Issue 1, March 2025

ANZBMS Newsletter

Welcome to the ANZBMS Newsletter

Thank you for joining us in the first ANZBMS newsletter of 2025!

As we celebrate the fifth anniversary of our launch, we extend our heartfelt thanks to **Mr HengKe Meas** for refreshing our newsletter design. He has given it a fresh, modern look, and we hope you enjoy the update.

We also take this opportunity to express our appreciation and bid farewell to **Dr Martha Blank, Dr Michelle Maugham-Macan, Dr Mícheál Ó Breasail, Dr Jakub Mesinovic, Dr Lucy Collins, and Dr Shejil Kumar**, who have stepped down from the Newsletter Editorial Board. At the same time, we warmly welcome **Dr Chelsea Tan, Dr Kai Chen, Dr Kaitlyn Flynn, Dr Karen Van, and Mackenzie Skinner** to the team—we look forward to their insights and contributions!

In this issue, you'll find a **Comment from ANZBMS President, Professor Mark Cooper**, as well as updates from the **Clinical Practice and Therapeutics Committee**. We also highlight key updates from the **ECIC co-chairs** and the **IFMRS HubLE** as they share their plans for 2025.

A huge congratulations to all **grant and award recipients** for their achievements, as well as ANZBMS members whose **publications** are featured in this issue. Be sure to check out **upcoming events** on pages 24–27 and mark your calendars!

Lastly, we are **recruiting new editorial board members!** If you're interested in joining our fantastic team, we'd love to hear from you. Please send a short biography to **newsletter@anzbms.org.au**.

Happy reading!

In this issue

ANZBMS Newsletter Editorial Board

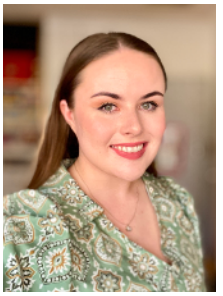
Dr Pholpat Durongbhan

Dr Haniyeh Hemmatian

Jacob Harland

Dr Kai Chen

Dr Kaitlyn Flynn



Mackenzie Skinner

Dr Chelsea Tan

Dr Karen Van

Next Issue: June 2025

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ANZBMS Early Career Investigators
@ANZBMSoc

From the President

For this newsletter I'd like to focus on ANZBMS efforts in relation to improving clinical practice through supporting the approval of medications and providing educational meetings to help navigate the changes in clinical practice in our field. In the not-too-distant past I was concerned that development of new pharmaceutical treatment approaches for bone diseases had stalled. We have had exciting progress in the use of exercise and nutrition to improve bone health but with highly effective medications for osteoporosis reaching their generic phase of life threatened to dampen innovation. However, in the last few months we have seen a wave of change with many new bone therapies working their way through the regulatory processes in Australia.

For osteoporosis we have seen the first line indication for Romosozumab through the Pharmaceutical Benefits Scheme (PBS) for people at very high risk of fracture. This opens up a more logical treatment approach for many people with osteoporosis that previously would have had to pay considerable amounts to access this drug when it would give them the most benefit. For Denosumab, the medication is fast approaching the end of its patent in Australia and a biosimilar medication (Denosumab-bbdz; marketed as Jubbonti/Wyost in its 60mg/120mg doses) is working its way through the regulatory system and has been recommended for listing on the PBS by the Pharmaceutics Benefits Advisory Committee (PBAC). This will be considered a direct like for like with the existing Denosumab formulations. There is also the prospect of another anabolic medication, Abaloparatide, becoming available in Australia. This has been used in the USA for many years but has recently been approved by the TGA and hopefully an application for this to be listed on the PBS will go forward soon.

For rare and ultra rare bone disorders there are also important developments. Palopegteriparatide, a long lasting PTH analogue formulation, has been TGA approved for the treatment of chronic hypoparathyroidism and is likely to be considered by the PBAC in the near future. The PBAC has recently recommended the listing of Palovarotene for people with Fibrodysplasia Ossificans Progressive (FOP). Palovarotene is a selective agonist of the retinoic acid receptor gamma (RARγ), which in turn inhibits the pathway responsible for heterotopic ossification. Including Burosumab for XLH we now have several drugs available for people with rare but important bone diseases.

