) FRAX(Aus) with BMD ($FRAX_{BMD}$), predicted major osteoporotic fractures (MOFs) in Australian men with dysglycaemia.

Methods: This study included 948 men, aged 40-90 y, enrolled in the Geelong Osteoporosis Study. FRAX and glycaemia status were identified assessed at baseline (2001-2006) or 5-y follow-up (2007-2010). Impaired fasting glucose (IFG) was defined as fasting plasma glucose (FPG) 5.5-6.9 mmol/L and diabetes as FPG ≥7.0 mmol/L, use of medication or self-report. Incident MOFs were verified radiologically over a 10-y follow-up period. There were too few hip fractures (n=20) to examine hip FRAX probabilities. The predicted number of fractures was calculated by multiplying FRAX scores by the proportion of time followed-up. A chi-squared test was used to assess differences between observed and predicted number of fractures. Sensitivity, specificity and AUC were calculated.

Results: $FRAX_{noBMD}$ underestimated MOFs in men with normoglycaemia (47 observed vs. 17 predicted, p<0.001) and IFG (33 observed vs. 10 expected, p<0.001), but not for diabetes (10 observed vs. 4 predicted, p=0.099). $FRAX_{BMD}$ underestimated MOFs in normoglycaemia (47 observed vs. 14 predicted, p<0.001), IFG (33 observed vs. 8 predicted, p<0.001) and diabetes (10 observed vs. 3 predicted, p=0.046). Both $FRAX_{noBMD}$ and $FRAX_{BMD}$ had similar AUCs. For men with normoglycaemia who sustained a MOF, two and one were considered high risk (≥20%) by $FRAX_{noBMD}$ and $FRAX_{BMD}$, respectively. For IFG, only one participant was considered high risk by $FRAX_{noBMD}$ and none using $FRAX_{BMD}$. $FRAX_{noBMD}$ and $FRAX_{BMD}$ did not consider any individuals with diabetes and a MOF to be at high risk. Sensitivity was low for both $FRAX_{noBMD}$ and $FRAX_{BMD}$ in all groups: normoglycaemia: (4.3 and 2.2), IFG (3.0 and 0.0) and diabetes (0.0 and 0.0).

Conclusions: $FRAX_{noBMD}$ and $FRAX_{BMD}$ underestimated the number of MOFs, except $FRAX_{noBMD}$ for diabetes.

P051

STRUCTURE RELATIONSHIP AMONG POLYPHENOL ON DIFFERENTIATION OF OSTEOCLASTS AND OSTEOBLASTS

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Objectives: Polyphenol exhibits anti-allergic, antidiabetic, antioxidant, antitumor effects. The present study was designed to evaluate the effects of flavonoid (4-hydroxyderricin, apigenin, sakuranetin, etc.) and nonflavonoid (oleuropein, hydroxytyrosol, carnosic acid, etc.) on differentiation of osteoclasts and osteoblasts by using cultured cells.

Methods: Multinucleated osteoclastic cells were formed from spleen cells by coculture with ST2 cells that had been stimulated by 100 nM 1α, 25-dihydroxyvitamin D_3, and we identified a molecular pathway of osteoclast differentiation mediated by polyphenol with real-time PCR method. By contrast, we investigated the indices of osteoblast differentiation such as alkaline phosphatase activity and deposition of calcium of preosteoblast MC3T3-E1 cells, at concentrations of 1-10 μM.

Results: All polyphenol tested dose-dependently inhibited the formation of multinucleated osteoclasts at concentration of 1-10 μM. The expression of RANKL mRNA in ST2 cells was inhibited. By contrast, apigenin and carnosic acid inhibited indices of osteoblast differentiation by MC3T3-E1 cells. Other polyphenol tested induced osteoblastic differentiation.

Conclusion: Our findings indicate that many polyphenols might have effects on inhibiting the osteoclast formation and inducing osteoblast differentiation.

P052

ASSOCIATION BETWEEN SERUM TUMOR MARKERS AND BONE MINERAL DENSITY IN HEALTHY CHINESE PEOPLE

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Objectives: This study was performed to investigate the association between serum tumor markers and BMD in healthy Chinese people.

Methods: This study composed of 6775 healthy Chinese people (4358 men and 2417 women) from January 2011 to December 2017, whose serum tumor markers (including CA199, NSE, CEA, CA242, ferritin, B-HCG, AFP, CA125, CA153, HGH, f-PSA, t-PSA) were measured. BMD was measured by DXA. We categorized subjects into three groups according to the level of BMD, and the difference of the serum tumor markers in these groups was compared with ANOVA. At last, associations between serum tumor markers and BMD were measured by correlation analysis and multiple regression analysis.

Results: In women, we observed that CEA, ferritin, CA125, CA153 and HGH levels were significantly different between the normal BMD, osteopenia, and osteoporosis groups ($p<0.05$). Both in men and women, femur and lumbar spine BMD were significantly correlated with age, height, weight, BMI and waist circumference($p<0.001$). By comparison, CEA, HGH, f-PSA, t-PSA had significant differences among these groups in men. Besides, the correlation analysis showed that in women the lumbar spine BMD was positively and significantly correlated with CA125, HGH ($p<0.05$), and was negatively and significantly correlated with CA199, CEA, ferritin, AFP, CA153 ($p<0.05$). In women, the femur BMD was negatively and significantly correlated with CA199, CEA, ferritin ($p<0.05$). In men, the lumbar spine BMD was positively and significantly correlated with CA153, B-HCG, ferritin($p<0.05$). The femur BMD was positively correlated with CA153 ($p<0.05$), and was negatively and significantly correlated with CEA, ferritin, HGH, f-PSA, t-PSA($p<0.05$). In the end, multiple linear regression analysis shows both femur and lumbar spine BMD was negatively associated with ferritin after adjustments for age, height, weight, BMI and waist circumference in women, while in men, there were no serum tumor markers associated with BMD.

Conclusions: The femur and lumbar BMD were both associated with ferritin levels among these serum tumor markers of Chinese women. Higher ferritin levels may have a negatively effect on bone loss in women. Further research is needed to elucidate the underlying mechanism of the association between ferritin and BMD.

	Q1	Q2	Q3	P
males (n)	3307	1003	48	
Age (yr)	50.9±10.2	55.2±12	59.4±13.4	**.000**
Height (cm)	171.6±6	169.2±5.6	167.6±5.1	**.000**
Weight (kg)	75.1±9.9	69.1±9.1	64.4±10.6	**.000**
BMI (kg/m 2)	25.5±2.9	24.1±3	22.9±3.4	**.000**
WC (cm)	86.7±7.3	83.7±7.6	81.6±8.8	**.000**
CA19-9 (U/ml)	7.67±7.35	7.77±5.66	9.64±8.49	.155
NSE (ng/ml)	2.31±1.15	2.37±1.26	2.05±0.58	.096
CEA (ng/ml)	1.44±0.96	1.52±1.01	1.66±0.94	**.028**
CA242 (U/ml)	3.13±2.43	3.15±2.22	3.32±1.97	.849
ferritin (ug/L)	147.1±94.1	143.6±93.1	144.9±102.3	.576
B-HCG (U/ml)	0.27±0.23	0.26±0.22	0.24±0.17	.695
AFP (ng/ml)	1.41±1.41	1.45±1.25	1.42±0.99	.812
CA125 (U/ml)	9.07±5.41	9.19±5.8	9.07±5.81	.843
CA153 (U/ml)	6.39±6.08	6.34±5.62	5.14±4.59	.351
HGH (ug/L)	0.26±0.42	0.3±0.44	0.39±0.64	**.016**
f-PSA (ng/ml)	0.24±0.24	0.29±0.3	0.31±0.31	**.000**
t-PSA (ng/ml)	0.71±1.13	0.9±1.3	0.87±1.17	**.000**
females (n)	1609	651	157	
Age (yr)	47.8±8.2	56.8±10.6	65.8±7.5	**.000**
Height (cm)	160.4±5	158.2±5.4	154.9±5.8	**.000**
Weight (kg)	60.2±8.2	58.6±7.9	54.7±8	**.000**
BMI (kg/m 2)	23.4±3.2	23.4±3.1	22.8±2.9	.067
WC (cm)	76.5±8.3	77.7±8.5	77.1±8.2	**.008**
CA19-9 (U/ml)	8.38±6.08	8.73±6.96	9.41±6.72	.115
NSE (ng/ml)	2.14±1.25	2.17±1.1	2.21±0.91	.715
CEA (ng/ml)	1.03±0.83	1.16±0.77	1.21±0.67	**.000**
CA242 (U/ml)	3.58±2.71	3.55±2.84	3.37±2.4	.669
ferritin (ug/L)	47.8±54.2	78.7±72.5	96.3±70.8	**.000**
B-HCG (U/ml)	0.27±2.4	0.22±0.23	0.24±0.2	.866
AFP (ng/ml)	1.26±1.48	1.29±1.16	1.26±1.21	.926
CA125 (U/ml)	9.49±9.74	8.62±8.05	7.5±3.87	**.008**
CA153 (U/ml)	6.03±5.39	5.76±5.13	7.89±8.27	**.000**
HGH (ug/L)	0.51±0.82	0.36±0.7	0.28±0.34	**.000**
f-PSA (ng/ml)	0.0426±0.0564	0.0441±0.057	0.04±0.0261	.847
t-PSA (ng/ml)	0.17±0.26	0.18±0.24	0.17±0.15	.707

Q1:normal BMD group ; Q2:osteopenia group ; Q3:osteoporosis group

Table 1. Baseline Clinical Characteristics According to BMD in Healthy Chinese Subjects

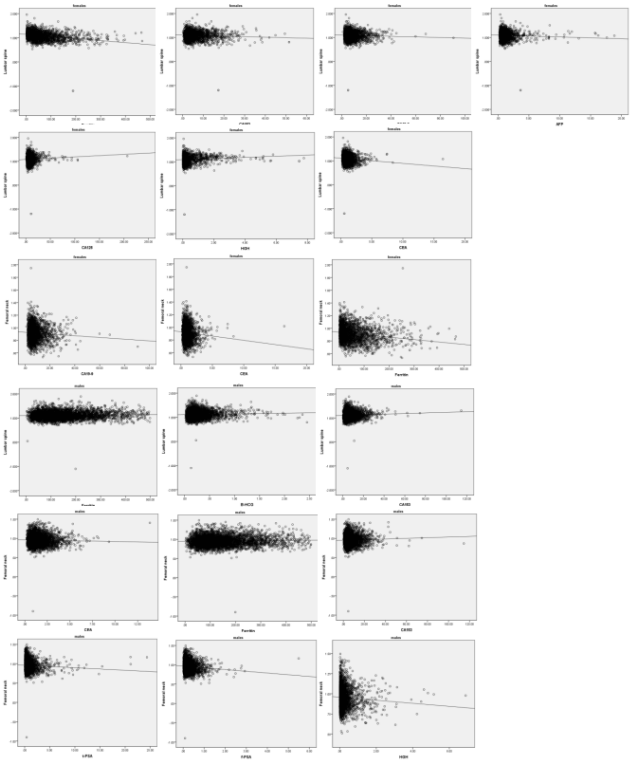

Figure 1. Correlations Between Serum Tumor Markers and BMD at Lumbar spine and Femoral neck

Variables	Males		Females	
	Lumbar spine	Femoral neck	Lumbar spine	Femoral neck
Age	.000	-.191**	-.517**	-.373**
Height	.181**	.209**	.295**	.265**
Weight	.243**	.352**	.141**	.322**
BMI	.172**	.280**	-.003	.199**
WC	.139**	.239**	-.093**	.090**
CA19-9	.026	-.027	-.044*	-.067**
NSE	.007	.009	-.021	-.013
CEA	-.026	-.032*	-.098**	-.083**
CA242	.009	-.008	.004	-.017
ferritin	.050**	.040**	-.298**	-.186**
B-HCG	.044**	.018	.005	-.015
AFP	.003	-.015	-.058**	.000
CA125	.005	.010	.053**	.020
CA153	.048**	.038*	-.070**	-.032
HGH	-.023	-.063**	.101**	.046
f-PSA	.006	-.086**	-.012	-.011
t-PSA	.013	-.058**	-.020	-.011

* P<0.05, ** P<0.01

Table 2. Correlations Between Serum Tumor Markers and BMD at Lumbar spine and Femoral neck

Variables	Males						Females					
	Lumbar spine(R^2=0.077)			Femoral neck(R^2=0.168)			Lumbar spine(R^2=0.316)			Femoral neck(R^2=0.283)		
	β	SE	p	β	SE	p	β	SE	p	β	SE	p
Age				-.002	.000	.000	-.008	.000	.000	-.005	.000	.000
Height				.005	.000	.000						
Weight	.007	.000	.000				.007	.001	.000	.007	.000	.000
BMI				.019	.002	.000						
WC	-.005	.001	.000	-.003	.001	.000	-.003	.001	.000	-.002	.000	.000
CEA				.008	.002	.001						
ferritin	.0000624	.000	.019				-.000327	.000	.000	-.000121	.000	.004
CA153	.001	.000	.011				-.002	.001	.021			

Table 3. Multiple Regression Analysis for Determinants of BMD at Lumbar spine and Femoral neck in Healthy Chinese Subjects

P053

ESTABLISHMENT OF A NORMAL REFERENCE VALUE OF SERUM FERRITIN IN A LARGE HEALTHY CHINESE POPULATION AND EVALUATION OF ITS AGE-RELATED CORRELATION TO BONE MINERAL DENSITY

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Objectives: To establish a normal reference value for serum ferritin, and to investigate age-related relationships between body iron stores and BMD.

Methods: This cross-sectional study included 11037 healthy Chinese subjects aged from 20-90 y. Serum ferritin concentrations were measured by electrochemiluminescence immunoassay and the reference values were calculated for all subjects according to gender and age. Among these subjects, 4979 individuals had measured BMD of lumbar spine and femur neck by DXA. The patterns of age-related BMD changes were presented and correlations of serum ferritin levels with BMD were statistically analyzed in different age-stratified groups.

Results: Reference values of serum ferritin were 24.66-395.25 ng/mL in males and 3.13-238.07 ng/mL in females among all subjects, respectively. The reference range of ferritin remained relatively stable in males and premenopausal females, while a dramatic change occurred in postmenopausal females. Based on the age-related change trend of serum ferritin concentrations, we categorized these subjects into three groups (≤45 y, 46-75 y, and ≥76 y) in each gender and then performed the analysis. Serum ferritin showed a negative correlation with BMD at the lumbar spines and the femoral neck, only in females at the age of 46-75 y after adjusting for confounders (r=-0.125 and -0.091 P< 0.001, respectively).

Conclusions: A reference range of serum ferritin was necessarily and importantly established in a large sample of healthy Chinese subjects according to gender and age. It's a new discovery that the negative correlation between serum ferritin and BMD only significantly existed at the age of 45-75 y in females, not all period after menopause.

Table 1. Principal clinical characteristics of study participants.

Variables	Male (n=6738)	Female (n=4299)	p value
Age (years)	48.0±11.9	46.6±12.5	<0.001
Height (cm)	171.7±6.0	160.2±5.6	<0.001
Weight (kg)	72.9±9.8	57.8±8.0	<0.001
BMI (kg/m^2)	24.7±3.0	22.5±3.0	<0.001
Waist circumference (cm)	84.6±7.4	74.8±8.1	<0.001
Ferritin (ng/mL)	122.96(77.64-200.43)	33.44(13.91-73.85)	<0.001
Hemoglobin (g/L)	154(147-160)	132(126-138)	<0.001
Alkaline phosphatase (IU/L)	71(61-84)	62(51-77)	<0.001
ALT (IU/L)	22(16-32)	13(10-19)	<0.001
AST (IU/L)	21(18-25)	18(15-21)	<0.001
Total Cholesterol (mmol/L)	4.96(4.41-5.55)	4.94(4.37-5.57)	0.49
Triglycerides (mmol/L)	1.45(1.00-2.17)	0.97(0.69-1.44)	<0.001
Creatinine (μmol/L)	74(68-82)	53(48-58)	<0.001
Uric acid (μmol/L)	358(315-411)	257(222-298)	<0.001
Fasting glucose (mmol/L)	4.84(4.51-5.21)	4.76(4.48-5.09)	<0.001

Table 2. Reference range (2.5th-97.5th) of serum ferritin concentrations according to gender and age

	Male					Female				
age	n	median	2.5th	97.5th	range	n	median	2.5th	97.5th	range
⩽30	461	137.8200	25.0090	390.3460	471.42	428	27.7150	3.4005	129.2580	248.73
31-35	505	132.2700	23.2615	395.6690	482.28	474	21.2850	2.9550	117.6863	184.27
36-40	838	121.3750	26.7855	388.2595	488.63	567	19.3800	2.9640	105.4400	398.18
41-45	1007	127.2500	29.5480	398.6280	491.12	580	20.8250	2.5710	110.1555	265.36
46-50	1288	123.2850	27.3825	402.9213	489.90	656	22.7500	2.8728	169.8255	391.96
51-55	1124	125.5000	26.1213	401.9363	491.75	627	46.4300	3.0810	272.9800	438.81
56-60	509	121.1400	24.1675	415.8350	495.45	319	79.9900	7.1600	330.2800	445.36
61-65	491	109.7200	20.9380	419.0140	482.75	339	84.2400	19.2400	275.0050	455.62
66-70	235	113.3000	16.1830	429.3980	479.60	165	91.0500	9.1440	329.5100	479.46
71-75	126	100.1100	14.5090	349.6458	459.63	78	114.3000	19.1888	353.9358	358.03
⩾76	154	100.0150	17.3988	336.5813	481.03	66	100.0500	17.3865	410.2925	441.83
Total	6738	122.9650	24.6638	395.2525	497.18	4299	33.4400	3.1250	238.0700	482.88

Table 3. BMD according to gender and age

	Male			Female		
age	n	L1–4 BMD (g/cm 2)	Femoral neck BMD (g/cm 2)	n	L1–4 BMD (g/cm 2)	Femoral neck BMD (g/cm^2)
⩽30	24	1.191±0.107	1.048±0.143	23	1.144±0.154	0.936±0.131
31-35	114	1.126±0.145	1.002±0.145	77	1.196±0.123	0.969±0.111
36-40	317	1.139±0.138	1.003±0.127	186	1.173±0.116	0.952±0.108
41-45	534	1.12±0.138	0.976±0.13	291	1.163±0.127	0.945±0.12
46-50	622	1.11±0.136	0.962±0.121	348	1.164±0.135	0.951±0.119
51-55	574	1.097±0.144	0.953±0.12	369	1.116±0.15	0.949±0.127
56-60	273	1.098±0.155	0.952±0.126	197	1.013±0.149	0.881±0.115
61-65	294	1.098±0.154	0.948±0.126	213	0.947±0.131	0.849±0.113
66-70	155	1.095±0.184	0.916±0.141	106	0.903±0.134	0.79±0.101
71-75	80	1.135±0.167	0.903±0.121	45	0.904±0.144	0.778±0.104
⩾76	102	1.15±0.219	0.878±0.144	35	0.878±0.139	0.751±0.107
Total	3089	1.113±0.150	0.960±0.130	1890	1.090±0.168	0.914±0.130

Table 4. Prevalence of osteoporosis and osteopenia in subjects (aged over 50 years old) in Suzhou area.

	n	L1–4 BMD (%)		Femoral neck BMD (%)	
		osteoporosis	osteopenia	osteoporosis	osteopenia
Male	1588	1.20%	15.49%	0.69%	22.29%
Female	1017	11.11%	33.04%	2.06%	25.96%

Table 5. The correlation coefficients between serum ferritin concentrations and BMD in each age group.

age	Male				Female			
	L1–4 BMD (g/cm^2)		Femoral neck BMD (g/cm^2)		L1–4 BMD (g/cm^2)		Femoral neck BMD (g/cm^2)	
	Not adjusted	Adjusted	Not adjusted	Adjusted	Not adjusted	Adjusted	Not adjusted	Adjusted
Total	0.029	0.022	**0.044***	-0.001	**-0.348*****	**-0.125*****	**-0.234*****	**-0.091*****
⩽45	-0.001	-0.002	-0.015	-0.038	0.076	0.014	0.028	-0.046
46-75	0.033	0.030	**0.048***	0.014	**-0.358*****	**-0.133*****	**-0.246*****	**-0.090*****
⩾76	0.098	0.192	0.093	0.105	0.248	-0.010	0.161	0.121

Data adjusted age, height, body weight, and waist circumference are given.

* $P < 0.05$. ** $P < 0.01$. ***$P < 0.001$.

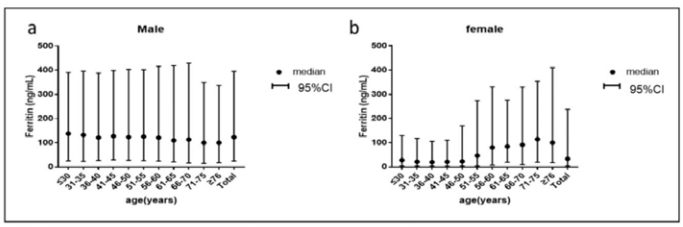

Fig. 1 Age-related reference values of serum ferritin in males and females. a Age-related changes of serum ferritin in males. b Age-related changes of serum ferritin in females.

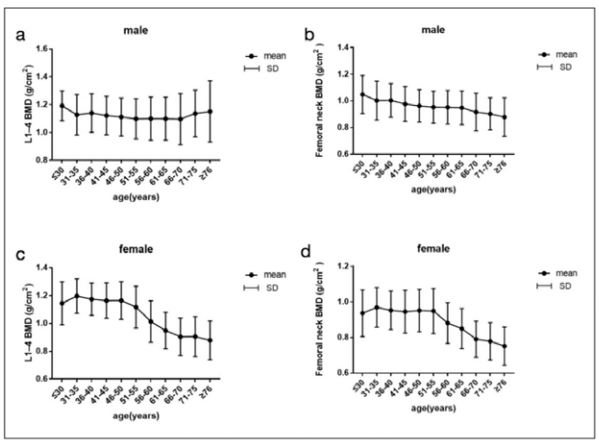

Fig. 2 Age-related changes in bone mineral density (BMD). a Age-related changes in L1–4 BMD in males. b Age-related changes in femoral neck BMD in males. c Age-related changes in L1–4 BMD in females. d Age-related changes in femoral neck BMD in females.

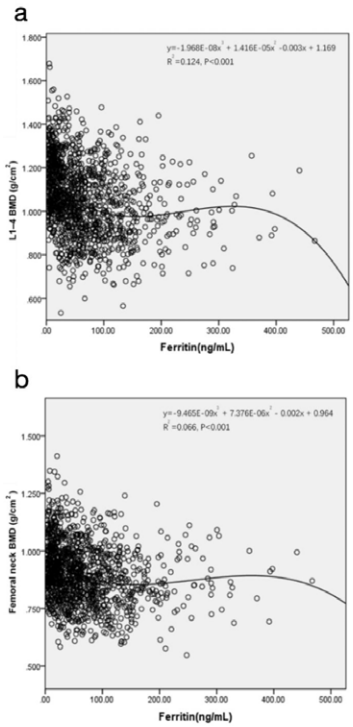

Fig. 3 Correlations of serum ferritin and BMD under the cubic model. a Correlation of serum ferritin and BMD of L1–4. b Correlation of serum ferritin and BMD of FN.

P054

DEPRESSION, ANXIETY AND OSTEOPOROSIS

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Objective: To determine whether the presence of depressive symptoms (depressive vs. nondepressive) and severity of anxiety (none to mild vs. moderate to severe) are associated with significant differences in BMD at either the lumbar spine (LS) or femoral neck (FN).

Methods: This prospective cross-sectional study enrolled women aged 45-69 y attending for 'well women' screening. It excluded women with cancer. The assessments included standardized questionnaires on sociodemographic variables; health and function; physical activity and sexual function; biophysical measures; short physical performance and grip strength; menopausal symptoms, pelvic floor function – incontinence and prolapse, presence of depressive and anxiety symptoms and sleep. A whole body composition DXA scan was performed. Analysis used SPSS Version 20. Multivariate analysis adjusted for age, BMI, HRT use, steroid use, SSRI use, average handgrip strength and generalized anxiety disorder

Results: The cohort comprised of 1201 women. 171 women (14%) and 70 women (6%) reported depressive symptoms and anxiety, respectively. More women in the depressive and moderate to severe anxiety category self-graded their health status as poor ($p<0.001$). There were no differences in age, HRT use, steroid use, smoking and alcohol consumption. Women who reported depressive symptoms were found to have a lower BMI ($p<0.05$). Lower handgrip strength was observed for women with both depressive symptoms ($p=0.01$) and anxiety ($p=0.01$). However, the presence of depressive symptoms and anxiety was not found to be associated with a significant difference in mean BMD (g/cm^2). Adjustment showed no significant BMD differences associated with mental health parameters between the groups.

Conclusion: The presence of depressive symptoms and severity of anxiety was not associated with differences in femoral neck or lumbar spine BMD. One limitation of our study is the use of self-reported questionnaires which is a source of methodological bias. Research supporting this relationship remains limited hence, the need for studies to address these conditions with high public health significance. Nevertheless, more studies are needed.

P055

DOES ANDROGEN DEPRIVATION THERAPY FOR MEN WITH PROSTATE CANCER ALTER CORTICAL AND TRABECULAR BONE STRUCTURE AND STRENGTH?

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Objectives: Androgen deprivation therapy (ADT) improves survival in men with advanced prostate cancer (PCa) but is associated with multiple adverse effects including increased fracture risk. Whether this is related to cortical or trabecular bone loss or changes in bone structure and strength remains uncertain as most previous studies have used DXA to quantify areal BMD (aBMD). Therefore, the aim of this study was to investigate the effects of ADT in men with PCa on cortical and trabecular bone density, structure and whole bone strength.

Methods: Cross-sectional study of 70 ADT men (mean treatment duration 25 months), 52 PCa controls and 70 healthy controls aged 50-85 y. Lumbar spine (LS), femoral neck (FN) and total hip aBMD, and osteoporosis prevalence were assessed using DXA. Distal tibia (4%) total and trabecular volumetric BMD (vBMD), total bone area and compressive strength (bone strength index, BSI) and proximal tibia (66%) cortical vBMD, total, cortical and medullary area, and bending strength (density weighted polar cross-sectional moment of inertia) were assessed using pQCT.

Results: ADT men had higher BMI than PCa ($P<0.05$) but not healthy controls. After adjusting for BMI, ADT men had 6.8-7.3% lower LS aBMD than PCa ($P=0.06$) and healthy controls ($P=0.02$), with a trend for lower hip aBMD (5.5%) than PCa controls ($P=0.07$). FN BMD did not differ significantly between groups, despite being 2.7-3.7% lower in ADT men than controls. Overall, 7.1% of ADT men were classified as osteoporotic (49% osteopenic), compared to 1.4-1.9% of controls ($P=0.18$). After adjusting for BMI and tibia length, distal tibia total vBMD was 7.0-7.4% lower in ADT men than both controls (both $P<0.01$), with trabecular vBMD being 3.8-4.1% lower (not significantly) in ADT men. Distal tibia total area was 5.1-6.3% greater in ADT men than PCa ($P=0.03$) and healthy controls ($P=0.06$), which may represent a compensatory response to reduced BMD. However, BSI was 7.3-9.8% lower than controls ($P=0.05$). Bone outcomes at the 66% tibia did not differ between groups.

Conclusion: ADT treatment in men with prostate cancer was associated with lower BMD, particularly at trabecular skeletal sites (lumbar spine and distal tibia), compared to PCa and healthy controls, but there were no adverse effects of cortical bone structure or bending strength.

P056

CORRELATION OF IRON OVERLOAD MARKERS, MRI T2-STAR LIVER/HEART AND BONE MINERAL DENSITOMETRY IN TRANSFUSION-DEPENDENT THALASSEMIA PATIENTS

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Objective: Osteoporosis remains an important complication of thalassemia patients. Proposed pathogenesis includes extramedullary haematopoiesis, genetic factors and acquired endocrinopathies due to iron overload. Iron deposition in osteoid also impairs bone mineralization causing focal osteomalacia. This study aims to find correlations between iron overload markers and bone density.

Methods: This is a cross-sectional study looking at transfusion-dependent thalassemia patients with iron overload attending thalassemia clinic of a government hospital in State of Pahang, West Malaysia. A total of 58 patients were included. Baseline BMD, serum ferritin, serum 25-hydroxy vitamin-D, MRI T2-star of liver and heart were done to look at their bone status and iron overload.

Results: 58 patients were screened for low bone mass. 34.7% has osteoporosis while 51.0% has osteopaenia. Mean T-/Z-score of femoral neck is -1.08(-3.3–1.3) and mean T-/Z-score of lumbar spine is -2.00(-4.5–0.7). Serum ferritin among normal BMD vs. low bone mass (LBM) is 3037.3 µg/L vs. 3044.2 µg/L (p=NS). Mean serum vitamin D among normal BMD was 43.57 pmol/L and LBM was 63.99 pmol/L (p=0.310). There is significant correlation between liver T2-star with T-/Z-score lumbar spine (p=0.008, B=-0.190) and a trend between liver T2-star and T-/Z-score femoral neck (p=0.058, B=-0.166). No correlation was found between T-/Z-score of lumbar spine/femoral neck with ferritin level or heart T2-star.

Conclusion: Prevalence of low bone mass was high(85.7%) among iron-overloaded thalassemia patients. This prompts for regular BMD screening for iron overload thalassemia patients. Ferritin is a poor predictor of iron overload as it is increased in inflammation and liver diseases. Hepatic T2-star does correlates with the degrees of endocrinopathies and osteoporosis. Our study findings found similar relationship between hepatic T2-star inversely correlates with T-/Z-score. However, heart T2-star doesn't corelate with both T-/Z-score of the patients as most patients are thalassemia intermedia with normal cardiac iron load. This is unlike a study in Iran that found similar inverse relationship between MRI T2-star of heart and liver and BMD. MRI T2-star liver is a good predictor of iron overload and low bone mass in thalassemia patient.

