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Editorial

By Ingunn Westerheim, OIFE president

More than just another survey...

We know you hate surveys. We truly do. Every time you buy an object, order take away, online grocery or come home from a holiday, you get a survey. Are you happy? Unhappy? Do you have something to complain about? Would you like to recommend our app? Do a review? Please, please, please provide us with your feedback! We need it to improve our product and services.

We therefore completely understand that survey fatigue is a real thing. And that you are all very tired of filling in surveys and questionnaires. Covid-19 for sure didn’t make it any better.

But unfortunately, this is one the many dilemmas the OI-organizations struggle with. Sometimes we really really really need big data and better statistics on a certain topic.
We need it for grant applications, for policy work and for our patient experts. We need it to improve our socalled “product” – which is the treatment and services you get in your countries and local hospital.

What is the best way to get big data? Unfortunately...through a survey. And for this we need the help of our member organizations, their individual members and sometimes from the whole international OI-community.

Last week we launched the English version of the IMPACT survey, and tomorrow seven more languages will be added. It’s a joint research project we have been working together with the OIF and Mereo on since April 2020. Before the survey itself was created, the company Wickenstones did a very thorough literature search and review of what the biggest knowledge gaps in OI-research were. Their conclusion was that significant knowledge gaps exist.

We feel that IMPACT is much more than just another survey. It’s the very first global research project exploring the real impact OI has on people’s lives. It is aimed at capturing and quantifying the true challenges of life with OI to enable better diagnosis, treatment and care, and to support availability of potential future treatments for OI. It will give us insight in which challenges people with OI deal with in different countries. And about differences between countries, when it comes to access to treatments, mobility aids & services for people with OI and their families.

Several rare disease federations similar to OIFE, are doing similar impact projects, simply because they see that access to orphan drugs and improved services for people with rare conditions relies on better data. Therefore our goal is to make IMPACT the biggest and best OI-survey possible. Bigger and better data matters – and with your help we can develop it.

This edition of OIFE Magazine is a special edition on databases and registries, which are also tools to fill the many knowledge gaps that exist for OI. But alas – we often encounter similar problems as for surveys. If registries and databases should give us new knowledge – we need people to contribute with their data. This includes clinicians – taking time to document their encounters with OI-patients. But it also requires input from people with OI and parents.

We need to fill in patient reported outcome measures (PROMS), which are used to assess our health status at a particular point in time. Do you have more pain now? Less fractures? Did the treatment improve your mobility?

And patient reported experience measures (PREMS) are also important. These are questionnaires measuring perceptions of your experience whilst receiving healthcare. Are you happy with the way treatment is being performed? Did you feel that the doctor had enough knowledge?

If we are going to reach a higher level of knowledge on OI and better treatment and services, we therefore need to take a collective deep breath and just keep on filling in surveys and questionnaires. Doctors need to document the boring stuff. OI-organizations need to advocate for more regular follow-up and centralized & coordinated care of both children and adults with OI. Because – if people are not seen by the same hospitals/professionals, no expertise will ever develop. And no systematic collection of data will happen.

Only by working together we can make it happen. And remember...IMPACT is more than just another survey. It’s a unique opportunity to increase the knowledge about OI on a global level.

Join us and make an impact!
Have an IMPACT on the future of OI research, treatment & care

**What**
The IMPACT Survey is an international research project aimed at capturing and quantifying the real impact OI has on the lives of people with OI and their families.

**Why**
Results will be used to enable better healthcare services for both children and adults and to support availability of potential future treatments for OI.

**Who**
The IMPACT Survey is for people with OI and parents/caregivers of children with OI.

**When**
Launching end of June 2021 and running until 10th September 2021.

Get involved
and find out more at www.impactsurveyoi.com
What is the OIFE doing?

Since the last magazine, many meetings with different stakeholders have taken place, new collaborations have been established and other projects have come to an end. More than ever is going on in OI-research and the OIFE is getting more and more requests to provide support and input from the patient perspective to different projects. Every year we forget how much time it takes to produce annual reports, financial reports and to plan an Annual General Meeting (AGM). Especially when you combine it with a seminar about news from research and other ongoing projects. But we did get through it this year as well. We’ll leave the highlights from the AGM until our next edition, which we hope will be a special edition on psychosocial aspects & OI.

