Guest editorial

By Alessandra Tolaccia, OIFE volunteer

WHEN OBSTACLES BECOME OPPORTUNITIES

I have been suffering from chronic pain for over 15 years now, and every time I have approached a new doctor looking for help, the answer has always been the same: pain in muscles/tendons has nothing to do with OI. But why doesn’t my pain go away with the common treatments for muscular pain? Why is the pain only worsening? These questions have been in my head for so long, and I could never get an answer.

The last time I have heard this “verdict” was at the beginning of February 2023. I remember that while leaving the hospital that day, I was literally in tears, because I could not accept that no-one could help me or should I say, believe me? Or at least make the effort of trying to give me an explanation that I could accept, and that would make sense to me.

For a few days I went on feeling very low, but then something clicked inside me. I took my iPad and started searching for medical articles and publications about “pain in adults with OI”. I finally found what I was looking for. A research article called “The prevalence of musculoskeletal pain and therapy needs in adults with Osteogenesis Imperfecta (OI) a cross-sectional analysis”.

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This study was giving me some of the answers that I have been looking for far too long. In the project from the UK, they found that 85% of the patients involved were suffering from musculoskeletal pain with no difference in pain between types of OI and age. 50% reported persistent pain for longer than 1 year. So, despite what I was told, I certainly wasn’t the only person with OI with a serious pain problem.

This was a very important starting point that led me to find out that in Europe there was an umbrella association called OIFE, that was organizing a conference called: “Balancing life with OI” – a topical meeting on the impact of pain in OI. I cannot express the mix of feelings that I had at the time, but I can tell you that on that exact day I booked my flight ticket to Stockholm and to the conference. And looking back at it, it has been one of the best decisions that I took in a long time about my health. Since then, for me there is a “BEFORE Stockholm” and an “AFTER Stockholm”.

This convention was one of a kind. It was the first time that so many studies on pain in adults, from literally all over the world, were presented to the OI community. Thanks to the findings that were shown, I now know, how many people are affected by this problem, and how much we all need to learn about it. Pain affects people’s lives in so many different ways that it becomes difficult to say which is the worse part of it. But certainly, it is fundamental to approach these issues one by one and to find a way to deal with them. And that is what research can do.

I came back home knowing that for now, there isn’t a therapy for my specific pain, but that there is a lot of interest in the scientific world to learn more about it and find solutions. Many studies are only at the beginning. There is also a new approach to this issue, in which the patient is more centric and our opinion matters. This is the time for us to be part of something important for the future. Pain is not something that we must accept passively, it is unfortunately something that we must live with. But it is also something we can learn how to fight. And knowledge is the first step towards this battle.

During those few days in Stockholm, I met some incredible people that inspired me to have a more active role as a patient. So now I am in the process of learning and motivating myself and I can say that, if in my “BEFORE Stockholm” version I used to see obstacles, in the new version of me, “AFTER Stockholm” I now see opportunities.

Last August I enrolled in the EUPATI Patient Expert Training Program. I am now learning a great deal about the role that patients can play if we have the right information and knowledge. I have also started the pre-training for the EURORDIS School On Scientific Innovation & Translational Research that will take place in Barcelona in June. Through this I have started to learn about genetics and how this field is becoming more affordable and precise and how it will have a key role for rare diseases. These courses are also giving me the opportunity to meet with different patients and association members of different rare diseases and exchange ideas and information.

So, in conclusion: pain is still here, and some days hurts worse than others. But now I am fighting back!

Kind greetings
Alessandra Tolaccia - proud to be “rare”.  

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What is the OIFE doing?
By Ingunn Westerheim, OIFE President

Between November and March, we have been busy planning activities for 2024 and the coming two years. We have also worked on our Rare Disease Day awareness campaign for 2024, which has focused on the impact OI has on various aspects of life. The facts and figures were collected from our Pain & OI Project and the IMPACT survey. The Pain and OI article from Baylor College of Medicine is under production and two more articles from the IMPACT survey have been submitted for publication and the third is being written right now. We’re hoping these articles will be available for the public soon. As usual, we have also had many meetings with various stakeholders involved in research and development, including the Cosmic and Orbit trials and the Remedi4All consortium.

### IMPACT analyses and publications

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In addition to many meetings with our regular collaborators, member organizations and volunteers, we have organized or attended these meetings between November and March:

- OIFE Board Meetings (Zoom), Jan 9 and 22, Feb 13
- IMPACT Data Management Committee, Jan 9 (IW)
- Steering committee Norwegian registry for rare bone disorders, Jan 10 (IW)
- OIF TeleEcho – research updates from the BBDC, Jan 10 (IW)
- Wickenstones, Jan 19 (IW)
- ISCBH (IW), Jan 26
- EuRR-Bone study group, Jan 26 (IW, RTS and TvW)
- Quality of Life 4 OI conference, Feb 3 (TvW)
- Meeting with Ultragenyx about fracture app, Feb 6 (IW)
- Introduction meeting NextCure, Feb 9 (IW)
- TeleEcho Growth and OI, Feb 14 (IW)

### EURORDIS Council of Federations (CEF) meeting Brussels

On December 13th OIFE was represented with 3 people at the meeting for national alliances (CNA) and federations (CEF) in Brussels. Ingunn attended on site and Bruno and Inger-Margrethe attended online. Topics included independent living, the proposed European pharma regulation, access to advanced treatments, cross border healthcare, Rare Barometer surveys and activities in the World Health Organization (WHO). Lots of useful information for future policy work! For dinner we met with representatives from the European Huntington Federation, who we have a lot in common with as a federation.
On December 14 there was another meeting for the European and international federations who are members of EURORDIS. We learned about how we as patients can work with industry in a transparent and constructive way, and heard about the youth project and fundraising of the European Huntington Association. Ingunn attended on site and Inger-Margrethe online.

**Activities connected to Remedi4All**

OIFE has been represented by Stephanie Claeys in the EU-funded multidisciplinary consortium REMEDI4ALL, which focuses on repurposing of medicines. The projects consist of four demonstrator projects, where the MOI-A Trial investigating the blood pressure drug Losartan in OI is one of them.

Within this project, Remedi4All are currently organizing their 2nd REMEDI4ALL Multi-stakeholder Meeting (MSM) “Ensuring patient centricity in Osteogenesis Imperfecta research” which will take place on the 13th of June 2024 in Bologna, Italy. This meeting will be organized back-to-back with the annual meeting organized by the Italian OI-Organization AS.I.T.O.I. held in the same location from the 14th to the 16th of June 2024. OIFE has agreed to be formal collaborator of the MSM in Bologna and will be represented by Anna Rossi. Since OIFE got involved in the planning of the event, there has been many meetings on the topic, including meetings with Nick Bishop, Luca Sangiorgi, Claudia Fuchs, several patient representatives. OIFE also joined the programme committee, with three people.

Remedi4All is also organizing a more general conference on repurposing of drugs called “Bridging Boundaries: Innovating, Connecting & Reshaping Drug Repurposing”. The event will take place in Barcelona from March 6-7 and OIFE will be represented by our MAB-member Miguel R. Molina. Read more about Remedi4All and the multistakeholder meeting another place in the magazine.
Rageema represented OIFE at Rare X 2024
The Third Biennial Rare Diseases Conference, Rare X 2024, took place in Johannesburg, South Africa from February 14 to 17, 2024 and OIFE and the OI-community was represented by Rageema Livingstone who is the chair of Brittle Bones South Africa. Rare-X 2024 - Rare Disease Conference in Africa was a conference where South African, African and International rare diseases communities came together to discuss policy and learn from each other. It's a coming together of patient organizations, innovators, policymakers, industry and those entrusted with healthcare and reimbursement matters. Read Rageema’s report from the meeting another place in the magazine.

The Remedi4All consortium & the MOI-A Trial (Losartan)
Information provided by Claudia Fuchs, EURORDIS

What is Remedi4All?
The EU-funded multidisciplinary consortium REMEDI4ALL (Repurposing Medicines for All) has an ambition to establish a European research and innovation eco-system that facilitates fast and cost-effective patient-centric development and implementation of repurposed medicines, meeting high unmet medical needs in any disease. The project is led by the European umbrella EURORDIS and patient involvement is supported by the non profit Beacon. OIFE was until recent represented by our Board member Stephanie Claeys.