P057

BONE HEALTH IN NEW ZEALAND YOUNG ADULTS: CAUSE FOR CONCERN?

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Objective: Peak bone mass (PBM) is a major determinant of the risk of fragility fracture. While many lifestyle factors may be important to attain PBM, little research exists regarding the lifestyle choices of young adults around the time of PBM acquisition. In this study we consider these issues: reporting excessive alcohol consumption, sporting physical activity and their relationship to bone health in a cohort of New Zealand young adults.

Methods: A lifestyle questionnaire was administered to 474 young adults. This detailed age, height, weight, ethnicity, smoking, alcohol history and sporting physical activity. Heel ultrasound was performed using an Achilles ultrasonometer to provide estimates of Stiffness Index, broadband ultrasound attenuation and speed of sound in order to assess bone health.

Results: There were 169 male (median age=21, IQR=5; mean BMI=24.5kg/m^2±7.6) and 305 female (median age=22, IQR=7; mean BMI=24.2kg/m^2±5.6) participants recruited. Ethnicities represented were Caucasian (67.6%), Māori/Pacific (9.5%), and other (22.8%). Over 80% of males and females reported at least weekly sporting physical activity. More males (21.7%) than females (10.3%) were current smokers; 431 (92.1%) of participants reported drinking alcohol, with a mean weekly alcohol consumption of 6.3 (SD=4.6) and 4.9 (SD=3.2) units in males and females respectively, though 6.1% males and 6.3% females drank more than the recommended number of units weekly. In this group of 16-35 y olds, 35.3% reported binge drinking (consumption greater than 6 drinks at one time) at least monthly, 50% reported drinking alcohol by the age of 15, and 83.6% reported alcohol exposure before the New Zealand legal alcohol purchasing age of 18. Individuals consuming more than the recommended units of alcohol per week were more likely to smoke ($p<0.001$). Clear associations between alcohol intake and heel ultrasound bone measures were not observed. Male participants who had participated in habitual sporting activity had higher heel mean stiffness index ($p<0.005$). There was no statistically significant association between sporting activity and bone density amongst female participants.

Conclusion: These data highlight the high rate of binge and underage drinking in young people, with potential long-term impact on bone health.

P058

USING FOCUS GROUP TO ASSESS THE NEEDS AND CHALLENGES OF AN ONLINE COURSE ON METABOLIC BONE DISEASES

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Objectives: To assess the needs and evaluate the challenges of an online course on metabolic bone diseases (MBD) for postgraduates (PG) using focus group discussions (FGD).

Methods: Two FGD (90 min each) were conducted at section of Chemical Pathology, AKU for PGs from Medicine, Radiology Chemical Pathology and Orthopedics in 2018 after informed consent. FGD were moderated by two faculties from AKU and PGs across Pakistan participated via ZOOM. Attendance was maintained. FGD took perspectives from PGs (n=14, residency years 1-6) into following themes; course need, time commitments, tools/technology, course content and assessment.

Results: The PGs (14/14) agreed on a dire need for MBD online course, expressed concerns that MBD burden was high (8/14), objectives were not covered in training (10/14) and would help them in their exit examination (11/14). Course time committed ranged from 15-20 min/d to 2-4 h/week. PGs were comfortable in accessing the course through cellphones/computers. PGs (2/14) were not comfortable in using social media for connecting with faculty/students enrolled because of busy schedules. PGs (10/14) responded that connectivity could be a hindrance to accessing the course and they might not be able to contribute discussions due to heavy duties. Majority wanted asynchronous course and micro presentations. They agreed in having MCQs on diagnostic approach as mode of assessment (14/14) and wanted a final assessment to complete the course (2/14).

Conclusion: Need for comprehensive MBD course was strongly felt in FGD. Challenges can be catered by developing asynchronous multiple modules with micro-video lectures and simulated clinical cases. Feedbacks, formative assessments, reading assignments can be shared using online platforms. Detailed information about PG's perceptions and opinions will help design a successful MBD online course tailored according to their needs.

Acknowledgement: Foundation for Advancement of International Medical Education and Research (FAIMER) as presenting author is FAIMER year 1 fellow and this is her project for FAIMER fellowship. ERC number: 5415-Pat-ERC-18

P059

ESTABLISHMENT OF A GOLD FRACTURE LIAISON SERVICE IN CHRISTCHURCH, NEW ZEALAND

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Objective: Canterbury is the second largest District Health Board (DHB) in New Zealand (NZ). Population of 543,820 people with 85,810 >65 years and increasing. Fracture Liaison Services (FLS) are relatively new to NZ, established first in Auckland in 2013. Christchurch Hospital's FLS is a Clinical Nurse and Specialist led service which began in February 2016. It uses the International Osteoporosis Foundation (IOF) Capture the Fracture and Osteoporosis New Zealand guidelines (https://osteoporosis.org.nz/clinical-guidance/). In 2016 there were 436 neck of femur fractures treated through Christchurch Hospital. To date we have assessed >6000 patients for all fragility fractures including >1000 vertebral fractures in both primary and secondary care. Our aim was to assess the number of FLS patients with undiagnosed osteopenia/osteoporosis and fractures requiring treatment with the aim of ensuring treatment implementation to reduce the number of hip fractures.

Methods: A retrospective electronic review of patient records was assessed by the FLS from February 2016 – December 2017. The cohort consisted of 932 patients >50 y. Overall hip fracture numbers in Canterbury and the implementation of recommended bisphosphonate treatments were reviewed.

Results: Our results identified 932 FLS patients. 34% (n=320) were aged >75 y. 379 had a bone density scan showing the majority had osteopenia 48% (n=180), 27% (n=104) had osteoporosis. Only 25% (n=95) had a normal bone density. Bisphosphonates were recommended for 57% (n=527). Electronic review at 4 months showed 56% (n=293) bisphosphonate compliance and at one year ending June 2017 showed 50% (n=63/127) compliance. Between 2009-2017 total hip fracture numbers have fallen (p=0.2) adjusted for the increase in population >65 y.

Conclusion: The Christchurch FLS has been effective in identifying and treating previous undiagnosed osteoporosis. The number of yearly hip fractures appears to be reducing in parallel with the introduction of the FLS.

P060

PSORIASIS IS ASSOCIATED WITH A HIGHER RISK OF FRAGILITY FRACTURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives: Psoriasis is an immune-mediated inflammatory skin disease and has been reported to have higher risk of comorbidities including osteoporosis. The aim of this study was to determine the risk of fracture and prevalence of osteoporosis among patients with psoriasis.

Methods: We conducted a systematic review and meta-analysis of cohort and case-control studies that reported the risk or odds of fracture or the odds of osteoporosis among psoriatic patients. We searched the Cochrane Central Register of Controlled Trials, MEDLINE, and Embase for relevant studies. We used the Newcastle-Ottawa Scale to assess the risk of bias of included studies. We did a random-effects meta-analysis in calculating the pooled risk estimates. The main outcomes were the risk and odds of fragility fracture including hip, vertebral, and overall fractures. The secondary outcomes were the odds of osteoporosis and osteopenia. We also performed subgroup analyses based on the severity of psoriasis and the presence of concomitant psoriatic arthritis.

Results: This meta-analysis included 14 studies with a total of 200,233,986 subjects (952,918 psoriatic patients and 199,281,068 healthy controls). Compared to the general population, psoriatic patients had increased risk of hip, vertebral, and overall fractures (HR=1.14, 95%CI 1.07~1.21; HR=1.35, 95%CI 1.03~1.73; HR=1.13, 95%CI 1.05~1.21, respectively). The subgroup analyses showed that female gender was associated with psoriasis (HR=1.12, 95%CI 1.06~1.19, *P*=0.0002), whereas male gender was not (HR=0.88, 95%CI 0.40~1.92). The severity of psoriasis also correlated with the risk of fractures (mild psoriasis: HR=1.10, 95%CI 1.04~1.15; severe psoriasis: HR=1.26, 95%CI 1.15~1.38; Subgroup difference, *P*=0.01). When compared to nonpsoriatic controls, psoriatic patients had an increased odds of osteopenia (OR=2.37; 95%CI 1.31~4.26) but not osteoporosis (OR=1.48, 95%CI 0.73~2.99). Neither psoriatic arthritis nor gender was associated with increased odds of osteoporosis or osteopenia.

Conclusions: Psoriasis is associated with a significant increase of incident and prevalent fractures, without increasing the prevalence of osteoporosis but osteopenia. Routine bone quality evaluation other than DXA and fracture prevention programs may be introduced into routine care of psoriatic patients.

P061

A HOSPITAL BASED STUDY OF BONE MASS IN ASIAN INDIAN NEWBORN SUBJECTS

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Objective: To study bone mass (whole body BMD, BMC and bone area) in Asian Indian newborn subjects and to study the associated factors.

Methods: Apparently healthy pregnant women (<16 weeks POG) recruited from Department of Obstetrics & Gynaecology, AIIMS. Data captured on maternal antenatal events: dietary intake (3-d, 24-h recalls) at first and third trimester, femoral volume (3D USG) at 19 and 34 weeks POG, placental weight and serum vitamin D levels at baseline and postdelivery. Newborn parameters included birth weight, length, head circumference; cord blood vitamin D and IGF-1 levels and bone mass assessment by DXA (Hologic Discovery A) within 15 d after birth. Association was sought between bone mass parameters and newborn and maternal factors using one-way ANOVA and linear regression.

Results: The study population included 150 term and AGA newborns from mothers with mean age at recruitment of 26.7±3.4 y, mean gestational age 14±1 weeks at recruitment and mean gestational age at delivery 38±1 weeks. The bone mass was: BMC 44.94±7.3 g, BMD 0.25±0.21 g/cm^2 (median 0.21, 0.15-1.38) and bone area 218.6±20 cm^2. The mean placental weight was 506.9±77.4 g (n=60) and mean femoral volume as assessed by 3D ultrasound was 0.77± 0.29 ml at 19 weeks and 4.49±1.28 ml at 34 weeks (n=30). The mean birth weight, birth length and head circumference were 2991.3±403.5 g, 50.7±2.2 cm and 34±1.3, respectively. Newborn BMC, BMD and bone area were significantly associated with placental weight and newborn birth weight, birth length and head circumference (all $p<0.001$) however newborn IGF-1 was also significantly associated with newborn BMC and bone area ($p<0.05$). None of the newborn bone mass parameter significantly correlated with maternal dietary intake and maternal or newborn vitamin D status.

Conclusion: Placental weight and newborn IGF-1, birth weight, birth length and head circumference could be the probable factors associated with newborn bone mass.

P062

EVIDENCE BASED GERIATRIC EXERCISES WITH DEPRESCRIPTIONAL PHYSICAL ACTIVITY FORMS MAINSTAY IN LIFE TIME FALLS PREVENTION EXERCISES PLAN

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Objectives: To demonstrate the importance of daily exercising for lifetime with minimum medications is the key for never to fall.

Materials and Methods: 100 Elderly persons from 58 yrs to 88 yrs were selected for the Falls Prevention Exercises Plan Of 10 Days. They were given pectoral and pelvic girdle exercises by keeping watch on all four types of exercises namely - Flexibility, Strength, Endurance and Balancing eg. by Heel To Toe Walk, Reverse Walk etc. Before starting the plan they were given consultations by an ophthalmologist, diet consultant and also an ECG was done. They were tested for Osteoporosis by doing DEXA Scan and the basic blood works were also done for Vit B12, Vit D3, Sr Calcium, Uric Acid, Hb%, Fasting and Post-meal Blood Sugar. During daily session everyparticipant's blood pressure, pulse rate and SpO2 was recorded three times namely: before starting, during midway and after the end of sessions. Most of the participants tolerated the plan very well. The duration was from 40 to 60 minutes each day depending upon the age, co- morbidity and enthusiasm to do it. All were also given guidance about Sarcopenia and Quality of Life. The weight cuffs were used as per the requirements of muscle groups eg. weight cuff of 1/2 kg, 1 kg, 11/2kg and 2 kg for quadriceps strengthening.

Results: The results of this experiment were excellent and extremely encouraging. This activity was named as GEDPA: Geriatric Exercises with Deprescriptional Physical Activity. The results are as follows: a) All participants were extremely confident after undergoing this plan. b) One 77 years old female participant, who is a K/C/O PD with Osteoporosis, suffered a Fall in front of her home but as she was enough trained so she did not suffer any injury and could fall in proper fashion avoiding the grievous hurt. c) One 68 year old obese, K/C/O T2 DM with Severe HTN male participant stopped using stick for walking. Now, he can climb five storey to his home in case of power failure without any difficulty. He can drive two wheeler with great confidence. d) Most of the participants are doing the exercises daily in two sessions [morning & evening] to avoid the fatigue. All are very happy and very regular in their physical activities and exercising. e) As all were given an ophthalmic consultation, all of them consulted their regular ophthalmologist for correction of visual impairments. f) Most of them are following the nutritional advise also given by the nutritionist. g) Falls can be prevented and falls is a disease is convinced to all. Now, they are creating awareness in the society and in the city regarding the importance of evidence based daily exercising and physical activities with minimum medications. h) The Geriatrician, Principal Investigator [PI], after studying each and every participant gave Geriatric Deprescription to each of the beneficiary resulting into reduction of no. of medications, reduction into cost of medications and finally reduction or stopping into the events of falls, repeated falls and fear of fall.

Conclusion: a) Geriatric Exercise forms the mainstay of the Life Time Falls Prevention Plan. Many exercises were taught with the help of an arm less sturdy chair. b) Before going for any exercise plan one must work out the plan of DEPRESCRIPTION, so that the medications can be kept to minimum. c) Geriatric Nutrition forms an important part in Falls Prevention Strategy. d) Correction of Visual impairments [of any sort like ARMD, glaucoma, cataract or refraction error] reduces no. of falls, repeated falls and fear of fall [FOF] significantly. e) REFERENCE (if appli-

cable) : National Council On Ageing Book On Geriatric Exercises and Physical Activity, 2017 edition. f) Acknowledgements (if applicable) : Presentation of "Falls Prevention" by Prof. Rene Rizzoli [MD, Professor of medicine] in Krakow, WCO 2018 at Poland. g) Disclosures (if applicable) : Not Applicable

P063

FEATURES OF DISTAL FOREARM FRACTURE IN PERSONS 50 YEARS OLD AND OLDER

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Objective: To identify the prevalent fracture risk factors in the group of persons 50 y and older. Assess their impact on BMD in patients with a distal forearm fracture (DFF-fracture of the radius) over 50 y at low injury.

Methods: A comparative study among patients with DFF in the age group 50 y and older. Study based on medical records of city hospital trauma department. Analysis period 2009-2012. All patients underwent R-densitometry on the unit DTX-200, provided by Nicomed Takeda in the framework of the Russian Osteoscreening program.

Results: Hospital records of patients 50 y and older who suffered from low-energy fracture of the distal forearm were analyzed retrospectively for the period of 2009-2012. 791 patients were interviewed using standardized Osteoscreening Russia questionnaires. According to the survey the metabolic syndrome (MS) diagnosed in 70.8% (560 persons). It included type 2 diabetes mellitus (T2DM) -14.8% (117 persons), prediabetes -22.9% (181 people) - (impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)), obesity (33.1%) - an isolated cohort of patients with overweight and obesity without disrupting glycemic indices. All patients had DFF that occurred at a low injury. Among the investigated cohort of patients with high-normal BMD (BMD above -1.0 SD)we revealed 66.0% of patients with MS; 64.1% - with obesity; 65.4% - with the presence of prediabetes; 65.3% - with a history of type 2 diabetes. BMD-1,0-2,5 SD: 20.6% with MS; obesity, 20.2%; prediabetes, 19.7%; type 2 diabetes -19.5% BMD below 2.5 SD: MS at 13.5%; obesity, 15.7%; prediabetes, 14.7%; type 2 DM -15.3%. Patients with low-energy DFF with a history of metabolic syndrome differed from the group of patients without this disease by its high and high-normal% normal BMD. Almost 2/3 (70.8%) of patients with metabolic syndrome have normal BMD.

Conclusion: The prevalence of low BMD in patients of investigated groups has not been established. Proposed mechanism of fracture is focused not on the performance of T-score (BMD) but the bone quality due to changes caused by abnormality of bone metabolism. Suppression of medullary osteoblastogenesis by adipocytes of bone marrow and stimulation of proinflammatory cytokines synthesis leads to increased bone fragility without decreasing BMD.

P064

LACTOBACILLUS RHAMNOSUS (LR) ENHANCES BONE HEALTH IN OSTEOPOROTIC MICE MODEL (OVX) BY REGULATING TREG-TH17 BALANCE

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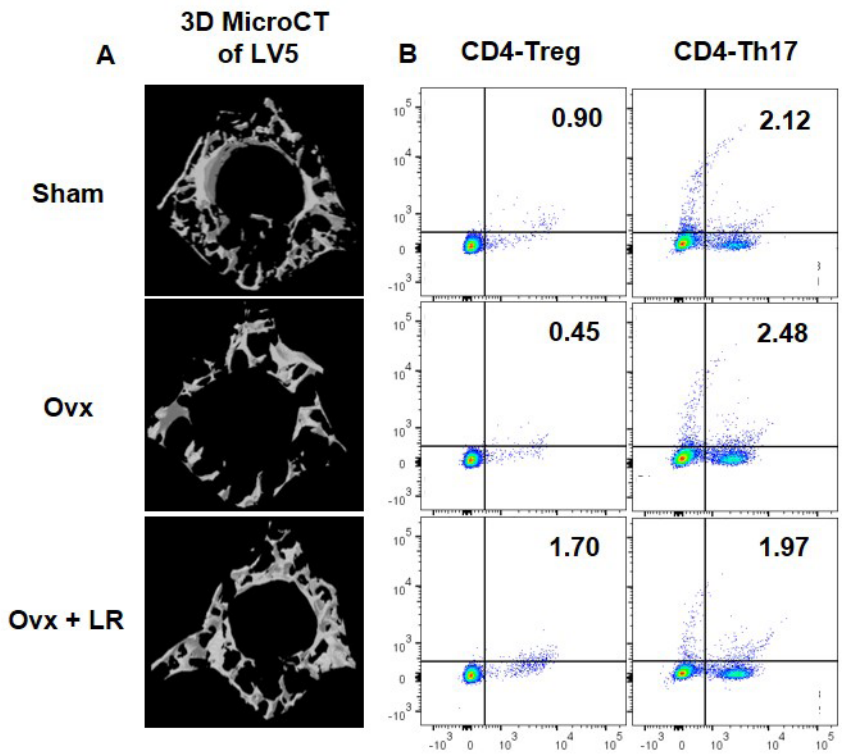
Objective: Probiotics compromise a group of living micro-organisms which upon administration in adequate amounts confer a health benefit on the host by altering the composition of the GM. Recently, various probiotic strains have been found with immense potential for regulating bone health. Taking cue from these studies we administered *Lactobacillus rhamnosus* (LR) strain for studying its effect on bone mass in ovariectomy (Ovx) induced osteoporotic mice model.

Methods: Mice were divided into three group's viz. Sham, Ovx and Ovx + LR. LR was administered orally and at the end of 6th week mice were sacrificed and analyzed for various parameters for accessing the role of LR on bone health by the use of different cutting-edge technologies such as AFM, SEM, FTIR, µCT, FACS, and ELISA.

Results: Interestingly, it was observed that administration of LR protected mice from Ovx-induced bone loss which was confirmed by SEM, AFM, FTIR and µCT analysis of bone samples. Mechanistic studies revealed that administration of LR significantly increased the percentage of Tregs in both primary and secondary lymphoid tissues along with simultaneously decreasing Th17 cells. Serum cytokine analysis further confirmed that LR administration significantly decreased proinflammatory cytokines (IL-6, IL-17, TNF-α) and increased anti-inflammatory cytokines (IL-10, IFN-γ) in ovx group.

Conclusion: Thus, we propose that the inhibitory effect of LR on bone loss is mainly mediated via its effects on the Th17 & Treg which in turn regulates osteoclastogenesis.



Lactobacillus rhamnosus enhances bone health in osteoporotic mice mod

P065

WE NEED TO TALK ABOUT YOUR BONES: A STUDY OF PATIENT OUTCOMES AND EXPERIENCES FOLLOWING CONVERSATION ABOUT SECONDARY FRACTURE PREVENTION

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Objective: To understand how the outcomes and experiences of fragility fracture patients are impacted by the context surrounding secondary prevention conversations.

Methods: Explanatory sequential mixed methods methodology underpinned an observational, non-experimental epidemiological study of consecutive patients accessing a Fracture Liaison Service (FLS) over a 3-month period. A subsequent phenomenological investigation, utilising semistructured interview, sought patient experience data.

Results: Patients with recent fragility fracture (n=123) discussed secondary fracture prevention with a FLS nurse. Twenty-three patients were referred for bone density scanning, with 14 patients completing the examination. A total of 59 patients were recommended to start bone-enhancing medication, with 18 patients initiating treatment within 6 months (31%). Specific aspects relating to the nurse-patient discussion were investigated, to see if contextual factors had an observable influence on the commencement of treatment. Telephone contact was found to be slightly more successful than in-person contact (at 41% and 26%, respectively). Timing of first contact was observed as having a greater influence on treatment initiation, with success rates ranging from 0-40% across the six intervals studied. Women interviewed about their osteoporosis conversation revealed three key themes. (1) *Life after fragility fracture* gave voice to a period after index fracture characterised by intense pain and greater than expected impact on emotional state. During this phase, energy was totally focused toward physical and psychological recovery. (2) *Person-centred communication* revealed how contextual features support or undermine the bone health conversation. The women spoke of being happy to talk about their bones, particularly when the discussion was well-timed, planned, and preferably undertaken face to face. (3) *Knowing, Learning, Accepting* emerged as the final theme, indicating that osteoporosis knowledge builds over time. Learning was aided by individualised information and a second opportunity to talk about bones.

Conclusion: We need to keep talking about bones. Conversations between patients and healthcare professionals that acknowledge vulnerability after first fracture, are person-centred, and facilitate adult learning about osteoporosis, will be most likely to motivate self-management.

P067

DISCORDANT INTERPRETATION OF SERIAL BMD MEASUREMENTS BY DXA USING VENDOR'S AND INSTITUTIONAL LEAST SIGNIFICANT CHANGES (LSCS): SERIOUS IMPACT ON DECISION MAKING

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Objective: BMD is measured serially to ascertain disease progress and treatment response evaluation. A meaningful change should be equal or higher than institutional least significant change (LSC). However, it is not uncommon that some facilities use vendor's LSC which is discouraged by ISCD. Aim of this study was to find impact of scan interpretation upon interval BMD changes using vendor's and institutional LSCs.

Methods: This prospective study was conducted at a Joint Commission International (JCI) accredited facility of Pakistan from April-June 2017 using Hologic Discovery-A. As per ISCD recommendations, precision error and LSC of two technologists were measured. Due to higher precision error, Technologist-B was sent for retraining and LSC of Technologist-A was used as institutional LCS. Serial BMD changes like deterioration or improvement interpreted based on vendor's and institutional LSCs were compared.

Results: Serial BMD changes in DXA studies of 102 patients were included, having a mean age, male:female ratio and mean BMI of 63 y, 94%:06% and 29.274 kg/m^2, respectively. Mean menopausal age was 47 y and mean duration between DXA studies was 03 y. BMD changes over hip were found significant in 55% and 53% cases against vendor's and institutional LSCs, respectively (nonsignificant discordance in 02% cases). BMD changes using vendor's and institutional LSCs were found significant over L1-4 spine (62% vs. 46%; discordance:14%) and distal forearm (77% vs. 35%; discordance:41%), respectively. Interpretations based on vendor's LSCs revealed significantly overestimated deterioration over forearm and improvement over L1-4 spine BMD values.

Conclusion: We conclude that vendor's provided LSC for interpretation of serial DXA is misleading and has significant negative impact upon patients' management. Every DXA facility must use its own LSC as per ISCD guidelines. Furthermore, ISCD must consider publishing cutoff values for precision error and LSC for distal forearm measurement.

P068

A MULTICENTRE COHORT STUDY OF RISK FACTORS FOR MORTALITY, FALLS, AND RECURRENT FRACTURES AMONG PATIENTS UNDER FRACTURE LIAISON SERVICE

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Objective: Significant care gap exists for those suffering from fragility fracture and osteoporosis. We reported the design and risk factors on 2-y mortality, falls, and recurrent fractures of a fracture liaison service (FLS) program.

Methods: Our FLS program enrolled patients with incident hip fracture and untreated vertebral fracture from both inpatient and outpatient services from 2 hospitals (N=600). Physician champions, and care coordinators followed protocols adapted from the 13 best practice framework (BPF) standards published by the International Osteoporosis Foundation and provided baseline assessments with scheduled follow-up for 2 y. Multivariate regression analysis was used to identify significant determinants of 2-y mortality, falls, and recurrent fractures.

Results: The mean age for this cohort was 77.5±10.5 y with 72% female. The implementation of FLS programs in this cohort reached level II or above for most of the 13 BPF standards. Two-year mortality was 14.2%, fall rate was 33.2%, and recurrent fracture rate was 6%.Cox proportional hazard model revealed that older age (HR 1.031, $p<0.05$), presence of chronic kidney disease (HR 3.466, $p<0.05$), cancer (HR 3.414, $p<0.05$), BMI <21 (HR 1,964, $p<0.05$) and serum albumin <3.8 (HR 2.49, $p<0.05$) were significant risk factors for mortality. The presence of heart disease (HR 2.093, $p<0.05$) increased the risk for incident fracture. Older age (HR 1.019, $p<0.05$), BMI >24 (HR 1.1.08, $p<0.05$), the presence of cancer (HR 1.571, $p<0.05$), and osteoarthritis (HR 1.568, $p<0.05$) increased the risk for fall.

Conclusion: Our FLS program compliant with best practice standards to provide quality care, and we identified risk factors for mortality, falls, and recurrent fracture among these patients.

P069

SEX HORMONE INTERACTION WITH TRABECULAR BONE SCORE AND MINERAL DENSITY IN MEN

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Objective: To evaluate the relationship of sex hormones with bone quality and mineral density in men.

Methods: We examined 72 men aged 40-87 y. Depending on their BMI, all the subjects were divided into 2 groups: Group I – 19 men with obesity whose BMI was ≥30 kg/m^2 (mean age 60.3±10.8 y, height 177.3±5.8 cm, weight 102.5±7.6 kg, BMI 32.6±1.9 kg/m^2), and Group II – 53 men without obesity and BMI of <30 kg/m^2 (mean age 60.5±13.5 y, height 174.6±6.9 cm, weight 79.2±10.3 kg, BMI 25.9±2.4 kg/m^2). The BMD of lumbar spine at the site L_1-L_4 and femoral neck were measured by DXA (Prodigy, GEHC Lunar, Madison, WI, USA). The TBS of L_1- L_4 was assessed by means of TBS iNsight® software installed on our DXA machine (product of Med-Imaps, Pessac, France). Total testosterone and SHBG were measured in all the subjects using an enzyme immunoassay method. The level of free testosterone was calculated using the ISSAM website calculator.

Results: In general, we found that obese men have a significantly higher BMD at the level of lumbar spine (group I – 1.402±0.232 g/cm^2, group II – 1.203±0.245 g/cm^2, F=9.08, p=0.004) and femoral neck (group I – 1.050±0.141 g/cm^2, group II – 0.925±0.164 g/cm^2, F=8.80, p=0.004) in comparison with men of no obesity. Significant differences between the groups for the TBS were not found. When assessing the hormonal status in men, it was revealed that obese men have a significantly lower total testosterone (group I – 12.55±3.48, group II – 17.64±6.10, F=11.74, p=0.001) and SHBG (group I – 43.03±20.27, group II – 58.15±25.39, F=5.46, p=0.02). However, the probable differences in the levels of free and bioavailable testosterone were not found. The level of SHBG increased with age and there was a probable negative correlation with BMD of femoral neck (r=-0.39; p<0.001). There was no significant correlation between total testosterone and BMD of femoral neck in men with a normal body weight (r=-0.19, p=0.2) and an obesity (r=0.02, p=0.93). Significant association between TBS and sex hormones in men was not revealed.

Conclusions: Men with obesity have a significantly lower total testosterone and SHBG, but their BMD is significantly higher than the one of men with a normal weight.

P070

ASSOCIATIONS BETWEEN METABOLIC SYNDROME, BONE MINERAL DENSITY AND TRABECULAR BONE SCORE IN POSTMENOPAUSAL WOMEN WITH NONVERTEBRAL FRACTURES

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Objective: Medical, social and economic relevance of osteoporosis is explained by the lowering quality of life, increasing disability and mortality of patients as a result of fractures due to the low-energy trauma (Bliuc D. et al., 2009; Maghraoui A. et al., 2014; Poiana C. et al., 2015; Huang C.Y. et al., 2015). This study is aimed to examine the associations of metabolic syndrome components, BMD and trabecular bone score (TBS) in menopausal women with nonvertebral fractures.

Methods: 1161 menopausal women aged 50-79 y old were examined and divided into three groups: A included 419 women with increased body weight (BMI - 25.0-29.9 kg/m^2), B – 442 obese women (BMI > 29.9 kg/m^2) and C – 300 women with metabolic syndrome (diagnosed according to the IDF criteria, 2005). DXA (Prodigy, GE Medical systems, Lunar, Madison, WI, USA, 2005) was used for measuring lumbar spine (L1-L4), femoral neck, total body and forearm BMD and bone quality indices (the latter by means of the Med-Imaps installation). Data were analyzed using Statistical Package 6.0.

Results: A significant increase of lumbar spine (L1-L4), femoral neck, total body and ultradistal radius BMD was found in women with obesity and metabolic syndrome compared to the pre-obese ones ($p<0.001$). TBS was significantly higher in women with increased body weight compared to obese and metabolic syndrome patients. Analysis showed significant positive correlation between waist circumference, triglycerides level and BMD of lumbar spine and femur. Significant negative association between serum HDL level and BMD of the examined sites was established. The TBS (L1-L4) indices positively correlated with HDL level. Low-trauma nonvertebral fractures occurred in 14.6% female with increased body weight, 17,4% of women with obesity and 21.3% of patients with metabolic syndrome.