I think these ongoing developments illustrate that the research that we do as a bone community is still essential for improving the outcomes of people with bone disorders. Some of these treatments have arisen from research studies that were originally very much at the bench but have now made it to the pharmacy. ANZBMS has, for its part, been providing evidence based support to the regulatory bodies that are making decisions about treatments in the bone field.

There continue to be some barriers. I am conscious that all of the medications listed above are going through regulatory processes

in Australia. The system is New Zealand is different and I fear that the smaller 'market' size is likely to be a barrier to patients and clinicians getting access to these medications. It is notable that our New Zealand colleagues continue to get the most mileage from what they have as evidenced by the NEJM article in January from the Auckland group looking creatively at using zoledronic acid is younger postmenopausal women.

With such changes in the availability of medications and how we might use them it is important that high quality CPD opportunities are available to our clinician members and also specialists that are not (yet) members of our society. To address this need, ANZBMS holds the Advanced Clinical Postgraduate Virtual Meeting. The latest version of this will be held in March with a great line up of speakers from Australia and New Zealand. This meeting has gone from a small in-person meeting for Advanced Trainees in Endocrinology to one that now has over 150 attendees, mostly comprising specialists in treating bone disease. My thanks go to the current and former Chairs and Members of our Clinical Practice Committee for evolving this meeting to address wider clinical needs. If you are a clinician working in the bone space and have not registered yet please take a look at the offerings through the ANZBMS website. You will likely get to know about some of the new treatment approaches being introduced into our field.

Mark Cooper
BMBCh PhD FRCP
(London) FRACP, GAICD

ANZBMS President
Head of Clinical School,
Concord Clinical School
Faculty of Medicine and Health
Patyegarang Precinct

Welcome to our new members...

Dr Kaitlyn Flynn

Postdoctoral Researcher, Mater Research, University of Queensland.

I am a recently submitted PhD candidate at Mater Research and the University of Queensland. I work in the Musculoskeletal Genomics Group at Mater Research, focusing on applying integrative biostatistical approaches to identify therapeutic targets for osteoporosis and osteoarthritis.

I recently joined the editorial board, after being an ANZBMS member for the past three years. I am excited to share our society's wonderful successes and get to know you all further.

Mackenzie Skinner

PhD Candidate, University of Adelaide.

I am a PhD candidate at the University of Adelaide in South Australia, supervised by Dr Melissa Cantley in the Myeloma Research Group. My project focusses on using mass spectrometry techniques to explore the lipidome and metabolome within the bone marrow microenvironment in multiple myeloma.

I am excited to join the ANZBMS newsletter, and share your exciting developments, as I delve further into the fascinating metabolism of bone!

Dr Kai Chen

Research Fellow, The University of Western Australia.

I am a Research Fellow and Lab Head working at UWA. My research interest mainly focuses on leveraging advanced imaging technologies to directly visualise and measure the biological processes (e.g., metabolism, drug transport) in the skeletal system and beyond.

I recently joined the ANZBMS Newsletter Editorial Board, and I am looking forward to highlighting the amazing work and opportunities available in ANZBMS.

Dr Chelsea Tan

PhD Candidate, Monash University.

I am an endocrinologist starting a PhD on breast cancer and bone health. I am new to both ANZBMS and the Editorial Board. I look forward to highlighting the amazing publications from members this year.

Dr Karen Van

PhD Candidate, Monash University. Endocrinologist, Monash Health.

I am an endocrinologist starting a PhD in diabetic kidney disease and bone health.

I am excited to join the ANZBMS Newsletter Editorial Board and look forward to the opportunity to engage with exceptional bone clinicians and researchers.

... and a big thank you to our outgoing members

Dr Martha Blank

Research Officer,
St Vincent's Institute of Medical Research, Melbourne.

With a heavy heart, I will be moving on from the Editor-in-Chief role of the ANZBMS newsletter to the ECIC Events subcommittee. I want to thank all team members (past and present) for their hard work and dedication to create and deliver the newsletter to our ANZBMS members.