Meetings and events

Videocalls & webinars in the last months have included many meetings related to The IMPACT survey, The Photo Voice Project (#RareBoneMobility) and the Pain & OI brainstorming project. Ingunn has also attended the monthly OI TeleECHO webinars hosted by the OIF. There have also been videocalls (VCs) with OIFE members, volunteers and individual members of OIFE MAB in addition to these videocalls and online events:

- EC-meetings March 16th, April 18th (expanded), May 18th, June 8th and June 15th
- Blueprint Genetics March 17th (IW and BVD)
- EuRR-Bone Annual Meeting online, March 25th (IW, TW and RTS)
- Key4OI Update March 30th (IW and more)
- Alexion (Walter Atzori), March 31st (IW)
- SBB (Belgian consultancy company), April 1st (IW and BVD)
- Project group OI Variant database, April 9th, May 12th, June 3rd (IW and TW)
- XLH Alliance (A stronger BOND between us), April 12th and May 10th (IW)
- Nordic Rare Disease Summit, April 12th – 13th (IW)
- Ultragenyx, April 14th and May 26th (IW)
- Patient Expert Summit for Novadip Stem Cell Technology, April 21st (IW)
- Webinar “Ways to prevent your non profit from being hacked”, April 27th (AW)
- Steering Committee IMPACT survey April 30th (IW and TvW)
- Advisory Committee of Norwegian Skeletal Dysplasia registry (IW and RTS)
- Retina Pigmentosa International – sharing experiences, May 7th (IW)
- OIFE Wishbone Day Party, May 7th (IW, AR, DL, BVD)
- ASMBR Webinar “Emerging therapies in OI”, May 25th (IW)
- VC BOOSTB4, May 25th (IW)
- OIFE MAB-meeting, May 31st (IW)
- TOPAZ PPI event (IW was invited speaker)
- Orphan drugs conference (European Expert Group on OD Incentives), June 11th (IW)
- Sanofi introduction, June 15th (IW)

OIF INVESTIGATOR MEETING

Usually the annual Investigator Meetings organized by the OI Foundation take place in Chicago. The target group is American researchers. But the last 3-4 years the OIFE has sponsored attendance for one researcher from Europe, to report back to the European community. The event in 2021 took place on Zoom and Tracy Hart was kind enough to invite both Dr. Lars Folkestad and Dr. Oliver Semler in addition to Ingunn Westerheim as an observer and patient representative. Read a summary another place in this magazine.
**31st ERTC WORKSHOP**

In the context of the ongoing consultation on the new public health programme from the European Commission, the 31st European Round Table of Companies workshop convened patient representatives, policy makers, regulators, industry and payers to focus on key elements of the EU Regulation on orphan medicinal products. Discussions were held on how multi-stakeholder collaboration can help to bridge public and private research and how important it is to ensure that an early dialogue with regulators, health technology assessment (HTA) bodies and payers is taking place. The discussions reflected on a common European approach that highlights the importance of continuous data generation to support health systems in providing equitable access to rare disease treatment and care. Ingunn Westerheim was invited as a speaker from OIFE, to talk about how the OI-community is preparing for future situations with European and national discussions on approval and reimbursements of new potential medicines and advanced therapies for OI, where the IMPACT survey is our main tool.

**EURORDIS MEETINGS**

After Ingunn’s talk at the ERTC, EURORDIS contacted the OIFE to hear more about the IMPACT survey. They thought IMPACT could serve as some kind of template project for other rare disease groups who need to collect big data for advocacy and access to treatment. Ingunn attended a meeting with EURORDIS staff about this on April 9th. Representatives from OIFE and our member organizations have attended several meetings and events hosted by EURORDIS the last months. We also initiated a meeting ourselves and on May 12th Ingunn Westerheim from OIFE and Astri Arnesen from the European Huntington Association (EHA) hosted an informal workshop for the rare disease federations, who were interested. Topics were sharing of experiences on burden of disease projects like the IMPACT survey and challenges and opportunities of running a rare disease federation in Europe. On May 13th and 14th we were several who attended parts of the EURORDIS Membership Meeting, which included tips on how to engaging organize online and hybrid events. There were also discussions on research, registries and access to orphan drugs. Ingunn represented OIFE at EURORDIS Annual General Meeting on June 10th, where long term strategy and policy work to achieve a new European action plan on rare diseases were the most important topics.
OIFE MEDICAL ADVISORY BOARD
On May 31st we hosted our first MAB-meeting in 2021. The meeting included a short update from OIFE about activities and projects, including the IMPACT survey. Ingunn also gave an update about ongoing initiatives on registries, databases and networks and asked the MAB for advice on what role OIFE should take and which knowledge gaps we should focus on. There were also discussions on how OIFE can support collaboration and networking between OI-researchers in Europe and conclusions were made that an investigator meeting similar to the one they have in the US, is something we want in Europe as well.