Conclusion: Menopausal women with obesity and metabolic syndrome have a significantly higher BMD at all the measured sites compared to females with pre-obesity. TBS is significantly lower in women with non-vertebral fractures and increased body weight or obesity. Despite the fact that BMD indexes were better in women with metabolic syndrome, the frequency of nonvertebral fractures was significantly higher in this group of patients.

P071

RELATIONSHIP BETWEEN BODY COMPOSITION ANALYSIS AND FRACTURE RISK IN MIDDLE-AGED AND ELDERLY PEOPLE LIVING IN COMMUNITY IN HOHHOT

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Objective: Adipose tissue is closely related to bone metabolism, and the relationship between obesity and bone health remains unclear. The purpose of this study was to investigate the relationship to fracture risk through body composition analysis.

Methods: The investigation included 249 middle-aged men and women living in the community of Hohhot, including 46 males and 203 females, aged 40-90 y. Body composition and BMD were measured using DXA, and fracture risk was further analyzed by a fracture risk questionnaire.

Results: The mean age was 62 y old, female BMI 29, male BMI 25, femoral neck BMD was 0.62 g/cm^2 for females and 0.72 g/cm^2 for males. The risk of major fractures in the next 10 y was 6.8 for females, 3.2 for males, and hip fracture for the next 10 y was 2.7 for females and 1.3 for males. The percentage of female body fat was 36%, and the percentage of male body fat was 25%. The amount of lean tissue in males was higher than that in females, and the percentage of fat was lower than that in females. The fracture of the main part of the female was related to the age and the percentage of body fat and was negatively correlated with the bone density of the femoral neck, the amount of lean tissue and the amount of lean tissue in the limbs, and the lean tissue index. Hip fracture was positively correlated with age, and was negatively correlated with femoral neck bone density, body lean tissue mass, and lean tissue mass in the extremities.

Conclusion: The results of this study suggest that body composition contributes to the analysis of fracture risk, analyzes the characteristics of body composition analysis indicators of community residents, and investigates relevant factors for disease prevention and treatment.

P072

25-HYDROXYVITAMIN D LEVELS, VITAMIN D DEFICIENCY AND INSUFFICIENCY IN PATIENTS WITH MUSCULOSKELETAL DISORDERS

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Objective: To examine 25(OH)D level, vitamin D deficiency and insufficiency prevalence in patients of various ages who have musculoskeletal disorders, and to reveal the influence of seasonal factors on these conditions.

Methods: 3460 patients of the Ukrainian Scientific-Medical Center of Osteoporosis Problems, aged 1-92 y (mean age 52.9±21.1 y). 25(OH)D and PTH analyses were performed by means of electrochemiluminescent method (Elecsys 2010 analyzer, Roche Diagnostics, Germany) and cobas test-systems.

Results: Among the patients with bone-muscular pathology, the highest 25(OH)D level was noted in the age group of 1-9 y (30.6±15.1 ng/ml) and the lowest in the age group of 80 and over (20.4±11.4 ng/ml). Prevalence of vitamin D deficiency among the patients with bone-muscular pathology was 37.3%, vitamin D insufficiency 30.6%, normal vitamin D status in 32.1%. Normal 25(OH)D concentration was found in 38.0% of children, 33.2% of adults and in 29.6% of elderly patients. Month of blood sampling had a significant influence on 25(OH)D concentration values ($F=7.49$: $p<0.0001$). The highest significant differences in 25(OH)D concentrations during the summer vs. winter months were observed in the age groups of 10-19 y (18.2%), 40-49 y (17.3%), 30-39 y (16.2%) and 1-9 y (16.1%). There were no significant seasonal differences observed in the elderly patients (60 y and older) with musculoskeletal pathology.

Conclusion: Despite the combined calcium and vitamin D supplementation utilized by most patients with a bone-muscular pathology, only 37.9% of children, 33.2% of adults and 29.6% of the elderly people had normal 25(OH)D concentration values.

P073

EPIDEMIOLOGY OF HIP FRACTURES IN UKRAINE: RESULTS OF STOP-STUDY

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Objective: Hip fracture is one of the most serious complications of osteoporosis, which has important medical, social and economic complications. It is well known that incidence of hip fractures gradually increases with age and depends on the sex, but similar epidemiological studies in Ukraine are limited. The aim of the present study was to estimate age- and sex-specific hip fracture rates in Ukrainian population.

Methods: The STOP study (Study of The prevalence of Osteoporotic fractures in Ukrainian Population) was conducted in 2011-2012. It was organized by Ukrainian Association of osteoporosis with the support of the Ukrainian Association of orthopaedist and traumatologists and was gathering the information about incidence of hip fractures in different parts of Ukraine.

Results: It was established that incidences per 100,000 persons in both sexes progressively increased with age. At younger ages, up to 67 y, incidence rates were higher in men than in women; but thereafter they were much higher in women, almost double at the age of 80–85 y. Overall incidence of hip fracture was comparable with data from neighboring countries (Poland and Romania).

Conclusions: As hip fractures are a serious health problem in Ukraine and around the world, the regional epidemiological data about hip fractures incidence is an important basis for the development of a national system of prevention and treatment of osteoporosis and its complications.

P074

EVALUATING SPINE MICROARCHITECTURAL TEXTURE (VIA TBS) IN THE DIFFERENTLY-AGED FEMALE POPULATION OF UKRAINE

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Objective: To create a reference database for the trabecular bone score (TBS) including the Ukrainian women of different ages.

Methods: We examined 1066 women aged 40-89 y old (age 62.47±9.57 y, height 1.61±0.63 m, body weight 73.48±6.27 kg) who were divided into the groups depending on their age: 40-44 y (n=33), 44-49 y (n=62), 50-54 y (n=137), 55-59 y (n=169), 60-64 y (n=215), 65-69 y (n=180), 70-74 y (n=151), 75-79 y (n=76), 80-84 y (n=31), 85-89 y (n=12). TBS was assessed using TBS iNsight (Med-Imaps, Pessac, France). BMD of the lumbar spine (L_1-L_4) was measured by DXA (Prodigy, GE Lunar, Madison, USA).

Results: Age has a significant effect on the variability of the TBS (F=26.78; p<0.0001). However, the effect of age on BMD L_1-L_4 wasn't detected (F=1.02; p=0.42). We determined the following parameters of TBS and BMD L_1-L_4 for the Ukrainian women depending on their ages: 40-44 y – 1.374±0.114 and 0.993±0.201; 44-49 y – 1.340±0.116 and 1.068±0.184; 50-54 y – 1.301±0.120 and 1.072±0.201; 55-59 y– 1.220±0.151 and 1.025±0.209; 60-64 y – 1.212±0.124 and 1.031±0.199; 65-69 y – 1.188±0.143 and 1.027±0.192; 70-74 y – 1.146±0.134 and 1.030±0.182; 75-79 y – 1.143±0.143 and 1.027±0.217; 80-84 y – 1.139±0.132 and 1.024±0.232; 85-89 y – 1.114±0.158 and 0.993±0.194.

Conclusion: TBS is a significant predictor of age-related bone changes in women.

P075

IS BREAST SIZE RELATED TO THORACIC VERTEBRAL FRACTURE RISK?

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Objectives: To examine breast size as an independent predictor of thoracic vertebral fracture in postmenopausal women.

Methods: This was a cross-sectional study of postmenopausal women. Objective measurements were collected on: thoracic vertebral fractures (defined as ≥20% loss in vertebral body height on lateral radiograph); breast size (bra size converted to breast form score); BMD (T-score of left neck of femur using DXA); upper back extensor muscle endurance (Isometric chest raise test); body composition (DXA) and thoracic kyphosis (radiograph). Data were analysed using binary logistic regression analysis with vertebral fracture (yes/no) as the dependent variable. Initially each physical characteristic was entered into univariable models. Those variables with a significant association with fracture were then entered into a multivariate model.

Results: 117 postmenopausal women, 17 (15%) with ≥1 thoracic vertebral fracture participated in the study. Women with fracture had a larger breast size (mean difference (MD): 1.38 sizes, 95%CI: 0.92-2.67 sizes), lower upper back muscle endurance (MD: 38.60s, 95%CI: 14.30-62.90s) and greater thoracic kyphosis (MD: 7.25° 95%CI: 1.7-12.78°), compared to those without fracture. There was no difference between groups in BMD. Characteristics that were associated with increased odds for vertebral fracture were an increased breast size (OR: 1.26, 95%CI: 1.01-1.57) and thoracic kyphosis (OR: 1.07, 95%CI: 1.01-1.13). Although greater upper back extensor muscle endurance was associated with a significant decrease in odds for vertebral fracture (OR: 0.99, 95%CI: 0.98-1.00) in univariable models it was not significant in the final multivariate model. The final multivariate model, containing breast size and thoracic kyphosis, was significant (p=.004) and explained 16% of the variance in vertebral fracture.

Conclusions: Breast size and thoracic kyphosis are associated with thoracic vertebral fracture in postmenopausal women. Thoracic vertebral fractures could be considered a burden of large breasts. Acknowledgments: Primary researcher supported by an Australian Government Research Training Program Scholarship and Curtin University Research Scholarship.

P076

IMPACT OF KNEE OSTEOARTHRITIS TO BONE MINERAL DENSITY AND DIAMETER RECTUS FEMORIS MUSCLE

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Objective: Knee osteoarthritis (OA) is characterized by degradation of articular cartilage and substantial loss of matrix. Intra-articular cell senescence and cartilage matrix degradation, extra-articular loss of skeletal muscle mass (SMM) and deteriorated proprioception contribute to development of OA. These causes chronic disability and can impact to risk of fall and decrease of extremity muscle strength. Early identification for osteoporosis and risk of decrease muscle strength in knee OA patients could reduce medical complications. Rectus femoris muscle as part of quadriceps places more superficial and have strong effect to extend and rise the knee. The present study had the objective to identify BMD, anthropometric characteristics and diameters of dominant femur of rectus femoris muscle in knee osteoarthritis patients who had difficulties to stand up after squat. To identify the relationship between diameter rectus femoris to BMD and to BMI.

Methods: Thirsty-five knee osteoarthritis patients participated in this study were assessed by DXA of femoral neck and spine to determine BMD. The diameter of rectus femoris muscle was assessed by musculoskeletal ultrasound on knee flexion ninety degree and quadriceps in relax position.

Results: The results shown 85.7% was women, BMI mean 27.1 kg/m^2 (SD±5,46) and 26 patients (74.3%) have osteoporosis. Mean of diameter rectus femoris was 1.68 cm (SD±0.32). There was no correlation between diameter rectus femoris and BMD (r=0.020; p>0.05) and so to BMI, there was no correlation (r=0.36; p>0.05).

Conclusion: Most of knee OA patients who have difficulties to stand up after squat were osteoporosis even they were overweight. Diameter of rectus femoris muscle as a part of quadriceps did not be determined by BMD and BMI.

P077

EFFICACY AND SAFETY OF 1-YEAR TREATMENT WITH DENOSUMAB IN POST KIDNEY TRANSPLANTATION RECIPIENTS

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Objective: Post kidney transplantation (KTx) patients are known to have high fracture risk especially during first year after KTx mainly due to immunosuppression therapy such as glucocorticoid. Anti-RANKL antibody denosumab has strong inhibitory effects on bone resorption, but its efficacy and safety after KTx is still uncertain. We have previously shown the efficacy and safety of denosumab during first year after KTx. In the present study, we explored the efficacy and safety of denosumab during two years after KTx.

Methods: This study was performed in Fujita Health University Hospital, and post-KTx patients were recruited (n=39, M/F=26/13, age 50±13 y old) from 2014-2016. Denosumab was administrated every 6 months during first year after KTx in 31 cases regardless of BMD at KTx. Other 8 cases who were not met to the criteria of glucocorticoid-induced osteoporosis would not like to take any anti-osteoporosis medicine (Control). The patients in denosumab-treated (Dmab) group also took 0.25-1.00 μg/d of alfacalcidol or 400 IU/d of cholecalciferol.

Result: Among Dmab group, two female patients dropped out of study because of retransplantation and moving to another hospital. The new clinical bone fracture was found in 1 case in Dmab group, while no patient had any fracture in control group. In Dmab group, lumbar and femoral neck BMD significantly increased during first year and returned to baseline in 2 y after KTx. In the control group, femoral neck BMD tended to continuously decrease during 2 y after KTx. The increase of serum creatinine levels in Dmab were not different from those in control groups after KTx.

Conclusion: The treatment with denosumab would be tolerable and effective in post KTx patients.

P078

THORACIC KYPHOSIS MEASUREMENT IN POSTMENOPAUSAL WOMEN: AN EXAMINATION OF THE FLEXICURVE METHOD IN COMPARISON TO RADIOLOGICAL METHODS

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Objectives: To examine and compare the validity of the flexicurve method using two separate "gold standard" radiological measurements of Thoracic kyphosis (TK) in postmenopausal women.

Methods: This was a cross-sectional study of postmenopausal women. Thoracic kyphosis was measured in each participant using 1) a flexicurve ruler and 2) a lateral thoracic x-ray. Flexicurve kyphosis angles were calculated using a mathematical formula and flexicurve dimensions. Cobb and centroid angles were measured from a single x-ray of each participant. Correlations (*r*) between methods were calculated and Paired-samples t-tests identified differences between the angles obtained from each method. Using a Bland and Altman analysis, each method was paired with another and assessed for agreement. Linear regression was used to assess if the differences in measurement between methods were significantly predicted by age (y), BMI (kg/m^2) and BMD (g/cm^2).

Results: 117 postmenopausal women (mean age: 61.43 y, SD 6.99 y) participated in this study. Thoracic vertebral fractures were identified in 17 women. The flexicurve kyphosis angles were more strongly correlated with the centroid angles (r=0.61, p<0.005) than with Cobb angles (r=0.55, p<0.001). The Bland and Altman analysis showed a fixed bias in the plots between flexicurve method and both the Cobb and centroid methods. The flexicurve method recorded smaller angles than the Cobb method (MD: 18.02°, 95%CI: 16.35-19.69°) and the centroid method (18.57°, MD: 95%CI: 16.99-20.17°). In relation to the Cobb method, the differences increased proportionally and progressively as the average values increased. The differences between radiological and flexicurve methods increased with increasing age which explained up to 6-8% of this variance.

Conclusions: Thoracic kyphosis measured in healthy postmenopausal women using the flexicurve method shows poor agreement with radiological methods regardless of whether the Cobb or centroid angles are used for comparison. Inaccuracy of the flexicurve increased with increasing angle of kyphosis and increasing age.

Acknowledgements: Primary researcher was supported by funding from an Australian Government Research Training Program Scholarship and Curtin University Research Scholarship.

P079

PREVALENCE AND RISK FACTORS OF OSTEOPOROSIS AMONG THAI MIDDLE-AGED MENOPAUSAL WOMEN

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Objectives: To evaluate the prevalence and risk factors of osteoporosis among Thai middle-aged menopausal women.

Study design:

Methods: Cross-sectional study. 150 eligible women, who visited menopause clinic of Phramongkutklao Hospital during May-August 2018, participated in this study. Demographic data and baseline characteristics were interviewed. Laboratory values and medical history were reviewed from hospital database. The participants were informed to record dietary diary for 7 d and average daily calcium intake (mg/d) was calculated by International Osteoporosis Foundation (IOF) calcium calculator. BMD was measured by DXA. The BMD outcomes were evaluated and reported by clinical experts.

Results: The prevalence of osteoporosis, osteopenia and normal BMD were 21.3%, 54.7% and 24%, respectively. The significant associated risk factors were increasing age (adjusted OR=1.3, 95%CI=1.2-1.5), low level of calcium intake (adjusted OR=9.7, 95%CI=3.6-27.2), lack of exercise (adjusted OR=7.1, 95%CI=1.4-36.1). Recent year since menopause and increasing waist circumference were found to be protective factors.

Conclusion: The prevalence of osteoporosis among Thai middle-aged menopausal women was 21.3% which was influenced risk by increasing age, low calcium intake and lack of exercise.

P080

STUDY DESIGN AND BASELINE CHARACTERISTICS OF THE POPULATION ENROLLED IN A MULTINATIONAL, OBSERVATIONAL STUDY OF TERIPARATIDE (ALAFOS)

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Objectives: Prospective observational studies analyzed use of teriparatide (TPTD) in USA, Europe and Japan. We describe the design and baseline characteristics of patients in the "Asia & Latin America Fracture Observational Study" (ALAFOS).

Methods: ALAFOS a non-interventional, prospective, observational study in postmenopausal osteoporotic women treated with TPTD up to 24 months, with a post-TPTD follow-up until 12 months. Baseline included demographics, risk factors for osteoporosis and falls, physical function, back pain (numeric rating scale-NRS), osteoporosis knowledge, and health-related quality of life (HRQoL).

Results: 3031 patients, 156 sites, 20 countries (Asia, Latin America, Middle East, Russia). Most participants were White (47.4%) or Asian (42.7%). Mean (SD) age and BMI: 72.5 (10.4) y and 24.9 (5.0) kg/m^2, respectively. Mean (SD) baseline lumbar spine, total hip and femoral neck T-scores were -3.06 (1.4), -2.43 (1.14), and -2.6 (1.05), respectively. 63.2% of subjects had history of fracture after age 40 (33% spinal, 14.2% hip), and 40.5% of patients had ≥1 fall the year before enrollment. At entry, 43.7% of patients were osteoporosis-treatment naïve, 2.9% were taking glucocorticoids. Most used osteoporosis drug was bisphosphonates (27.6% of subjects). Found comorbidities: type 2 diabetes (12.7%) and rheumatologic disorders (9.1%). The mean (SD) NRS worst back pain in the last day was 4.6 (3.3). Mean (SD) EQ-5D-5L utility total score, EQ-5D-5L visual analog scale, and physical function score in OPAQ were 0.50 (0.36), 61.0 (21.8), and 45.1 (30.6), respectively.

Conclusions: Baseline characteristics indicate that patients prescribed TPTD have severe osteoporosis, highly prevalent fractures, disabling back pain, and poor HRQoL; use of osteoporosis drug therapy was lower than in other studies.

Disclosures: Sponsored by Lilly

P081

INCREASED HUMAN FEMORAL CORTICAL POROSITY INDICATES POSSIBLE OCCURRENCE OF OSTEOPOROSIS IN PREHISTORIC TONGA

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While osteoporosis is well studied in living human populations, little is known about the occurrence of this condition in prehistoric societies in the Pacific. This study investigated abnormal cortical bone porosity in archaeologically derived ancient Tongan femora to establish whether poor bone quality and quantity may have been present in this region as early as approximately 3000 years ago.

Using static histomorphometry and 3D laser scanning confocal microscopy, cortical bone remodelling and endo-cortical porosity were examined in four male and female (n=8) adult femoral midshaft samples from 2650 BP archaeological site of Talasiu, Kingdom of Tonga. A quantitative assessment of bone vascularity and remodelling rate was undertaken by estimating secondary Haversian canal density in the cortical wall of each femoral thin section. Subsequently, abnormal bone porosity was also measured from the endocortical to subperiosteal region in each sample.

When compared to males, Haversian canal density indicative of cortical bone vascularity was lower in females. Females also showed the highest variation within their sex category, with males exhibiting an overall consistent rate of bone remodelling. Increased endocortical porosity was observed in every single female sample, with an average 36% of overall section affected by poor bone quality. In contrast, only an average 15% of total bone section area was abnormally porous in males.

Results indicate sex-specific differences in bone quality and quantity at the midshaft femur in these ancient individuals. The accelerated bone loss at the microstructural level in females may relate to a manifestation of menopause-driven bone turnover changes. However, the presence of increased cortical porosity in almost all cases is possibly evidence of osteoporosis inflicting the prehistoric societies of Tonga. Our findings align with high incidence of metabolic disorders (such as diabetes) in the contemporary Pacific, and previously reported ancient skeletal manifestation of possible gout and diffuse idiopathic skeletal hyperostosis. Taken together, poor bone quantity and quality in ancient Tongans may have been a result of complex metabolic changes underpinned by sex, lifestyle, diet, and genetic factors.

P082

COMPARISON OF THE PHARMACOKINETICS OF ORAL 150 MG IBANDRONATE BETWEEN EUROPEAN AND TAIWANESE POSTMENOPAUSAL WOMEN

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Objectives: Oral monthly doses of ibandronate have been reported to be significantly efficacious for osteoporosis. Studies investigating the interethnic difference in the pharmacokinetics of oral ibandronate are still lacking. This work aims to compare the disposition of ibandronate after oral administration between ethnic European and Taiwanese postmenopausal women.

Methods: The interethnic comparison utilized patient level data from two phase 1 studies of oral ibandronate to assess the pharmacokinetic properties including the area under the concentration-time curve (AUC), peak concentration (Cmax), the time to reach Cmax (Tmax), elimination half-life, urinary drug recovery (Ae%), renal clearance (CLr), apparent total clearance after oral administration (CL/F) and apparent volume of distribution by the oral route (Vd/F).

Results: Oral ibandronate was rapidly absorbed into the blood, reaching Cmax at 0.94 and 1.50 h after oral administration in Caucasian and Taiwanese participants, respectively. In Taiwanese subjects, the mean AUC, Cmax and Ae% were 2.41-, 1.69- and 2.95-fold greater, respectively, than in European subjects. The average CL/F and Vd/F were 2.48- and 2.46-fold smaller in Taiwanese subjects, respectively, compared with European subjects. There was no statistical difference in the mean values of CLr and half-life in both groups. For nitrogen-containing bisphosphonates, the total body clearance is close to CLr because it is not metabolized in the body and the renal excretion is the predominant route of elimination. These data suggested a larger bioavailability (F) in Taiwanese group and the difference of bioavailability leaded to the differences in CL/F and Vd/F between two groups. The multiple linear regression analysis demonstrated ethnicity influences the pharmacokinetic properties after adjusting for the other variables.

Conclusion: The process of drug absorption from the gastrointestinal tract is largely responsible for the interethnic difference of the pharmacokinetics following oral administration of 150 mg ibandronate.

P083

PERSISTENT HIGH-IMPACT ACTIVITY AND FITNESS DURING ADOLESCENCE AND EARLY ADULTHOOD AND BONE DENSITY AND MICROARCHITECTURE IN EARLY ADULTHOOD

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Objective: This prospective study aimed to investigate whether persistent high-impact activity (HIA) and fitness during adolescence and early adulthood were associated with BMD and microarchitecture in early adulthood.

Methods: We followed 201 participants from birth to 25 y. Outcomes were areal BMD (aBMD) at the lumbar spine (LS), hip and total body (by DXA) and trabecular and cortical bone measures (by HR-pQCT) at the radius and tibia. Exposures were HIA participation (by questionnaire) and physical fitness (by physical work capacity (PWC_{170})) at ages 16 and 25 y. Multivariable linear regressions were used to assess associations of different HIA and fitness patterns between age 16-25 with bone measures at age 25.

Results: There were significant interactions between HIA/fitness patterns and sex for most bone measures. Compared to those with persistently low HIA, males with persistently high HIA (n=36) had better bone outcomes at age 25 (aBMD at all sites; trabecular volumetric density (Tb.vBMD), trabecular number, trabecular separation, trabecular bone volume fraction (Tb.BV/TV) at both radius and tibia, and cortical thickness (Ct.Th) and inner transitional zone porosity at the tibia). Persistently high fitness was also associated with higher LS and hip aBMD, higher Tb.BV/TV at the radius and higher Tb.vBMD, Tb.BV/TV, trabecular and cortical thickness (Tb.Th, Ct.Th), lower inner transitional zone porosity at the tibia compared with persistently lower fitness. For females, compared to those with persistently low HIA, participants with persistently high HIA (n=12) had higher total volumetric density and lower inner transitional zone porosity at the tibia only. Persistently high (n=28) compared to lower fitness was only associated with higher Ct.Th at the tibia.

Conclusions: Maintaining high HIA and fitness from adolescence to young adulthood appears beneficial for bone density and microarchitecture in early adulthood particularly in males. This supports health promotion messages highlighting the lifelong potential benefits of physical activity for bone.

P084

LOWER SERUM SODIUM CONCENTRATION IS ASSOCIATED WITH REDUCED CORTICAL THICKNESS AND CORTICAL DENSITY AT 66% SITE OF TIBIA IN YOUNG FEMALES

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Objectives: Hyponatraemia (serum [Na+] <135 mmol/L) is associated with increased risk of osteoporosis and fractures and is more prevalent in females. In addition, postmenopausal females have a greater prevalence of osteoporosis and incidence of fracture than males. However, associations between hyponatraemia and bone health have not been investigated in young healthy females to the best of authors' knowledge. We aimed to investigate associations between serum sodium concentration and BMD and fractures in young females to search for an independent pathophysiological association.

Methods: This cross-sectional study included female participants, aged 16-25 y from Victoria, Australia, who had serum sodium concentrations and bone health measures including reported fracture history, BMD, bone mineral content (BMC) by DXA and pQCT of 4% and 66% sites of the tibia available from two studies. All bone measures were adjusted for age, height and weight. Clinical data, including medical history, fracture history and health behaviours were obtained via questionnaires.

Results: 434 participants were recruited. Cortical thickness was positively correlated with serum sodium concentrations (rho=0.100, p=0.042) and those with hyponatraemia had lower tibia cortical density at the 66% site than those with normonatraemia (1119.4 (1105.7-1138.6) vs. 1150.6 (1131.0-1167.5) mg/cm^3; p=0.017). Lower metabolic equivalents categories were significantly associated with reduced total hip BMD ($\chi^2(3)=12.948$, p=0.005) and total trabecular area at the 4% tibia site (F(3,402)=2.817, p=0.039). 25-hydroxyvitamin D levels also were positively correlated with cortical thickness (rho=0.137, p=0.005).

Conclusions: Even from a young age, hyponatraemia and lower physical activity may be associated with poorer bone health. Further prospective studies with a larger sample size are required to investigate an independent physiological association between serum sodium concentrations and bone health, and the effect of its reversibility with electrolyte restoration, to improve preventative management of bone health in females.

P085

SERUM SODIUM CONCENTRATION, BONE MINERAL DENSITY, FRACTURES AND FALLS IN ANTIEPILEPTIC DRUG USERS

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Objectives: Hyponatraemia (serum [Na+] <135 mmol/L) is associated with increased risk of osteoporosis and fractures. Antiepileptic drugs (AEDs) are also independently associated with increased risk of osteoporosis and fractures and can induce hyponatraemia. The aim of the study was to evaluate associations between serum sodium concentration and bone health measures in AED users, to help elucidate how AEDs relate to bone health.

Methods: This cross-sectional study included patients, aged 18-75 y, who had been treated with AEDs for more than one year at the time of BMD scan. Serum sodium concentrations in the 10 y prior to their index BMD scans during AED use were included. Questionnaires were used to obtain clinical data, including falls and fracture history, AED use and duration.

Results: Sixty patients were recruited. No significant associations were found between serum sodium concentrations and adjBMD or fractures. The number of hyponatraemic events was positively correlated with the number of nonseizure-related falls in the previous 12 months (rho=0.321, p=0.04), independent of fractures. Those who reported a history of fracture had longer durations of AED use in general (17.5 (8.8-36.3) vs. 8.0 (4.0-12.0) y; p=0.011) and NEIAED use (8.5 (3.8-30.5) vs. 3.0 (1.0-7.3) y; p=0.011), in particular sodium valproate (20.0 (3.0-31.0) vs. 2.5 (1.0-8.0) y, p=0.009).

Conclusions: Although longer duration of AED, especially NEIAED and sodium valproate, was associated with poorer bone health, serum sodium concentration did not appear to be an explanatory mechanism for poor bone health associated with specific AED use. Hyponatraemia may, however, increase the risk of fractures due to greater likelihood of falls. Further prospective studies with a larger sample size are required to investigate the association between serum sodium concentration, bone health and falls in AED users, and the effect of its reversibility with electrolyte restoration, to improve preventative management of bone health in AED users.

P086

BONE MINERAL DENSITY MEASUREMENT IN ADULT POPULATION USING QUANTITATIVE ULTRASOUND (QUS) OF CALCANEUS IN A COUNTRY WITH CHALLENGING RESOURCES: A CROSS-SECTIONAL STUDY FROM NEPAL

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Objective: To evaluate the BMD of Nepalese population to assess general bone health using calcaneal QUS.

Methods: QUS is a relatively inexpensive, portable and radiation free technique to assess the risk of osteoporosis in elderly women (1). A cross-sectional screening survey was conducted among male and female participants of 40 y and above. SONOST 2000 Heel Scanner was used for the screening procedure. Speed of the sound (SOS) and broadband ultrasound attenuation (BUA) was measured, Bone quality index (BQI) was calculated and T-score was generated for the analysis. T-test and chi-square test are used for continuous and categorical outcome, respectively, and logistic regression for analysis of covariates. P<0.05 is taken as a statistically significant. Statistical analysis performed through STATA (©STATA 15).

Results: 239 (mean age: 53.75±10.73), 159 females (mean age 52.90±10.41) and 80 males (mean age: 55.44±11.23), participated in the screening. The mean calcaneal T-score of all the participants was -2.04 ±.80 (females: -2.11±.82, range: -4.5 to -.1 and males: -1.81±.73, range: -3.1 to -0.7). Calcaneal T-score decreased with increasing age (P=0.001), menopause (P=0.001), and in subjects who were vegetarian (P=0.634), did not perform regular physical exercise (P=0.160) and lack a history of sun exposure (P=0.353).

Conclusion: Calcaneal QUS data showed poor bone health with increasing age in both female and male subjects. Postmenopausal females had statistically significant low calcaneal T-score. Calcaneal QUS can be a useful and a cost-effective alternative tool to assess general bone health and screen people for risk of osteoporosis in developing countries like Nepal where DXA is not readily available and economically affordable.