What is drug repurposing?
Drug repurposing consists of finding new therapeutic uses for existing medicines. Building on the knowledge previously generated on safety and effectiveness for a specific drug, researchers can explore new indications, potentially leveraging those steps already completed during the drug development process. This means that scientific knowledge and resources are used efficiently, and research can move faster to provide patients with innovative therapeutic options where no treatments are available.

The MOI-A trial (Losartan) – one of four demonstrator projects in Remedi4All
The Remedi4All consortium are currently working on four different repurposing demonstrator projects, including a project on OI called the MOI-A trial led by Prof. Nick Bishop from Sheffield, UK and Dr. Luca Sangiorgi from Bologna, Italy. The purpose of the MOI-A Trial is to investigate if the blood pressure drug Losartan will reduce bone turnover in older adolescents and adults with OI by reducing circulating levels of TGFβ and TGFβ pathway signalling. The project aims to identify the dose of Losartan that is effective in reducing circulating levels of CTX, a bone resorption (destruction) marker, without causing undue side effects. The trial will have sites in UK and Italy. Read more on the project website or on this page.
Remedi4All Multi-stakeholder Meeting (MSM) on OI in Bologna
Remedi4All are currently organizing their 2nd REMEDI4ALL Multi-stakeholder Meeting (MSM) "Ensuring patient centricity in Osteogenesis Imperfecta research" which will take place on the 13th of June 2024 in Bologna, Italy. This meeting will be organized back-to-back with the annual meeting organized by the Italian Patient Organization AS.I.T.O.I. held in the same location from the 14th to the 16th of June 2024.

The overall goal of the meeting is to discuss patient centric approaches to research, drug repurposing and medicines development for OI in a multi-stakeholder environment. The gathering of stakeholders will tackle topics relevant to the OI patient community and patient centricity will run as the core narrative in all sessions – ensuring that each stakeholder is considering the patient perspective in their current and future work. In particular, the sessions will tackle the three main topics:

1. Multi-national strategies for Patient Advocacy in OI
2. Current Treatment Options in OI – a multistakeholder perspective.
3. Patient-centered clinical trial design in OI.

In addition, a final panel discussion on innovative outcome measures in OI clinical trials and an "Ask the experts" session is foreseen.

OIFE is a formal collaborator
OIFE has agreed to be formal collaborators of the MSM and will be represented by Anna Rossi. We are also represented with three people in the programme committee. In addition, there will be many different people suggested by OIFE contributing as speakers, panelists and moderators.

RareX conference in South Africa

By Rageema Livingstone,
President of the South African OI-association

For four days, Johannesburg pulsed with the collective energy of hope and collaboration as RareX unfolded, hosted by Rare Diseases South Africa (RDSA). This pivotal event, held from February 14th to 17th, 2024, brought together a diverse tapestry of voices – patient groups, healthcare professionals, government representatives, and international advocates – united by a single, powerful purpose: empowering individuals living with rare diseases in South Africa and the African Continent.

The conference buzzed with a unique energy. One of the conference's most powerful and unique facets was the platform given to patient voices. For many attendees, it was the first time they could connect with others facing
similar challenges, fostering a sense of belonging and shared understanding. Patient groups, representing a spectrum of rare conditions, shared their lived experiences, challenges and triumphs.

Young adults diagnosed at a young age, radiated resilience and determination to forge their own paths. Tears flowed during emotional testimonials, while laughter erupted during sessions exploring the unique joys and struggles of living with a rare disease. The air crackled with the shared understanding of living a life with rare disease, fostering a sense of solidarity and belonging.

Beyond patient voices, the conference saw a powerful confluence of healthcare professionals. Doctors, researchers, geneticists, and pharmaceutical representatives all engaged in lively discussions, seeking solutions to diagnostic hurdles, treatment access barriers, and the need for more specialized care. The presence of representatives from the World Health Organization (WHO) and the national government health department signalled a crucial step towards building stronger partnerships and prioritizing rare diseases in national healthcare agendas.

The exchange between patients and healthcare professionals was equally crucial. Doctors, researchers, policymakers and the rare disease community engaged in open dialogues, seeking to bridge the knowledge gap and identify solutions to improve diagnosis, treatment, and access to care.

Ms. Alexandera Heumber Perry, the Chair of Rare Diseases International, graced the event with her presence, lending her expertise and amplifying the South African experience on a global platform. Her keynote address resonated deeply, highlighting the importance of international collaboration and advocacy in achieving equitable access to healthcare for all, regardless of the rarity of their condition.
The conference went beyond mere dialogue. Action plans were formulated, aiming to improve early diagnosis, enhance research efforts, and streamline access to treatment and support services. The commitment from government representatives to investigate allocating resources and implement policy changes offered a glimmer of hope for the future. The conference culminated in the development of a collaborative action plan, outlining key areas for improvement. These include:

- **Improving access to diagnosis and treatment**: This includes advocating for streamlined referral systems, creating centres of excellence, and affordable access to essential medications.

- **Raising awareness and reducing stigma**: The conference emphasized the need for education campaigns aimed at both the public and private healthcare professionals to dispel myths and increase understanding of rare diseases. They also incorporated the training of traditional healers to assist in getting patients in traditional communities to hospitals and dispel stigmas by working with the doctors to get the patients the care needed while still respecting their cultures and traditions.

- **Building research capacity**: Investing in research specific to rare diseases prevalent in South Africa and Africa is crucial for developing effective treatments and improving patient care. The Undiagnosed Disease Programme (UDP) in South Africa, run by Prof. Shahida Moosa at Stellenbosch University provides an African example of how the above can be achieved: cutting-edge research using the latest in OMIC technologies to provide diagnoses to those still undiagnosed. At the same time, the UDP provides a platform to train the next generation of African healthcare workers, medical geneticists, genetic counsellors, scientists and bioinformaticians in anticipation of the genomic revolution reaching our shores. The UDP also incorporates patient and parent voices and provides access to community and an opportunity for us to play a pivotal role in the research which affects us and our families.

The impact of the conference extends far beyond the walls of the venue. The connections forged, the knowledge exchanged, and the renewed sense of purpose will ripple outwards, empowering patient groups, influencing policy decisions, and ultimately, improving the lives of countless individuals and families.

The conference added an extra workshop day designed to upskill patient support group leaders. Topics such as leveraging social media for NGO’s, fundraising, driving patient-centred healthcare policies in healthcare and addressing compassion fatigue and burn-out were covered acknowledging the important role of patient leaders and supporting them in their respective patient communities.

The Rare Diseases Conference in South Africa was more than just an event; it was a symbol of hope, a testament to the power of collaboration, and a call to action for a more inclusive, holistic and equitable future for all.

The journey to RareX mirrored the diagnostic odyssey we endured - meandering paths littered with dead ends and misdiagnoses. Each session mirrored the battles we fought – for accurate diagnosis, for access to specialists, for clinical trials, for simply being heard. But unlike the isolation of navigating these battles alone, RareX was a chorus of shared experiences, a symphony of unwavering support.
I saw myself reflected in the tired eyes of other parents, yet their spirit remained unbroken. Each story was a poignant reminder of the invisible scars etched by the diagnostic odyssey; a silent war waged upon families. This war transcends generations, casting a long shadow of uncertainty on our children’s futures.

Therefore, I plead - not just for my child, but for the countless others trapped in similar battles - that RareX be more than a memory. I see her, my daughter, being amongst this vibrant community, absorbing the energy, the knowledge, the unwavering hope. I envision her future, not defined by limitations, but empowered by the collective fight for better diagnostics, more research, and a healthcare system equipped to handle the complexities of rare diseases.

I would like her to attend future conferences witnessing others thrive with rare diseases to fuel her own resilience and inspire her to become an advocate for herself and others. It will provide her with knowledge to access cutting-edge research and clinical trials which opens doors to potential treatment options and improves her understanding of her own condition. A sense of community connecting with peers and mentors creates a vital support network, fostering a sense of belonging and reducing isolation. Exposure to success stories and patient-led initiatives ignites her passion to contribute to the rare disease community and contribute to future advancements.

RareX offered a glimpse into a world where my daughter's rare disease doesn't define her future. This conference marks a significant step forward, echoing the sentiment of nothing about us without us, but the journey is far from over. The rare disease community in South Africa and across Africa will continue to advocate for their needs, collaborate with stakeholders, and work tirelessly to build a brighter future for all those living with these complex conditions. Let’s continue weaving this tapestry of hope, ensuring that future generations of rare warriors have the tools and support they need to thrive.