It was my absolute pleasure to work together with lots of creative minds and great personalities and I am looking forward to reading future editions of the newsletters. I wish Dr Pholpat Durongbhan, the upcoming Editor-in-Chief, and the new team all the best for their work and hope to see many of you at the ASM later this year.

Dr Lucy Collins

PhD Candidate, Monash University.
Endocrinologist, Western, Northern & Monash Health, Victoria.

It has been wonderful assisting in delivering the newsletter each quarter to our ANZBMS members! We have highlighted excellent basic and clinical research. Special thanks to Martha Blank for steering the ship so smoothly! I am moving on to a new role within the ANZBMS ECIC clinical subcommittee. I look forward to seeing everyone at the next ASM.

Dr Michelle Maugham-Macan

Lecturer, University of the Sunshine Coast

It has been an absolute pleasure serving on the Newsletter editorial board and working with the wonderful team with Martha at the helm. Thank you to all the labs and ECIs that have taken part, it has been a joy collating and reading your highlights. I look forward to reading the 2025 newsletters and hopefully seeing everyone at the ASM!

... and a big thank you to our outgoing members

Dr Jakub Mesinovic

Research Fellow, Deakin University

Being part of the newsletter board has been a wonderful experience. I've really enjoyed showcasing the brilliant research and achievements of this society while working alongside an awesome team. While I'm stepping down, I'll still be cheering from the sidelines and looking forward to future editions. See you all at the next ASM!

Dr Shejil Kumar

PhD Candidate & Clinical Lecturer, University of Sydney

It has been a pleasure working with the ANZBMS newsletter committee this past year. Spotlighting ECI publications has been a very rewarding role and has also helped keep me up to date with the latest research in bone and musculoskeletal health. I look forward to continuing my PhD studies and my new role as co-chair of the ANZBMS Early Career Investigator Committee.

Dr Mícheál Ó Breasail

Research Fellow, Monash University

Being a part of the editorial board and serving as the copy editor for this newsletter has been a very rewarding and enjoyable experience. This role has given me an opportunity to engage with many exceptional bone researchers across Australia and New Zealand. I wish the best of luck to the team and look forward to reading future editions!

Clinical Practice Committee

The primary focus for the **Clinical Practice Committee** the last few months has been the 'Advanced Postgraduate Clinical Meeting' which will be hosted on March 15 and 16. This will provide a practical and up to date education in the expanding field of bone and mineral medicine. Targeted at Advanced Trainees, it is also ideal for all specialists with a bone interest including endocrinology, nephrology, rheumatology, rehabilitation and geriatric medicine. The virtual only event should allow greater accessibility as it is also a recognised requirement from the RACP for endocrinology advanced trainees.

An outstanding faculty of experts will present the latest updates in bone and mineral medicine. The seminar will be offered over 2 half-days and cover a wide range of themes:

- Bone Health Management in Younger Adults and Through the Menopause Transition
- Cancer and Bone Health
- Managing Complications of Bone Health Therapies (atypical femoral fractures and osteonecrosis of the jaw)
- Mineral Balance (hyperparathyroidism, hypoparathyroidism)
- Hot Topics

Presentations will be interactive, pragmatic and have a clear clinical focus.

The committee once again sincerely thanks contributors including speakers and chairs who will generously give up their time to advance the knowledge of their peers and share their skills and insights.

We have several other educational activities planned for later in the year and at the ASM in Cairns.

We're always happy to hear your suggestions on how we can better engage with clinicians. If you'd like to hear more or have ideas around clinician engagement/education, please feel free to email **Jasna Aleksova** on *jasna.aleksova@hudson.org.au*.

Yours Sincerely,

Dr Jasna Aleksova

ANZBMS Clinical Practice Committee Chair 2025

Therapeutics Committee

The **Therapeutics Committee** held their latest meeting on the 26th February 2025. The updates from this meeting are noted as follows:

- ANZBMS supported PBAC application for palopegteriparatide in the management of chronic hypoparathyroidism
- ANZBMS will draft a position statement on avoiding concurrent iron infusions and potent anti-resorptive therapy
- ANZBMS will be holding a post-graduate seminar on diagnosis and management of atypical femoral fractures
- ANZBMS will draft a guideline for diagnosis and management of hypophosphataemia
- ANZBMS will draft a brief report to supplement recent RACGP guidelines

Yours Sincerely,

Professor Roderick Clifton-Bligh

ANZBMS Therapeutics Committee Chair 2025

ECIC Co-Chairs Report

What a busy start to the year we've had!