Reference: Chen SJ, Chen YJ, Cheng CH, et al. Medicine (Baltimore) 2016;95:e3415

P087

ADVANCED GLYCATION ENDPRODUCTS SUPPRESS LYSYL OXIDASE EXPRESSION VIA SECRETION OF TNF ALPHA IN OSTEOBLASTIC CELLS

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Objectives: To investigate the reason why advanced glycation endproducts (AGEs) can induce the suppression of lysyloxidase (LOX) in osteoblastic MG63 cells.

Methods: MG63 cells were cultured by 0~100 μg/ml AGEs and assayed LOX mRNA expression. To elucidate the pathway to regulate LOX, the cells were stimulated with a JAK2 inhibitor. The cells were cultured with 100 μg/ml AGEs for 0~12 h and the phosphorylated-JAK2 level was analyzed by western blotting. To elucidate whether the phosphorylated-JAK2 level was increased in a dose dependent manner of AGEs, the phosphorylated-JAK2 level were assayed at 30 min and 6 h after exposure to 0~100 μg/ml AGEs. TNF α, IL1 β and IL6 mRNA levels were assayed for 6 h treatment with 100 μg/ml AGEs. Finally, to investigate effect of TNF α on pathway that AGEs suppress LOX mRNA expression, the cells were cultured with AGEs and TNF α antagonist, and subsequently LOX mRNA level was assayed.

Results: LOX mRNA expression was significantly inhibited after treatment with 100 μg/ml AGEs ($p<0.01$ vs. control). JAK2 inhibitor treatment led to increase in LOX mRNA expression in a dose dependent manner. Phosphorylated-JAK2 level showed an increased tendency at 30 min and 6 h after 100 μg/ml AGEs treatment. In addition, at 6 h after AGEs treatment, phosphorylated-JAK2 level was increased in the dose dependent manner. TNF α mRNA level was increased in a dose dependent manner for 6 h AGEs treatment. Treatment with TNF α antagonist induced the increase of LOX mRNA level in the dose dependent manner of TNF α antagonist.

Conclusions: It is suggested that AGEs decreased LOX mRNA level via secretion of TNF α from MG63 cells.

P088

USING ARTIFICIAL INTELLIGENCE MODEL TO IDENTIFY PATIENTS IN FRACTURE LIAISON SERVICE

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Objectives: Fracture liaison service (FLS) is an excellent model to improve the care quality of fragility fracture patients. To identify the care demanded patients is the most important step. However, manually identifying the patients by case manager is inefficient and to omit the patient easily.

Methods: The E-Da Hospital in southern Taiwan, with approximately 1,000,000 outpatients and 40,000 inpatients per year, launched the FLS program in 2016. The thoracolumbar X-ray and DXA were all interpreted and reported formally by radiologists. By the best practice standard of IOF, the case managers manually reviewed the reports to identify the fragility fracture patients. In 2018, E-Da FLS team established the artificial intelligence (AI) model by supervised machine learning in python for automatically identifying the hip and vertebral fracture patients from the formal reports. A total of 1,500/500 reports in X-ray/DXA were used to train the models and 500/500 reports in X-ray/DXA were used for testing the accurate rate of the AI model. The time consuming was measured by reviewing 100 different reports and the omitted-patients, defined as the subjects with osteoporosis/hip fracture/vertebral fracture in DXA/X-ray reports were not identified, were calculated by either manually review or AI model.

Results: The average time consuming in reviewing 1 DXA/X-ray report was 10.7 and 0.04 seconds in manually review method and AI model, respectively. The omitted-patients rate (osteoporosis/hip fracture/vertebral fracture) was 2.0/8.0/7.0% in manually review by case managers, but 0/0/0% in AI model. Furthermore, the accurate rate of AI model was 100% in identifying osteoporosis/hip fracture/vertebral fracture.

Conclusions: Using artificial intelligence model may improve the efficiency of FLS by rapidly and accurately identifying the patients with lower omitted-patients rate.

Acknowledgments: This study is supported by I-Shou University, Taiwan (grant number: ISU107-GOV-07) and research project of E-Da hospital, Taiwan (grant number: EDAHP106002)

P089

HIGH INCIDENCE OF OSTEOPOROSIS AND CACHEXIA IN PATIENTS WITH NEWLY DIAGNOSED POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS: A CROSS-SECTIONAL ANALYSIS

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Objectives: The objective of this cross-sectional analysis was to evaluate the incidence of osteoporosis and body composition aberrations in polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) patients at time of diagnosis.

Methods: This is an ongoing prospective study. 37 consecutive patients with newly diagnosed PMR/GCA were included. The patients were requested to perform a total body DXA at time of diagnosis or shortly after. Data from Swiss population of healthy adults (2986 men, 2649 women) were used to classify our patients according to body composition [1,2].

Results: Of 37 patients, 3 pts. were excluded from the study because of lack of interest or a change in the initial diagnosis. Statistical analyses were performed for the rest 34 pts. Results of DXA scan were available for 30 pts. Of all included pts. 61.8% were female and mean age (confidence interval) was 71 (69-74) y. At diagnosis, 24 pts. presented with pure PMR symptoms, 2 pts. with pure cranial GCA, 8 pts. with concurrent PMR and GCA. Results of body composition assessed by DXA scan are summarized in Table 1. 23.3% of patients had low muscle mass (underlean, FFMI<10th percentile) and 40% of patients had high FMI (obese, FMI>90th percentile). 20% of the patients were categorized to have cachexia (FFMI<10 and FMI>25) and 3.3% (FFMI<10 and FMI<25) to be wasted. 30% and 53.3% of pts. had osteoporosis (T score ≤ -2.5) and osteopenia (-1≤ T score <-2.5) respectively at time of diagnosis.

Conclusion: About every fifth patients had already cachexia at time of diagnosis irrespective of age and gender which was surprising. This is a chronic condition resulting in increased morbidity and functional disability in the patients. Furthermore, there was high incidence of osteopenia/osteoporosis in this patient population at diagnosis, which should be taken into consideration in the clinic.

References:

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Acknowledgement: Study data were collected and managed using REDCap electronic data capture tools hosted at University of Southern Denmark.

Disclosure: The present study is funded by the Region of Southern Denmark, The Danish Rheumatism Association, Department of Rheumatology Svendborg Hospital, Department of Medicine Svendborg Hospital, University of Southern Denmark and Odense University Hospital.

Table 1. Body composition assessed by DXA

Variables	Male	Female
Total body DXA area, cm^2	2284.8 (2171.4-2398.3)	1932.0 (1839.9-2024.1)
Total body DXA BMC, g	2.548.5 (2192.7-2904.3)	*1773.1 (1684.4-2073.7)
Total body DXA BMD, g/cm^2	1.1 (1.0-1.2)	1.0 (0.9-1.0)
FM, g	24724.4 (20761.1-28687.7)	*27379.6 (22648.0-35065.8)
LBM, g	52691.5 (49038.0-56344.9)	39728.2 (36683.6-42772.8)
FFM, g (=LBM+BMC)	55239.9 (51556.4-58923.4)	41638.6 (38484.9-44792.3)
Total, g	79964.3 (73150.0-86778.7)	70802.5 (63482.0-78122.9)
FM, %	30.5 (27.2-33.9)	43.3 (37.5-40.4)
FMI, kg/m^2 (=FM/(height*height))	7.9 (6.7-9.2)	*9.6 (8.8-12.8)
FFMI, kg/m^2 (=FFM/(height*height))	17.7 (16.7-18.8)	15.3 (14.4-16.2)
Total body DXA T-score	-1.0 (-2.2-0.1)	-1.6 (-2.2--1.0)
Total body DXA Z-score	-0.4 (-1.4-0.7)	-0.2 (-0.7-0.3)
Hip area, cm^2	47.6 (44.9-50.4)	36.6 (34.3-38.9)
Hip BMC, g	41.9 (36.9-47.0)	27.6 (25.1-30.1)
Hip BMD, g/cm^2	0.9 (0.8-1.0)	0.7 (0.7-0.8)
Hip T-score	-1.0(-1.6--0.3)	-1.5 (-2.0--1.1)
Hip Z-score	-0.3 (-0.9-0.4)	0.0 (-0.4-0.4)
Spine area, cm^2	*62.8 (49.2-73.4)	52.5 (46.8-58.2)
Spine BMC, g	58.0 (43.3-72.8)	46.8 (38.6-54.9)
Spine BMD, g/cm^2	1.0 (0.8-1.1)	0.9 (0.8-0.9)
Spine T-score	-1.2 (-2.4-0.0)	-1.5 (-2.2--0.9)
Spine Z-score	-0.2 (-1.5-1.0)	0.6 (-0.2-1.3)

BMC: bone mineral content, BMD: bone mineral density, FM: fat mass, LBM: lean body mass, FFM: fat free mass, FMI: fat mass index, FFMI: fat free mass index. Data are presented as mean (confidence interval) or *median (interquartile range) depending on their distributions.

P090

EVALUATION OF BIOCHEMICAL PARAMETERS AND BONE MINERAL DENSITY IN POSTMENOPAUSAL OSTEOPOROTIC WOMEN

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Objectives: Osteoporosis is the most common metabolic bone disease in postmenopausal women, which is associated with bone mass and increased fracture. Bone mineral densitometry in the area of the lumbar spine and hip is considered a safe method to measure bone mass, which can determine the risk of fracture. DXA is a kind of measurement system for thorough noninvasive BMD with low error and uncomplicated feature. The aim of the study is to evaluation the parameters calcium, phosphorus, alkaline phosphate, vitamin D, magnesium and BMD of postmenopausal women referred to Isfahan Osteoporosis Center.

Methods: This case-control study, 87 postmenopausal women were chosen by considering study inclusion and exclusion conditions. Bone mineral densitometry in the area of spine and hip was performed by DXA system. The serum level of calcium, phosphorous, alkaline phosphatase and magnesium were measured by an auto-analyzer device, and the serum level of vitamin D was measured by high performance liquid chromatography. Data was analyzed using SPSS software (version 21) by means of a t-test between two independent groups and Pearson correlation coefficient and a correlation test between two variables.

Results: This study, after recording the results of T-score and BMD, etc. from 87 postmenopausal women, 55 individuals were placed in the patient group and 32 in the control group, in that no significant correlation existed between the values of the parameters calcium, phosphorous, alkaline phosphatase, vitamin D and magnesium in both groups ($P>0.05$). Moreover, Pearson correlation coefficient did not show a significant correlation statistically between the values of the parameters for calcium, phosphorous, alkaline phosphatase, vitamin D, magnesium with BMD and T-score, etc. in the area of the spine (L1-L4) and hip of the patient group ($P>0.05$).

Conclusion: The present study did not show a significant correlation between the values of the parameters calcium, phosphorous, alkaline phosphatase, vitamin D, magnesium with BMD (spine and hip) in postmenopausal women.

P091

PROCESS FOR IDENTIFYING VERTEBRAL FRACTURES AT COUNTIES MANUKAU HEALTH (CMH), AUCKLAND, NEW ZEALAND

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Objectives: It is well known that a significant proportion of vertebral fractures do not come to clinical attention for various reasons. The clinical relevance is often overlooked, particularly of vertebral fractures identified incidentally. Standard 4 of the IOF Capture the Fracture: Best Practice standards relates to 'Vertebral fractures' and states the 'institution has a system whereby patients with previously unrecognised vertebral fractures are identified and undergo secondary fracture prevention evaluation'. On this basis, the CMH Fracture Liaison Service (FLS) initiated a process to identify vertebral fractures (and other fragility fractures), which were reported on in radiology reports. Our aim was to outline the CMH FLS process for identifying vertebral fractures from radiology reports, and review data from the first year of data collection (October 2016 – Sept 2017).

Methods: A daily electronic report was generated containing radiology reports based on searching truncated keywords. The FLS coordinator screened each report to identify any patient with old, but previously unrecognised, or new vertebral fractures. Those aged less than 75 y were referred for a DXA scan, if appropriate. A retrospective review of the CMH FLS database was carried out to identify the number of patients with vertebral fractures (either requiring further assessment or eligible to start treatment if aged ≥75 y); the number of patients aged under 75 who proceeded to have DXA scan; and proportion of those identified as having osteoporosis or osteopenia.

Results: A total of 2320 radiology reports were received. Of these, 326 patients (14.1%) had vertebral fractures. There were 129 patients aged under 75, and 92 of these had a DXA scan. Of these, 26.1% were confirmed as having osteoporosis (T-score ≤ -2.5) and 44.6% had osteopenia (T-score between -1 and -2.5).

Conclusions: Accessing radiology reports via an electronic search based on key terms is a viable way of identifying previously unrecognised vertebral fractures. Further work can be done to optimise and streamline these reports for more effective capture of appropriate patients.

Disclosure: Amgen (financial support to cover conference registration costs)

P092

THE RELATIONSHIP BETWEEN THE OSTEOPOROSIS VERTEBRAL COMPRESSION FRACTURE PATIENTS AND THE RISK OF VENOUS THROMBOEMBOLISM: A NATIONWIDE, POPULATION-BASED CASE-CONTROL STUDY

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Background: Percutaneous vertebroplasty (PV) is a therapeutic procedure for osteoporosis vertebral compression fracture. Venous thromboembolisms (VTE) have been reported as procedure complications. The relationship between PV and the risk of VTE is unclear.

Methods: We conducted a retrospective, population-based case-control study using the National Health Insurance Research Database (NHIRD) to investigate the relationship between osteoporosis vertebral compression fracture patients receiving PV and risk of VTE. We identified 1639 patients with receiving PV and 14,887 subjects without receiving PV from 2000-2013. After development of 1:1 propensity score-matched cohort study, 1639 PV patients and 1639 control patients were followed up for more than 12 y. Using the application of PV as the exposure factor, cause-specified Cox's proportional hazard model was performed to examine the association between PV and VTE. We used three different adjusted models, including covariate adjustment using the propensity score, traditional measured confounders and confounder selection model using backward elimination procedure.

Results: The incidence and risk of VTE between patients receiving PV and matched participants were insignificantly different after propensity matching and using three different adjusted models. In the subgroup analyses, age, sex, comorbidity and cancer were not to increase the risk of VTE between the two cohorts. However, osteoporosis vertebral compression fracture patients with the history of heart failure, arrhythmia, cancer, with using antihypertension medications, and aged were significantly increase the risk of VTE regardless receiving PV or not, and patients receiving analgesic drugs decreased the risk of VTE.

Conclusion: Osteoporosis vertebral compression fracture patients who received PV seems not to increase the risk of VTE but should be monitored cautiously in subgroup prone to developing VTE.

P093

QUETIAPINE AMELIORATES OSTEOCLAST FORMATION IN COLLAGEN-INDUCED ARTHRITIS AND OSTEOPOROSIS MICE VIA THE SUPPRESSION OF THE AKT AND ERK SIGNALING PATHWAYS

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Objective: To investigate the amelioration effects of quetiapine on the osteoclast formation in the rheumatoid arthritis with RAW 264.7 macrophage and collagen-induced arthritis (CIA) DBA/1J mouse model.

Methods: Subjects: RAW 264.7 macrophage and DBA/1J mice, Osteoclast. Treatment: lipopolysaccharide (LPS) and collagen. RAW 264.7 macrophages stimulated by LPS followed by quetiapine treatments were investigated. Activations of CD80 and CD86 were analyzed by flow cytometry. Pro-inflammatory cytokines such as IL-6, TNF-α and IL-1β were analyzed by ELISA. Proteins involved in signaling pathways related to the formation of rheumatoid arthritis were assayed by Western blotting. Therapeutic efficacy of quetiapine in CIA mouse model was also assayed. 18F-FDG/micro-PET was used to monitor the inflammation status in the joints, and the severity of bone erosion was evaluated with micro-CT and H&E staining. To observe these cells in the joints of CIA mice, immunohistostaining using markers for macrophages and neutrophils and TRAP staining for osteoclasts were performed. Infiltration of macrophages and neutrophils and accumulation of the osteoclasts in the joints of the control (normal), CIA and quetiapine-treated CIA mice were demonstrated.

Results: The inhibition of pro-inflammatory cytokines by quetiapine was found through the ERK and AKT phosphorylation and subsequent NF-κB and CREB signaling pathways. Pro-inflammatory cytokines such as IL-17, IL-6 and IL-1β were decreased, while immunosuppressive factors such as TGF-β and IL-10 were increased in CIA mice treated with quetiapine. Notably, no uptake of 18F-FDG and bone erosion was found with micro-PET images on days 32 and 43 in the quetiapine-treated and normal control groups. However, significant uptake of 18F-FDG could be observed in the CIA group during the same time course. Similar results were further verified with ex vivo autoradiography. Decrease in macrophages, neutrophils, and osteoclasts in the joint of quetiapine-treated CIA mice were noted. Infiltration of inflammatory cells and accumulation of osteoclasts play the important role in the progression of arthritis. To observe these cells in the joints of CIA mice, immunohistostaining using markers for macrophages and neutrophils and TRAP staining for osteoclasts were performed. Infiltration of macrophages and neutrophils and accumulation of the osteoclasts in the joints of the control (normal), CIA and quetiapine-treated CIA mice were demonstrated. These cells were significantly decreased in the joints of quetiapine-treated CIA mice as compared to those of untreated CIA mice by quantification analysis. The results suggest that administration of quetiapine could suppress the infiltration of inflammatory cells and accumulation of osteoclasts in the joints of CIA mice.

Conclusion: Taken together, these results suggest that quetiapine is a potential anti-inflammatory drug, and may be used to suppress osteoclast formation in the rheumatoid arthritis osteoporosis mice model.

P094

ROLE OF INDIVIDUAL COMPONENTS OF SARCOPENIA IN FRACTURE RISK PREDICTION IN ELDERLY WOMEN AND MEN

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Objectives: As the relationship between sarcopenia and fracture is controversial, we aimed to assess the independent contribution of individual components of sarcopenia (muscle mass, strength and performance) and their decline rate to fracture risk prediction.

Methods: The study involved 912 women and 502 men 60+ years from the longitudinal Dubbo Osteoporosis Epidemiology Study, who had a total body BMD scan and/or muscle strength and function measurements. Fractures were ascertained by X-ray report between 2000-2017. Clinical data, lean muscle mass (MM), BMD, quadriceps strength (QS), gait speed (GS), sit-to-stand (STS) and timed get-up-go (TGUG) were measured biannually. Cox proportional hazards models adjusted for age, BMI, prior fracture, falls, smoking, alcohol and comorbidities quantified the association between components of sarcopenia and their decline rate with fracture risk.

Results: There were 262 incident fractures in women and 79 fractures in men over a median of 10 years follow-up. In women, none of the sarcopenia components measured at baseline independently contributed to fracture risk. By contrast, in men, QS, STS, TGUG and GS were associated with increased fracture risk. The decline rate of QS, STS, TGUG and GS were associated with fracture risk in women but not in men. MM correlates with QS but did not correlate with muscle performance. MM and its decline rate did not contribute to fracture risk.

Conclusion: In the sarcopenia framework, muscle function (strength and performance), and not muscle mass, appears to be the major contributor to fracture risk and should be measured in addition to other risk factors in elderly people.

P095

MEDICARPIN PREVENTS POSTMENOPAUSAL ARTHRITIS CONDITION BY INHIBITING TH17 CELLS AND PROMOTING T REGULATORY CELL EXPANSION

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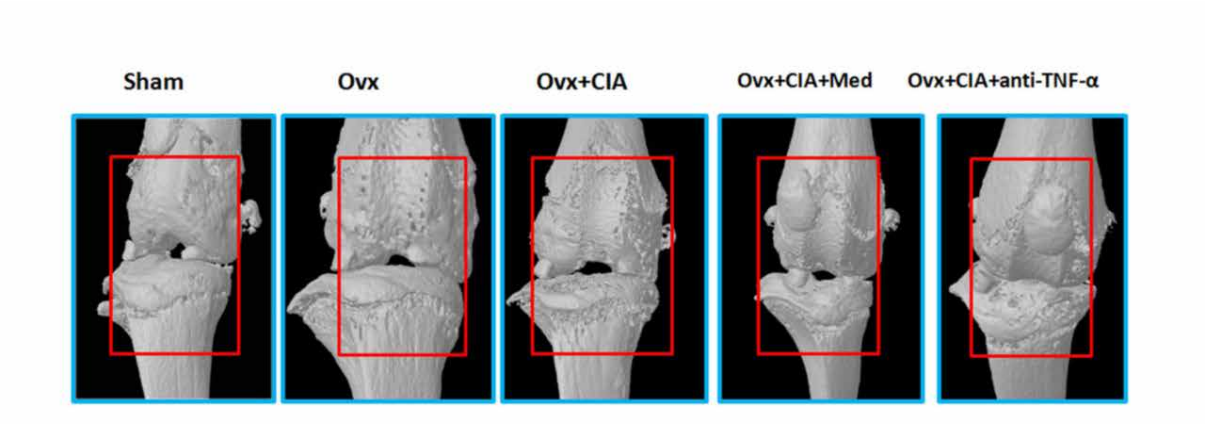
Objectives: Rheumatoid arthritis leads to cartilage destruction at knee and hands. One of the common autoimmune model for rheumatoid arthritis is collagen-induced arthritis (CIA) model. In this study, investigate the therapeutic role of medicarpin, a natural pterocarpan with known anti-resorptive and bone-protective activity, in postmenopausal polyarthritis model of DBAJ/1 mice.

Methods: Female DBA/1J mice were taken for the study. Groups were Sham + Vehicle, Ovariectomized (Ovx) + vehicle, Ovx + CIA induced, Ovx + CIA + Medicarpin (Med) and Ovx + CIA + TNF-α. Number of animals per group were eight. Mice were ovariectomized and after one week, 100 µl of collagen: FCA (1:1 ratio) emulsion was injected into the tail dermis of the mice. Twenty-one days later a secondary booster dose of 100 µl was given in the ratio of 1:1 (collagen: IFA), followed by Med treatment (10.0 mg/kg body weight) for another 4 weeks. Subsequently, mice were sacrificed and long bones were isolated for micro-CT and histological studies. Spleen was isolated for PBMCs isolation. Blood serum was collected for ELISA Assays.

Results: Treatment with Med prevented alteration of TH-17/Treg ratio in CIA model leading to decreased osteoclastogenesis. Micro-CT analysis demonstrated that Med treatment prevents cartilage erosion in joints and restores loss of trabecular parameters in distal tibia. Cartilage oligomeric matrix protein (COMP), a biomarker for arthritis, levels were upregulated in CIA induced mice while treatment with Med significantly restored the serum level of COMP. Safranin-O cartilage staining indicated that cartilage destruction in joints of CIA mice was prevented by Med treatment.

Conclusions: Medicarpin was effective in arresting postmenopausal polyarthritis by inhibiting TH-17 and promoting Treg cells, thereby preventing cartilage destruction and bone erosion. Overall, these studies demonstrate the therapeutic potential of Medicarpin in management of menopause induced arthritis condition.

Acknowledgement: This work is supported by the Council of Scientific and Industrial Research (BSC0103 and BSC0201), New Delhi, India.



P096

FRACTURE IN TYPE 2 DIABETES CONFERS EXCESS MORTALITY

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Objectives: Despite higher BMD, type 2 diabetes mellitus (T2DM) may increase fracture risk. Both fragility fractures and T2DM independently increase mortality, but the mortality risk after a fracture in T2DM is unknown. We aimed to determine the fracture and post-fracture mortality risk in T2DM.

Methods: In the Dubbo Osteoporosis Epidemiology Study, the longest running population-based osteoporosis study internationally, radiologically confirmed fractures, BMD and date of T2DM diagnosis and comorbidities were collected from 1989-2017. Fracture and survival analyses were performed using Cox proportional hazard ratios with time-to-event for fracture and T2DM diagnosis (censored at death).

Results: There were 272 participants with, and 3346 without, T2DM at recruitment. T2DM participants had higher BMI, BMD, prevalent fractures and comorbidities at baseline. T2DM was relatively mild at baseline (median duration 6 y, 17% managed with insulin). Over 43,215 person-years, there were 796 incident fractures in women (64 in T2DM) and 240 in men (27 in T2DM). T2DM did not increase fracture risk in either gender in univariate or multivariate modelling (adjusted for age, BMI, BMD, falls, smoking, alcohol, prior osteoporosis treatment and prior fracture). After multivariate adjustment for age and baseline comorbidities, mortality was increased in T2DM women (HR 1.45, p=0.0004) but not men (HR 1.09, p=0.47). Incident fracture was associated with increased mortality in both women (HR 1.94, p<0.0001) and men (HR 2.04, p<0.0001). Mortality was highest in T2DM with fracture (HR 2.30, p<0.0001 in women, HR 2.72, p=0.0008 in men). Post-fracture mortality was increased in T2DM women (HR 1.50, p=0.044), especially in T2DM of greater than 5 y duration (HR 2.83, p=0.0004), but not men (HR 1.24, p=0.51).

Conclusions: There was no increased fracture risk in this cohort of mostly non-insulin treated T2DM of relatively short duration. The combination of T2DM with fracture confers significantly elevated mortality risk. Thus, bone fragility may affect a subset of T2DM patients and methods to identify and treat those at risk are warranted given the severe consequences.

P097

FRACTURE TYPE ON THE OUTCOME OF PATIENTS MANAGED WITHIN THE FRACTURE LIAISON AND OSTEOPOROSIS MEDICATION MANAGEMENT SERVICES

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Objective: Patients within Fracture Liaison Services (FLS) have lower mortality and subsequent fracture rates but the outcomes of patients having different fracture types were not discriminated. We reported the different one-year outcomes of patients who have different fracture type within the FLS and Osteoporosis Medication Management Services (MMS).

Methods: The FLS enrolled new hip fracture (HF) inpatients and untreated vertebral fracture (VF) including both inpatient and outpatients (N=600). The MMS enrolled patients with potential osteoporosis medication management but not necessary with fractures (N=499). Care coordinators followed similar protocols adapted from the 13 best practice framework (BPF) standards by the International Osteoporosis Foundation to provide baseline assessments, and telephone follow-up every 4 months for one year. This sub-group analysis reported outcomes on patients receiving osteoporosis medication from two services (N=974, 475 from FLS, and 499 from MMS) and reclassified subjects as no hip/vertebral fracture (N=147), hip fracture only (N=166), vertebral fracture only (N=575), and both hip fracture and vertebral (N=86). Comparisons were made among 4 groups. Within group comparisons were made between baseline and 12 months data. Logistic regression analysis was performed to identify baseline correlates of selected one-year outcomes.

Results: The mean age for this cohort was 76.1±10.2 y with 81% female. Four groups have significant by different baseline characteristics. Overall, one-year mortality rate was 5.3%, fall rate was 23.8%, and subsequent fracture rate was 4.5%. Patients with only hip fracture have highest mortality rate and those having both hip and vertebral fracture has highest subsequent fracture rates. After adjusting other correlates, patients with only hip fractures have highest risk of morality (odds ratio: 6.78) and patients with both hip and vertebral fracture have highest risks of subsequent falls and fractures.

Conclusion: Patients with different fracture types within FLS and MMS have different results of mortality, subsequent fracture and fall risks.

P098

VISCERAL FAT AND INSULIN RESISTANCE ARE ASSOCIATED WITH LOWER BONE TURNOVER

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Objectives: Despite higher BMD in obesity and type 2 diabetes (T2DM), fracture risk may be elevated, possibly due to reduced bone quality. Not all individuals with obesity develop T2DM, and insulin resistance (IR) is associated with increasing visceral adipose tissue (VAT) rather than subcutaneous or total body fat. The relative effects of obesity, VAT and IR on bone health remain unclear. We aimed to assess the relationship between bone turnover markers (BTM), BMD and body composition in insulin-sensitive lean (IS-L), insulin-sensitive overweight (IS-O), insulin resistant (IR) and T2DM subjects.

Methods: In a cross-sectional analysis of 525 subjects from the Dubbo Osteoporosis Epidemiology Study, concurrent whole body scans (by DXA) and fasting plasma samples were analysed for BMD, body composition, VAT (using CoreScan), IR (defined as Homeostasis Model Assessment [HOMA] ≥2.5, calculated from glucose and insulin levels) and BTM (osteocalcin [OC], procollagen type 1 N-propeptide [P1NP] and C-terminal telopeptide [CTx]). Repeated measured ANOVA with Bonferroni adjustment was used for continuous variables. Predictive multivariate modelling for the most parsimonious models was performed using Bayesian Model Averaging.

Results: BMD was lower in IS-L compared with IS-O, IR and T2DM (no differences within the obese groups). VAT increased progressively from IS-L to IS-O, IR and T2DM (0.6±0.4, 1.2±0.6, 1.5±0.8, 1.8±0.9kg, $p<0.0001$, respectively). BTM were lower only in T2DM. VAT independently predicted bone formation (-6.6%/kg VAT for P1NP, $p=0.02$; -9.3%/kg VAT for OC, $p<0.0001$) while HOMA independently predicted bone resorption (-0.11%/% change in HOMA for CTX, $p=0.005$).

Conclusions: Although higher BMD was associated with obesity, BTM were lower only in T2DM. VAT correlated strongest with bone formation while IR correlated with bone resorption. Thus, VAT and IR, not total body fat, is associated with lower bone turnover and may contribute to fracture risk in T2DM. Future studies evaluating the metabolic effects on bone remodelling and quality are warranted.

P099

HIGH LEVEL OF ADHERENCE TO OSTEOPOROSIS PROPHYLAXIS MEDICATIONS IN STEROID-TREATED POLYMYALGIA RHEUMATICA (PMR)/ GIANT CELL ARTERITIS (GCA) PATIENTS: A PROSPECTIVE COHORT STUDY.

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Objectives: Adherence to the osteoporosis prophylaxis medications can play a significant role to prevent steroid-induced osteoporosis. The objective of this study was to evaluate the level of adherence to osteoporosis prophylaxis medications in newly diagnosed steroid-treated polymyalgia rheumatica (PMR)/giant cell arteritis (GCA) patients.