Welcome new OIFE Associate Member Brazil (ANOI)!

Information provided by Henrique Benincaza dos Santos, ANOI

How many people with OI does Brazil have?
The exact number is unknown; we have an estimate of around 14 thousand people living with osteogenesis imperfecta in Brazil.

Tell us about the situation for OI-people in Brazil!
In Brazil, we have 15 Reference Centers for Osteogenesis Imperfecta (CROI), where registered patients receive multidisciplinary care. We have a Clinical Protocol and Therapeutic Guidelines (PCDT) for OI under the Unified Health System (SUS), which is public and establishes criteria for the diagnosis, pharmaceutical and non-pharmaceutical treatment for children and adults. However, we still face challenges in telescopic rod surgeries, as few practitioners master the technique.
When was ANOI founded? How is it managed?

Associação Nacional de Osteogênese Imperfeita (ANOI) was founded in May 2017, as a restructuring of the former ABOI (Brazilian Association of Osteogenesis Imperfecta), established in December 1999. It is a private entity, legally constituted as a civil association with no economic purposes. Operating on organizational, welfare, and educational principles, with no political or religious affiliation, ANOI is governed by its bylaws, internal regulations, and other legal provisions. ANOI has been active, particularly in the production and dissemination of information about the condition, its characteristics, and treatment possibilities. ANOI also represents civil society in various arenas of public authorities. The organization is managed by a board of 5 members, an executive council of 3 members, and a fiscal council of 3 members. In all 27 Brazilian states, we have regional coordinators who closely follow individuals with OI and their families. All members are volunteers.

How many members does ANOI have? How do you recruit more members?

Currently, we have 1,862 individuals with OI registered. This number has been achieved through partnerships with reference centers, establishing a network of contacts. Upon the birth of a child with OI in these reference centers, ANOI is notified. This marks the beginning of crucial initial contacts with the parents and guardians of the child with OI. In many cases, it is highly likely that the parents and family members also join ANOI as legal representatives of these children.

What are the biggest challenges for your organization?

Our greatest challenge is to structure ANOI so that it can stand on its own feet. In the realm of ANOI’s actions, this involves training healthcare and education professionals, as well as promoting research for gene therapy.

What has been your biggest success so far?

We believe that ANOI’s greatest success or achievement was when the SUS (Brazil’s Unified Health System) took over the funding of treatment and established the 15 Reference Centers for OI (CROI). This included guidelines for registering OI reference centers nationwide, the appointment of a Coordinator for CROI in Brazil, the adoption of the Montreal Protocol, and specific funding for the OI program.

Regarding projects, we can mention: Priority access in public hospitals for orthopaedic and surgical emergencies, surgical procedures, and ensuring the purchase of telescopic rods for the treatment of OI for all Brazilian states.
Why is it important for you to be associate member of OIFE?

It is a significant step for ANOI to be part of an international community addressing crucial issues related to OI. We share a similar mission, but encounter different opportunities due to our economic, social and cultural reality, and the vast dimensions of our continent. ANOI believes that we stand to gain much in terms of new knowledge and approaches to OI by being a part of this community. Sharing our journey, struggles, victories, and, why not, difficulties could be highly interesting for OIFE in terms of problem-solving: How did we get here, being an association that needed to redefine/rebirth itself to preserve its history that began in 1999! It’s worth mentioning that ANOI is part of a group of OI-Organizations in Latin America. We exchange information and gather in a virtual environment.

What are your plans for the future?

ANOI has plans and several projects in development. This includes training healthcare professionals—promoting technical training for orthopedists, radiologists, nurses, plaster technicians, attendants, social workers, and other healthcare professionals directly involved with OI. The goal is to find ways to make childbirth as little traumatic as possible, given that any mechanical shock can cause fractures. The organization aims to expand physiotherapy services, enhance psychological support for patients and their families undergoing OI treatment.

OIFE Investigator Meeting – a success

By Gabriela Beug & Ingunn Westerheim

On the 17th of November 2023, OIFE hosted the second Virtual OIFE Investigator Meeting for the OI research community. 273 people from 48 countries signed up and more than 160 individuals attended the online event. Attendees were a mix of health professionals, scientists, OI clinicians and a lower number of representatives from industry and patient groups.

The meeting’s objectives included highlighting recent advances in OI research, providing a collaborative space for researchers in Europe and beyond, attracting fresh talent to European OI research, and offering support to the younger generation of OI researchers. With a focus on fostering a spirit of cooperation and innovation, this meeting aimed to contribute to the growth and development of OI research globally.
EUROPEAN RARE DISEASE RESEARCH COLLABORATION

Dr. Luca Sangiorgi (ERN BOND coordinator) from Bologna, Italy gave a presentation on possibilities and challenges of European research collaboration. The ERICA (European Rare Disease Research Coordination and Support Action) initiative seeks to enhance collaboration among European Reference Networks (ERNs) for rare diseases. It focuses on improving the quality and impact of clinical trials. One of the tools mentioned was the ERICA PROMs repository.

Challenges include the diverse geographical distribution of Health Care Providers (HCPs) and varying national regulations, for which ERICA has organized webinars that offer insights and tools for clinical trial activities. The last part of the talk was dedicated to the European Rare Diseases Research Alliance (ERDERA) will replace the European Joint Programme for Rare Diseases (EJP RD).

NEWS FROM BASIC SCIENCE

Advances in Osteogenesis Imperfecta (OI) research include the development of a new conditional knock-in mouse model for COL1A1, which is tissue-specific. Current mouse models express mutations globally (i.e. in all tissues). This new model will help understand the effect of mutations in one tissue i.e., by only expressing the mutation in the lung (instead of all tissues) it is easier to isolate the impact of the mutation on the lung versus the effects of the mutation on the skeleton.

Furthermore, a new potential therapeutic target is endoplasmic reticulum (ER) stress. The endoplasmic reticulum (ER) is important for the proper folding and processing of type I collagen, which is impaired in OI due to the COL1A1/COL1A2 mutation. Targeting the ER stress response through chemical chaperones is thought to improve collagen processing and bone properties in OI mouse models and eventually patients. 4-phenylbutyric acid (4PBA) is a chemical chaperone that is currently being investigated. It is hypothesized to reduce ER stress and improve cell homeostasis.

TECHNIQUES TO ASSESS BONE DENSITY, STRUCTURE, STRENGTH, AND MOBILITY IN OI

High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) was introduced as an imaging method that gives information on the bone’s structure and mineral density in the arms and legs. It helps medical professionals estimate the bone’s strength and ability to resist fractures.
The presenter Enrico Schileo from Italy leads a working group around the use of HR-pQCT OI. If you are interested in participating, please contact him on Email.

**Motion analysis** in osteogenesis imperfecta (OI) is a valuable tool for improving clinical decision-making, particularly the assessment and treatment of gait issues. The evaluation of individuals with OI by means of motion analysis and selected functional assessments, along with an accurate biomechanical model of the lower and upper extremities aims to better understand and predict OI disability and improve quality of life.

**A Danish 10-year follow up study of adults with OI**

Plans for a 10-year follow-up study to reassess bone status in adults with OI were announced by Bente Langdahl from Denmark. The planned study aims to reevaluate approximately 80-100 adults with OI, that participated in a clinical trial 10 years ago.

The methods to conduct skeletal studies, re-evaluate bone health and identify fractures include: Dual-energy X-ray Absorptiometry (DXA) to measure areal BMD for lumbar spine, hip and the entire body, High-resolution peripheral quantitative computed tomography (HRpQCT) to measure volumetric BMD of the distal radius, distal tibia, and investigate bone architecture, and spine X-rays. Combining data from multiple assessment methods may help better understand fracture risk long-term.

**NOSOLOGY & CLASSIFICATION – CATEGORIZATION OF OI TYPES**

The purpose of nosology (classification of diseases) is to create a common naming system to facilitate diagnosis for the growing number and variety of skeletal phenotypes (clinical manifestations of a disease) with a genetic basis.

The dyadic naming system, which was recently adopted in the 11th revision of the “Nosology of genetic skeletal disorders” is a classification system used in osteogenesis imperfecta (OI) that incorporates both genotype (the underlying genetic mutation) and phenotype (clinical manifestations).