The **ANZBMS ECIC Fellowship Coaching Program** is back for 2025, after the success of the past three years. It is an incredible opportunity for **ANZBMS ECIs re-applying for NHMRC Investigator Grants** or who have a grant currently under consideration to receive personalised feedback from experienced Mid-Career Researchers. The program will focus on the impact and leadership capability sections of the application. If you are considering re-applying, please do visit our information page and submit an expression of interest: ANZBMS-FCP.

The **Bridging Overseas Network Exchange (B.O.N.E)** program planning for 2025 is currently underway. The reciprocal program with ASBMR is expected to return for 2025 – eligibility criteria for Australian and New Zealand applicants include receipt of an ASBMR Young Investigator Award for their abstract for 2025, so we encourage all those eligible and interested to please apply! Dr Melissa Cantley has been invited to present her work at the Japanese Society of Bone Mineral Research (JSBMR) later this year and will be supported by ANZBMS for her travel expenses, with reciprocal arrangements currently under negotiation.

The ANZBMS-JBMRPlus special issue on hypophosphataemic bone disorders, an ECI-focussed initiative supported by an independent medical education grant by Kyowa Kirin Australia, is now in its final stages of publication. The accepted manuscripts are being added to JBMRPlus online, with ten manuscripts expected to be included – please do view the amazing work of our Australian and New Zealand colleagues here.

The clinical subcommittee are finalising the **RACP-ANZBMS webinar series** with six highly-relevant topics to be presented through the year by prominent and experienced clinicians. Further details will be provided through ANZBMS communication channels as well as through RACP. We encourage our Endocrinology Advanced Trainees (both paediatric and adult!) to start thinking of clinical cases that can be presented at the Metabolic Bone Diseases Complex Clinical Cases Series planned for the Annual Scientific Meeting this year. Abstract submission portal is now open until Friday, 4th July 2025!

We are also cognisant that great research is enabled through strong collaborations. The ECIC is working towards developing ECI-focused networks with other relevant Australian and New Zealand societies. We look forward to providing you with more details as the year goes on.

All ECIC news and opportunities will also now be communicated through our ANZBMS Early Career Investigators LinkedIn Group and the ANZBMS Facebook Group (QR code below) which you can join to stay updated on upcoming opportunities. A huge thanks to our amazing Comms team for all the work!

ECIC Co-Chairs Report

You can view the 2025 committee members on the ANZBMS ECIC page.

The ANZBMS ECIC is focused on empowering you, the ECIs. We would love to share your news and successes through our various communication channels; feel free to share through our LinkedIn page, Facebook Group or contact us at ecic@anzbms.org.au.

Yours Sincerely,
Dr Shejil Kumar
ANZBMS ECIC
Co-Chairs 2025

Yours Sincerely,
Dr Madhuni Herath
ANZBMS ECIC
Co-Chairs 2025

IFMRS
INTERNATIONAL FEDERATION OF MUSCULOSKELETAL RESEARCH SOCIETIES

HubLE

IFMRS HubLe Update

Update - February 2025

This month, IFMRS HubLE is excited to announce several upcoming initiatives aimed at furthering our mission of supporting the musculoskeletal research community. We are planning to launch a series of podcasts featuring expert discussions, interviews with leading researchers, and insights on the latest developments in orthopaedics and musculoskeletal science. Additionally, we will be introducing research highlights in the form of graphical abstracts, allowing complex findings to be shared in a visually engaging and accessible format.

During the recent ORS 2025 Annual Meeting in Phoenix, Arizona, we had the pleasure of meeting many early-career researchers whose innovative work promises to shape the future of our field. In the coming weeks, IFMRS HubLE will be featuring their research on our platform, offering an opportunity to showcase these emerging voices and their contributions to musculoskeletal science.

As always, if you have any comments or suggestions, feel free to reach out to our Editor-in-Chief, Mustafa Unal, at mustafa@huble.org.