Method: This is an ongoing prospective study. 37 consecutive pts. with newly diagnosed PMR/GCA were included in the study. The patients were requested to perform a total body DXA at time of diagnosis or shortly after. Hereafter, patients were contacted by nurses after a week of treatment initiation to evaluate the effect of treatment and to review the details. After 4 weeks of treatment with prednisolone, all included patients were interviewed about their compliance towards osteoporosis prophylaxis using a standardized questionnaire at first follow up visit. Patients were asked if they had remembered to take their prescribed medications. The standard treatment for prevention of osteoporosis was calcium (1200 mg/d) plus vitamin D (800 U/d) and 70 mg alendronate weekly (if T-score ≤−1).

Results: Of 37 pts., 3 pts. were excluded from the study because of lack of interest or a change in the initial diagnosis. Statistical analyses were performed for the rest 34 pts. Results of DXA scan were available for 30 pts. Of all included pts. 61.8% were female and mean age (confidence interval) was 71 (69-74) y. 24 pts. had pure PMR symptoms, 2 pts. pure cranial GCA, 8 pts. with concurrent PMR and GCA. The cumulative prednisolone dose was 696.2 (516.9-1123.1) (median (interquartile range)). The mean of erythrocyte sedimentation rate 61.8 and C-reactive protein 44.9 at diagnosis decreased to 10.7 and 4.0, respectively, after 4 weeks of treatment. At time of diagnosis, 30% and 53.3% of pts. had osteoporosis (T-score ≤ -2.5) and osteopenia (-1≤ T-score <-2.5), respectively. Of included patients, 92.6% were (100%) and 7.4% were (50-100%) adherent to their prescribed medications [Figure1]. Forgetfulness was mentioned as the most important reason for the decreased adherence.

Conclusion: Though previous research was in favor of low level of adherence to osteoporosis prophylaxis drugs, we found a high level of adherence in this specific group of patients at first follow up visit. These findings are in line with our earlier results that showed a high level of adherence in PMR/GCA patients [1,2].

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Acknowledgement: Study data were collected and managed using REDCap electronic data capture tools hosted at University of Southern Denmark.

Disclosure: The present study is funded by the Region of Southern Denmark, The Danish Rheumatism Association, Department of Rheumatology Svendborg Hospital, Department of Medicine Svendborg Hospital, University of Southern Denmark and Odense University Hospital.

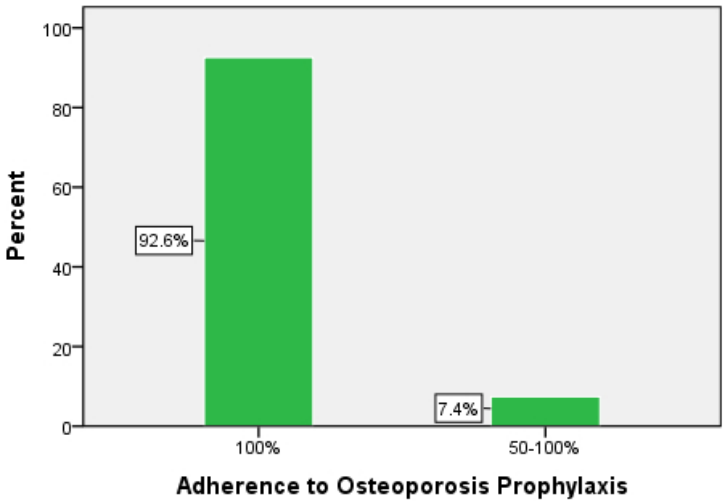

Figure 1: Level of adherence to osteoporosis prophylaxis medications among PMR/GCA patients at first follow up visit.

P100

HIGH-IMPACT EMULATION AND MINIMUM DOSE RESPONSE FORCE ABSORBTION FOR OSTEOGENIC ADAPTATION STIMULUS

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Objective: To determine when bio-feedback mediated hip joint compression in impact ready positions achieves the minimum dose-response levels of force to stimulate an osteogenic adaptation upon 2 applications of therapy intervention with 1700 males and females between 40-85 y of age.

Methods: Recent research provides a better understanding of the magnitude of force that must be applied to the human hip joint in order to initiate a BMD adaptation [1]. While high forces that exceed 4.2 multiples of body-weight (MOB) can be osteogenic, high impact exercise protocols may not be practical for adult populations [2], therefore an apparatus that displays computerized biofeedback in the positions normally associated with high impact force absorption can provide loading of relevance for BMD adaptation with minimized risk of injury. Previous studies with impact emulation therapy had positive BMD outcomes after 6 months [3], but in this analysis we look at specific load exposures and the force absorbed by the lower extremities. Globally networked emulation devices provide computerized protocols. Query for data analysis included patients/subjects who utilized the devices for 5 or more sessions and agreed to participate in this research; partaking in the therapy at a clinically focused, supervised facilities in the US, Spain, and Sweden.

Results: The MOB force/loading levels in the first load exposure were 11.01±2.81 MOB through the lower extremities (N=1762) with 77% exceeding the minimum dose response for BMD adaptation (4.2MOB), and 84% were capable of exceeding this level one week later.

Conclusion: These data present a broad nonexercising population, and for those who choose to engage in this targeted bone loading, an option for increasing BMD in adult and older adult years of life. A more comprehensive analysis will follow.

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Disclosure: J.J. has ownership/financial interest in Jaquish Biomedical, Inc., intellectual property holder apparatus.

P101

CARE OF ELDERLY PATIENTS WITH HIP FRAGILITY FRACTURE BY SPECIALIZED HIP SURGEONS AND TREATMENT OF UNDERLYING DISEASE AFTER DISCHARGE REDUCES ONE-YEAR MORTALITY

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Objectives: Osteoporotic fractures are a major cause of morbidity in the general population. Hip fractures cause acute pain and loss of function and often lead to hospitalization. The principal treatment for hip fracture in elderly patients is surgery. However, after acute hip surgery, the in-hospital mortality and 1-y mortality rates may be as high as 9.5% and 14%–36%, respectively. After acute hip surgery, the 1-y mortality rate is high. Orthogeriatric care provided by geriatricians and orthopedic surgeons in elder patients with hip fracture can reduce mortality rates as well as institutional costs through reduced length of inpatient stay. However, despite the promising results of the care provided by orthogeriatricians, most hospitals still lack an orthogeriatrician. Therefore, this study investigated the risk factors for 1-y mortality in elderly patients with hip fracture undergoing surgery to determine whether care by orthopedic surgeons acting as orthogeriatricians reduces 1-y mortality.

Methods: This retrospective cohort study was conducted at a tertiary referral hospital. All patients with fragile hip fracture who were aged >65 y and who underwent surgery between January 2009 and December 2010 were included in this study. The exclusion criteria were concomitant fractures other than hip fracture and concomitant injury that required surgery. This study was approved by the institutional review board of the hospital. Those with multiple fractures or combined trauma were excluded. The outcomes of interest were demographic characteristics (i.e., sex, age, and BMI), clinical characteristics (e.g., fracture type, cause of fracture, comorbidity, American Society of Anesthesiologists [ASA] grade, and time to surgery), surgical characteristics (e.g., transfusion, type of surgery, surgical time, blood loss, and bone grafting), and type of medical provider (general orthopedic surgeon or a specialized hip surgeon acting as an orthogeriatrician). Medical effectiveness was based on 1-y mortality. Descriptive statistical analyses were performed using an independent t-test, analysis of variance, chi-square test, linear regression, and logistic regression.

Results: This study included 313 patients received surgery for hip fragility fracture. The male-to-female ratio was 3:7, and the BMI of approximately 90% of patients was within the normal range. Their mean age was 78.8 y. The overall 1-year mortality rate was 12.1%. A total of 106 (33.9%) of patients received care from one high-volume specialized hip surgeon acting as an orthogeriatrician (geriatric orthopedic) group. The other 207 patients were cared by other orthopedic surgeon (general orthopedic) group. The geriatric orthopedic group exhibited longer hospitalization (11.6±7.9) than did the general orthopedic group (7.0±3.2; p<0.001). Moreover, the geriatric orthopedic group received more consultation (2.6±1.2) than did the general orthopedic group (0.7±0.7; p < 0.001). Besides, the geriatric orthopedic group received more follow-up of comorbidities other than orthopedics one month after discharge (4.1±1.3) than did the general orthopedic group (1.3±0.8; p<0.001). During hospitalization more expenditure was noted in the geriatric orthopedic group (3054±2177 USD) than in the general orthopedic group (2367±696 USD; p=0.001). The 1-y mortality rate was much lower in the geriatric orthopedic group (4.7%) than in the general orthopedic group (14.0%). The Kaplan–Meier survival curves revealed that 1-y mortality was related to the presence of three or more comorbidities (p<0.001), surgeon (p=0.014), blood transfusion (p=0.033),

and complications (p=0.005), but not fracture type, type of surgery, time to surgery, blood loss, or surgical time. The most critical risk factor was the hip specialist acting as an orthogeriatrician (geriatric orthopedic surgeon), which significantly reduced the 1-y mortality rate (p=0.014). Although ASA grade IV seemed to lead to higher 1-y mortality, this increase was not statistically significant (p=0.094). Multiple logistic regression Cox analysis of the risk factors for 1-year mortality revealed that patients with CCI ≥3 had higher 1-y mortality (hazard ratio [HR]: 6.35, 95%CI: 1.81–22.31; p=0.004). Patients who received care from a hip specialist acting as an orthogeriatrician (geriatric orthopedic surgeon) had lower 1-y mortality (HR: 0.33, 95%CI: 0.12–0.88; p=0.027). Postoperative complications were also related to 1-y mortality (OR: 2.97, 95%CI: 1.19–7.39; p=0.019).

Conclusions: This study demonstrated that the presence of three or more comorbidities and the occurrence of postoperative complications were associated with high 1-y mortality, consistent with the findings of previous studies. However, the most crucial finding of this study is that care by a hip specialist acting as an orthogeriatrician (geriatric orthopedic surgeon) is associated with a 1-y mortality rate of 4.7% and a 67% reduction in mortality compared with care by general orthopedic surgeons. The most significant reduction in mortality is in age>80 (from 18.3% to 4.1%), ASA grade IV (from 29.2% to 0), CCI≥3 (from 31.5% to 8.3%), transfusion (from 22.1% to 3.8%) and complication (from 21.0% to 4.8%). The reduction in mortality in high risk patients can efficiently reduce total mortality rate. This finding has not been reported previously. Although the geriatric orthopedic group had longer hospitalization, more consultation during hospitalization, more follow-up of comorbidities one month after discharge and more expenditure, the group had a much lower 1-year mortality rate. We infer that encouraging the patients to receive treatment of underlying diseases at the Medical departments such as cardiology, endocrinology and pulmonology may be the most important factor to reduce 1-year mortality rate. A high-volume surgeon specializing in hip fracture patient care can significantly reduce mortality. Treatment of comorbidities after discharge is important. Nevertheless, the co-care of these patients with geriatric specialists is strongly recommended, particularly for those with more than three comorbidities.

P102

FACTORS INFLUENCING BONE DENSITY AND MUSCLE VOLUME IN JAPANESE FEMALE LONG-DISTANCE TRACK RUNNERS IN HIGH SCHOOL

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Objective: For sports athletes to achieve success in sport matches, nutritional intake is important to prevent injuries and enhance body strength. Sports training exerts a positive influence on the body composition of athletes by increasing bone density, etc. However, its effect on young female athletes with lower bone density has not been clarified. In this study, data on the change in body composition and nutritional intake conditions of female long-distance track runners for three years during high school was collected and the effects of training and meal intervention on bone density and muscle volume was considered.

Method: Five female long-distance track runners in high school in Prefecture O, Japan were targeted, and consent was obtained. Research was carried out for three years, between 2016-2018, and nutrition/meal habits were surveyed, body and body composition (DXA method) measurements were taken, and blood and urine tests were carried out each year. After the survey, and explanation of the results and meal intervention were carried out. Furthermore, implementation of this study was carried out with the approval of Okayama University and Ethical Committee of Okayama Prefecture Southern Health Development Center.

Results: Subjects measurements were body height 156.2±2.5 cm (mean±SD), weight 45.1±5.5 kg, BMI18.6±2.0 (rate of underweight 60.0%). During the three years in high school, height increased 1.4 cm, weight 4.2 kg. Regarding bone density, lumbar spine BMD was 0.86±0.11 g/cm, YAM rate less than 80% was 1/3 overall. No change in bone density was observed over the three years. Moreover, all of the subjects had amenorrhea, and their estradiol value decreased over three years ($p<0.05$) At the initial meal survey, protein intake was excessive. However, after meal intervention, protein intake was reduced ($p<0.05$) and was within the appropriate range. The muscle volume (arms, legs, body trunk, whole body) increased ($p<0.05$).

Conclusion: Continuous training for female long-distance track runners in high school students resulted in increased muscle volume. However, bone density was not improved. After meal intervention, intake volume of protein was adjusted to the appropriate level, and muscle volume increased. A positive effect by meal intervention was indicated. In the future, support with the aim of strengthening bone density is needed.

P103

ACCURACY VARIATIONS IN DXA BONE MINERAL DENSITY: A MULTICENTRE PHANTOM STUDY

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DXA is the gold standard for the diagnosis of osteoporosis. To date in Australia there are no studies assessing the diagnostic accuracy of different DXA Imaging Centres. We have conducted a multisite study of spine and hip phantoms to compare the accuracy of 13 GE-Lunar and 6 Hologic DXA scanners. Both phantoms were measured at each site 3 times on the same occasion with all in clinical use no repositioning between scans. The observed average of the 3 scans were then used as an unbiased estimate of the "true mean" BMD at the lumbar spine (L1-L4), femoral neck and total proximal femur.

The within-centre variation was less than 0.01 g/cm^2 (or less than 1% relative to the mean) for BMD at all two sites. The between-centre variation for BMD at the three sites was larger than the within-centre variation, and the largest between-centre variabilities are observed at the femoral neck site measured using Hologic scanners (Table).

Scanner	Site	Mean BMD (g/cm^2)	Largest Between-Centre Absolute Difference -(g/cm2)	Largest Between-Centre Absolute Difference (%)
Lunar	L1-L4	1.208	0.0127	1.5
Lunar	Femoral neck	0.800	0.0247	3.1
Lunar	Total Proximal Femur	0.888	0.0122	1.4
Hologic	L1-L4	1.035	0.043	4.2
Hologic	Femoral neck	0.675	0.060	8.8
Hologic	Total proximal femur	0.778	0.033	4.2

Thus, while the within-centre variation in measured values of BMD at all sites was small, the between-centre site variation was clinically relevant. The magnitude of the observed difference in measured femoral neck BMD could potentially affect therapeutic decisions and assessment of serial changes in BMD, when patients are measured at different centres. The results indicate a need for further studies of DXA accuracy and underline the need for a standardization of BMD measurements across scanners.

P104

TREATMENT OUTCOME BY MEASURING TREND OF BMD VS. BMC BY DUAL-ENERGY X-RAY ABSORPTIOMETRY (DXA) OF SPINE:

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Objectives: To determine the change in BMD vs. bone mineral content (BMC) as the measure of osteoporosis treatment outcome of the spine.

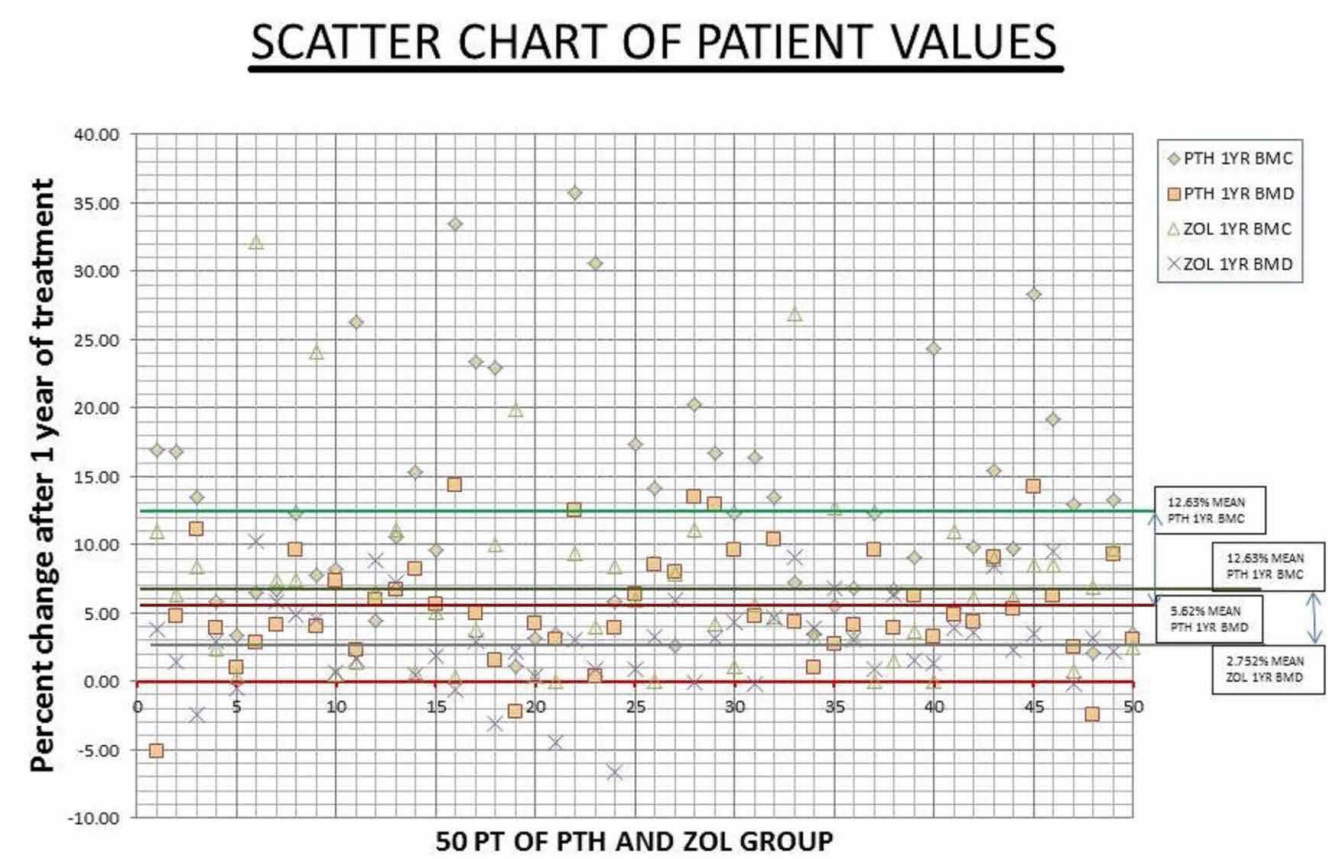
Methods: Data from the BMD and BMC trend analysis of patients treated for osteoporosis were evaluated. The region of interest (ROI) was taken as L2, L3 and L4. (1) The total BMD change of ROI was compared with total BMC change. Study group of 50 random patients from those treated with Teriparatide 20 µg/d (PTH) and 50 from those treated with zoledronic acid (ZOL) 5 mg i.v. infusion per year were chosen. Those studies with artefacts in ROI were excluded.

Results: The percentage change in BMC vs. BMD was 12.63 & 5.62 with PTH, and 6.85 & 2.75 with ZOL respectively. The data is summarised in Figure 1.

FIGURE - 1

% CHANGE	FINDINGS	PTH	ZOL
BMC	Average	12.63	6.85
	RANGE	34.19	32.21
	MAX to MIN	35.7 to 1.51	32.23 to 0.02
BMD	Average	5.62	2.75
	RANGE	19.53	16.88
	MAX to MIN	14.38 to -5.15	10.21 to -6.67

The scatter graph of both study groups showing the range and maximum and minimum values are presented in Figure 2.



Conclusions: The least significant change (LSC) of Spinal BMD is 2.6% when evaluated on a single machine while evaluating treatment outcome. (2) The LSC in BMD often shows negative values (6% on PTH group and 18% in ZOL group) while the BMC in the same patients was always positive. This fallacious reading is due to associated increase in area as a result of treatment. The BMC change is more consistent, and so should be taken as the value to evaluate treatment outcomes. Our study further shows a BMC change is 2.25 to 2.50 times that of BMD, suggesting an LSC for BMC of 5.84% to 6.47%.

References:

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P105

BONE MARKERS IN POSTMENOPAUSAL OSTEOPOROSIS WOMEN WITH DIABETES

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Objectives: Bone turnover markers have useful in fracture risk assessment and monitoring treatment efficacy in postmenopausal osteoporosis. The aim of this study is to evaluate the bone turnover markers and fracture risk in postmenopausal osteoporosis women with diabetes.

Methods: This is a cross-sectional study investigated subjects who were diabetes postmenopausal osteoporosis women at endocrine clinic. In this study, country-specific fracture risk for 10-y probability of a hip or major osteoporotic fracture, were calculated by the WHO Collaborating Center, using the FRAX algorithm. The FRAX algorithm includes femoral neck BMD, age, sex, BMI, previous history of fracture, parental history of hip fracture, current smoking, recent use of corticosteroids, presence of rheumatoid arthritis, and at least 3 alcoholic beverages per day. A single, fasting blood sample to assess bone markers, and other biochemical tests were performed in the study visit. Patients were measure the serum sugar, glycosylated hemoglobin (HbA1c), bone specific alkaline phosphatase (BSALP), and beta-crosslaps (b-CTx) analyzed the bone turnover markers.

Results: In this cross-sectional study, we investigated 52 Taiwanese postmenopausal women, with 30 subjects diabetes and 32 non-diabetes at osteoporosis clinic, aged between 50-77 y, had high risk for fractures by FRAX, defined as 10-y major osteoporotic fracture probability (≥20%) or hip fracture probability (≥3%), and found both bone formation and resorption markers were elevated.

Conclusions: Our findings suggest that high risk for fractures by FRAX, with 10-y major osteoporotic fracture probability or hip fracture probability and high bone markers in diabetes osteoporosis women, but no significant difference bone markers in diabetes and nondiabetes osteoporosis women.

P106

FRACTURES AND FRACTURE-ASSOCIATED MORTALITY ATTRIBUTABLE TO LOW BONE MINERAL DENSITY AND ADVANCING AGE: A TIME-VARIANT ANALYSIS

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Objective: Although BMD is causally related to fracture, the burden of fractures attributable to low BMD has not been investigated. In this study, we estimated the fraction of different fracture types occurring in older people that can be attributed to low BMD.

Methods: The study involved 2320 women and 1380 men aged 50 y and older, whose bone health has been continuously monitored for up to 20 y. During the follow-up period, the incidence of fractures was ascertained by X-ray report. Femoral neck BMD was measured at baseline by GE-Lunar DXA and expressed as T-scores. Osteoporosis was defined as T-scores being <-2.5. Advancing age was categorized as age from 70 y old. The estimation of time-dependent attributable fraction was based on the Cox's proportional hazards model.

Results: Overall, 21% of women and 11% of men had osteoporosis by BMD. Approximately 21% and 16% of total fractures in women and men, respectively, were attributable to osteoporosis. When osteoporosis was combined with advancing age, the two factors accounted for 46% and 51% of total fractures in women and men, respectively. The two factors (age and osteoporosis) accounted for ~80% of all hip fractures. Fracture was associated with increased risk of mortality. Approximately 63% and 53% of postfracture mortality in women and men, respectively, were attributable to advancing age, osteoporosis and fracture; however, most of the attributable fracture was ascribed to advancing age.

Conclusion: While 80% of hip fractures were attributable to advancing age and osteoporotic BMD, these factors contributed to less than 50% of total fractures. Most of postfracture mortality was attributable to advancing age.

P107

EFFECT OF DENOSUMAB ON BONE FORMATION MARKER P1NP

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Objective: Type I procollagen N-terminal propeptide (P1NP) is considered the most sensitive bone formation marker and is useful for monitoring osteoporosis treatment using antiresorptive therapy. In our hospital, we have administered denosumab, an anti-RANKL antibody, as a treatment for osteoporosis. In addition to bone mineral assessment using DXA, P1NP and serum N-terminal telopeptide of type I collagen (NTx) are used as osteogenic and bone resorption markers, respectively, for determination of therapeutic efficacy. Previous reports have indicated that there are many cases in which P1NP falls below the standard lower limit (17.1 μg/L) in patients using bisphosphonate (BP). The purpose of this study was to investigate P1NP levels in cases treated with denosumab.

Methods: Between January 2015 and December 2017, we evaluated P1NP and NTx levels in 50 patients with osteoporosis who received denosumab at our hospital. The percentage of cases below the baseline lower limit of each marker was determined.

Results: Denosumab administration resulted in a P1NP level below the reference lower limit in 24 cases (48%). NTx level did not decrease below the reference lower limit in any cases. There were no cases of atypical femoral fractures during the follow-up period. In 38 patients with measurement of P1NP with initiation of denosumab, a transition in the level was observed. All cases were within reference limits before the initial prescription but were below the reference lower limit in 18 cases (47.4%) during administration of denosumab for an average of 6 months.

Conclusion: Denosumab strongly suppresses bone turnover and also decreases bone metabolism markers. When both bone formation and bone resorption markers are below the reference lower limits, the patient is serologically in a state of severely suppressed bone turnover (SSBT) and may be at risk for atypical fracture (Kitaori et al., 2004). In this study, P1NP was below the lower limit in half of the cases treated with denosumab, but it is unlikely that all of these were in SSBT status. There are reports of cases in which P1NP is even below the lower limit in patients receiving BP (Eastell et al., 2011). It is difficult to use P1NP as a risk marker for SSBT in patients receiving bone resorption inhibitors such as denosumab. It may be necessary to set new reference values for P1NP for cases using bone resorption inhibitors. In patients using denosumab, P1NP fell below the reference lower limit in 48%. In patients receiving bone resorption inhibitors including denosumab, it may be necessary to establish new reference values for P1NP.

P108

EOSINOPHIL RATIO COULD BE A MARKER IN PATIENTS WITH SARCOPENIA

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Objectives: Increasing data suggests that chronic inflammation has a crucial role in the development of muscle dysfunction and progression of sarcopenia in the aging population. The aim of the present study was to compare leukocyte count in sarcopenic and nonsarcopenic individuals and to present the correlation between subtypes of white blood cell counts, including eosinophils, monocytes, neutrophils, and lymphocytes and diagnostic criteria for sarcopenia.

Methods: We performed a retrospective study to survey the prevalence of sarcopenia in elderly nursing home residents (age >65 y old). A total of 124 subjects with sarcopenia (male/female: 64/60, mean age 84.3±7.3) and 128 subjects as nonsarcopenic (male/female: 77/51, mean age 83.4±8.4) were enrolled in this cross-sectional study. Sarcopenia was diagnosed according to The European Working Group on Sarcopenia in Older People criteria. The comprehensive geriatric assessment was performed to participants. Complete blood counts, biomarkers of inflammation (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)) of all subjects were measured.

Results: We could not find statistical differences in acute (CRP) and chronic (ESR) inflammatory factors between sarcopenic and nonsarcopenic participants. However, compared to non-sarcopenic participants, red blood cell (RBC), hematocrit, hemoglobin and lymphocyte levels were lower in the sarcopenic group. On the contrary, we found higher eosinophil ratio in the sarcopenic group (3.44±3.05 vs. 2.77±2.59, $p<0.05$, respectively). Furthermore, the result of the logistic regression analysis depicted that higher eosinophil ratio (>6%) is an independent predictor for sarcopenia (OR=1.87; 95%CI=1.54–2.23, $p<0.05$). Most of important, we found all subjects with eosinophil ratio over 6% (N=20), whether sarcopenic or not, their gait speeds were under 1.2 m/s.

Conclusion: Increased eosinophil ratio can indicate slower walking speed and may have a significant role in the development of sarcopenia in the elderly population.

P109

THE PERFORMANCE OF CALCANEAL QUANTITATIVE ULTRASOUND AND OSTEOPOROSIS SELF-ASSESSMENT TOOL FOR ASIANS IN IDENTIFYING MALAYSIAN WOMEN AT RISK FOR OSTEOPOROSIS

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Objectives: Quantitative ultrasound (QUS) and Osteoporosis Self-assessment Tool for Asians (OSTA) are two commonly used screening tools for osteoporosis but their performance in the Malaysian population has not been validated. This study aimed to determine the performance of calcaneal QUS and OSTA in identifying women with low BMD and osteoporosis.

Methods: A total of 198 women aged 40 y or above (mean age=56.6±8.65 y) from central Malaysia without apparent risk for osteoporosis were recruited in a cross-sectional study. They underwent basic anthropometrical, calcaneal QUS and BMD measurements. OSTA was calculated using the formula 0.2 x (body weight in kg – age in years). T-score of the hip or spine generated from BMD measurement was used to define low BMD (T-score of hip/spine ≤-1) and osteoporosis (T-score of hip/spine ≤-2.5). Crosstabulation was used to calculate the sensitivity and specificity of QUS and OSTA. Receiver-operating (ROC) curve was used to estimate the performance and optimal cutoff values of both instruments.

Results: At the standard cutoff, QUS (cutoff ≤-1; sensitivity=83.0%; specificity=50.8%) performed better than OSTA (cutoff ≤-1; sensitivity=48.1%; specificity=92.1%) in identifying subjects with low BMD. Both instruments were ineffective in identifying osteoporotic subjects (cutoff for OSTA ≤-4, QUS≤-2.5; sensitivity for OSTA=23.7%, QUS=10.5%; specificity for OSTA=97.5%, QUS=95.6%). Modifying the cutoff values based on ROC curve significantly improved the sensitivity of OSTA in identifying subjects with low BMD (cutoff ≤-1.69; sensitivity=84.4%; specificity=49.2%), while the standard cutoff remained effective for QUS. Altering the cutoff values of OSTA to 0.52 and QUS to -1.28 improved the sensitivity of both instruments in identifying subjects with osteoporosis (sensitivity for OSTA=86.8%, QUS=89.5%; specificity for OSTA=50.0%, QUS=50.0%).

Conclusions: Modification to the standard cutoff values of OSTA and QUS is necessary to increase the sensitivity and performance of these instruments in identifying women at risk for osteoporosis. These should be calibrated prior to deployment in local settings for osteoporosis screening.

Acknowledgements: We thank Universiti Kebangsaan Malaysia for funding this study via research grants GUP-2017-060 and AP-2017-009/1.