The session started with 3 introductory talks from Valérie Cormier Daire (France), Joan Marini (USA) and Dimitra Micha (The Netherlands) who gave their thoughts on how a classification system of OI should look like – and whether the genetic mutation or the clinical picture should come first in a dyadic system.

This was followed by a panel debate, where Fleur van Dijk and Lena Lande Wekre joined.

There was no consensus reached during this meeting, but all the participant agreed that this is an important discussion, and that our goal should be to find a classification system that both clinicians, researchers and people with OI can live with.
Resources for adults with OI

ADULT HEALTH RESOURCE GROUP - MEETING IN FLORIDA ABOUT CARDIOVASCULAR ISSUES IN OI
Due to common interests in adults with OI, Dr. Eric Orwoll identified researchers and clinicians who have worked on adult care. One of the clinicians who got involved was Dr. Lars Folkestad from Denmark. During the summer of 2022 the group started meeting online to discuss a potential collaboration to identify the gaps in knowledge related to adult care.

The group consists of the Chair Eric Orwoll and members from the US, Laura Tosi, Cathleen Raggio, Sandesh Nagamani and from Europe, Lars Folkestad, Jannie Dahl Hald, Bente Langdahl, Stuart Ralston and Oliver Semler. The OI Foundation (OIF) helps facilitate the meetings.

In the middle of January, the group gathered in Orlando, Florida to write what will be their 3rd paper together. The Delphi process study will review the current literature related to the risk of and follow up for cardiovascular disease in OI. The group had great discussions.

OIFE was represented by Lars Folkestad and Oliver Semler (online). Due to difficult winter weather, the planned meeting went from an on-site meeting to a hybrid meeting, which worked relatively well. Read an interview with Dr. Eric Orwoll and Dr. Lars Folkestad about the initiative from a previous magazine.

ADULT RARE BONE NETWORK & ADULT CARE PATHWAYS IN THE UK
When adults with rare bone conditions turn 18, they mostly have no dedicated adult clinics or services to transition to. Because of an initiative from the BBS, there is now an official Rare disease collaborative network (RDCNs) established for adults with different rare bone conditions, including OI. The priority areas of existing RDCNs include: (across the UK)

- Raising awareness of the rare disease
- Improving co-ordination of care
- Sharing of expertise and best practice
- Establishing a disease registry to improve the understanding of the epidemiology of the rare disease
- Research on treatment options and diagnostics
- Establishing a support network for patients and families, including co-ordinated transition from paediatric to adult services.

In addition to delivering a virtual multidisciplinary structure for rare bone clinicians the network also has as its goal to develop care pathways (guidelines) for the different conditions, which will serve as resources for professionals and patients. Read more about the UK initiatives in an interview with Patricia Osborne and Kassim Javaid elsewhere in the magazine.
TEAMS FOR ADULTS WITH OI IN SWEDEN
At the conference in Stockholm, we learned that there are now two national teams for the assessment and follow up of adults with OI in Sweden – one in Uppsala Academic Hospital and one in Linköping University Hospital.

According to the information at the Swedish health authorities webpages, adults with newly diagnosed OI should be assessed in adult National highly specialized unit (NHV) at least once. Adults with severe illness should be followed regularly by an NHV team for adults. People with milder forms should be followed by an osteoporosis specialist at the local hospital and receive individual care plans from the adult NHV. The care plan includes follow-up with bone density measurements, dental care, hearing examinations among other topics. The intervals between follow-ups are determined by individual needs, the severity of the disease and the type of treatment.

ADULT HEALTH TOOLKIT FROM THE USA
"The Adult Health Toolkit" is made by the OI Foundation in the US. The brochure is called "Information for adults Living with OI, Their Families, and Medical Professionals“ and is created to help adults with OI navigate the many aspects of managing their health. Learn more and check out this resource at www.oif.org/adulthealth.

ADULT WEEK-ENDS
Several of our member organizations have started to organize gatherings for adults in addition to the more common family meetings. Such meetings can be a great place to get together and share experiences between people living with OI in addition to learning from professionals. This photo is from DOIG (German group) who earlier this year got together in Kassel, Germany.

Care pathways & Adult OI networks in UK
Written by Patricia Osborne CEO of Brittle Bone Society and Professor Kassim Javaid

WHO ARE YOU (BOTH) AND WHAT IS YOUR RELATIONSHIP TO OI?
I am Patricia Osborne, Chief Executive of the Brittle Bone Society (BBS). I manage the UK charity, working with individuals and families with OI. Prof. Kassim Javaid from the University of Oxford is the Chair of the BBS Medical Advisory Board (MAB).

TELL US ABOUT THE RDCN ADULT RARE BONE NETWORK:
The Rare disease collaborative networks (RDCNs) are an important part of the National Health Service (NHS) architecture initiated by NHS England and NHS Improvement to improve care and support for patients with rare diseases.

Prof Javaid and other HCP colleagues decided to submit an application to establish a RDCN for adults with rare bone diseases and this was fully supported by the BBS and other rare bone groups. There are now 20 networks approved and monitored by the NHS, with the Adult Rare Bone, being the latest. 22 x NHS Hospital Trusts have signed up to the network, with more in the wings. The network includes approximately 35 – 40 healthcare professionals (HCPs).
The priority areas of existing RDCNs include: (across the UK)
- Raising awareness of the rare disease
- Improving co-ordination of care
- Sharing of expertise and best practice
- Establishing a disease registry to improve the understanding of the epidemiology of the rare disease
- Research on treatment options and diagnostics
- Establishing a support network for patients and families, including co-ordinated transition from paediatric to adult services.

To achieve this the goal of RDCN for Adults with Rare Bone Diseases is to
- Deliver virtual national and supporting regional multidisciplinary structures for all clinicians caring for adults with rare bone diseases
- Develop four rare disease patient pathways that will include minimum clinical indicators both generic and disease specific and resources for professionals & patients.

At the RDCN Launch Event - Prof Javaid, Trustee of the BBS Thines Ganeshamoorthy, Patricia Osborne, and patient representatives & colleagues from various groups involved in the new RDCN, Oliver Gardiner XLH UK, Heather Delaney FDDSUK, Helen Bedford-Gay.

HOW IS THE NETWORK MANAGED?
A steering committee is responsible for implementation and management of network, including prioritizing deliverables, assigning tasks, organise an annual meeting, reporting to the NHS and be a point of contact for other organisations including from patient groups. A key essence for the RDCN for Adults with Rare Bone Diseases is patient co-production. We have therefore integrated patient engagement at every level of the RDCN governance. BBS Trustee Thines Ganeshamoorthy (left of the photo) is appointed co-chairman of the Steering Group in year one of the project alongside ProfJavaid.

The NHS England will provide ‘light touch’ support to RDCNs. Each network is allocated a named commissioning manager. RDCNs is also assigned an NHS England approved logo which they can use on publications and correspondence with patients, patient groups, other stakeholders and when applying for research funding for example. The establishment of an RDCN is not accompanied by additional funding; set up and running costs are not reimbursed.
WHAT ROLE DOES THE BBS HAVE?
BBS hosted the formal launch event alongside other patient support groups in London November 2023. The BBS also provide initial resources, staff time and have committed to providing back office support including joint secretariat duties alongside Metabolic Support UK. The network also involves an expert group of co-applicants and friends whose members include reps from: XLH UK, Fibrous Dysplasia Support UK, FOP, and Softbones UK - HPP (informally). So far BBS have helped co-ordinate meetings online with HCP’s, steering groups etc, to help formalise due governance procedures and similar. Metabolic Support UK have kindly agreed to host a map finder for the network and other useful info on their website. BBS is hosting OI specific information on our website and other groups will do likewise.

WHY RARE BONE AND NOT JUST OI?
While traditionally RDCN have been single disease focused, the BBS and clinical community recognised the aims and objectives of the RDCN were relevant across rare bone diseases. Working collaboratively with the other patient groups made sense as those groups all share the same unique set of highly skilled healthcare professionals/clinicians. Working in a larger group also gives a stronger voice for better understanding and future care plans for those with rare bone conditions.

TELL US ABOUT THE OTHER INITIATIVE – THE CARE PATHWAYS
The BBS have long campaigned for a formal set of clinical care guidelines for OI to be put in place. For some years we have consulted and worked with leading healthcare professionals in the UK and the OI community to gather strong evidence and data to help shape that missing formal guidance. The care pathways document is aimed at the whole OI community from specialists, generalist in hospital and primary care, patients and their families to clarify the minimum standard of care that patients with OI can expect wherever they live in the UK.