Stay tuned for more exciting updates and initiatives from IFMRS HubLE as we continue to foster collaboration and knowledge-sharing in the global research community.

Warmly,
Dr Mustafa Unal
Editor-in-Chief, HubLE

ECIC Funding Opportunities

Grant/Fellowship Scheme*	Application Period
NHMRC Ideas Grants	Applications open 12 March 2025, closing 7 May 2025
Children's Research Foundation (Channel 7) Annual Research Grant	Expression of interest for Grant Opportunities closing 31st of March 2025
Australian Museum Eureka Prizes	Entries now open, closing 7pm AEST Monday 14 April 2025
Al & Val Rosenstrauss Fellowship	Applications open 1 April 2025, closing 30 April 2025
Rebecca Cooper Fellowship	Applications open 1 August 2025, closing 29 August 2025
Christine and T.Jack Martin Research Travel Grant	TBC
ANZBMS Travel Grant	TBC
ANZBMS Bone Health Foundation Grant	TBC

**Clicking on the scheme name will redirect you to the grant/fellowship website.*

***Davey lab** (left to right): Ellen Davies (Honours Student), Bronte Green (Honours Student), Sue Golub (Senior Research Assistant), Rachel Davey (Lab head), Varun Venkatesh (Postdoctoral Researcher).*

The Molecular Endocrinology and Musculoskeletal Research Group, Department of Medicine, Austin Health, The University of Melbourne

Featuring: Professor Rachel Davey (Lab Head), Dr Varun Venkatesh (Research Fellow) and Ms Bronte Green (Honours Student)

Professor Rachel Davey, Lab Head

How long have you been in this lab/group? 27 years! We moved from the Royal Melbourne Hospital to Austin Health 23 years ago and I started my own lab group 17 years ago.

What topics are researched in your lab? Our group's primary aim is to understand how hormones regulate the musculoskeletal system and fat metabolism, with a particular focus on sex steroids. We combine physiological studies with novel, cutting-edge preclinical genetically modified models to investigate the cellular and molecular pathways through which hormones act. Our goal is to identify new pathways for treating highly prevalent musculoskeletal and metabolic diseases, including osteoporosis and obesity. Additionally, we are studying the effects of gender-affirming hormone therapy, both during puberty and in adulthood, on bone cell metabolism, structure, and strength — an area with important implications for maintaining the bone health of transgender individuals.

What was your career trajectory leading to this moment? I completed a Bachelor of Science degree at the University of Adelaide and first entered the field of bone research during my Honours year. I was incredibly fortunate to have Professor Howard Morris as my supervisor — his mentorship and passion for rigorous, well-designed research inspired me to pursue my goals. His guidance also gave me the confidence to undertake a PhD, something I hadn't previously considered. After completing my PhD, I moved to Melbourne to work with

Professor Jeffrey Zajac, where I gained invaluable experience and expertise in the field of molecular endocrinology that eventually enabled me to lead my own lab group. Throughout my career, I have been privileged to work with some amazing researchers both within my own lab as well as outstanding mentors, both in Australia and internationally, who have played a crucial role in shaping my path and leading me to where I am today.

What's your mentorship style? I try to be a hands-on and supportive mentor, always making time for my team and encouraging them to ask questions and share ideas. I'm a big believer in teamwork and creating an environment where everyone feels heard and valued. Since everyone works differently, I adapt my approach to fit each person's personality and needs. At the same time, I encourage critical thinking and independence to help my team build the confidence they need to succeed in their research careers.

What's a fun fact about your lab? My lab bench was stolen by a post-doc, and I've been benchless ever since.

Dr Varun Venkatesh, Postdoctoral Researcher

How long have you been in this lab? I started here in September of 2019 so nearly 6 years, though I'm not sure the lockdown years count!

What inspired you to choose the lab? The research done in this lab is highly exciting fundamental research that seeks to identify novel therapies for underserved chronic diseases which I am very passionate about. Some of the fundamental work the lab did on the mechanisms of androgen activity were really inspiring and as a cell biologist by training I'm always fascinated by cell signalling. I came from a cancer research/cell signalling background where I was starting to touch on the heterogeneity of tumours and how they might communicate. These complicated cell to cell interactions really excite me as there are opportunities to dissect and leverage signalling molecules as new therapeutics using the knowledge I gained from an adjacent field.