P110

SODIUM BENZOATE (NAB) - A FOOD ADDITIVE, INHIBITS BONE LOSS BY UPREGULATING ANTI-OSTEOCLASTOGENIC T CELLS

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Objective: Nab, a commonly used food additive has been recently associated with upregulation and development of Tregs cells. Also, Treg cells have proven osteoprotective role in bone health. Based on these findings we hypothesized to study the effect of NaB on bone health in ovariectomy (ovx) induced osteoporotic mice model.

Methods: Mice were divided into three groups viz. Sham, Ovx and Ovx + NaB. NaB was administered orally (100 mg NaB/kg bw) and after 50 d mice were sacrificed and analyzed for various parameters for accessing the role of NaB on bone health via various cutting edge technologies such as SEM, AFM, FTIR, µCT, FACS, and ELISA.

Results: Interestingly, it was observed that oral administration of NaB protected mice from ovx-induced bone loss which was confirmed by SEM, AFM, FTIR and µCT analysis of bone samples. In our present study, we found that NaB-intake enhanced bone density in both cortical and trabecular bones of ovx mice. Interestingly, it was observed that NaB-intake induces in vivo differentiation of Foxp3$^+$Treg cells along with inhibiting differentiation of Rorγt$^+$Th17 cells in bone marrow, the prime sites of osteoclastogenesis (Figure 1).

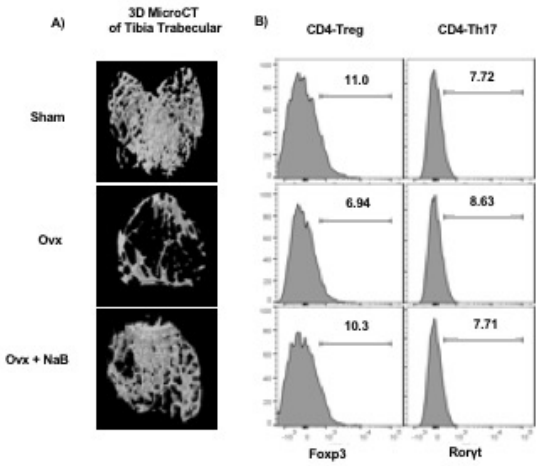

Figure 1. NaB enhances bone health by modulating Treg-Th17 cell axis in ovx mice. **A).** 3D MicroCT images of Tibia trabecular, **B).** FACS analysis of Bone marrow showing CD4$^+$Foxp3$^+$Treg & CD4$^+$Roryt$^+$Th17 cell population in sham, Ovx and Ovx + NaB group respectively.

Conclusion: Taken together, our results for the first time establish an osteoprotective role of NaB-intake on bone health via modulation of Treg/Th17 cell axis in host immune system.

P111

THE IMPACT OF DIFFERENT TYPES OF SEDENTARY BEHAVIORS ON FRAILTY

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Objective: To determine the association between different types of sedentary (sitting) patterns and the frailty states.

Methods: A total of 142 participants, 65+ (between 65-90, average age 73) completed a survey with 35 questions, referring to their demographic data, lifestyle habits and ability to perform repeated chair stands (as a measure of lower limb strength/physical performance).

Results: There was a significantly positive association between sedentary time and frailty but with different calculated probabilities for the various sitting occupations (p=0.002/watching TV and p=0.45/other sitting behaviors).

Conclusions: Various sedentary behaviours differ significantly in terms of their impact on frailty.

P112

IMPROVING OSTEOPOROSIS CARE IN FAMILY PRACTICE USING AN ELECTRONIC MEDICAL RECORD (EMR)

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Objectives: Evidence suggests a fracture risk assessment and screening for osteoporosis with BMD can help prevent osteoporotic fractures in women ≥65 y [1]. Systematic EMR queries and visit templates can improve the process for osteoporosis recall, screening and risk assessment in primary care.

Methods: Our EMR queries during the period of Aug 1-Sept 15, 2018 retrospectively identified (1) patients with an ICD-9 of 733 (Osteoporosis) or 729 (Fracture), and (2) patients ≥65 y with or without BMD

Results: Among a patient roster (n=1637) for a single family physician within a group practice. We had 66 patients with an ICD-9 733 (Osteoporosis); of these, 16.6% were male and 83.4% female. We had 8 patients with an ICD-9 729 (Fracture); of these, 62.5% were male and 37.5% female. We had 373 patients age ≥65; of these, 55.5% were male and 44.5% female. 15.5% of patients already had a diagnosis of osteoporosis. 40.2% already had a BMD and 59.8% did not have a BMD. Thus, we had 223 patients eligible for a fracture risk assessment visit. Quality improvement (QI) themes identified suggested we need to implement:

1. standardized visit templates for initial and follow-up visits
2. standardized lab and imaging templates
3. clinic-wide standardization of reports classification and use of ICD-9 codes
4. a regularly scheduled EMR query to identify patients with osteoporosis care gaps
5. a team-based approach for a nurse to recall patients for an osteoporosis education visit and fracture risk assessment.

Conclusions: Our primary care Osteoporosis EMR quality improvement project identified care gaps, gender differences and opportunities to streamline care and to develop a sustainable proactive team-based approach. We plan to recall 223 patients to review their osteoporosis risk and this data, QI themes and queries to identify patients for recalls will be shared with our primary care physicians to implement for improved osteoporosis care.

Reference: US Preventive Services Task Force, Curry SJ, et al. JAMA 2018;319:2521.

P113

MULTIMORBILITY CONTRIBUTES TO POST-FRACTURE MORTALITY: A LATENT CLASS ANALYSIS

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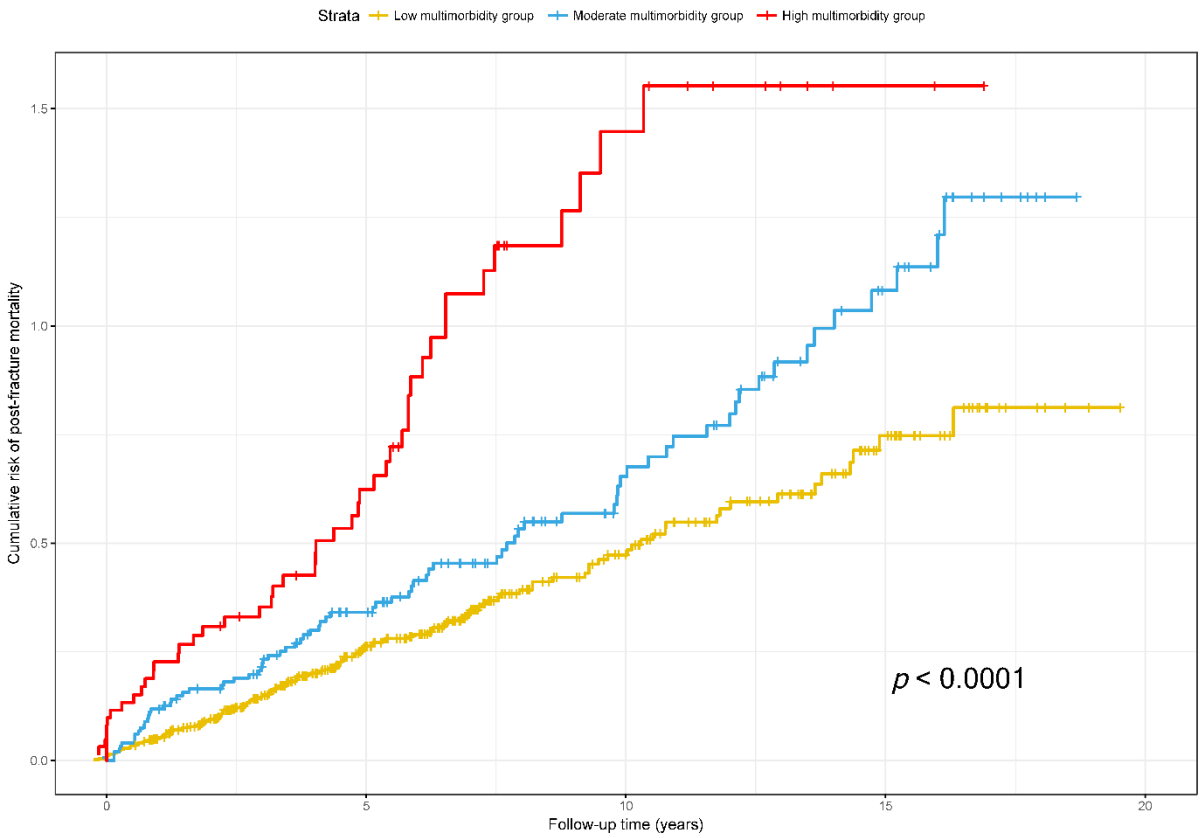
Objective: Osteoporotic fracture is associated with increased risk of mortality. Individuals with a fracture frequently have other chronic diseases. Multimorbidity is defined as the co-occurrence of two or more chronic diseases. The present study sought to define the pattern of multimorbidity and its impact on the risk of post-fracture mortality.

Methods: This is a prospective, population-based study that involved 890 women and 244 men with a fracture. Health status of the individuals had been monitored for over 20 y. Osteoporosis was defined as femoral neck BMD T-score ≤ -2.5. Seven broad diseases were considered: osteoarthritis, cardiovascular disease, type II diabetes, cancer, rheumatoid arthritis, neurological illnesses, and mental illnesses. The diseases were self-report ascertained at baseline. A latent class analysis (LCA) was used to define the pattern of co-occurrence of diseases within an individual. The relationship between the LCA-derived clusters of diseases and post-fracture mortality was assessed by the Cox's proportional hazard model.

Results: During the follow-up period (1989-2009), the mortality rate for men was 54%, approximately 2-fold higher than that for women (30%). The prevalence of multimorbidity was 38% in women and 35% in men. Multimorbidity was associated with increased risk of post-fracture mortality (HR 2.4, 95%CI: 1.68-3.38). The LCA identified 3 clusters of patients: low multimorbidity group (68%), moderate multimorbidity group (20%), and high multimorbidity group (12%). The 5-y risk of post-fracture mortality among the high multimorbidity group was 45%, which was 1.64-fold higher than the moderate multimorbidity group, and 2.3-fold higher than the low multimorbidity group. The increased risk of death was mainly seen among individuals with cardiovascular disease (HR 1.6, 95%CI: 1.2-2.3), type 2 diabetes (HR 1.8, 95%CI: 1.0-3.2), rheumatoid arthritis (HR 1.8, 95%CI: 1.1-2.9) and neurological illnesses (HR 2.74, 95%CI: 1.2-6.3). The proportion of post-fracture mortality attributable to multimorbidity in women and men was 33% and 28%, respectively.

Conclusions: More than one-third of men and women with a fracture have multimorbidity. The coexistence of multimorbidity accounts for one-third of post-fracture mortality. These data emphasize the need for a wholistic management of patients with a fracture.


Strata
Low multimorbidity group
Moderate multimorbidity group
High multimorbidity group
Cumulative risk of post-fracture mortality
0.0
0.5
1.0
1.5
0
5
10
15
20
Follow-up time (years)
p < 0.0001

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SENSITIVITY AND SPECIFICITY OF PLAIN RADIOGRAPHS IN SCREENING OSTEOPOROSIS AMONG HEALTH EXAMINEES IN TAIWAN

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1. Introduction

The prevalence of osteoporosis in people aged over 50 years in Taiwan was 23.9% in men and 38.3% in women.[1] Osteoporosis combined with accidental falls incurred significant morbidity and mortality. Early detection and intervention are therefore important.

Vertebral fractures are a common hallmark of osteoporosis.[2-5] Some 65% of vertebral fractures cause no symptoms.[2] Recognizing and reporting fractures incidental to radiologic examinations has the potential to reduce health care costs.[6] However, vertebral fractures are often unrecognized or denied by physicians and patients.[2,7]

Dual energy X-ray absorptiometry (DXA) is the gold standard for measuring BMD. The major disadvantages of DXA are non-portable, not easily accessible and expensive. DXA for screening purposes is not included in the reimbursement scheme of the Taiwanese National Health Insurance. Calcaneal quantitative ultrasound (QUS) is another option. Nevertheless, calcaneus is not representative of the vertebral status.[8] The results of QUS does not reliably exclude or confirm osteoporosis and is not widely used. A consensus regarding its accuracy for identifying patients with osteoporosis does not exist.[9] There is a need to support the use of a simple screening tool administered in primary care, such as plain radiographs, to improve the detection of osteoporosis.

As population age, periodic health examination is a common practice in East Asia. Plain radiograph particularly chest radiograph is readily available in most medical settings and is widely used as the first choice of all images. The accessibility of radiography far exceeds that of QUS. Plain radiograph is mostly used to diagnose orthopedic diseases, such as vertebral fractures. Morris et al. suggested that recognition of incidental vertebral fractures identified from chest radiographs may represent a missed opportunity for osteoporosis management.[10] Plain radiographs can also give an approximate estimate of BMD.[11] In addition, plain radiograph has the advantages of good accessibility, low cost and time frugality which all make it a potential choice for screening osteoporosis.

Although the idea that radiographs can identify osteoporosis is convincing, minimal previous studies compared the agreement between incidental radiographic findings of osteoporosis and DXA confirmed osteoporosis. Recent performance of digital radiographs in screening osteoporosis was not reported. Years ago, Wagner et al. reported the sensitivity and specificity were 72% and 47% for digital radiographs, respectively.[12] However, this study was limited by the small number of cases and the inclusion of both conventional and digital radiographs which is different from current practice. The study also failed to discuss whether increasing the types of plain radiographs would improve the validity. Moreover, they enrolled participants under 50 years who are not recommended to receive DXA examination.

Plain radiographs have long been faulted for their low sensitivity in diagnosing osteoporosis. The validity of using plain radiographs as a screening tool was not established. In epidemiologic studies, a common method to increase sensitivity is by parallel testing several exams. Hence, we hypothesized that by parallel testing several plain radiographs, we can improve the validity.

The purpose of this study was to estimate the validity of digital plain radiographs in screening osteopenia/osteoporosis among apparently health people aged over 50 years.

2. Materials and methods

2.1 Recruitment of participants

This is a diagnostic cohort study. Data of all consecutive series of private-pay health examinees who came to Renai Branch, Taipei City Hospital in year 2012 were retrieved from the electronic Health Examination Automatic Logic System. Participants requested the radiographic tests for screening purposes. There were several predefined sets of health exams to choose from, and the choices were mainly based on participants' request. Inclusion criteria were examinees aged 50 to 90 years old who underwent both DXA and plain radiograph examinations. Exclusion criteria included inability to provide reliable DXA data owing to orthopedic implant or fracture, those who did not have a final X-ray report, and duplicate or incomplete data.

2.2 Measurements

Plain radiographs could be any of the following ones: plain radiographs for (1) chest; (2) kidney, ureter, bladder (KUB); (3) cervical spine (C1-C7 included); (4) lumbar spine (T12-L1 included). Chest radiograph was taken mainly to check lung or heart disease. KUB was taken to evaluate abdominal or retroperitoneal disease. Cervical spine or lumbar spine radiographs were taken to detect spinal pathology. A single participant underwent one to four kinds of X-ray examinations, one of each. These plain radiographs and the DXA exam were performed in the same morning.

All radiographs were digital and acquired with storage phosphor technology on an Agfa ADC Compact system and viewed on a Siemens Magic View workstation. The radiographs were read by eight board certified radiologists who were all trained in the same center. The agreement on osteoporosis/osteopenia between radiologists was about 80%~90%. For comprehensiveness, the radiographs of the same participant were read by a same radiologist. The radiologists only knew the age and gender of the examinees and were otherwise blinded to the rest of the participants' clinical information, including DXA results. To increase inter-rater reliability and for quality control purposes, there is a common pool of frequently used phrases with standardized wordings to allow the radiologists to choose from when issuing the reports.

We adopted the Genant semi-quantitative approach of vertebral fractures.[13] Prevalent vertebral fractures were defined at a given vertebral level as a reduction of ≥ 20% and 4 mm in any vertebral height.[14] There was no need to exclude traumatic fracture because our participants were mostly asymptomatic health examinees.

As objective criteria, we defined six radiologic descriptions as meaningful indicators, including: reduced bone mineralization, osteopenic change, osteoporosis, reduced vertebral height, vertebral wedge deformity, and vertebral compression fracture. The presence of either one was considered positive for osteopenia/steoporosis.

Using a Norland Excell and XR-600™ bone densitometer (Norland Products Inc., New Jersey, USA), DXA value of the femoral neck or lumbar spine was used as our reference standard. To ensure the stability of the device, the scanner was calibrated every morning before use using QC phantom with a coefficient of variation (CV) of 0.5%. The T-scores was compared with a young Chinese population. According to World Health Organization, participants were classified into three categories: normal (T-score≧-1), osteopenia (-2.5＜T-score＜-1.0) or osteoporosis (T-score≦-2.5).[15] In health examinees who received DXA of both femoral neck and lumbar spine, the lower value was used for analysis. Subjects who had osteoporosis/osteopenia at one or both of these sites were defined as having "overall osteoporosis/osteopenia". This study was approved by the Institutional Review Board of Taipei City Hospital, Taiwan [TCHIRB-1030418-E].

2.3 Statistical analysis

SPSS 22.0 was used for statistical analysis. Odds ratio (OR) was used to determine the possibility of true osteopenia/osteoporosis, and 95% confidence intervals (CI) were used to quantify uncertainty. Receiver operating characteristic curve (ROC curve) presents the performance of different discrimination thresholds. Area under curve (AUC) was used to determine the best strategy of screening with digital radiographs.

3. Results

A total of 4218 health examinees were identified in 2012. Among them, 2289 participants were excluded (Fig. 1). We recruited 855 men (44.3%) and 1074 women (55.7%). The majority (99.6%) had DXA of only one site (L-spine DXA only: 990 (51.3%); hip DXA only: 932 (48.3%); both sites: 7 (0.4%)).

Participants aged between 50 and 59 were the majority (67.2%) (Table 1). The prevalence of osteopenia and osteoporosis were 38.3% and 5.0%, respectively. Osteoporotic cases were mainly women (96.9%). For participants who took only one kind of X-ray, chest X-ray was the main image (> 99%). Table A.1 presents cross tabulation of the test results. As BMD decreases, the percentage of participants with positive plain radiographic findings increases from 17.4% to 45.8%. In patients with a T-score > -2.5, the majority (80.4%) had negative plain radiographic findings.

Of the participants, 22 had radiographic fractures other than vertebral fractures, mainly rib and clavicular fractures. The majority of these cases were aged between 50 and 59 (n=16 (72.7%)). There is no statistical difference between T-scores of fractured and non-fractured participants (TableA.2). Of the 1991 unique radiographic findings, the most common keywords were reduced bone mineralization (11.2%) followed by wedge deformity (5.8%) and osteopenic change (4.5%) (Table A.3).

Table 2 presents the validity of plain radiographs using one or two plain radiograph findings. Generally, using any plain radiograph criterion for osteopenia/osteoporosis performs better than using two, particularly for osteoporosis diagnosed by femoral neck DXA T-score (AUC=0.748, 95%CI=0.582-0.913) (Fig.A.1). Using one keyword as cutoff, the sensitivity of plain radiographs in screening osteoporosis alone was up to 70.0%. The specificity could be up to 81.3%. The negative predictive values (NPV) were 79.5% to 99.6%.

Table 3 displays the validity of using different kinds (numbers) of plain radiographs. Plain radiographs were most accurate in predicting overall osteoporosis by using two radiographs with a cutoff of one X-ray keyword. The sensitivity was 69.8% and the specificity was 60.3% (AUC=0.650, 95%CI=0.564-0.737).

4. Discussion

We found that to screen overall osteoporosis, using two digital radiographs with a cutoff of one plain radiograph criteria might be a potential strategy. Using one plain radiograph criteria as cutoff, the specificity can be up to 80.4%, respectively. Wagner et al. reported that the sensitivity and the specificity of digital radiographs in screening osteoporosis were 72% and 47%, accordingly.[12] In contrast to their results, specificity was higher than sensitivity in this study. In Wagner's study, the readers were aware of taking part in a study assessing osteoporosis which might have led to overestimation of osteopenia/osteoporosis and therefore an increased sensitivity. Also, chest plain radiographs despite being the most common radiographic type prescribed were performed with 0.1 mSv and were hence not as good a choice for the evaluation of bony structures as lumbar spine plain radiographs performed with 1.5 mSv,[16] as in Wagner's study. In our study, 36.2% of participants took only chest plain radiograph. This might be the cause of the lower sensitivity we observed. Our healthier and younger study population might contribute to the good NPV. A higher specificity of screening infers that exempting healthy examinees from unnecessary DXA exams might potentially save U$20 (New Taiwan Dollar 600). We postulate that if digital radiographs were used to screen populations at higher risk, positive predictive value would be increased.

We found that any one plain radiograph criterion performs better than using two plain radiograph criteria. Using two plain radiograph findings as cutoff for screening confers higher specificity at the expense of sensitivity. Therefore, we suggest a DXA scan for people with any positive radiographic finding of bone loss, in addition to individuals with evident clinical risk factors for osteoporosis.

There is some discordance in the performance of different radiographic keywords. However, this discordance points to the most relevant keywords and can be very useful for clinicians. As with the kinds of X-rays, parallel testing two kinds of plain radiographs increases the sensitivity as compared to one single radiograph. More plain radiographs, although offer some benefit in increasing specificity, does not enhance the overall validity, which can be contra-intuitive at first glance. However, validity comprises of both sensitivity and specificity. Any sacrifice in either one might lower validity. Therefore for screening screening purposes, we recommend combining two kinds of digital radiographs.

Our study has some advantages. We included asymptomatic individuals aged over 50 years and the sample size was large. This study group is more close to the general population as compared to symptomatic patients. This is a diagnostic cohort study, and the diagnostic accuracy is less likely to be overestimated. Our results might serve as a reference for future population screening strategy. All plain radiographs were digital radiographs and DXA was used as the gold standard. All radiographs were read by experienced radiologists. Participants were recruited from a single center, and all the radiologists were trained in the same center so that inter-rater variability was minimized. This is a retrospective study and the radiologists were unaware of study participation. Hence, our study might resemble real clinical practice more. Last and most important of all, we compared the validity of screening using different numbers of digital radiographs (one, two, three or four) and suggested the best number of radiographic keywords as cutoff. As far as we know, this is the first study to do so in literature.

There are some limitations. The majority of participants only took DXA of one body part. The number of X-rays taken differs among subjects, and cervical spine is not the preferred region to determine osteoporosis. Radiation dose needs to be considered. Some AUC results are barely satisfactory. Our study population is specific in many aspects: health screening participants, young mean age, low prevalence of osteoporosis, and possible economic and social bias owing to private-pay. The ability to extrapolate our findings to other populations at much higher risk warrants further study.

5. Conclusions

Among private-pay health examinees aged over 50 years, we suggest a DXA scan referral for individuals with any suspicious radiographic finding of bone loss. To screen osteoporosis, using two existent digital radiographs with a cutoff of one keyword criterion might be a potential strategy.

Our proposed method is best suitable for asymptomatic examinees receiving routine health checkups including plain radiographs or patients receiving plain radiographs for whatever other reason, particularly women. We do not intent to promote radiographs as a substitute for DXA but rather as a pre-screening for prudent DXA referral. Further study based on prevalent fracture risk is needed to determine the cost-effectiveness of this method.

Funding

This study was funded by the Department of Health, Taipei City Government (The validity of plain radiographs in screening osteoporosis among private-pay health examinees).

Disclosure of potential conflicts of interest

Conflict of Interest: The first author has received research grant from the Department of Health, Taipei City Government. The sponsor has no role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Ethical approval: "This study was approved by the Institutional Review Board of Taipei City Hospital, Taiwan [TCHIRB-1030418-E]. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

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Acknowledgements

The authors acknowledge the Department of Radiology, Renai Branch, Taipei City Hospital, Taiwan for providing the original reports used in this study.

Contributors

TY Wu designed the study and wrote the manuscript. KT Chen was responsible for statistical analysis of the data. CK Liaw, RS Yang, WC Chie, and KL Kuo contributed intellectually to the work in important steps. All authors revised the paper critically and approved the final version. All authors agreed to be accountable for the work and to ensure that any questions relating to the accuracy and integrity of the paper were investigated and properly resolved.

Tables

Table 1 Demographic characteristics of the participants (n=1929).

Characteristics (n (%) or mean±SD)	Total	Men	Women
Participants	1929 (100%)	855 (44.3%)	1074 (55.7%)
Age (years)	57.7±6.4	57.9±6.3	57.6±6.5
50-59	1296 (67.2%)	555 (64.9%)	741 (69.0%)
60-69	524 (27.2%)	252 (29.5%)	272 (25.3%)
70-79	88 (4.6%)	39 (4.6%)	49 (4.6%)
80-89	21 (1.1%)	9 (1.1%)	12 (1.1%)
Body height (cm)	162.2±8.6	169.3±6.0	156.5±5.6
Body weight (kg)	63.0±11.8	71.0±10.0	56.6±8.9
Waist circumference (cm)	80.8±10.1	86.7±8.5	76.1±8.8
Body mass index (BMI) (kg/m^2)	23.8±3.3	24.7±3.0	23.0±3.4
Underweight (BMI＜18.5)	76 (3.9%)	12 (1.4%)	64 (6.0%)
Normo-weight (18.5≦BMI＜24)	985 (51.1%)	350 (40.9%)	635 (59.1%)
Overweight (24≦BMI＜27)	558 (28.9%)	312 (36.5%)	246 (22.9%)
Mild obesity (27≦BMI＜30)	231 (12.0%)	141 (16.5%)	90 (8.4%)
Moderate to severe obesity (BMI≧30)	79 (4.1%)	40 (4.7%)	39 (3.6%)
Lumbar spine bone mineral density (BMD) (T-score)	-0.8±1.3	-1.0±0.6	-0.8±1.3
Femoral neck BMD (T-score)	-0.7±0.9	-0.7±0.8	-1.0±1.1
Overall normal BMD (T-score≧-1.0) [a]	1094 (56.7%)	541 (63.3%)	553 (51.5%)
Overall osteopenia (-1.0>T-score>-2.5) [a]	739 (38.3%)	311 (36.4%)	428 (39.9%)
Overall osteoporosis (T-score≦-2.5) [a]	96 (5.0%)	3 (0.4%)	93 (8.7%)
Kinds[b] of plain radiographs taken			
One	694 (36.0%)	363 (42.5%)	331 (30.8%)
Two	208 (10.8%)	125 (14.6%)	83 (7.7%)
Three	325 (16.8%)	59 (6.9%)	266 (24.8%)
Four	702 (36.4%)	308 (36.0%)	394 (36.7%)

[a] For examinees who took both dual energy X-ray absorptiometry (DXA) of lumbar spine and femoral neck, the lower T-score was chosen for analysis.

[b] Kinds means both the number and also the site of the images.

Table 2 The validity of plain radiographs in screening osteopenia/osteoporosis under different definition of positive screening results.

Definition of positive screening results	Sensitivity	Specificity	PPV	NPV	OR (95%CI)	P-value	AUC (95%CI)
Any plain radiograph criterion for osteopenia/osteoporosis							
Osteoporosis diagnosed by lumbar spine DXA T-score value	43.0%	81.3%	17.9%	93.8%	3.29 (2.08-5.21)	<0.001	0.622 (0.555-0.689)
Osteoporosis diagnosed by femoral neck DXA T-score value	70.0%	79.5%	3.6%	99.6%	9.08 (2.33-35.43)	0.001	0.748 (0.582-0.913)
Overall osteoporosis[a]	45.8%	80.4%	10.9%	96.6%	3.47 (2.29-5.28)	<0.001	0.631 (0.569-0.693)
Osteopenia/osteoporosis diagnosed by lumbar spine DXA T-score value	64.7%	56.7%	28.2%	86.0%	2.41 (1.75-3.31)	<0.001	0.571 (0.535-0.606)
Osteopenia/osteoporosis diagnosed by femoral neck DXA T-score value	40.1%	61.9%	21.8%	79.5%	1.09 (0.79-1.50)	0.615	0.507 (0.469-0.545)
Overall osteopenia/osteoporosis[b]	52.9%	59.2%	25.5%	82.6%	1.63 (1.31-2.03)	<0.001	0.541 (0.515-0.567)
Any two plain radiograph criteria for osteopenia/osteoporosis							
Osteoporosis diagnosed by lumbar spine DXA T-score value	5.8%	98.7%	29.4%	91.7%	4.62 (1.59-13.45)	0.008	0.522 (0.457-0.588)
Osteoporosis diagnosed by femoral neck DXA T-score value	30.0%	95.9%	7.3%	99.2%	10.05 (2.50-40.38)	0.001	0.630 (0.427-0.832)
Overall osteoporosis[a]	8.3%	97.3%	13.8%	95.3%	3.24 (1.49-7.05)	0.005	0.528 (0.466-0.590)
Osteopenia/osteoporosis diagnosed by lumbar spine DXA T-score value	94.1%	53.1%	3.4%	99.8%	18.09 (2.39-136.92)	<0.001	0.516 (0.480-0.552)
Osteopenia/osteoporosis diagnosed by femoral neck DXA T-score value	46.3%	61.8%	5.2%	96.2%	1.40 (0.75-2.62)	0.295	0.507 (0.469-0.545)
Overall osteopenia/osteoporosis[b]	60.3%	57.2%	4.2%	97.9%	2.04 (1.19-3.48)	0.008	0.510 (0.484-0.537)

Abbreviations: AUC (area under curve), CI (confidence interval), DXA (dual energy X-ray absorptiometry), NPV (negative predictive value), OR (odds ratio), PPV (positive predictive value).

[a] Overall osteoporosis means osteoporosis diagnosed by lumbar spine/femoral neck DXA T-score value.

[b] Overall osteopenia/osteoporosis means osteopenia/osteoporosis diagnosed by lumbar spine/femoral neck DXA T-score value.

Table 3 The validity of plain radiographs in screening osteopenia/osteoporosis under different kinds of X-rays taken.