In 2020 BBS were given an award in ‘care’ and part of the prize was a chance to work with the company WPP (now called VMLYR Health). This included access to pro bono support in ‘project managing’ to develop a formal set of care guidelines/pathways. We benefitted greatly from this and went on to purchase (at much reduced rates) expertise in project management from VMLYR Health to conduct the collation of the documents for Pathways for severe OI. Prof Javaid agreed to lead on this, and our formal process began.

Expert working groups with individuals with OI worked alongside BBS staff to co-develop the content and format, including which areas of health/topics that should be covered in the best practice pathway document. The final pathway draft was completed and presented at the 2023 BBS family day. Once all topics were agreed we then invited 22 healthcare experts to input into the document. It is now in its final stage of being written up into a paper for publication including a Patient checklist. We are aiming to submit for publication by the summer of 2024. BBS have now embarked on the 2nd phase of work in care pathways which will include similar documents for adults with all other types of OI.

WHAT ARE THE FURTHER PLANS?
Creation, completion and publication of formal care pathways for both severe and all other types of OI, together with the new NHS RDCN network, heralds an exciting step forward for OI in the UK. To grow understanding of both management of care of those with OI alongside recognised pathways can only mean that those with OI will receive better treatment, and lead to a better understanding and better health outcomes for the OI community. BBS also plan to compliment this programme with webinars and members will be involved throughout.
My name is Meena Balasubramanian. I am a clinician-scientist specialising in bone genetics at the University of Sheffield and Sheffield Children’s Hospital in the UK. I have worked in Sheffield over the last 15 years. I started here as a Clinical Genetics trainee having previously worked as a paediatrician and did my higher research degree on atypical presentations of OI. I subsequently started as a Consultant Clinical Geneticist in the Highly specialised OI service in Sheffield looking after a number of children with OI. I set up the bone genetics clinic in 2012 to streamline diagnostic pathways and address the diagnostic odyssey that some families go through when trying to get a genetic diagnosis of OI. Those were the days when access to genetic testing was limited and expensive, so my work was around ensuring robust clinical pathways to ensure equitable access to such testing across the highly specialised services in England.

In addition, realising there was lack of continuity with Genetics services when children were transitioned to the adult services, I set up links with the adult metabolic bone clinic in Sheffield. This led to setting up a regular Genetics-metabolic bone team meeting since 2015 to discuss shared families and referrals to Genetics for young adults to access genetic testing prior to starting a family.

My research over the last 15 years has been on improving diagnostic outcomes in OI especially the more rare, atypical presentations. I previously led studies on applying advanced genetic technologies in unresolved OI families where a diagnosis was uncertain and developing pathways for robust interpretation of genetic variants identified on testing. I was able to identify and publish a novel cause of bone fragility/OI which led me to establishing a lab working on zebrafish models for bone fragility.

Are you working on any other OI-related research?

Yes, I have a number of OI-related research projects which transcends the clinical and translational science. Most of my research ideas have always started with a child or family with OI that I care for. In the clinical space, my research is around understanding the natural history of the rarer forms of OI and mining genomics data for identifying new genes causing OI. In addition to this, we are working on a project to better understand why some adults develop significant fractures at a young age but clearly do not have OI as we understand it.

In the translational space, I am very interested in bench-to-bedside medicine, taking knowledge from the lab back into clinic like my work on zebrafish models for bone fragility. I also work with a number of colleagues in other disciplines such as engineering (looking at collagen orientation in OI vs control cells) and stem cell biology (developing iPSC models for gene therapy in OI). I have a PhD student working on reclassification of variants of uncertain significance identified on OI testing and another project on drug repurposing in OI. So quite a lot of research happening in this space.
Another major area of my research is on neurodevelopmental disorders where children present with seizures and developmental delay. I am working on developing gene therapies for specific conditions in this space and using all the knowledge gained from this work to apply to OI. As it happens, I have also identified a number of children in my clinic with significant fractures who have faults within genes causing severe developmental delay, so currently looking into the association with bone and brain so called BRONE association.

Do you think all people with OI should have the offer to get tested to know their mutation?

Yes, with the latest advances in genomic technologies, testing has got more accessible and cheaper which means there should be a discussion around genetic testing and what this means for the individual regardless of their consideration around family planning. There is some data on correlating the genetic variant on what the evolving phenotype would be, so this would be another reason to consider testing in individuals with OI. The longer I do this job, the lesser I second-guess whether testing would be useful or not and always discuss this as an option in all the families and adults I see in clinic with OI.

OI has been listed on Genomics England’s published list of conditions that will be screened for as part of the New-born Genomes Programme research study (“the Generation Study”). Normally the new-born screening programmes have been only for diagnoses, where it is important to start an advanced treatment very early. What is the rationale of including more conditions (incl. OI)?

The Generation study is a research study to explore the benefits, challenges, and practicalities in use of whole genome sequencing to look for rare genetic conditions in new-borns, to see if this is feasible and can help enable early treatments to be instituted. The conditions include those were there are treatment options available, and an early diagnosis could change outcomes. The decision about which conditions are screened for was decided following a wide-ranging consultation.

Why are only the genes Col1A1/A2/ IFITM5 chosen?

OI is included as there are treatments available as a pilot and it may show us what the challenges are and what the uptake is. I guess the genes were chosen based on how common they are as a cause of OI as we know genes encoding type 1 collagen (COL1A1/A2) account for >85% of OI. IFITM5 has been included, I suspect, because it is part of the autosomal dominant OI panel of genes.

Illustration borrowed from Dimitra Micha, OIFE Investigator Meeting
Based on your opinion - what are the pros and cons for including OI?

The pros are the using power of genome sequencing and harnessing the advances in genomic technologies to inform management of children born with OI long before they sustain a fracture and diagnostic odyssey that many families suffer from. The cons are that early diagnosis in the newborn period may come with its own challenges about knowing what the course of the condition might be and the uncertainty in these situations.

Will we find many "hidden" OIs, that would never have gotten their diagnosis until much later in life?

That is possible, just by nature of the study but I suspect most of the severe presentations in OI would have been picked up by prenatal scans. Some of the ‘hidden’ OI may have normally been picked up after a child sustains their first fracture, but involving in this study may allow an earlier diagnosis to be made.

Can this prevent accusations of child abuse?

As I mentioned above, that is possible and I know from my own professional experience, it is not nice for families that find themselves in this situation. However, the possibility of this needs to be balanced with the unnecessary anxiety this may generate.

Yes, can it also cause unnecessary worry to know of a diagnosis that you would otherwise not have cared about until later? Can this make it harder to access insurance or other similar consequences?

That is a possibility that such testing may reveal unexpected diagnosis causing unnecessary worry for the parents. However, the testing will only report back those genetic changes which are associated with the condition tested for and there is strong association with OI. It may then require further clinical work up in the metabolic bone clinic and follow up to ascertain that the child indeed has clinical features of the condition and if so, decisions need to be made around starting treatments for OI where required.

At the moment, with any genetic testing, there is a moratorium which means there is no obligation to reveal genetic testing results for insurance purposes, so hopefully that will not be an issue unless there is a clinical presentation of the condition.

Why do you think some have called it controversial?

It is a research study to check feasibility and parents would be counselled about the nature of the study and what testing is being undertaken. Of course, with any of these studies there is a potential to uncover diagnoses that may not have come to light until much later and having the diagnosis made when the family are not ready to receive such a news.

Any other messages to our readers?

Thank you for everything you do, I am always amazed by how generous families and adults with OI are with their involvement in research. It is always motivating to see the resilience and the unbreakable spirit which inspires me to do even more within my capacity to improve the lives of children, families, and individuals with OI. I work closely with Brittle Bone Society and always humbled by the overwhelming support I get whenever I have contacted colleagues at BBS be it Patricia or Coreen for support with my research.
My name is Rubén Muñoz Cortés and I work as a psychologist at Fundación AHUCE. I am specialized in clinical psychology, and my primary role involves offering psychological therapy to individuals with osteogenesis imperfecta (OI) or other dysplasias, and to their families, if they require support. I have been working at AHUCE since 2015, providing assistance to individuals with OI on various issues. In recent years, the management of chronic pain has acquired a prominent role in therapy work. In addition to direct patient care, Fundación AHUCE actively promotes the development of psychosocial research projects related to OI. My doctoral dissertation originated in this field of study.