“SHINING A LIGHT ON OI” WEBINAR ON THE TOPAZ TRIAL
On June 8th Ingunn Westerheim from OIFE, joined Patricia Osborne from the BBS as a speaker at the webinar “Shining a light on Osteogenesis Imperfecta” with an update about the TOPAZ trial and OI-research. The event was hosted by the university of Edinburgh and included an update from professor Stuart Ralston about the TOPAZ trial and a testimony from one of the patients who is taking part in the clinical trial. Read an update on the trial another place in the magazine.

Meet the OIFE delegates

Malene Sillas Jensen, Denmark

My name is Malene Sillas Jensen, I’m 26 years old and I have OI type 4. I’m a delegate from the Danish society for Osteogenesis Imperfecta.

Tell us about the organization you represent!
The Danish name of our organization is Dansk Forening for Osteogenesis Imperfecta (DFOI). We have around 300 members and the organization is entirely run by volunteers.

What do you do when you’re not doing OI-work?
I have just finished my master thesis at Aarhus University where I have been studying education science. I still have one semester left before I’m finished with my degree. I’m very active in the Student’s council at my university, and I’m currently a board member at the center for teaching environment under the Danish ministry of Education. Other than that, I have just started being a volunteer at the danish child helpline and I find that very intriguing. In my spare time I like to knit, hang out with friends and travel.
If you were the OIFE president for a week, what would you do/change?
I would try the raise more awareness about how awesome OI people are. Personally, I get very inspired by meeting or hearing about OI-people doing things that I never thought was possible.

What is the most important job for the national organizations and OIFE?
My national organization has been and still is very important to me. I have met some of my best friends through different meetings, and I know that it is the same for my parents and siblings. I therefore think that the most important area for the national organizations is to facilitate meetings for parents, siblings, OI-people and even grandparents to meet people who are in the same situation. I think that the most important job for OIFE is to create a forum for the national organizations to share knowledge and experiences. But I also think that OIFE is important for sharing information about new treatments, drugs, knowledge from different European and American studies and so on.

Willemijn Döpp - van Berkum,
The Netherlands

I am Willemijn. I am married with Manuel, I live in Emmen, in the Netherlands with our two dogs: Pucky (means little), a Jack Russell terrier and Pluis (means fluff) a Yorkshire terrier.

I was born in 1983 and when I was six weeks old I became a member of the VOI. In our family I am the only one with OI. I have type 3. I can stand and walk with support. But being only 93 cm long I use my electric wheelchair all the time. I didn’t have lots of fractures the last 20 years, but tiredness and muscle strain is a constant work in progress.

When I was young, my father was in the board of the VOI and he did go to the first international meetings. I was raised with the VOI, and it meant a lot to me and my family. As a child we had fun activities like dressing up and watching Disney movies. When I was a teenager, I came to the annual meetings just to meet my friends. I also attended youth weekends and International Youth weekends which are some of the greatest memory’s I have. It has always been a great adventure to go to an international youth weekend and I learned a lot of meeting youth from different countries.

Please tell us about VOI!
Since October 2020 I am a board member of the Vereniging Osteogenesis Imperfecta (VOI) of the Netherlands. We have 292 members, and we are all run by volunteers. At the moment, we have a project going on to find out where people with OI find their expertise (doctors, specialists, physiotherapist and so on) so we could help others to find professionals with knowledge on OI. We have a completely new board since December and it takes time to learn how everything works. There are lots of things to review and think over, like our association statutes which are not adapted since 1996.
What do you do when you’re not doing OI-work?
I have a degree in social law and a bachelor theology. Because I became too tired all the time, I had to quit my paid job. I now do volunteer work for a Christian political party in our local council and I am an active member of our church. Besides that, I craft a lot: knitting, crochet, sewing, painting. There is just too much I like to do. I think I am a serial hobbyist.

In your opinion - what is the most important job for the national organizations?
There are two and I cannot place one above the other: first the contacts with other people with OI. I think it is important to find understanding with few words and the option to truly learn from each other’s experiences, which I only find possible with other OI-people. The other is improving the health care for people with OI in our country by discussing medical treatments, having good contacts with specialists, and giving information and share experiences. The medical world needs us to know what to do.

In your opinion - what is the most important job OIFE should focus on?
Having international contacts and learning from other countries is very important in my eyes. Learning that living with OI and the health care can be different in different countries. We can learn from each other and use each other’s experiences. I think the youth weekends are very important to give youth a chance to experience this and to give them a change to travel and see something of Europe, meet other young adults and have a little adventure.