What are you excited to do? I'm excited to build my research career within molecular endocrinology, by trying to develop new and exciting research directions and learn new techniques. I think there are a lot of new technologies that haven't been applied to musculoskeletal research and there's a lot of opportunities for growth. I'm also excited to try and find a way to embed clinical research (through collaboration) into our research programme as I think the future of research will be done by labs with both fundamental and clinical research arms.

What's a fun fact about your lab? We all have big sweet tooths and bring some form of treat to our bi-weekly lab meetings.

Bronte Green, Honours Student

How long have you been in this lab? I have been in this lab since early 2024 when I completed an undergraduate research project.

What inspired you to choose the lab? I was inspired to choose this lab because of its integrative approach to studying the intersections of endocrinology, metabolism, and bone physiology. I think there is so much we are yet to know about the relationship between hormonal regulation, fat metabolism and bones, and it is an exciting area to be a part of. Many of the lab's projects also relate to transgender health which I think is an important area of research which has been previously very understudied.

What are you excited to do? This year I am excited to learn more about the relationship between androgens, bone mesenchymal pre-cursors and fat mass, applying several advanced techniques I haven't yet used before.

Dr Simon Ryder

Staff Specialist Endocrinology, Logan Endocrine and Diabetes Service (LEADS), Logan Hospital

Research Category: Clinical

Research interests: I consider myself an endocrine all-rounder and an early career researcher with specific interests including adrenal disease and metabolic bone disorders. I am establishing a fracture liaison service at Logan Hospital which has been undergoing an expansion recently. As seen more broadly, locally there is a major care gap in post-fracture secondary prevention which we hope to address.

What I hope to gain from joining ANZBMS: I'm excited to be joining the ANZBMS to join a network of enthusiastic, like-minded people, while learning more and more about metabolic bone disease.

Grant Recipients

NHMRC Ideas Grants

Dr Kylie Alexander

The University Of Queensland
AUSTRALIA

"Mechanisms and first prophylactic treatments of neurogenic heterotopic ossifications."

A frequent complication of traumatic brain and spinal cord injuries is the formation of extra bones in muscles called neurogenic heterotopic ossifications. These extra bones develop around the joints in the weeks after a neurological injury to become so large that they stop joint movement, resulting in increased disability and pain. This Ideas grant aims to understand why these bones develop after spinal cord injury and to develop new effective treatments to prevent their development.

CIA: Prof Jean-Pierre Levesque, CIB: Dr Kylie Alexander, CIC: Prof Sebastien Banzet, CID: Miss Marjorie Sanda

Congratulations

Dr Kai Chen

THE UNIVERSITY OF WESTERN AUSTRALIA

"Advancing RNA therapy for arthritis."

Reducing the population-level burden of skeletal disorders (e.g., osteoporosis, osteoarthritis) is an unmet need. RNA is a molecule that carries genetic information and plays a crucial role in building proteins within our cells. Powered by an innovative imaging technique, we will develop small pieces of RNA to bind to the existing RNA in our cells, switching off genes that lead to skeletal disease development. This project will develop novel add-on therapies for skeletal disorders.

CIA: Dr Kai Chen, CIB: Dr Xianfeng Lin, CIC: Prof Killigudi Swaminatha-Iyer, CID: Dr Haibo Jiang

Rebecca L. Cooper
Medical Research Foundation

Al & Val Rosenstrauss Fellowship

Congratulations

Dr Jiao Jiao Li

"Joint diseases, such as osteoarthritis, are the leading cause of disability and unhealthy aging, affecting 600 million people globally. In Australia, these diseases account for 13% of the total disease burden amounting to $14 billion in direct healthcare costs. Current treatments focus on pain relief rather than a cure, driving an urgent need for innovative therapies that can offer long-term solutions. Joint diseases and their treatments, despite their huge impact on quality of life and the economy, still pose a severe unmet need and remain an under-investigated realm of research.