Please tell us about your PhD project!
Firstly, I want to express my gratitude to all the people who actively participated in the study and to the organizations that provided invaluable support, such as OIFE, OIF, BBS, among others. A special appreciation goes to Fundación AHUCE and its Director, Julia Piniella, as well as my thesis supervisors, Jose F. Soriano and Vicente Monsalve.

This research aimed to broaden our understanding of the experience of chronic pain in adults with OI. While there has been a growing interest about this topic in recent years, there were very few studies when we started our investigation. Given our own experiences and those of our colleagues, chronic pain appeared to be a significant and pervasive aspect in the lives of individuals with OI, prompting us to consider it a crucial area worthy of exploration.

Our objective was to assess the frequency and characteristics of chronic pain in a diverse sample of adult individuals with OI. We sought to explore its correlations with clinical, sociodemographic, and particularly psychological variables, including cognitive perceptions of pain, coping strategies, personality traits, and its impact on daily activities and overall quality of life. The study was entirely funded by the AHUCE Foundation, thanks to donations from the OI community.

Which methods were used?
With the intention of obtaining a substantial sample size, we decided to conduct the assessment through an online survey, available in both Spanish and English, based on various standardized questionnaires. Through the collaboration of several organizations, the survey was widely disseminated. We successfully obtained a sample of over 400 participants from different countries worldwide. Once we collected the data, we were able to employ statistical analyses to establish frequencies and relationships among the various variables.

Why did you choose to focus on pain as a topic?
The defective synthesis of collagen not only affects bones but also involves other parts of the body, such as muscles, tendons, and various organs. This implies that issues stemming from the condition extend beyond bone fragility alone. There are diverse clinical manifestations that can significantly impact the lives of individuals with OI. And based on our experience, chronic pain appeared to be one of them. Furthermore, we observed a notable lack of research on this matter within the context of OI.
What were your most interesting findings?
Firstly, we looked at what other studies had already indicated: chronic pain, not solely attributed to fractures, was highly prevalent in adults with OI. Pain was a daily experience in over 80% of our sample, aligning it with findings from other researchers. Furthermore, it appeared to be problematic, interfering with daily activities such as household chores, physical activity, and work, among others, and correlating with a decline in both physical and mental health. Despite treatments, pain seemed to persist, as noted by other researchers, and no differences were found between types of OI and severity levels.

Focusing on psychological variables, we confirmed a significant relationship between how individuals perceive pain and its impact. Consistent with similar studies, we observed that a more threatening appraisal of pain was associated with higher intensity and greater interference in daily activities. We consider that this relationship could be bidirectional: undoubtedly, the more intense and debilitating the pain, the more threatening it appears. However, a more catastrophic appraisal of pain can also lead to increased concern and heightened fear, resulting in avoidance of various daily activities.

Furthermore, we found that personality was related to pain. Specifically, individuals with higher scores in the "neuroticism" dimension seemed to experience pain more frequently and intensely. Additionally, in line with the aforementioned findings, these people had a tendency to perceive pain as more threatening. This is not surprising, considering that this personality trait describes individuals prone to worry and more frequent experiences of emotions such as anxiety.

Any surprising findings?
Perhaps the most surprising finding was that there seemed to be no coping strategy for pain that was more effective than another. In reality, the relationship observed between coping style and pain adaptation was limited. One possible reason may lie in the study's descriptive and cross-sectional design, preventing the establishment of a cause-and-effect relationship between the way pain is coped with and its impact on people's lives. Another possible underlying cause is that coping strategies were designed to decrease pain. In recent years, psychological therapy has been attempting to focus interventions on facilitating coexistence with pain rather than controlling it, emphasizing the construction of a satisfying life even in the presence of pain.
What is the most important take home message for clinical work?
We believe that this study, along with other publications that have emerged in recent years, contributes to raising awareness among clinicians about the prevalence of chronic pain in OI and the importance of considering it in clinical consultations.

Were patients/patient organizations involved in the planning/implementation? How?
Patient organizations played a crucial role in the study's development, assisting in disseminating the online survey among participants and promoting visibility for the project and its results. Fundación AHUCE expresses its gratitude to the AHUCE and AMOI associations in Spain, as well as to OIFE, OIF, BBS, Care4brittleBones, and many other organizations that collaborated with us in other countries.

What are you currently doing? Future plans involving OI research?
I continue to provide psychological support to individuals with OI or other dysplasias, and their families upon request. Simultaneously, we are launching a new research project aimed at assessing the effectiveness of a group psychological therapy for adapting to chronic pain in adults with low-prevalence bone dysplasias. We look forward to sharing more information shortly.

In your opinion, what are the biggest knowledge gaps in OI?
There are many research fields that fall outside my area of expertise, and I cannot confidently identify neglected topics within them. However, from my professional perspective, there are very few studies addressing psychosocial aspects of the pathology. For instance, we have limited knowledge about the overprotection experienced by children with OI from their surroundings and its consequences for their future. Additionally, there is a lack of understanding regarding how OI interferes with the attainment and development of employment.

Any messages for the readers of OIFE Magazine?
I would like to thank you for taking the time to read this interview. If you have any questions about the chronic pain research in OI, feel free to reach out to me via email at psicologia.fundacion@ahuce.org. We hope to share more information with you in the near future.
Who are you & what is your relationship to OI?
I am Silvia Storoni, a physician specializing in internal medicine with a particular interest in endocrinology. A few years ago, I came in contact with Dr. Marelise Eekhoff and Dr. Dimitra Micha, who inspired me with the research projects conducted at Amsterdam UMC on OI. What struck me about OI and motivated me to continue this path is the fact that there is still too little known about this condition. I find it important that patients with OI receive the right attention. Despite being a relatively rare condition, research should aim to understand not only the skeletal but also the extra-skeletal issues in OI patients which also affect their health a lot. Only through this knowledge, new effective therapies can be found. By extra-skeletal, we mean issues that do not relate to the bone/skeleton, but has to do with soft tissue.

Can you tell us about your PhD project?
During my PhD, I initiated and completed various diverse projects. The common thread among them was the exploration of extra-skeletal complications in OI patients. We conducted a large study on the entire Dutch OI population (over 800 people) to understand how many hospitalizations are truly related to extra-skeletal complications. Other projects aimed to understand the relationship between genetic defects and clinical symptoms. A major project involved the TOPAZ trial, where we proposed Teriparatide as a new therapy for adult OI patients.

In my dissertation, I included 8 articles published between 2021 and 2023. The first 3 articles focused on the Dutch OI population and hospitalizations, comparing them with the general Dutch population. The next 3 articles concentrated on OI lungs, exploring what is known about lung OI pathology, lung histology, and the development of an innovative clinical diagnostic method to measure lung function in OI. The last articles focused on genetics, describing new genetic defects in OI patients.

The entire project was financed with funding from various projects and grants, and each project used different methods. For example, the first three articles involved matching information from all OI patients in the Netherlands with a genetic diagnosis with statistics from CBS (Centraal Bureau voor Statistiek). We collected anonymous information about hospitalizations, outpatient visits, and medication use in OI patients and compared it with the general population.

Why did you choose to focus on other issues than bone?
I chose to focus on other tissues because there is a lack of knowledge about these tissues. Unfortunately, although extra-skeletal complications seem less debilitating than bone issues, they significantly reduce the quality of life and can be as debilitating as bone problems.
What were your most interesting findings?
Some of the most interesting findings revolve around pulmonary complications. For the first time, we demonstrated that lung tissue in OI may have intrinsic alterations, especially in lethal forms of OI. This needs further study in other types. It is important to be aware that collagen type 1 can have a significant effect on lung development and structure which warrants attention and monitoring.

What is the most important take-home message?
The most important take-home message for clinical work is that patients must conceptually agree with the study. This helps them to be actively involved, which increases the success of the clinical study in providing meaningful outcomes for the patients.

Were patients/patient organizations involved?
Yes, and we strive to increasingly implement this aspect. Involving patients and organizations is crucial to understand patient needs and priorities, and to inform them about new therapeutic options and research findings.

What are you currently doing and what future plans do you have?
Currently, I am continuing my specialization in internal medicine and endocrinology. Alongside this, I am involved in more studies exploring extra-skeletal issues, with a particular focus on the heart and lungs. We are trying to study and introduce a new clinical method to assess lung function quickly and easily in OI patients, which can prevent the detection of lung complications when it is too late.