OIF Investigator Meeting

Summary by Ingunn Westerheim, Oliver Semler and Lars Folkestad

The OIF investigator Meeting is normally held in Chicago, but took place online on April 15th 2021. The program chair this year was Dr Deborah Krakow who is Professor and Chair of the Department of Obstetrics and Gynecology at UCLA. This year’s program had a clinical focus and not so much on basic research. Topics included:

- Findings from the Brittle Bone Disorders Consortium (BBDC)
- Orthopedic research – non union fractures
- Cardiovascular and pulmonary health
- Biomarkers in OI-research
- Dental issues
- Mouse Models to study pain as disease outcome
- Patient Centered Outcomes Research (PCOR)

A first presentation was given by Misty Richards from Los Angeles about the impact of the Covid pandemic on mental health in OI. In general, the incidence of depression has increased during the last year. The rate of anxiety disorders tripled, and the prevalence of depressive disorders even quadrupled in the US population. A special problem is that many patients who had mental problems already before the pandemic have stopped their therapy due to lockdowns etc.
Chronic pain is a risk factor for depression, and it was assumed that due to reduced availability of medical treatment and reduced possibilities for physiotherapy or physical training the pain level in persons with OI increased. Additional stressors like fear of fractures and insufficient medical care in case of injury aggravated the risk factors. Therefore there is a recommendation, which is also supported by the OIF to implement mental health strategies in the daily care of people with OI and to focus on additional goals like:

- Minimize fracture risk and especially chronic pain
- Realize and treat mental health co-morbidities early
- Stay in contact with other people in your community and with other OI people
- Prepare for a potential hospital stay and check with your doctor what needs to be "prepared" regarding the pandemic.

An orthopedic talk presented by Dr. Spencer focused on the issues of «Non-Union Fractures». Non-union is a failure of bone healing 6-9 months after a fracture or an osteotomy after surgery. Even in a well healing fracture an ongoing remodeling of the bone may take many years before the original structure is re-built by osteoblasts. To decide if a surgical treatment is necessary, it is important if non-union is only a radiographic finding, or if the patients is affected by pain and instability of the extremity. It was also emphasized not to stop bisphosphonate treatment in children due to a non-union, regardless of the reason being an osteotomy or fracture. To prevent non-unions, unstable fracture treatment should be avoided. During and after surgery a good blood supply in the area is required. In case of an asymptomatic non-union which is only detected on radiographs, no surgical intervention or other treatment is necessary. A surgical treatment is only required in cases of severe pain or impaired mobility due to the non-union. During the discussion after the talk, it was stated that very little experience in the use of bone morphogenic protein (BMP) to increase fracture healing in patients with OI is available.

Prof. Judge from University of South Carolina gave a talk about the involvement of the cardiovascular system in OI. The most critical points are valve diseases, dilatations of the aortic root and aneurysms in combination with hypertension. In different studies and case series a moderate higher incidence of insufficiencies of the mitral valve has been detected in up to 7-10% of patients with OI. Therefore, it might be recommended to check cardiac function and aortic root in patients with OI specially when patients have a comorbidity of high blood pressure.

Preliminary data on a respiratory study was presented. The researchers wanted to investigate if respiratory impairments are directly associated with OI or if these problems are only consequences of scoliosis, chest deformities and impaired cardiac function. They included adults with genetically confirmed OI and performed lung function tests, chest CT, echocardiography, and tests to assess physical function of the probands. The first results strengthen the hypothesis that respiratory problems are intrinsic to OI and are not just a complication of other co-morbidities. The chest-CT showed a thickening of the bronchial wall which needs to be investigated further.

Dr. Laura Tosi gave an update on the Patient Centers Outcome Research (PCOR), where the goal is to have community members active through the whole process from determining research questions, interpreting results and dissemination etc. She praised the OIF for reorganizing their services quickly and for organizing 12 videocalls connected to Covid-19 in 2020, which were shared with the worldwide OI-community on YouTube. She also presented some data from the OIF Covid-19 survey and one of the most worrisome facts was that 50% of people with OI who had Covid-19 reported symptoms longer than 4 weeks. People with OI had also become less active during the lockdown, but the vaccination rate is better in the OI-community than the average US
population. She encouraged all people with OI to join the OIF Registry, to make it easier to recruit people to surveys and research. She also stressed that future surveys need to have more diversity and better distribution in age, sex and race. Click here to join: https://www.rarediseasesregistry.org/Registration/Registration/RegStart/9797