With her vision of developing new solutions to help people age healthily without pain, the Al & Val Rosenstrauss Fellowship will fund Dr Li's research in regenerative medicine that combines therapeutic discovery, delivery, and testing for joint diseases into a single pipeline. Drawing from the knowledge and techniques in stem cell biology, materials science, nanotechnology, biofabrication and AI, this program seeks to develop translation-ready products that can transform our understanding and treatment of joint diseases. With the Foundation's support, Dr Li's research will harness stem cells as 'bio-factories' to produce a suite of bio-therapeutics with the ability to provide customisable anti-inflammatory and pro-healing functions in joint diseases. Concurrently, new hydrogel materials will be developed to controllably deliver these therapeutics into patients, and new models of human mini-joints will be created to help better understand disease mechanisms and to test the treatment effects of new therapeutics. This combinational strategy seeks to provide new solutions for people suffering from joint diseases, improve their quality of life, and reduce the staggering socioeconomic impacts of associated disability and healthcare costs."

Summary courtesy of the Rebecca L. Cooper Medical Research Foundation (https://www.cooperfoundation.org.au/dr-jj-li/)

Bolland MJ, Nisa Z, Mellar A, Gasteiger C, Pinel V, Mihov B, Bastin S, Grey A, Reid IR, Gamble G, Horne A. Fracture prevention with infrequent zoledronate in women 50 to 60 years of age. N Engl J Med . 2025; 392:239-248. DOI: 10.1056/NEJMoa2407031.

Featured authors:

Distinguished Prof Ian Reid & Associate Prof Mark Bolland
University of Auckland
E: i.reid@auckland.ac.nz ; m.bolland@auckland.ac.nz

What is the background of the study?

Zoledronate prevents fractures in older women when administered every 12-18 months. However, studies have shown that the effects of a single 5mg zoledronate dose on bone mineral density (BMD) and bone turnover persist well beyond 5 years. Current clinical guidelines for fracture prevention recommend treating people at higher risk of fracture or with low BMD. But a view often expressed by patients and clinicians is "Why delay treatment until people are older, at higher risk of fracture, and may already have experienced irreversible loss of bone density or had a fracture themselves?". Given its long-lasting effects, very infrequent zoledronate seemed a promising agent to test whether early intervention in younger women can prevent fractures and maintain BMD.

What did you find?

We performed a 10 year, double-blind, placebo-controlled RCT of 5-yearly 5mg zoledronate or a single 5mg dose in 1054 women aged 50-60 years with a BMD T-score of more than -2.5. The primary endpoint was new morphometric spinal fractures on x-rays at baseline, 5 and 10 years. The mean age was 56y, and 95% of women completed 10 years of follow-up. There was a 44% (95%CI 8-66%) reduction in vertebral fractures with two zoledronate doses, and a 41% (95% CI 3-64%) reduction with a single dose. For any fracture, risk was reduced by 30% (95% CI 12-44%) with two zoledronate doses, and 23% (95% CI 3-38%) with a single dose. At 5 years, the differences in BMD between the zoledronate and placebo groups were 4.9-6.6%. At 10 years, the differences were 7.4-8.8% with two zoledronate doses, and 5.0-6.3% with a single dose. At 5 years, bone turnover markers were 30-40% below placebo in the zoledronate groups. At 10 years, they remained similar to 5 year with two zoledronate doses, whereas with a single dose, the effects slowly wore off but were still below baseline and placebo. There were no new safety concerns in the study.

Bolland MJ, Nisa Z, Mellar A, Gasteiger C, Pinel V, Mihov B, Bastin S, Grey A, Reid IR, Gamble G, Horne A. **Fracture prevention with infrequent zoledronate in women 50 to 60 years of age. N Engl J Med . 2025; 392:239-248. DOI: 10.1056/NEJMoa2407031.**

What is the application of these findings?