Screening criteria	Plain radiograph keywords (n)	Sensitivity	Specificity	PPV	NPV	OR (95%CI)	P-value	AUC (95%CI)
Kind [a] of X-ray taken=1								
Overall osteoporosis [b]	1	13.3%	97.2%	17.4%	96.2%	5.29 (1.68-16.65)	0.002	0.553 (0.439-0.666)
	2	-[d]	99.7%	-[d]	95.7%	-[d]	1.000	0.499 (0.393-0.604)
Overall osteopenia/ osteoporosis [c]	1	5.1%	98.0%	65.2%	58.5%	2.64 (1.10-6.31)	0.024	0.515 (0.472-0.559)
	2	0.7%	100.0%	100.0%	57.9%	-[d]	0.349	0.503 (0.460-0.547)
Kinds [a] of X-rays taken=2								
Overall osteoporosis [b]	1	69.8%	60.3%	21.1%	92.9%	3.50 (1.75-7.01)	<0.001	0.650 (0.564-0.737)
	2	11.6%	96.1%	31.3%	87.7%	3.24 (1.07-9.84)	0.029	0.539 (0.442-0.635)
Overall osteopenia/ osteoporosis [c]	1	50.5%	66.7%	69.7%	47.0%	2.04 (1.29-3.24)	0.002	0.586 (0.523-0.649)
	2	7.7%	99.2%	93.8%	41.4%	10.61 (1.38-81.32)	0.005	0.534 (0.471-0.598)
Kinds [a] of X-rays taken=3								
Overall osteoporosis [b]	1	28.6%	74.1%	3.7%	96.8%	1.15 (0.22-6.09)	0.873	0.514 (0.293-0.734)
	2	14.3%	93.0%	6.7%	96.9%	2.23 (0.25-19.80)	0.462	0.537 (0.308-0.765)
Overall osteopenia/ osteoporosis [c]	1	29.7%	75.7%	35.2%	70.8%	1.31 (0.68-2.54)	0.414	0.527 (0.441-0.613)
	2	10.9%	94.4%	46.7%	70.5%	2.09 (0.72-6.03)	0.166	0.527 (0.440-0.613)
Kinds [a] of X-rays taken=4								
Overall osteoporosis [b]	1	50.0%	74.0%	4.3%	98.4%	2.85 (1.05-7.71)	0.031	0.620 (0.473-0.767)
	2	12.5%	96.6%	8.0%	97.9%	4.07 (0.87-18.95)	0.053	0.546 (0.393-0.698)
Overall osteopenia/ osteoporosis [c]	1	28.8%	75.0%	43.5%	61.2%	1.21 (0.86-1.71)	0.269	0.519 (0.475-0.563)
	2	4.0%	96.6%	44.0%	60.1%	1.18 (0.53-2.65)	0.682	0.503 (0.459-0.547)

Abbreviations: AUC (area under curve), CI (confidence interval), DXA (dual energy X-ray absorptiometry), NPV (negative predictive value), OR (odds ratio), PPV (positive predictive value).

[a] Kinds means both the number and also the site of the images.

[b] Overall osteoporosis means osteoporosis diagnosed by lumbar spine/femoral neck DXA T-score value.

[c] Overall osteopenia/osteoporosis means osteopenia/osteoporosis diagnosed by lumbar spine/femoral neck DXA T-score value.

[d] These values are not calculable because some of the numbers are zero.

Appendix Tables

Table A.1 Cross tabulation of the results of the radiographs by the results of DXA (dual energy X-ray absorptiometry).

	Number of plain radiograph findings					
DXA results (n (row%))	**Negative**	**Positive**				**Total**
	0	**1**	**2**	**3**	**All**	
Overall normal BMD (T-score≧-1.0) [a]	903 (82.6%)	167 (15.3%)	22 (2.0%)	1 (0.1%)	190 (17.4%)	1093 (100%)
Overall osteopenia (-1.0>T-score>-2.5) [a]	571 (77.2%)	142 (19.2%)	24 (3.2%)	3 (0.4%)	169 (22.8%)	740 (100%)
Overall osteoporosis (T-score≦-2.5) [a]	52 (54.2%)	36 (37.5%)	8 (8.3%)	0 (0%)	44 (45.8%)	96 (100%)

[a] For examinees who took both dual energy X-ray absorptiometry (DXA) of lumbar spine and femoral neck, the lower T-score was chosen for analysis.

Table A.2 Bone mineral density (BMD) among fractured & non-fractured participants.

BMD	Fractured participants (n=22)		Non-fractured participants (n=1907)		P-value
	Mean	SD	Mean	SD	
Lumbar T-score	-0.52	1.59	-0.81	1.32	0.592
Femoral T-score	-0.98	0.87	-0.72	0.85	0.231
Overall T-score	-0.86	1.09	-0.77	1.12	0.726

Table A.3 Distribution of the keyword findings (total n=1991 findings).

Keywords	n	%
None	1525	76.6
Reduced bone mineralization	223	11.2
Osteopenic change	89	4.5
Osteoporosis	2	0.1
Reduced vertebral height	11	0.6
Wedge deformity	115	5.8
Compression fracture	26	1.3

Illustrations

Figure caption

Fig.1 Flow chart of the selection of the participants (DXA: Dual energy X-ray absorptiometry)

Fig.A.1 ROC curve of different numbers of plain radiograph criteria using osteoporosis diagnosed by femoral neck T-score as outcome. Blue line: any one X-ray criterion as cutoff; Green line: any two X-ray criteria as cutoff; Vertical axis: sensitivity; Horizontal axis: 1-specificity.

P115

FRAILTY IN THE FEMALE COHORT OF THE GEELONG OSTEOPOROSIS STUDY

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Objectives: Frailty is an age-related clinical condition associated with adverse health outcomes that can be debilitating. Few Australian studies have investigated the prevalence of frailty in the general population. This study aimed to determine the prevalence of frailty in a population-based sample of women and to examine the relationship between frailty and comorbidities.

Methods: Women (n=360, ages 60-90 y) were assessed as part of the Geelong Osteoporosis Study (GOS) between 2011-2014. Frailty was identified using a modified Fried frailty phenotype, a five-item tool (comprising unintentional weight loss, exhaustion, low physical activity, slowness and weakness), that segregated participants into frail, pre-frail or robust groups. Prevalence estimates were standardised to the 2011 Australian population. Comorbidities and lifestyle factors were self-reported. ANOVA, Kruskal Wallis and chi-square tests were used to investigate associations between frailty groups.

Results: Of 360 women (median age 71 y, IQR 65-77), 49(13.6%) were frail, 183(50.8%) pre-frail and 128(35.6%) robust. Frailty prevalence increased with advancing age: 60-69 y(7.8%), 70-79 y(14.4%) and 80+ y(27.4%).Overall population-standardised prevalence for frailty was 14.2% (95%CI 10.5-18.0), pre-frail 50.9% (44.2-57.6) and robust 34.9% (29.0-40.5). Women who were frail were older, shorter, weighed less and tended to have lower BMI compared to the pre-frail and robust groups. The proportions of cardio-metabolic, pulmonary and musculoskeletal conditions were higher in the frail and pre-frail groups. The proportions across frail, pre-frail and robust groups [n (%)] were: cardio-metabolic conditions 46(93.9)-vs-160(81.4)-vs-101(78.9) (p=0.021); pulmonary conditions 15(30.6)-vs-41(22.4)-vs-15(11.7) (p=0.008); and musculoskeletal conditions 47(95.9)-vs-155(84.7)-vs-101(78.9) (p=0.020). Cancer was not associated with frailty 12(24.5)-vs-31(16.9)-vs-17(13.3) (p=0.199).

Conclusion: Just over 14% of older women in our study were frail and a further 50.9% were pre-frail. These estimates fall within the range reported by other similar studies. Additionally, the prevalence of frailty increased with age. These findings have important implications for public health, clinical practice and service utilisation, given the association between frailty and comorbid conditions in the context of an ageing population.

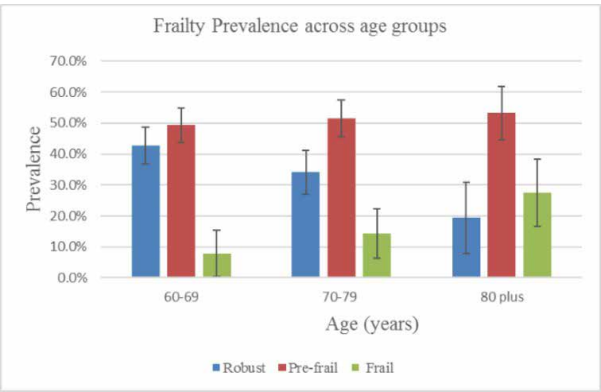

Figure 1. Frailty Prevalence stratified by age groups. Error bars represent standard error

P116

NO RELATIONSHIP BETWEEN WIDE RANGE OF SERUM 25 HYDROXYVITAMIN D LEVELS AND PHYSICAL FUNCTION PARAMETERS IN OLDER WOMEN: FINDINGS FROM VITAL D SUBSTUDY

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Objectives: To investigate the relationship between serum 25-hydroxyvitamin D [25(OH)D] levels and physical function parameters in women aged ≥70 y who took part in the Vital D study. The Vital D study has previously reported increased falls and fractures in older women[1] on an annual high-dose vitamin D.

Methods: The Vital D study was a randomized trial of 500,000 IU vitamin D or placebo given annually to 2256 women aged ≥70 y residing in, Australia. A substudy of 137 participants had blood and physical function tests in 2006 and 2007. Serum 25(OH)D levels were measured pre-dose and at 1-and 3-months after the annual dose of study medication. Muscle strength (hip flexion, quadriceps, hip abduction), balance (Balance Master), 'timed up and go' and 7 gait parameters (Gait Rite) were assessed 3 months post dose. This analysis uses the pooled participant data irrespective of treatment allocation to investigate relationship(s) between serum 25(OH)D and physical function parameters. Linear and nonlinear relationships between serum 25(OH)D levels measured at 1- and 3-month post dose and physical function parameters measured 3-month post dose were examined using linear mixed models (LMM) and generalized additive mixed models (GAMM), with adjustment for pre-dose serum 25(OH)D, baseline physical function parameters, age, BMI and time in study.

Results: 56% of substudy participants received the annual high dose vitamin D (age 76.0±4.3 y; BMI 28.0±4.8 kg/m^2). Mean pooled serum 25(OH)D levels before the annual dose, 1-month and 3 months post dose were 62±25; 87±50 and 69±34 nmol/L, respectively. Correlations at 1- and 3-month post dose serum 25(OH)D with physical function parameters ranged from -0.2 to 0.2. Analyses with LMM and GAMM did not identify any significant associations between serum 25(OH)D levels and any of the physical function parameters ($p>0.05$).

Conclusions: Our results showed that correlations between serum 25(OH)D levels vitamin D and physical parameters measured 3 months following annual high-dose vitamin D or placebo in older women were only very weak and were unable to identify either linear or nonlinear associations. Further analysis is required to study the effect of serum 25(OH)D levels and physical function parameters to explain increased falls in Vital D study.

Reference: [1]Sanders KM, et al. JAMA 2010;303:1815.

P117

IMPACT OF OSTEOPOROTIC FRACTURE TYPE AND SUBSEQUENT FRACTURE ON MORTALITY IN TROMSØ, NORWAY

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Objectives: Norway has one of the highest rates of osteoporotic fractures and life expectancies worldwide. However, limited evidence exists about the impact of those fractures and their subsequent fractures on mortality in this ageing population. This study examined the contribution of initial fracture type and subsequent fractures over and above other factors on mortality risk in Tromsø, Norway.

Methods: The Tromsø Study is a prospective population-based cohort. Women and men aged 50+ y were followed from 1994-2010. All incident non-vertebral fractures were registered. Fractures analysed were hip and nonhip nonvertebral (NHNV) fractures (classified as proximal or distal). Self-reported comorbidities including diabetes, stroke and heart disease and lifestyle factors including smoking, physical activity, general health and education level were collected. Multivariable Cox models were used to quantify mortality risk after accounting for potential confounders. Incident and subsequent fractures were analysed as time-dependent.

Results: Of 5214 women and 4620 men, 1549 (30%) and 504 (11%) sustained a fracture, followed by 589 (38%) and 254 (51%) deaths over 10,523 and 2820 person-years, respectively. There were 403 (26%) subsequent fractures in women and 68 (13%) in men. Hip fracture was associated with a 2-fold increase in mortality risk (HR 2.07 95%CI1.75-2.45 in women, and 2.49 95%CI 1.99-3.11 in men). NHNV proximal fracture was associated with 51% and 78% increased mortality risk in women (HR 1.51 95%CI 1.22-1.86) and in men (HR 1.78 95%CI 1.34-2.37), respectively. NHNV distal fractures were not associated with mortality. Subsequent fracture was associated with 74% increased mortality risk in women (HR 1.74 95%CI 1.35-2.22), while in men it was not significant (HR 1.39 95%CI 0.79-2.43). In women this increased mortality risk was seen following hip (HR 3.07 95%CI 2.25-4.20), proximal NHNV (HR 2.01 95%CI 1.39-2.91) and distal NHNV fractures (HR 1.42 95%CI 1.05-1.91) but only following hip fractures in men (HR 3.05 95%CI 1.72-5.42).

Conclusions: This study highlights the impact of: 1) hip and proximal NHNV fractures on mortality risk and 2) subsequent fractures following hip (women and men) and NHNV (women) on mortality risk. Hence, early intervention pre and post-fracture is warranted.

P118

ORAL BISPHOSPHONATE USE AND ALL-CAUSE MORTALITY IN PATIENTS WITH ADVANCED (STAGE IIIB+) CHRONIC KIDNEY DISEASE: A POPULATION-BASED COHORT STUDY

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Objectives: Chronic kidney disease (CKD) is associated with significantly increased risk of fractures and mortality. Oral bisphosphonates (oBP) have been associated with better survival. However, their risks and benefits are unclear in patients with severe CKD. This study examined the association between oBP use and all-cause mortality in stage IIIB + CKD.

Methods: A population-based cohort study including all subjects with an eGFR<45/ml/min/1.73m2 aged 40 y or older, with at least one year of run-in data from the UK Clinical Practice Research Datalink (CPRD) linked to Office for National Statistics (ONS) mortality data. Previous and current users of anti-osteoporosis drugs other than oBP were excluded. GP prescriptions of oBP were identified using BNF codes. oBP use was modelled as a time-varying exposure to avoid immortal time bias. Treatment episodes in oBP users were created by concatenating prescriptions until patients switched or stopped therapy (refill gap in prescriptions of 180+ d) or were censored (end of study or transfer out) or have died. A washout period of 180 d was added to (date of last prescription +180 d). Propensity scores (PS) were calculated using multivariable logistic regression modelling. Prespecified predictors of mortality including age, gender, baseline eGFR, socioeconomic status, comorbidities (including Charlson Index), previous fracture, concomitant medications and hospital admissions in the previous year were included in the models. Cox models were used to perform adjustment for PS before and after PS trimming (at the first and last quintiles) where 40% of subjects whose PS have little or no overlap were removed.

Results: Of 19,351 oBP users and 210,954 non-oBP users, 5,234 (27%) and 85,105 (40%) deaths were recorded over 45,690 and 915,867 person-years of follow-up, respectively. oBP users had 8% lower mortality risk compared to non-oBP users (HR 0.92 95%CI 0.89-0.95). Following PS trimming this became not significant (HR 0.98 95%CI 0.94-1.04).

Conclusions: oBP use is not associated with increased mortality amongst patients with advanced CKD (stage IIIB+). However, they may be associated with 8% decreased mortality risk. Hence, use of oBP could be supported in this population, who have a high risk of fracture and no alternative treatment.

P119

LIFESTYLE FACTORS ASSOCIATED WITH TRABECULAR BONE SCORE VALUES

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Objectives: The recently developed trabecular bone score (TBS) indirectly assesses trabecular microarchitecture at the lumbar spine, providing complementary information to areal BMD. Many studies have investigated the effects of lifestyle factors on BMD, but limited research has been directed towards TBS. The aim of this study was to assess the cross-sectional relationship between lifestyle factors and TBS in Australian men and women.

Methods: This study involved 894 men and 682 women (aged 24-98 y) enrolled in the Geelong Osteoporosis Study. TBS was assessed by analysis of lumbar spine DXA scans (Lunar Prodigy) using TBS iNsight software (Version 2.2). Bivariate and multivariable linear regression were used to explore the associations between TBS and lifestyle factors, including alcohol consumption, physical activity, smoking status, prior fracture, medication use, calcium and vitamin D intake.

Results: Median age for men and women was 60.1 (IQR 46.4-73.3) and 55.3 (IQR 42.1-68.1) respectively, while median weight was 82.0 (IQR 74.1-91.8) and 70.0 (61.9-81.4). Mean height was 174.8±7.3 for men and 162.1±6.5 for women. In bivariate regression modelling, physical activity and the use of antiresorptive medication were associated with lower TBS in both men and women (all $p<0.05$). Prior low trauma fracture, use of glucocorticoids, and total calcium intake were associated with lower TBS in women only ($p<0.001$, $p=0.016$ and $p<0.001$ respectively). The final adjusted model for men included age, weight and BMD, and for women included age, height, BMD, and physical activity. No interaction terms were identified in the models.

Conclusion: Factors associated with lower TBS included older age, heavier weight and lower BMD in men, and older age, shorter stature, lower BMD and physical activity in women.

P120

INFLAMMATION AND BONE: GEELONG OSTEOPOROSIS STUDY

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Objectives: Osteoporosis is a disease state possibly underpinned by systemic inflammation. Thus, we aimed to determine whether serum interleukin 6 (IL-6), a marker of systemic inflammation, is associated with BMD in a population-based sample of men.

Methods: This cross-sectional study utilised data from 1143 men aged 20-96 y (median 61.5, IQR 44.5-75.5) participating in the Geelong Osteoporosis Study. Serum IL-6 was measured following an overnight fast using ELISA (R&D Systems). BMD (g/cm^2) was measured at the PA-spine, femoral neck, total body and forearm using DXA (Lunar). Anthropometric measurements and socioeconomic status (SES) were determined and information on medication use and lifestyle was obtained via questionnaire. IL-6 values were natural log transformed (ln-IL6) and associations between ln-IL6 and BMD were tested using Pearson's correlation. Multivariable regression models were developed to test the association between ln-IL-6 and BMD after adjusting for age and weight.

Results: Ln-IL-6 (median 1.9 mg/ml, IQR 1.2-3.2) was positively correlated with age (r=0.52, p<0.001) and negatively with BMD at the femoral neck (r=-0.27, p<0.001), total body (r=-0.16, p<0.001), distal-forearm (r=-0.17, p<0.001) and mid forearm (r=-0.19, p<0.001) sites. After adjustments, ln-IL-6 was associated with decreased BMD at the femoral neck (β -0.014, se±0.006, p=0.015), total body (β -0.010±0.004, p=0.010), distal (β -0.010±0.003, p=0.050) and mid forearm (β -0.009±0.003, p=0.011), but not spine BMD (β -0.010±0.010, p=0.237). These associations persisted after further adjustment for smoking, physical activity, SES, alcohol consumption, medications (statins, antidepressants, nonsteroidal anti-inflammatory drugs) and arthritis.

Conclusion: These population-based data suggests IL-6 is independently associated with BMD in adult men. This supports an aetiological role for inflammatory activity in the pathophysiology of osteoporosis, suggesting a possible target for therapy.

P121

QUANTITATIVE HEEL ULTRASOUND (QUS) AND ANTICONVULSANT USE IN A POPULATION-BASED STUDY

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Objectives: Anticonvulsant use has been previously linked with decreased bone density. QUS is a cost-effective, portable screening tool used to assess fracture risk. We aim to determine the association between QUS measures and anticonvulsant use in a population-based sample of men.

Methods: Complete information on medication use and QUS measures were available for 849 men (age range: 24-98) participating in the Geelong Osteoporosis Study. Bone quality was assessed using QUS, which provided the following measures: stiffness index (SI), broadband ultrasound attenuation (BUA) and speed of sound (SOS). Height and weight were measured and BMI calculated (kg/m^2). Medication use, activity levels and smoking status were self-reported. Multiple linear regression was used to assess the relationship between QUS and anticonvulsant use.

Results: Fifteen men (1.8%) reported using anticonvulsants. Anticonvulsant users were less physically active compared to non-users [physically active: 6 users (40%) vs. 599 non-users (72%), p=0.007]. Before and after adjustment for age (y), BMI and agents affecting calcium, anticonvulsant users had lower SI (mean: 84.4±26.9% vs. 100.1±20.2%, users vs. non-users, p=0.04), BUA (106.4±17.6 dB/MHz vs. 120.7±15.9 dB/MHz, p=0.01) and SOS (1540.0±57.0 m/s vs. 1572.7±40.9 m/s, p=0.05) compared to non-users. Further adjustment for smoking, physical activity and medications known to affect bone did not affect the relationships.

Conclusion: Our data suggest that bone quality, as assessed using QUS, is reduced for men using anticonvulsants. QUS may therefore be a useful screening tool to identify anticonvulsant users at risk of fracture.

P122

ROLE OF PLAQUE CHARACTERISTICS IN THE ASSOCIATION BETWEEN CORONARY ATHEROSCLEROTIC PLAQUE AND BMD: THE WOMEN HEALTH REGISTRY STUDY FOR BONE, BREAST, AND CORONARY ARTERY DISEASE (BBC STUDY)

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Objectives: Although the associations between BMD and atherosclerosis are still inconclusive, several mechanisms have been proposed to underly the potential link between bone and atherosclerosis. This study sought to evaluate the association between presence and severity of coronary artery calcification (CAC) and coronary atherosclerotic plaque (CAP), and BMD, and also to investigate whether plaque characteristics of CAP could affect this associations between bone and vessel in asymptomatic women.

Methods: Asymptomatic 2100 women aged 40 y and older (median age, 52 y, range 40-80 y) who underwent DXA, digital mammography, and coronary computed tomography angiography simultaneously for their routine health checkup were consecutively enrolled. The study subjects were further stratified into normal, osteopenia, and osteoporosis groups according to their BMD T-score grades. We evaluated the presence and severity CAC and CAP. The CAPs were further classified as calcified, mixed, or noncalcified plaque according to the proportion of calcified tissue (>50%, <50%, and none, respectively).

Results: Both CAC score and CAC severity showed significant increasing trends with BMD grades, normal to osteoporosis. The CAP was found in 15.6% of all participants and was proportionally increased in subjects with normal, osteopenia and osteoporosis (12.6%, 20.2% and 28.8 respectively, $p<0.001$). The proportion of extensive CAP was also significant higher in osteoporotic subjects compared to other two groups (1.8% in osteoporosis vs. 0.8% in osteopenia and 0.8% in normal group). Moreover, the numbers of CAP were significantly increased according to the BMD grades even after adjusting for age. According to the plaque characteristics, the number of calcified plaque only provided increasing trends with BMD grades after adjusting for age, but mixed or noncalcified plaque did not.

Conclusions: The presence and severity of CAC and CAP were significantly associated the levels of BMD in asymptomatic women, especially for the calcified plaque presence. Further studies are needed the association between vascular calcification and bone health status.

P123

PICOLINIC ACID (PIC) AS A NOVEL OSTEOANABOLIC: POSSIBLE MECHANISMS OF ACTION

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Objectives: PIC is a potent bone anabolic. We have earlier reported a concentration-dependent osteoanabolic effect of PIC on human mesenchymal stem cells (hMSCs) *in vitro*. In this study, we hypothesised that PIC may play a role in activating essential osteogenic pathways in hMSCs. Therefore, the aim of this study was to investigate the role of PIC in regulating Wnt/β-catenin signalling and the nitric oxide (NO) pathway in hMSCs.

Methods: hMSCs were cultured under standard osteogenic conditions in the presence of an osteoanabolic concentration of PIC (100 μM) or vehicle control. Nitrite levels were determined using Greiss' method. Expression of β-catenin (stabilised form), CK1, GSK3-β and iNOS were studied using western blotting. Runx2 binding to its consensus sequence was determined using an ELISA-based method.

Results: At 8 h post PIC treatment in hMSCs, we found a significant ($p \leq 0.05$) upregulation of stabilised non-phosphorylated (Ser45) β-catenin levels (3.1±0.96-fold in PIC treated cells, as compared to 0.7±0.07 fold in their respective controls). Concomitantly, there was a significant ($p \leq 0.05$) gain in β-catenin gene expression at 8 h post PIC treatment. RUNX2 binding was also significantly ($p \leq 0.05$) increased by PIC treatment (0.3±0.01) as compared to untreated controls (0.2±0.08). Our preliminary results also suggest that LRP5 knockdown alters PIC-induced osteogenic gene expression. Additionally, we found that PIC treatment not only significantly reduced nitrate levels and iNOS expression ($p \leq 0.05$) in hMSCs but also elevated the expression of eNOS by day 7 post-treatment.

Conclusion: Our results clearly demonstrate the influence of PIC on two distinct pathways. In the β-catenin pathway, PIC induced early stabilisation of β-catenin. However, it did not alter protein levels of GSK3β and CK1. PIC significantly inhibited iNOS production also, confirmed by two separate approaches. We also observed a significant increase in eNOS levels in hMSCs treated with PIC. Overall, we conclude that PIC acts as an osteoanabolic by activating the Wnt/β-catenin pathway of osteogenesis in hMSCs, and also inhibits nitric oxide in these cells, thus promoting their osteogenic differentiation capacity. Further investigations are still required.

Acknowledgements: This study was funded by the Australian Institute for Musculoskeletal Science, University of Melbourne, Melbourne, Australia.

P124

HEALTH LITERACY AMONG FRAIL AND PRE-FRAIL WOMEN

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Objective: The declines in physical and cognitive function that characterise frailty often leave individuals managing complex comorbidities, including an increased risk of falls and fracture, with reduced abilities. We aimed to investigate the health literacy needs of frail women.

Methods: Data were collected as part of the 15-y follow-up of women in the Geelong Osteoporosis Study, a population-based cohort study. Participants aged ≥60 y were included in analyses. Frailty scores were calculated using a modified Fried frailty phenotype. Participants were categorised as 'robust', 'pre-frail' or 'frail'. Health literacy was determined using the multidimensional Health Literacy Questionnaire (HLQ). One-way Analysis of Variance (ANOVA) was used to investigate differences in mean HLQ scale scores across frailty groups.

Results: Among 282 women (median age 69.9 y [IQR 64.7-75.0yr]), 113 (40.1%) were categorised as robust, 145 (51.4%) as pre-frail and 24 (8.5%) as frail. Trends for differences in mean HLQ scale scores were observed between groups for scales 'Navigating the healthcare system' (mean [95%CI]; 'robust' 4.18 [4.08, 4.28], 'pre-frail' 4.05 [3.96, 4.15], 'frail' 3.76 [3.32, 4.19] *p*-value=0.07) 'Actively managing health' (mean [95%CI]; 'robust' 3.06 [2.97, 3.14], 'pre-frail' 2.95 [2.89, 3.02] 'frail' 2.93 [2.73, 3.13] *p*-value=0.09) and 'Understanding health information' (mean [95%CI]; 'robust' 4.27 [4.17, 4.38], 'pre-frail' 4.16 [4.07, 4.26], 'frail' 3.98 [3.62, 4.34] *p*-value=0.09). Differences in HLQ scores occurred largely between 'robust' and 'frail' categories.

Conclusion: Frail women may experience difficulties in understanding health information, navigating healthcare systems and actively managing health. This suggest the need to provide health information and services in ways that meet the health literacy needs of frail individuals.

P125

RELATIONSHIPS BETWEEN SARCOPENIA, COMORBIDITY AND MEDICATION USE IN ELDERLY PEOPLE

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Objective: To investigate how sarcopenia was related to comorbidity and medication use in community-dwelling older people.

Methods: Inclusion criteria of this retrospective cross-sectional study were: age 60 or more years, unrestricted mobility, MMSE score ≥21. Sarcopenia was diagnosed according to the criteria made by European Working Group on Sarcopenia in Older People (2010). Muscle mass was measured by iDXA (GE Lunar, USA), muscle strength was evaluated by handgrip by dynamometry (Jamar, Patterson Medical, UK). Physical performance was measured using the Short Physical Performance Battery (SPPB) test. Number of diseases was assessed by physician. Polypharmacy was defined as regular use of ≥5 medications. Associations between sarcopenia and number of diseases or medications were assessed using Spearman correlation coefficient.

Results: In total, 166 subjects were included into this study: 67 (40.4%) men and 99 (59.6%) women. Average age of investigated subjects was 78.38±6.45 years, ranging from 62.8-94.7 y. Sixty-three (38%) subjects were identified as having sarcopenia. All participants had comorbidities, ranging from 1 (60 participants, 36.1%) to 5 diseases (1 participant, 0.6%). Most prevalent diagnoses were: hypertension (58.4%), coronary artery disease (13.9%), diabetes mellitus (9%), stroke (8.4%), cold (6.1%), heart attack (4.2%). Number of participants taking no drugs was 17 (10.2%). Polypharmacy was observed in 25 (15.1%) participants. Statistically significant correlation was found between sarcopenia and number of diseases ($r=0.744$, $p<0.001$). Sarcopenia was also associated with polypharmacy and number of medications ($r=0.504$, $p<0.001$; $r=0.767$, $p<0.001$, respectively).

Conclusion: In older adults sarcopenia was associated with number of diseases and number of medications taken.

P126

HIGHER BODY MASS INDEX IS ASSOCIATED WITH LOWER BONE MATERIAL STRENGTH INDEX IN MEN

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Objectives: BMD does not fully explain fracture risk, as the largest absolute number of fragility fractures occur in people without severe deficits in BMD. Impact microindentation is an emerging technique, which measures bone material strength index (BMSi) in vivo. Recent studies have reported that a significant percentage of fractures occur in obese people (1). Therefore, we aimed to evaluate whether adiposity is associated with BMSi.