The panel discussion at the end included three very different topics. Dr. Charlotte Philips asked if the OIF could play a role in saving the different mouse models of OI and raised the question if there should be OI-research in bigger animals like sheep and dogs. Dr. Eric Rush was frustrated about the lack of knowledge on challenges of adults with OI after a certain age. There is also a lack of good treatment options to gastrointestinal problems, which he stated was surprisingly common. We also need more knowledge on pain and muscle weakness, which can cause functional limitations. As the last introduction to a short debate, dr. Frank Rauch emphasized that new treatment methods need to offer something more than what bisphosphonates can offer today. New drugs need to produce more bone and bone of better quality. And we need to develop better methods of measuring when a treatment is efficient or not.

Research on the potential therapy Fresolimumab (TGFb)

Interview with Brendan Lee, M.D. Ph.D., Baylor College of Medicine, Houston, Texas

I am a pediatrician and clinical geneticist who has engaged in basic, translational, and clinical research in skeletal dysplasias for over 25 years. Our group has been focused in identifying the first recessively inherited OI genes, understanding how mutations in these genes cause OI using cell and mouse models, and testing new therapies in OI as part of the National Institutes of Health (NIH) Brittle Bone Disorders Consortium (BBDC). The OI Foundation (OIF) has been a primary partner in all these activities. I have had the honor of serving on the OIF Medical Advisory Committee as well as chairing previous research meetings of the OIF.
Can you tell us about the research project on Fresolimumab?
The project’s goal was to identify common mechanisms of how mutations in collagen and collagen processing enzymes cause brittle bone and then translate this into a potential “targeted” therapy more effective in OI. We hypothesized a therapy focused on the underlying changes in OI might be more beneficial, than therapies that only increase bone mass. We discovered that an important growth factor called TGFb (beta) is elevated in OI bones and that by reducing this level, we may have beneficial effects not only in OI bones but also soft tissues like the lung.

Who came up with the idea and when did it start?
The idea came to us when we observed a lung picture in an OI mouse model that was reminiscent of other situations where TGFb was elevated. We then went on to test this in OI mouse models (COL1A2 mouse model and the CRTAP mouse model). We have now moved this preclinical study into a clinical trial as part of the BBDC, studying the safety of an anti-TGFb antibody called Fresolimumab. The aim of the study is to test the safety of Fresolimumab in OI type III and IV patients. We are also studying the effects on bone and other tissues. The antibody has been studied by Sanofi (and previously Genzyme) as a treatment of cancer and fibrotic disease. We are using it at a much lower interval than previous studies as bone turns over more slowly than soft tissues and cancers. This increases the safety profile of the drug.

And how is it progressing?
The study is in two parts. The first part or stage A is a single dose study. We have completed that, and we are now in the second part which is Stage B. Here we are doing repeated injections either every 3 or 6 months. We follow bone mass by DEXA scan and safety measures. In Stage B, we will also evaluate quality of life, mobility and pulmonary function. We are about to submit the paper describing Stage A results. The drug has had significant effects on increasing bone mass in some but not all patients even after a single dose at the 3 and 6 month time points. This was a very impressive result. It was also very well tolerated.

We have now recruited subjects for Stage B, the repeated dose study. Unfortunately, COVID19 has affected our ability to recruit as patients have not been able to safely travel as needed for the study. We hope the study will encourage companies like Sanofi to pursue clinical studies of efficacy (or phase 3 studies) that may lead to FDA or EMA approval.
Who is sponsoring the project?
The study is sponsored by the National Institutes of Health first as research grants to my group for the preclinical study and now as part of the Brittle Bone Disorders Consortium (BBDC) of the Rare Diseases Clinical Research Network (RDCRN). Sanofi, who is the maker of the antibody used in our trial, donated the antibody to the study and provided data to help with our regulatory applications. They do not participate in the performance, design, or interpretation of the study. This is purely what we call an “Investigator-initiated study”. The OIF also supports the project as they support all the activities of the BBDC.

What is the difference between Fresolimumab and other antibodies being investigated in OI?
Fresolimumab blocks the growth factor TGFb. Setrusumab and romozosumab blocks another protein call sclerostin. There are many different antibodies that each block specific proteins. Denosumab is another antibody that blocks RANKL, a growth factor that stimulates bone resorbing cells. This is also being studied in OI.