The results offer a new evidence-based option for women at lower risk of fracture who are concerned about preventing fractures (or maintaining BMD). Both a single zoledronate infusion or 5- yearly dosing prevents fractures and maintains BMD over the next 10 years. We are now doing an extension study to see whether the benefits from these dosing strategies will continue over the next 10 years. We think these results are likely to change practice. Having several infrequent zoledronate infusions over a lifetime is likely to be an attractive option for many individuals, and since zoledronate is now off-patent, it is a cheap and cost-effective option for healthcare systems. In our own experience in NZ, primary care providers have been enthusiastic providers of the infusions for their patients, and secondary care providers have set up infusion centres where zoledronate, as well as other IV agents such as biologic therapies for rheumatoid arthritis, are administered. Patients need to be informed carefully about the risk of an acute phase response after zoledronate, but this risk can be decreased substantially with 4mg oral dexamethasone given pre-infusion and daily for 2 days post-infusion, and/or symptoms can be mitigated with regular paracetamol for 48 hours post dosing.

Kim AS, Taylor VE, Castro-Martinez A, Dhakal S, Zamerli A, Mohanty ST, Xiao Y, Simic MK, Pantalone A, Chu J, Cheng TL, Croucher PI, Center JR, Girgis CM, McDonald MM. Early and multiple doses of zoledronate mitigates rebound bone loss following withdrawal of RANKL inhibition. J Bone Miner Res. 2025 Jan 23:zjaf008. doi: 10.1093/jbmr/zjaf008.

Featured author:

Dr Albert Kim
Staff Specialist in Endocrinology, Department of Endocrinology and Diabetes, Westmead Hospital.
PhD Candidate, Garvan Institute of Medical Research
E: Albert.Kim@sydney.edu.au

What is the background of the study?

Denosumab discontinuation leads to rebound bone loss and fractures. Current sequential treatment strategies fail to prevent this bone loss. We developed a mouse model of denosumab discontinuation and showed that the processes driving rebound bone loss occur earlier than previously understood and can be detected by serum markers of osteoclast differentiation and activity. In this study, we use our model to examine novel sequential treatment strategies to prevent bone loss.

What did you find?

Our model shows an early rise in serum TRAP which precedes detection of bone loss by DXA. Early administration of zoledronate at the time of rising serum TRAP was able to attenuate bone loss and a second dose at the time of expected bone loss was able to prevent bone loss, consolidating bone gains made with RANKL inhibition. This was seen in both young, growing mice and older, skeletally mature mice with improved vertebral fracture resistance seen in older mice receiving early sequential zoledronate.

What is the application of these findings?

To date, human clinical studies examining sequential therapy after denosumab have timed the intervention to 6 months following the last dose based on denosumab's dosing schedule. Our studies show that this is likely too late to be efficacious as the processes during bone loss are already active. Therefore, intervening earlier and with multiple doses of zoledronate may be able to prevent bone loss in patients stopping denosumab. Our novel findings support the need for clinical trials using earlier and multiple doses of zoledronate following denosumab discontinuation.

Sandy, J. L., Ford, N., Bevc, S., Rodda, C., Siafarikas, A., Simm, P., Collins, L., Wall, C.-L., Biggin, A., & Munns, C. F. What is it like living with X-linked hypophosphataemia?: results from an Australian consumer survey. JBMR Plus. 2025. https://doi.org/10.1093/jbmrpl/ziaf027

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What is the background of the study?

X linked hypophosphataemia, or XLH, is a genetic condition that predominantly impacts bones and teeth.The extra-skeletal and psychosocial manifestations are being increasingly recognised as important contributors to overall impact of disease.This manuscript describes the results of a survey-based study describing the life experience and burden of disease for children and adults living with XLH in Australia. This study was conducted in collaboration with patient support and advocacy group, *XLH Australia Inc*.

What did you find?

Forty-six affected individuals and their carers responded, reporting that XLH had a significant physical and psychosocial impact. This included a high surgical burden, with two thirds reporting having had 5 or more surgeries and one third of responders having undergone previous major dental procedures. Participants reported many psychosocial and financial challenges, including mental health disorders (depression, anxiety, suicidal ideation, self-harm), discrimination, and social isolation. Just over half rated emotional and physical burden of disease as equally impactful.

What is the application of these findings?

This study emphasises the substantial physical, emotional, psychosocial, and mental health burden of XLH, and the importance of improving awareness and knowledge of this disease in health professionals and the wider community.

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