In your opinion, what are the biggest knowledge gaps in OI?
Areas where there is still much to learn include extra-skeletal complications and the correlation between genotype and phenotype. Better understanding of these aspects is crucial for developing new therapies and improving clinical care.

Any messages for the readers of OIFE Magazine?
The message I would like to convey, both to medical professionals and patients or patient families, is the importance of collaboration. Collaboration between different research centres and between doctors and patients or patient associations is essential. Researchers need to know the needs of the patients, in order to direct research in that direction. And patients need to understand the challenges and recommendations of the doctors.
School kit for children with OI

Starting school or changing school is a big step in the life of a child or adolescent, and very likely a lot more if a have condition that makes their bones more fragile than their peers. A tool was created to ease these transitions as much as possible for students with OI.

In collaboration with students and their caregivers, the Individualized School Plan for Optimal Inclusion of Students with Osteogenesis Imperfecta (ISP – OI) can be filled out by any healthcare professional who is assisting a child/adolescent beginning or change school.

Patient and parent representatives, Shriners Hospitals for Children-Canada (SHC-Canada), McGill University, Sunnaas Rehabilitation Hospital (Norway) and the Montreal School Services Center collaborated on this project. They collaborated to describe a global view of the activities that students take part in throughout their school day and the adaptations and recommendations that could be made to optimize their schooling experiences. The ISP-OI includes 16 sections supplying the student and school staff with education and accommodations the student can receive in all aspects of their school day. In the format of a fillable PDF, the ISP-OI is available in French and English. It is intended for students ranging from kindergarten to high school.

Lastly, one of the annexes of the ISP-OI is a list of suggested items to be included in an OI Splint Kit, this idea was the initiative of a patient from the SHC-Canada. OI Splint Kit is intended to empower patients and families with the appropriate knowledge and equipment to immobilize fractures and manage pain. The list of content is available to help anybody interested into created their own splint kit.

Artist with OI: Jon Wos

Jon Wos was born in Lena, Wisconsin in 1981. He was diagnosed with OI at birth. Though this condition limited his physical ability, it heightened his sensitivity to the world around him, and, out of his love of creation, Jon began drawing as a very young child. When Jon was a sophomore in college, he won a $10,000 grand prize in a national competition for disabled artists. In 2005, Jon graduated from the University of Wisconsin-Oshkosh, receiving a Bachelor of Fine Arts with an emphasis in drawing, painting, and sculpture. Mr. Wos has exhibited his various pieces of artwork throughout North America.

Tell us a bit about yourself!
I was born in 1981 in Green Bay, Wisconsin. My family lived about a half hour drive north of Green Bay on a dairy farm near a town with a population of less than 500. It was very rural, so many of the activities that most kids engaged in, were pretty physical, and it could be hard for me to keep up. Especially when I had a fracture. Out of all the things I did to keep myself busy when I was in a cast, creating visual art of any kind was something I loved to do very early on. Whether it was drawing, building blocks, or doing crafts, creating things gave me great joy.
And I needed as much joy as I could get, because there were a lot of fractures early on. Most of the fractures were of both femurs and my right arm. I had plates put in and then eventually rods when I was in my late teens.

But after all that, it has been more than 20 years since I have had a fracture. Family, friends, and creating art is what got me through all those years of fractures. My fracture rate declined as I grew up, but my love of creating art did not. I knew I wanted to become a professional artist, pretty early on in my life. So with the strong encouragement, and support of my family and friends, I pursued art as more than just a hobby in my life. I started painting with oil paints around the age of 12, partly due to my religious commitment to watching Bob Ross on TV. Then when I was about 16, I tried stained glass in high school and fell in love with that. This led to experimenting with glass bead making. In college I studied drawing, painting, and sculpture. During this time, I worked on my portrait painting skills as well as studying glass torch work independently in sculpture. I graduated in 2006 with a Bachelor of Fine Art from the University of Wisconsin, Oshkosh. I have been selling my work in galleries and doing commission work ever since.

How do you live?
I live in my own home and have my art studios within. I primarily use a manual wheelchair to get around, but can walk short distances, unaided, thanks to having both my femurs rodded. My house is a ranch with a ramp to get in, which is really all I need, other than a few grab bars here and there. I also have a van with a ramp, hand controls, and a rotating driver's seat that I transfer into. I currently live alone but have friends and family coming by often and they help me to reach things if need be.

In what way has OI affected your art?
Well, my art is affected by OI for obvious physical reasons. My limited size and strength make doing small or medium sized work more practical. Otherwise, I hire others to help me with projects that are too big to handle my myself. I have also broken my right arm and wrist many times which has negatively impacted my range of motion and strength of my dominant hand. So, painting tends to be the most comfortable for me to execute because pencil drawing requires too much of my wrist to accomplish. This fact about my right arm has also pushed me to learn to paint with both hands in some cases.

But OI has also had an impact on my work by pushing me to use my work to deal with and improve life rather than try to escape from life and dwell on the negative. Having been through many painful experiences, I do not see the point in thinking of them a moment longer than what is necessary to overcome them.
What are you currently working on?
Currently I am in between commissions, so I am taking care of smaller projects and making blown glass ornaments and wine glasses while I prepare for my next large commission. I often juggle a few different projects at the same time, working a little bit on each throughout the day. This allows me to work on something while the paint is drying, or glass is cooling. I also find this allows me to get away from projects when they become frustrating or just to have time away and then to come back at a project with fresh eyes. Just before the holidays I finished a 36" x 48" oil painting of a Viking longboat on a stormy sea. Soon I will be starting another even larger commission of 3 paintings that hang together as a triptych, totalling almost 45 sq feet of painting surface.

Why do you do what you do?
There are so many reasons I do what I do. First and foremost, I do it because I love to create, I love the doing, the experimenting, and the fact that after this process, that I enjoy so much, I am left with something that is real, that has not existed before me. And the fact that I can bring joy to others from my creations by doing what I love most, makes it such an easy decision of what to do. It is essentially a spiritual win-win for me as well as my clients.

What themes do you pursue?
I want to use my work to show people that life is worth living. I choose my themes centred around the fundamental values that help people to thrive, in spite of the struggle and challenges of life. Out of the fundamental values that make life worth living, your loved ones and the people you surround yourself with, are at the top. So, I do a lot of portraiture commission work. As well as portraits I also like to create still life paintings that show objects and moments in life that are often overlooked because of their mundane nature. I want people to see that the way they view something changes the way they feel about it, even seemingly boring objects. I have also done many self-portraits around the theme of how to keep one’s passion for living strong. I think this is best done by surrounding yourself with beauty, with your values and what reminds you of them. Which brings me back to my main goal of showing life is worth living if you make it so.

What kind of work do you most enjoy doing?
This is a very tough question for me. I equally love to create portraits, still life, stained glass, and blown glass torch work. As long as I feel like I am bringing beauty into existence, then the medium isn’t necessarily important. So long as the work involves both a mental and a physical aspect to it, then I will enjoy it.

What was the scariest experience in your life?
It was most certainly when I tried to take my own life in college. I have never felt so alone as when I almost lost myself. I didn’t really want to die but had enough of the struggles of life. I was afraid my love of life would never return. This event greatly impacted the goal of my work as it started me on a quest to find what fuels the human soul. And by soul I don’t mean anything mystical or supernatural. I mean the desire to live: a passion for and love of life.
What was one of the happiest moments in your life?
It is a bit harder for me to choose what the happiest moment in my life has been. But it is a tie for the top two. The first was when I had the opening reception for my first solo show at Ripon College. I was asked to fill their gallery exclusively with self-portraits which took me more than a year to prepare for. It was an incredibly fulfilling and happy experience. The second moment that I was equally as happy was the first time my fiancé told me he loved me.

What’s your favourite artwork?
Well, this is an extremely tough question, but certainly one of my favourite paintings is "The Astronomer" by Vermeer. As with all Vermeer's work, the sense of light is wonderful. In addition to that the feeling of eagerness the figure portrays is perfect as well as the sense of wonder the whole painting elicits. I find it to be a perfect portrayal of the human desire to understand.