OI-registries in the USA

Interview with Brendan Lee, M.D. Ph.D., Baylor College of Medicine, Houston, Texas

In Europe we are developing the EuRR-Bone - which OI-registries do you have in the US?
There is a contact registry with ca 3000 individuals signed up, which is sponsored by the OI Foundation (OIF). The main purpose is to keep patients informed on development in OI, but it is also a mechanism to engage patients in research as full partners. There is also natural history of close to 1000 OI patients which is the core project of the Brittle Bone Disorders Consortium (BBDC). The OIF finances the contact registry and the National Institutes of Health (NIH) together with the OIF support the natural history study as part of the BBDC.

Can people from other countries than the US sign up for the contact registry?
The contact registry is open to anyone in the world and we encourage all to join. It is stronger if it includes OI individuals from all over the world.
OI is taken care of differently in different parts of the world and understanding commonality and differences in practices is very important. Similarly, OI’s natural history is different in different parts of the world and understanding how different environment affects this is critical.

**What about the natural history study?**
Natural history studies are important. Without understanding how a disease evolves with time, we can never know how to prevent and treat complications of the disease. Similarly, we would not be able to develop appropriately designed trials to test efficacy of different interventions. There is now close to 1000 individuals in the study and some people have been followed close to 7 years. We are still recruiting, especially the rare forms of OI. We usually see patients once a year to once every other year. We do many studies that would normally be done as standard of care. We try to align the protocol to standard of care, to minimize burden on families. We collect the data in a systematic fashion which is what makes it a research study. When it comes to patient reported outcome measures (PROMS), we have studied PROMIS, PODCI, and SF12 versions of PROMs.

### BBDC Studies

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**Do you have patient involvement in the project?**
We have extensive involvement as partners in the BBDC. Tracy Hart the executive director of the OIF is a co-principal investigator of the BBDC. The OIF also leads the patient engagement and training elements of the BBDC. Many of our studies beyond the natural history study include focus groups with OI patients.

**What have been the most important findings from the natural history study so far?**
The study is by far the largest study of OI patients to date and the information sometimes confirms what has been reported in smaller studies, sometimes changes their conclusions, and sometimes identifies completely new issues in OI. I would direct those interested to go to the BBDC or OIF websites where the publications are listed. There are publications on growth, bone density, craniofacial and dental malocclusion, patient reported outcomes, hearing, mobility, and pulmonary function just to name a few.

**In your opinion - where are the biggest knowledge gaps in OI?**
The biggest knowledge gaps are still how mutations in collagen and all the other genes actually cause brittle bones and non-skeletal issues. This might sound surprising but knowing which genes that cause a disease, is only the first step in really understanding what the disease affects and how it occurs at a tissue level. This is why natural history studies and registries are so important. It is also why supporting basic science studies is very important.
The European Registry for Rare Bone & Mineral Conditions (EuRR-Bone)

Interview with Natasha Appelman-Dijkstra, M.D. Ph.D., Leiden University Medical Center (LUMC), Netherlands

Who are you and what is your relationship to OI?
I am Natasha Appelman-Dijkstra internist-endocrinologist in Leiden University Medical Center and specialized in Bone and Mineral Disorders and thus treating patients with OI. I have worked in the Leiden University Medical Center (LUMC) for almost 10 years now and since the founding of the European Reference Networks (ERNs) our center has been involved in the European Reference Network on Rare Bone Diseases (ERN BOND). Since 2020 I am the coordinator of EuRR-Bone, where OI is an important part.

How did it start?
The EuRR-Bone project started in April 2020 officially. During the summer of 2019 we wrote the grant proposal for the EU to get funding for the registry. Faisal Ahmed is the lead for EuRRECa registry, which is the registry for the European Reference Network on Rare Endocrine Conditions (ENDO-ERN). Together with Faisal’s help and the connection to EuRRECa, we were able to develop a plan and got everything up and running rather quickly. At this moment we are funded for three years. In the meantime we are developing a sustainability plan.

Who owns and maintains the registry?
I am the custodian of the data, but in the end the patients always own the data. People can retract their information anytime. At this moment the servers are in Glasgow, Scotland, but we expect to host them in Leiden (The Netherlands) anytime soon. Maintenance is performed by our database creator and a team at Leiden University.
What is the purpose of the registry?
To collect data on rare bone and mineral conditions to learn more about the natural history of the different bone conditions, to evaluate the level of care throughout Europe and to gather patient related outcomes (PROMS). In the future the registry might be used for active surveillance of newly introduced drugs. It can be used to quickly identify potential subjects for studies and patients can use it to report on their disease and engage with the caregivers involved in the registry. Everybody who fills in a data request form can get access to the data if the request is deemed ok by the data access committee.