Methods: BMSi was measured using the OsteoProbe for the first 336 men (ages 33-96 y) assessed in the current phase of the Geelong Osteoporosis Study. Pearson product moment correlation was used to test for a linear association between BMSi and BMI. Multiple regression models were used to adjust the association for age, prior fracture, parental fracture, alcohol consumption and smoking.

Results: Mean (±SD) for age, weight, height, BMI and BMSi were 64.1±13.3 y, 81.4±11.1 kg, 174.1±6.8 cm, 26.8±3.2 kg/m^2 and 83.0±7.5, respectively. BMSi was negatively correlated with BMI before (r=-0.16, p=0.004) and after adjusting for age (β=-0.06, p=0.008). No other confounders were identified.

Conclusion: We report that BMSi is negatively correlated with BMI, independent of other risk factors for fracture. Findings from recent studies suggest that excessive adipose tissue may negatively affect bone quality. These findings support the notion excessive body fat, that is known to reduce bone quality, might contribute to reduced bone material strength. Further work is in progress to confirm this. Taken together, our data support the notion that IMI using the OsteoProbe may be a useful technique for identifying men with bone fragility.

Reference: (1) Nielson CM, et al. J Bone Miner Res 2010;25:496.

P127

FALL RELATED OUTCOMES AND HEALTHCARE SERVICES IN ELDERLY WOMEN

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Objective: In elderly, falls are the most recognized problems leading to serious health and psychosocial consequences. The aim of this study was to analyse the outcomes and healthcare services provided for falls in community-dwelling elderly women.

Methods: Participants of this cross-sectional study were women over 65 y. Falls, their outcomes, and contacts with medical care services were registered. Fear of falling was evaluated using short version of FES-I. Women were also asked to describe any health care procedures performed at out-patient clinic, emergency department or at hospital. The statistical analysis was performed using SPSS software for Windows (version 18.0). All p-values less than 0.05 were considered as statistically significant.

Results: The study population consisted of 878 community-dwelling women (mean age 72.2±4.8 y). Falls were reported by 310 (35.3%) women. Of all women who fell, 280 (90.3%) reported different injuries, and 77 (15.3%) falls led to bone fractures. The fear of falling was reported by 76.4% respondents; the score of FES-I was 20.43±6.43. Different types of outpatient healthcare were used by 43.5% of women who fell. Family doctor was visited by 19.4% of fallers. The majority of specialists visited were traumatologist, surgeon, and radiologist. Of all fallen subjects, 18 (5.8%) women were hospitalised. Rehabilitation was provided to 5 subjects with fractures. The mean number of health care procedures was higher in women who sustained a fracture, as compared to those who did not: 4.9 (95%CI 4.4–5.4) and 0.67 (95%CI 0.29–0.76), respectively; p<0.0001.

Conclusions: Majority of all self-reported falls in women over 65 years resulted in injuries, consequent fear of falling was reported by three-fourths of subjects. Health care services were provided almost to half of women fallen.

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FDPS, GGPS1, OPG, RANKL GENE POLYMORPHISM AND BONE RESPONSE TO ANTIRESORPTIVE THERAPY OF POSTMENOPAUSAL OSTEOPOROSIS

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Objective: Osteoporosis (OP) therapy is primarily focused on decreasing the bone resorption or promoting the bone formation. Among drugs which inhibit bone resorption, the bisphosphonate family, SERM and denosumab are mostly used by clinicians. The genetic variations of the *FDPS*, *GGPS1* genes, which participate in mevalonate pathway, and of the *OPG*, *RANKL* genes, playing important roles in NF-κβ pathway, play important role in regulation of bone remodeling and are possible markers of effectiveness of antiresorptive therapy. Purpose of work was to analyze the association between *FDPS*, *GGPS1*, *OPG* and *RANKL* gene polymorphisms and effectiveness of bisphosphonate therapy in Belarusian and Lithuanian postmenopausal women.

Methods: Forty-seven Belarusian patients were recruited from Center for Osteoporosis Prevention (Minsk, Belarus), while 88 Lithuanian patients were recruited from National Osteoporosis Center (Vilnius, Lithuania). The study was approved by local research ethics committees. The women were given bisphosphonates (alendronate) orally for 2 y. The BMD at the lumbar spine and femoral neck were measured (GE Lunar). Polymorphic variants in *FDPS* (farnesyl diphosphate synthase, rs2297480) *GGPS1* (geranylgeranyl diphosphate synthase, rs10925503) *OPG* (osteoprotegerin, rs3102734) and *RANKL* (receptor activator of the NF-κβ ligand, rs9594759) genes were determined using PCR analysis with TaqMan probes (Thermo Scientific). Significance was assessed using χ^2 test and multivariate logistic regression (R-package).

Results: The genotyping revealed a statistically significant association of *FDPS* and *GGPS1* gene variants with the effectiveness of OP bisphosphonate therapy. No association was observed between *OPG* and *RANKL* gene variants and response to bisphosphonate therapy. In a further work, we will compare these markers with response to denosumab therapy. We also revealed statistically significant association between vitamin D receptor gene polymorphisms and BMD level in both population groups.

Conclusion: The analyzed genetic markers may correlate to the effectiveness of bisphosphonate therapy of osteoporosis. Considering the effects of unfavorable gene variants, genetic testing will help to improve effectiveness of OP therapy.

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FACTORS ASSOCIATED WITH OSTEOPOROSIS IN MALE COMMUNITY-DWELLING OLDER PEOPLE: A CROSS-SECTIONAL STUDY

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Objectives: To investigate the association of metabolic factors and osteoporosis among male community-dwelling older people.

Methods: This retrospective cross-sectional study recruited male older people aged 60 y and older who visited a health examination center in southern Taiwan for a routine checkup and received DXA between January and December 2017. Participants who had hyperthyroidism, rheumatoid arthritis, recent steroid usage, excessive alcohol consumption (>210 mg/week) and regular hemodialysis were excluded. Femoral neck and lumbar spine BMD were measured by DXA. Osteoporosis was defined according to the WHO as BMD T-score ≤-2.5. Multiple logistic regression analysis was applied for determining independent factors associated with osteoporosis.

Results: In total, 725 male participants (mean age 65.68±5.39) were recruited for the study, and 139 (12.9%) were diagnosed with osteoporosis. After adjusting for age, BMI, waist circumference (WC), serum fasting glucose, hemoglobin A1c, total cholesterol, high density lipoprotein, low-density lipoprotein, uric acid, hemoglobin, corrected calcium, alkaline phosphatase (Alk-p), exercise frequency (>150 min/week), current smoking status and alcohol consumption amount, we found higher BMI remained at a significant level for lower risk of osteoporosis (OR=0.847, 95%CI, 0.760-0.943, *p*=0.003) in multiple logistic regression. In addition, we also found higher serum Alk-p level was associated with osteoporosis (OR=1.016, 95%CI, 1.002-1.029, p=0.023).

Conclusions: Lower BMI and higher serum Alk-p concentration were associated with osteoporosis among community-dwelling male older people. Further intervention studies should be designed for those who had identified with a higher risk of osteoporosis.

P130

EFFECT OF TERIPARATIDE TREATMENT ON RISK MARKER OF CARDIOVASCULAR DISEASE

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Objective: Primary hyperparathyroidism is associated with increased occurrence of cardiovascular disease. The N-terminal fragment of the propeptide of brain natriuretic peptide (NT-proBNP) has been shown to be elevated in PHPT patients, indicating that continuously high concentrations of PTH affect the heart. The aim of this study was to investigate whether teriparatide treatment is associated with changes in plasma NT-proBNP.

Methods: A total of 30 patients receiving teriparatide treatment were included in the study. Plasma concentrations of NT-proBNP were measured at baseline, and after 6, 12, 18 and 24 months of treatment. BMD for the lumbar spine and total hip was recorded at baseline and after 12 and 24 months.

Results: No effect of teriparatide on plasma concentrations of NT-proBNP was observed at any time points. Spine and hip BMD T-score was significantly increased after 12 months of treatment.

Conclusion: After 24 months of treatment with teriparatide, there is no significant change of the concentration of NT-proBNP in plasma. Intermittent exposure to therapeutic levels of teriparatide may not affect heart function.

P131

ASSESSING A FRACTURE RISK CALCULATOR AS A SCREENING TOOL FOR WOMEN AT RISK FOR SARCOPENIA

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Objective: The identification of sarcopenia requires densitometry or bioelectric impedance analysis to measure muscle mass, dynamometry for muscle strength, or assessment of gait speed. A simple, feasible tool is needed for identifying individuals at risk for sarcopenia. As there are shared characteristics between individuals with sarcopenia and osteoporosis, we aimed to test the performance of FRAX for discriminating individuals at risk for sarcopenia.

Methods: In this longitudinal component of the Geelong Osteoporosis Study, baseline FRAX(Australia) scores were determined for 310 women, and sarcopenia assessed 15 years later using DXA-derived low relative appendicular lean mass (Lunar; rALM <5.5 kg/m^2) and poor handgrip strength (Jamar; HGS <20 kg). We tested FRAX scores for hip fracture and major osteoporotic fracture (MOF), with and without BMD. The area under the receiver operator characteristic (AUROC) curve quantified the discriminate performance of FRAX scores for predicting sarcopenia.

Results: At baseline, median(IQR) values were age 54(48-61) y, HIP-FRAX(noBMD) 0.20(0.10-0.80), MOF-FRAX-(noBMD) 1.70(1.0-3.63), HIP-FRAX(+BMD) 0.10(0.00-0.43), MOF-FRAX(+BMD) 1.60(1.00-3.33). At follow-up, sarcopenia was identified for 14(4.5%) of participants. (i) FRAX-without-BMD: AUROC was 0.859 for Hip-FRAX, and 0.839 for MOF-FRAX. Optimal thresholds were 1.0 for Hip-FRAX (sensitivity 78.6%, specificity 74.3%) and 4.2 for MOF-FRAX (sensitivity 71.4%, specificity 72.3%). (ii) FRAX-with-BMD: AUROC 0.808 for Hip-FRAX, and 0.802 for MOF-FRAX. Optimal thresholds were 0.6 for Hip-FRAX (sensitivity 64.3%, specificity 77.0%) and 3.9 for MOF-FRAX (sensitivity 64.3%, specificity 73.0%).

Conclusions: FRAX scores calculated without BMD predicted the risk for sarcopenia with reasonable sensitivity and specificity. Given that the clinical risk factors are identified without the need for equipment, and that the on-line calculator is widely accessible, there is potential for this assessment modality of FRAX to be used for screening individuals at risk of sarcopenia. Our results suggest that individuals with a Hip-FRAX score above 1.0 (8th decile) are at risk for sarcopenia and may require further investigation and management.

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SPINACIA OLERACEA EXTRACT ATTENUATES OSTEOARTHRITIS IN SURGICALLY INDUCED ACLT RAT MODEL

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Objective: To check effect of *Spinacia oleracea* extract on ACLT induced model of Osteoarthritis. Previously our study reported the positive effects of the leaves of *Spinacea oleracea* extract (SOE) on cartilaginous cells to enhance the fracture healing in rats and in MIA induced rat model of osteoarthritis, however its positive effects on more mimic osteoarthritis model like ACLT model remains unknown. The purpose of this study was to evaluate its anti-osteoarthritic and chondroprotective effects in ACLT induced OA model.

Methods: Histology and staining, ELISA, u-CT, H&E, Toluidine blue, CTX-II and COMP ELISA. Osteoarthritis (OA) is highly prevalent and debilitating disorder of the joints.

OA surgery model in rats were developed by cutting of ACL (anterior cruciate ligament) in knee joint by fine forceps. *In vivo* doses of SOE 125 $mg.kg^{-1}day^{-1}$ and 250 $mg.kg^{-1}day^{-1}$ were given orally for 28 d daily. We assessed the chondro-protective effect of SOE by micro-CT analysis of knee joint, gross appearance of knee joint, Histology of tibia sections and their staining by H&E and toluidine blue. Statistics: One-way ANOVA test done between all the group Control, ACLT, ACLT+SOE 125 $mg.kg^{-1}day^{-1}$ and ACLT +250 $mg.kg^{-1}day^{-1}$.

Result: Serum analysis indicated that SOE down regulated cartilage oligometric matrix protein (COMP), and CTX-II expression which were increased in ACLT model. SOE maintained surface architecture, smoothness and prevented clustering of chondrocyte cells which is a characteristic marker of OA.

Conclusion: Data showed that SOE acts as a strong anti-oxidant and an anti-inflammatory. ACLT induced loss of articular cartilage and changes in thickness of calcified cartilage and loss in subchondral bone were significantly prevented by SOE. As we know pain relieving and anti-inflammatory drugs have their own side effects, so if we use natural source/dietary content it may be more promising.

References:

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Choudhary D, Kothari P, Tripathi AK, et al. BMC Complement Altern Med 2018;18:69

P133

THE ASSOCIATION BETWEEN LONG-TERM SEDENTARY BEHAVIOR DURING CHILDHOOD AND MUSCLE MASS AND FUNCTION: THE HAPPY STUDY

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Objectives: In adult populations, there is evidence to suggest that sedentary behaviour in older age is associated with deleterious effects on lean mass and function. However, there are no studies in paediatric populations. Thus, we aimed to determine the association between sedentary behaviour (SB) in children and lean mass and function in the weight-bearing lower extremities.

Methods: Participants were recruited as part of the HAPPY Study (Victoria, Australia). Data for these analyses pertain to a subset of participants (mean age 12.2±0.8 y) with sustained high and low levels of SB based on measurements collected at 3-y intervals from preschool age (≤100 counts/min, Actigraph accelerometer) (n=71, 46.5% girls, 46.5% high SB). Lean mass was assessed by DXA (GE, USA), and by pQCT (Stratec, Germany) at the mid tibia (66% site). Lower extremity leg power (W) was calculated from maximal vertical jump height, using Sayer's equation. Group comparisons of lean mass and strength outcomes were made using linear regression modelling adjusting for sex, height and bone age.

Results: There were no significant sex interactions, thus data was pooled. After adjustment, there was no significant mean differences between groups for muscle cross sectional area as measured by pQCT, however those with sustained high SB had a lower muscle density (β-0.682, 95%CI-1.305,-0.060). Those with sustained high SB also had lower muscle mass in the lower extremities as measured by DXA (β-769, 95%CI-1390,-148). There was no difference in muscle power between groups.

Conclusions: Long-term SB during childhood is associated with deleterious effects on the amount of lean mass and density in the lower extremities but not on function. Interventions could be targeted from childhood to ameliorate reductions in muscle mass and prevent potential progression to loss of function.

P134

IS THERE SEX-SPECIFIC ASSOCIATIONS BETWEEN BONE MASS AND MUSCLE PARAMETERS? FINDINGS FROM THE VITAMIN D IN PREGNANCY STUDY

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Objectives: Post puberty, bone mass displays clear sex-specific patterns. However, some research has suggested that a sexual dimorphism in bone mass is evident in younger children and is likely attributable to differences in lean mass. Thus, we aimed to determine whether the association with both overall lean mass and/or muscle strength was different between the sexes in a paediatric population.

Methods: Participants were children recruited as part of the Vitamin D in Pregnancy Study (median age: 10.9 (IQR 10.2-12.1 y). Of the 402 children measured at birth, 209 (52.3%) returned for 11-y follow-up, and 172 had complete data for the current analyses. Children had an assessment of bone mineral content (BMC), BMD and lean mass by DXA (Lunar). Handgrip strength was measured using a dynamometer (Jamar). Linear regression models were adjusted for height, weight, age and pubertal stage.

Results: Compared to girls, boys had a trend for greater lean mass (29.3 vs. 28.1 kg, p=0.06), and had greater handgrip strength (15.7 vs. 15 kg, p=0.01). Sex interaction terms were significant in models predicting bone mass. When stratified by sex, both muscle strength and total lean mass were associated with BMD and BMC for boys and girls. In adjusted models, including both muscle strength and lean mass, the observed association differed between boys and girls. At the spine in boys, BMC and BMD were associated with muscle strength (β 0.34 [95%CI 0.09-0.59] and 0.008 [95%CI 0.003-0.014], respectively) but not total lean mass. In girls, spine BMC and BMD were associated with total lean mass (β 0.95 [95%CI 0.61-1.3] and β 0.01 [95%CI 0.005-0.02], respectively). The same pattern of association remained when those who self-reported being in a higher pubertal stage were removed from the analyses.

Conclusions: A clear sexually dimorphic pattern in bone mass was exhibited in association with muscle parameters in this paediatric cohort.

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LIPOPOLYSACCHARIDE BINDING PROTEIN AND BONE MINERAL DENSITY: EVIDENCE FROM A MALE COHORT OF THE GEELONG OSTEOPOROSIS STUDY

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Objectives: Increased risk of osteoporosis and related fractures are associated with gastrointestinal diseases, including Crohn's disease and irritable bowel syndrome, yet a possible link between bacterial lipopolysaccharides (endotoxins), intestinal activity and downstream effects on bone remain unknown. We aimed to investigate lipopolysaccharide binding protein (LBP) levels and BMD in a randomly selected population-based cohort of men.

Methods: Serum LBP (ng/mL) was measured using enzyme-linked immunosorbent assay (ELISA; R&D Systems) for 1149 men (ages 20-96 y, median 61 y) enrolled in the Geelong Osteoporosis Study (GOS). BMD (g/cm^2) was measured at the PA-spine, hip, total body and forearm using DXA (Lunar). Weight and height were measured; medication use, physical activity and smoking status were self-reported. LBP values were natural log transformed (ln-LBP) and associations between ln-LBP and bone measures were tested using Pearson's correlation. Multivariable linear regression models were developed to test associations after adjusting for age, weight, height, physical activity and medications affecting bone (thyroid medication, bisphosphonates, oral glucocorticoids).

Results: Relationships between ln-LBP (median 16.5 ng/mL, IQR:11.5-23.1) and age (r^2=0.06, p=0.04), weight (r^2=-0.08, p=0.005), total body (r^2=-0.09, p=0.003), spine (r^2=-0.05, p=0.08), distal- (r^2=-0.02, p=0.003) and mid-forearm BMD (r^2=-0.15, p=<0.001) were significant, but not hip BMD (r^2=-0.04, p=0.14). After adjustments, LBP was associated with decreased BMD at the mid-forearm (β -0.013, SE±0.004, p<0.001) and showed a trend with decreased spine (β -0.012±0.009, p=0.19) and total body BMD (β -0.006±0.004, p=0.13). No associations between LBP and hip (β -0.002±0.006, p=0.77) and distal-forearm BMD (β 0.001±0.003, p=0.66) were evident.

Conclusions: While acknowledging potential unrecognised confounding, these data suggest LBP is independently associated with mid-forearm, and potentially spine and total body BMD, in men. These results support a positive correlation with age, though a negative correlation with weight. Given the paucity of data, replication and future studies to confirm this relationship are warranted.

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COGNITIVE FUNCTION AND SKELETAL MUSCLE IN OLDER MEN

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Objective: Cognitive impairment is associated with obesity, but it is unclear whether cognitive function is associated with skeletal muscle, another metabolically active tissue. Our aim was to examine specific domains of cognitive function in relation to muscle mass and strength in older men.

Methods: For 174 men (ages 60-92 y) in the Geelong Osteoporosis Study, cognitive function was assessed in four domains: psychomotor function, visual identification/attention, visual learning, and working memory/attention (CogState-Brief-Battery). Higher scores represent poorer cognitive performance in all domains except visual learning. We measured DXA-derived relative appendicular lean mass (rALM kg/m^2, Lunar) and maximum handgrip strength (HGS, kg) by dynamometer (Vernier, LoggerPro3). Associations between cognitive function scores and muscle parameters were tested using Pearson correlation and age-adjusted partial correlations.

Results: There was an age-related decline in cognitive function in each domain (r=+0.19, +0.30, -0.19, +0.34, respectively; all p<0.001) and HGS (r=-0.40, p<0.001), whereas the decline with rALM was not significant (r=-0.08, p=0.28). Inverse associations between psychomotor function (r=-0.16, p=0.04) and visual identification/attention (r=-0.24, p=0.002) and rALM were sustained after adjustment (partial r=-0.14, p=0.08; r=-0.22, p=0.003). No associations were detected between scores for working memory/attention or visual learning and rALM either before or after accounting for age. There was an inverse association between psychomotor function and HGS which was sustained after adjustment (r=-0.29, p<0.001; partial r=-0.22, p=0.004), while the association between visual identification/attention and HGS was attenuated (r=-0.22, p=0.003; partial r=-0.11, p=0.15). Associations between scores for working memory /attention and visual learning and HGS were explained by age (r=-0.20, p=0.01, partial r=-0.07, p=0.36; r=+0.13, p=0.098, partial r=+0.02, p=0.80).

Conclusion: Our results suggest that cognitive declines affecting visual function and psychomotor skills are associated with lower muscle mass and strength. These cognitive and physical declines in tandem could place the ageing individual at increased risk for personal injury, including falls.

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ATYPICAL FEMUR FRACTURES IN AN AUSTRALIAN HOSPITAL SETTING: INCIDENCE, PATIENT RISK FACTORS AND DENSITOMETRIC CHARACTERISTICS.

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Objectives: Atypical femur fractures (AFFs) are feared complications of antiresorptive drugs (bisphosphonates/denosumab). Reported incidence rates are 0.3-11 per 100,000 person-years[1], but the incidence of AFFs in an Australian hospital setting is unknown. We aimed to investigate the incidence of AFFs at our institution (largest in Australia), and describe clinical/densitometric characteristics.

Methods: Patients aged 50 y with a femur fracture between 2009-2017 at Monash Health, Victoria, were identified using hospital ICD codes. Radiographic review of subtrochanteric (ST) and femoral shaft (FS) fractures identified AFF cases fulfilling the revised ASBMR case definition[1]. An age- and sex-matched control group was obtained from typical ST/FS fractures. Demographic data, medication use was obtained from hospital records. Lunar DXA data [spinal bone density T-score /trabecular bone score (TBS)] were extracted. To calculate the incidence rate, the at-risk population was identified as the number of patients aged 50 y admitted over the study period. Statistical analysis used Stata/IC 15.1.

Results: A femur fracture was identified in 3427 patients during the 9-y period, of whom 342 (10%) had a ST/FS fracture. Radiographic review identified 72 AFFs in 58 patients. Incidence rate was therefore 3.5 per 100,000 person-years. AFF cases were younger [median(IQR) years: 73(69, 79.3) vs. 81(71.5, 88), p=<0.001] and more likely to be female (86% vs. 70%, p=0.012) compared with typical ST/FS fracture patients. AFF cases had greater antiresorptive drug use [84% vs. 24%; OR 16.1 (95%CI 6.4-40.9), p<0.001] and Asian ethnicity [39% vs. 16%; OR 3.5 (95%CI 1.4-8.5), p=0.007] compared to an age- and sex-matched control group. DXA data were available for 19 AFF cases, and median(IQR) spine T-score and TBS were -1.3(-2.2, -0.4) and 1.17(1.09, 1.23), respectively. Degraded TBS (TBS<1.20) affected 13/19 of AFF cases, whilst 4/19 had spinal osteoporosis (T-score<-2.5).

Conclusions: As with international cohorts, AFF incidence in an Australian hospital setting is low, with similar risk factors. High rates of degraded TBS suggest AFF patients remain at increased fracture risk, with limited treatment options. This study has direct implications for the management of osteoporosis.

Reference: [1] Shane et al. JBMR 2014;1:1.

P138

ARTHROPATHIES IN ALKAPTONURIA: CASE SERIES AND LITERATURE REVIEW FROM A DEVELOPING COUNTRY

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Objective: Alkaptonuria, is characterized by the deficiency of the hepatic enzyme homogentisate 1,2-dioxygenase (HGO) resulting in accumulation of homogentisic acid in the connective tissue. To determine the spectrum of clinical presentation of cases of alkaptonuria from Pakistan.

Methods: Reported cases of alkaptonuria diagnosed on homogentisic acid detection on gas chromatography mass spectrometry (GCMS) between 2013 and March 2018 at biochemical genetics laboratory (BGL) were retrieved. Demographics and clinical data were collected from structured questionnaire used in BGL and telephonic interview. Literature review was done independently by three reviewers for studies published from 1947-2017 on alkaptonuria and Pakistan.

Results: Twelve cases of alkaptonuria were reported, male to female ratio was (2:1). Median age of patients was 21.05 y (32 d - 55.5 y); 6 cases presented within 2 y of life. All patients had dark urine on standing. Musculoskeletal involvement was seen in 6 patients (mean age of presentation 41 y), while ochronotic pigmentation was noted in 5 patients (men age of presentation 45 y).

Literature review identified 8 case reports and 1review article in past 70 y of Pakistan, with male to female ratio of 3:1. Presenting age in 6 case reports were after fourth decade of life except two cases presenting in infancy and second decade. Almost all patients were harboring symptoms for 10-15 y before diagnosis. Musculoskeletal involvement was seen in all cases from literature with joint pain reported in all cases, 5/9 also reported restriction movements, while 1 patients each had a height loss of 15 cm and flexion contractures. Ochronotic arthropathy was common in wrists, elbows, shoulders, knees, and ankle joints. Joint pain was also identified in patients reported from BGL, 6/12. Patients in whom joint problems were not identified were of age <2 years.

Conclusion: High prevalence of musculoskeletal involvement is seen in patients. Alkaptonuria being a rare autosomal recessive disorder of metabolism is likely to be missed by physicians as a cause of arthropathy unless specifically looked for. The cases in Pakistan were being diagnosed late due to nonavailability of diagnostic testing earlier. Twelve cases in 5 y indicates that the burden of disease may be high in Pakistan.

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INCREASED PREVALENCE OF SELF-REPORTED FRACTURES IN INDIAN PATIENTS WITH DIABETES: RESULTS FROM THE ICMR-INDIAB POPULATION BASED CROSS-SECTIONAL STUDY

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Objective: Diabetes mellitus (DM), has been associated with increased fracture risk. However, there are no data pertaining to the prevalence of fractures or its risk factors for patients with DM in India. Aim of the study was to examine the association between diabetes and risk of fracture in a population based sample of Indian individuals.

Methods: The study used the data of Indian Council of Medical Research–India Diabetes (ICMR–INDIAB) study, a community-based cross-sectional survey conceived with the aim of obtaining the prevalence rates of diabetes in India as a whole. A stratified multistage design was used to obtain a community-based sample of 57,117 individuals aged 20 y or older. All the study subjects underwent anthropometric measurements and oral glucose tolerance tests were done using capillary blood (except in self-reported diabetes). Fractures were self-reported. A structured questionnaire was used to obtain details of fracture including site of fracture. In addition, history of extent of trauma leading to fracture (serious injury or low trauma fracture) was obtained in patients who had suffered hip and spine fracture.

Results: Fracture data were available in 54,093 subjects out of which, 1416 (2.6%) had fractures. Overall prevalence of diabetes and pre-diabetes was 7.1% and 10.5%, respectively. Diabetes was associated with significantly higher number of fractures (4%) compared with prediabetes (3%) and those without diabetes (2.4%). In multivariate logistic regression analysis, diabetes was associated with an increased risk (1) of any fracture (OR=1.3, 95%CI: 1.1-1.6) and (2) of low trauma fracture (hip and spine combined) (OR=1.8, 95%CI:1.1-2.8). Age (>40 y, OR=1.3, 95%CI:1.2-1.5), male gender (OR=1.5, 95%CI:1.3-1.7), alcohol consumption (OR=1.6, 95%CI:1.4-1.8) and urban population (OR=1.3, 95%CI:1.2-1.5) were also significant contributors to the risk of any fracture in multivariate analysis. Among the various fracture sites, lower limb fractures were significantly higher in subjects with diabetes (44.2%) compared with prediabetes (33.9%) and those without diabetes (33%).

Conclusion: Diabetes is associated with increased prevalence of self-reported fractures in this population-based study from India.

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INVESTIGATION OF FACTORS THAT INFLUENCE CONCENTRATION OF SERUM 25-HYDROXYVITAMIN D

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Objectives: Vitamin D (VD) deficiency/insufficiency is a risk factor for osteoporotic fractures and falls. It is important to maintain an adequate level of 25-hydroxyvitamin D ([25 (OH) D]). Previous studies demonstrated that the level of 25 (OH) D is influenced by the level of exposure to sunlight and VD intake, as well as renal function and body fat content. In addition, FGF23 has been shown to induce the conversion of 25 (OH) D to 24, 25 (OH) D. Collectively, these studies suggest that the level of 25 (OH) D is influenced by various factors. In the present study, we investigated the factors that influence the level of 25 (OH) D.

Methods: The study examined 200 healthy postmenopausal women who had undergone osteoporosis screening. Serum levels of 25(OH)D, intact PTH, CTX, and FGF23 were measured. Lumbar (L) and femoral neck (FN) BMD were measured by DXA. Nutrient intake was calculated using a food frequency questionnaire.

Results: Mean values of age was 63.4 y with the following measurements: 25(OH)D 16.2±4.3 ng/mL, creatinine clearance (CCr) 99.5±21.3 mL/min, Ca intake 656±192 mg/d, VD intake 9.9±3.9 (range:1.3-24.6) μg/d, and the mean level of exposure to sunlight 1.9±1.6 h (range: 0-7.0 h). The level of 25 (OH) D revealed a significant association with the age and VD intake ($p<0.001$). On the other hand, the level of 25 (OH) D was not associated with the level of exposure to sunlight. Multiple regression analysis demonstrated that VD intake was associated with 25 (OH) D after adjusting for age, BMI, body fat percentage, the levels of Ca, P, PTH, CCr, CTX, FGF23, BMD, exposure to sunlight, and intake of other nutrients ($p<0.01$).

Conclusion: We demonstrated that VD intake significantly influenced the concentration of 25 (OH) D after adjusting for various factors including the level of exposure to sunlight and renal function. Our findings suggest that nutritional interventions focused on VD intake are important to ensure VD sufficiency and to prevent osteoporosis.

IOF REGIONAL SYDNEY'18
7TH ASIA-PACIFIC OSTEOPOROSIS CONFERENCE

IOF Regional 7th Asia-Pacific Osteoporosis Conference
Sydney, Australia – 2018

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