What is your dream project?
My dream project is a collection of paintings I would love to complete, that centre around the idea of keeping one's inner fire for living always burning bright. I have completed a few self-portraits centred around this theme already. It would consist of a series of oil paintings and stained-glass lanterns. The lanterns are symbols of the inner burning passion people can have for life and would be depicted in the paintings as the sources of a thriving life. My goal in this series would be to remind the viewer that it is of utmost importance to protect and fuel your inner fire to always stay burning.

Do you have any messages for readers of OIFE Magazine or for OIFE?
Well as someone who has dealt with anxiety and depression for the majority of my life, what I have learned is that much of it comes from a subconscious evaluation of the question, "Is life worth it?" And the answer I have come up with is that, yes, it is worth it, if you make it so.

Fundamentally I am the only one that can make my life worth living. No one else can judge what makes life worth living for you and you cannot passively sit and wait for the moments that make life worth living. You have to seek out, or even create, the moments that make life worth it, for you. Find what fuels you individually and protect that with all you can. Just as you protect the physically essential aspects of life, like your heart, your eyes, or the food on the table, your inner fire must be looked after just as carefully. Some may seem to be able to survive without that fundamental burning, but they certainly cannot thrive without it.
TIPS & TRICKS - STOLEN WHEELCHAIR
In January, the electrical wheelchair of Lars Nesset Romundstad was stolen in Oslo city center. A few days later, the chair was found again via a collaboration between the local police, Lars himself and Permobil. Why? Because Lars two days prior to the theft had installed the app My Permobil, which allows GPS tracking of the chair. Maybe something for other users with newer Permobil wheelchairs as well?

FUNDS FOR PAIN PROJECTS IN OI & RARE BONE CONDITIONS
Good news from the National Advisory Unit on Rare Disorders in Norway. Two projects related to pain in OI and rare bone conditions have been funded:
1) Pain in Osteogenesis Imperfecta Classified According to the International Classification of Diseases 11th Revision
2) Developing pain rehabilitation for people with rare bone conditions

INNER DENTAL CARE WITH BBS SUPPORT
Dental issues are the 6th biggest health issue adults with OI struggle with, according to the IMPACT survey. And in many countries access to dental care is problematic. There is a lack of knowledge and people with OI have to pay high costs for dental problems, that are obviously connected to the condition.

The Brittle Bone Society has awarded a grant to the University of Dundee School of Dentistry. The grant will help conduct an important first step in improving oral healthcare for people who are born with OI.

SOCIAL POLICY ACTION GROUP (SPAG).
The new policy group of EURORDIS called the Social Policy Action Group (SPAG) was launched on January 17, 2024. The goal of the SPAG is to raise awareness of the barriers faced by people living with rare diseases, to advocate for policies and services that address their unmet needs, and to facilitate the participation of rare disease representatives in relevant consultations, bringing their voice to specific projects.
PODCAST ABOUT OI & HISTORY BEHIND IT
Do you like podcasts? Do you want to learn more about OI, the mechanisms behind it and the history behind the rare condition in a not too complicated way? Then check out the latest episode of the This Podcast Will Kill You made by two medical students. The episode is 100% about osteogenesis imperfecta including an intro by famous author Natalie Lloyd.

FEMUR FRACTURES & OI
How can we avoid spica casts with femur fractures in OI? Check out this article from Children’s Hospital Los Angeles to see how functional braces are being proven to provide healing equal to spica casts for femur fractures!

OIFE AFFILIATED MEMBER OF ESE
The OIFE has recently been accepted as a Patient Advocacy Group (PAG) affiliated member of the European Society of Endocrinology (ESE). ESE see this as a two-way partnership, since PAGs play an essential role in ensuring that patients throughout Europe have access to the best information about their condition as well as to diagnosis and care.

OI IN CENTRAL AMERICA
This is Nicole Mesén Sojo who is a disability activist from Costa Rica. She has been talking about "inclusive leadership" at the Rotary Youth Leadership Awards, together with youth from El Salvador and Panama.

CONGRATULATIONS VIRGINIE!
We congratulate Virginie-Bros Facer with her new and very important position as the new CEO of EURORDIS. And a big thank you to Yann Le Cam for 25 years of service for the rare disease community.
Research Announcements

Ultragenyx-led ORBIT Study
Ultragenyx, in partnership with Mereo, are leading the Orbit clinical study, which is for individuals living with osteogenesis imperfecta (OI) Types I, III and IV. The purpose of this study is to investigate the efficacy and safety of setrusumab, a monoclonal antibody, for the potential treatment of OI in pediatric and young adult patients. The study aims to understand the potential reduction in fractures as well as other impacts of OI. Study participants are at least 5 but not yet 26 years of age, have a confirmed diagnosis of OI Types I, III, or IV, and are willing not to receive bisphosphonate therapy during the study. Learn more about this study here or visit https://www.ultraclinicaltrials.com/OI

Ultragenyx-led COSMIC Study
The purpose of this study is to evaluate the effect of setrusumab, a monoclonal antibody, against intravenous bisphosphonates (IV-BP) in children living with Types I, III or IV OI. It is also led by Ultragenyx, in partnership with Mereo. The study is focusing on reduction in fracture rate, including morphometric vertebral fractures, in younger paediatric participants as well as other parameters.

Currently enrolling patients aged 2 but less than 7 years old with OI Types I, III, and IV. Learn more about this study here or visit https://www.ultraclinicaltrials.com/OI

For more information on both of these trials, please reach out to trialrecruitment@ultragenyx.com or OIStudyInfo@ultragenyx.com

AMGEN
A multicenter phase 3 clinical trial is being conducted to study the efficacy and safety of a clinical trial drug compared to bisphosphonates in children and adolescents who have OI. The trial is open to eligible children from age 5 to less than 18 years of age who have a diagnosis of OI Type I through IV. The clinical trial will have sites participating in the following countries: Canada, United States, Australia, Japan, Austria, Belgium, Hungary, Poland, Slovakia, Switzerland, France, Germany, Spain, Turkey and United Kingdom. For more information, please visit the clinical trial registry page at: https://clinicaltrials.gov/study/NCT05972551.

POISE 1 (SANOFI)
Sanofi is conducting an early phase study in adults with OI Types I and IV with an anti-TGFβ antibody called SAR439459. This study is called Poise 1 and is a Phase 1 study, where the researchers evaluate the treatment’s safety and determine a safe dosage range.

This study involves a single administration of SAR439459 given intravenously (IV) into the arm, with a 6-month follow period. At this early stage in development, Sanofi is recruiting a limited range of study participants, but we will consider expanding enrollment criteria in future studies. TGFβ is a signaling molecule, which is a way cells communicate and coordinate with each other. Specifically, it is an important part of the bone remodeling environment, playing a role in the balance of forces which remove and build new bone. It even has roles in pain. In OI, signaling related to TGFβ is dysregulated, so controlling that signaling with SAR439459 may be a way to influence symptoms caused by OI.
Participants in the Poise 1 study are not likely to experience benefits from SAR439459, and 25% will receive a placebo, but all participants will help with the scientific understanding of OI and SAR439459 as we prepare for future long-term studies. The assessments in this study include digital, non-invasive strategies to better understand how OI patients move and are active throughout the day as well as direct patient feedback on daily activity and pain. Study participants will be compensated for their travel and accommodation associated with visits to the study site. Such travel and accommodation can be arranged directly by Sanofi or a third-party service provider appointed by Sanofi.

For this early study, our two sites in Europe are located in France. The other sites are in the US, Canada and Australia. Additional information on participating study sites and how to contact Sanofi, if interested, is available under ClinicalTrials.gov NCT05231668.

**DISCLAIMER**
The OIFE is not involved in the design or management of research studies we announce and as such, is neither endorsing nor supporting these studies. The mission of the OIFE is to keep the OI community informed of all relevant studies. This information is made available as a service to the OI community. We are available to answer questions on this or any other research announcements. Please contact the OIFE at office@oife.org if you have any questions.

**Future Events**

**ICCBH**
11th INTERNATIONAL CONFERENCE ON CHILDREN'S BONE HEALTH
22-25 JUNE 2024
SALZBURG, AUSTRIA

**ECE 2024**
26th European Congress of Endocrinology
11-14 MAY 2024
Stockholm, Sweden

**OIFE Calendar**

Ingunn Westerheim (President): president@oife.org
Ute Wallentin & Maria Barbero (Coord. Social Network): socialnetwork@oife.org
Stefanie Wagner (newsletter editor and secretary): secretary@oife.org
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