Can you explain about the different parts of the registry?

Core dataset
This collects a core dataset with minimal information on patients: age, sex, way of diagnosis, mobility and height, EQ5D (quality of life).

The E-Rec
Through the E-Rec we are counting new cases seen in a center for rare bone conditions.

The OI-module
This is a disease specific module on OI. So next to the Core dataset, we will collect more details specifically on OI with the purpose to have a centralized registry throughout Europe and beyond with clinical and patient info on OI.

Covid-19 module
This module is counting new cases of covid19 in patients with a rare bone disease.

Who can contribute with data to the various parts?
Anyone who considers themselves as an expert center can contribute with data.

Are you thinking of developing some kind of "patient facing platform"?
Yes, patients can already have access to their data and fill out PROMS. The next step would be that we could also use that platform perhaps to pass information to patients etc.
Do you have some kind of interaction with other OI-registries?
We have interaction with the RUDY registry (UK) and iFOPA (registry for FOP), but not with specific OI registries yet. Read more about RUDY another place in the magazine!

What has been the biggest challenge when developing a registry like EuRR-Bone?
Getting everybody moving into the same direction and sometimes the lack of consent on definitions and local differences of approaches.

It's been a year with EuRR-Bone now - what are you most happy with so far?
That the e-rec is working, core is being set up and we were able to decide on what to include in the modules. Despite the COVID 19 pandemic, everybody has been doing a great job.

Which impact did Key4OI have on the development of EuRR-Bone?
Key4OI has not impacted EuRR-Bone in general, but it did have an impact on the development of the OI module. Since Key4OI already went through all the phases with focus groups, we were able to have a quicker view of the potential items to collect. We were also informed on discussions that were already done on certain topics. It also made it clear for us, that we should decide on fewer items to collect, to ensure commitment from all centers in Europe. In addition, it made it clear that our niche should be to collect data that were not yet being collected.

What are the drop in sessions for?
Every other Friday at 14.00 CET, we have free drop in sessions online. They are there to give people answers or help with the registry or you can just drop by for a chat about the registry. Find out more on https://eurr-bone.com/

If you had a magic wand to make your job with EuRR-Bone easier – what would you change?
I would like to have a fulltime datamanager/programmer, perhaps also an EU liaison or so to help people setting their ethics up in their own center and help them to start registering.

Any messages for the readers of the OIFE Magazine?
I have to say that I am very impressed by the work OIFE is and has been doing. Not only the commitment from patient representatives in ERN BOND and EuRR-Bone, but also now with the help from OIFE with the LOVD OI variant database. I am really looking forward to intensify our collaboration with the EuRR-Bone module on OI and also to possible future projects.

The creation of the OI-module in EuRR Bone

The OI working group led by Dr Wolfgang Högler (photo) had as mandate to suggest clinician reported outcomes (CROMS) and patient reported outcomes (CROMS) for children and adults in the OI-specific module. Ingunn Westerheim, Rebecca Tvedt Skarberg and Taco van Welzenis represented OIFE in the OI working group. Dagmar Mekking represented Care4BB and Claudia Finis (DOIG). The OIFE representatives used input from OIFE’s Adult Health Facebook-group to have input from the larger community during the process. We asked some of the people involved in the process to develop the OI-module about their thoughts on the interaction between patients and professionals, the process and the outcomes of the process. And what their thoughts are on the biggest knowledge gaps in OI.
Claudia Finis, Germany
I’m a psychologist from Germany. My daughter and I have OI. I found the interaction between physicians and patients beneficial. Even if there was not always an immediate agreement, an important process was carried on here. Incidentally, the doctors also often had different opinions between each other. I was very positively, surprised at how committed some people were to the decision-making process. Due to structural requirements, we had to limit ourselves to very few topics. I think we all would have liked to have considered more. For me, the focus right now is on the potentially life-threatening complications and effects of OI. What does it help to strengthen our bones into old age if we die long before from other symptoms caused by OI?

Dagmar Mekking, Care for Brittle Bones, Netherlands
I am a mother of a 15 year old daughter with OI and director of the Care4BrittleBones foundation, which aims to improve quality of life for people with OI through research. There was a good dialogue between professionals and patients, and both sides listened to each other and learned from each other. I really liked the leadership style of Dr. Högler who kept the group focused. Well done!

Given the short amount of time, a lot was achieved. So I am ok with the outcome. I think EuRR-Bone is absolutely critical for all of us, going forward. Given its importance in the long run, I wished we had applied even stronger scientific approaches to select the best outcome domains and the right measures based on evidence or anonymous survey (Delphi). I really hope everyone who can, will provide input to EuRR-Bone to help understand OI better than we do today. In my opinion the biggest knowledge gaps in OI are psychosocial aspects, pain, fatigue, lung issues and also rodling surgery.

Prof. Dr. med. Ralf Oheim, Germany
I am an orthopedic and trauma surgeon working as an osteologist in Hamburg, Germany. The perspective of people with OI and other rare bone conditions is especially valuable and highly relevant to this project. I had the feeling that we discussed the topics as equals and was very impressed by the professionalism of the ‘non-professional’ participants. Working together with many strong-minded people does always mean to make compromises, which is perfectly fine! But, when creating a database, it is very hard to find the perfect balance between collecting as many (relevant) data as possible and the suitability of the system for clinical routine. The length and intensity of our discussions could be frustrating. Even issues that seemed pretty simple and clear to me got quite complex due to the different perspectives of the participants. This showed me once again how important such discussions are! In my opinion the knowledge gap is specific OI treatment options and the effect of our current treatment regimens on the quality of life of OI patients.
The systematic spiral – how clinical work, registries, research, guidelines and quality improvement are connected

Interview with Lena Lande Wekre, M.D. in the Skeletal dysplasia team at TRS National Resource Centre for Rare Disorders, Norway

Who are you and where are you currently working?
My name is Lena Lande Wekre and I am a Medical Doctor in the Skeletal dysplasia team at TRS National Resource Centre for Rare Disorders. I’m involved in the project of developing The Norwegian Registry for Rare Congenital Bone Diseases, which is a combined quality- and research registry where our endeavour is to map persons with rare bone conditions and follow them over time in a lifetime perspective.

I am working together with physical therapy specialist and coordinator for the registry, Anne Marthe Svendsen Rysst-Heilmann and Associate Professor Joachim Horn at the Section of Children's Orthopedics and Reconstructive Surgery, Oslo University Hospital, OUS (both in photo).

What is the purpose of the Norwegian registry?
The main purposes are

- To provide data for research at a national level within different subgroups of patients with skeletal dysplasias. By this we hope to increase the knowledge of epidemiological conditions, disease mechanisms and interactions between genetic, environmental and clinical factors affecting the disease.
- To secure the quality of drug therapy and other treatment.
- To identify, implement, monitor and optimize treatment and services for persons with rare bone conditions in Norway.

An important side purpose is to adapt our variables to those, which will be considered for the European registry (EuRR-Bone), to give us the possibility to map and compare different aspects of different diagnoses and treatment given in different countries.

In which way does this registry/database differ from the patient database you have in TRS?
The database at TRS is more a patient record system and does only contain an overview of those who want to register at the centre and use our services. The TRS database does not register data systematically over time as you do in a registry.

How is the registry managed and funded?
The registry is a collaboration between the Section of Children’s Orthopedics and Reconstructive Surgery at Oslo University Hospital, who is the owner of the Registry, and TRS National Resource Centre for Rare Disorders. The registry is funded by Oslo University Hospital (OUS). However, TRS has so far funded 20% of costs related to a registry coordinator to facilitate the collaboration between the healthcare service at OUS and the competence service at TRS.
**Who can get registered and how?**
In principle, all persons in Norway who have a rare skeletal disorder, all age groups included. However, we will probably try to start with the same diagnostic groups as EuRR-Bone (OI, XLH, Achondroplasia, FD/MAS and MO). The patients will be asked to register when coming to a consultation at the Children’s Orthopedic department or to one of the special outpatient clinics for OI, Achondroplasia or Skeletal dysplasias. We will also ask all the users (patients) of TRS, who are relevant for this registry, if they want to register. It will also be possible to contact us directly, or through your GP, or other doctor.

**In what way do you get the data?**
We will use a combination of historical data from the patient’s records, and new data delivered by the clinicians during a consultation. Then we will have patient reported data from the patients themselves, filling out several forms.

**What is the biggest challenge when setting up a new registry?**
To decide what we want to know – which, and how many, data variables we should collect. And, to get the best possible coverage. Which in turn requires that both professionals and patients know about the registry – and use it.

**Do adults with OI have see a specialist on a regular basis for a registry to work?**
It would definitely help if adults could also see a specialist responsible for a holistic follow-up on a regular basis. For the time being, we have to collaborate closely with the person having the diagnosis and their family doctor/GP. We have not yet decided if we will send out a follow-up survey regularly to those who are registered (ex: every 3rd year) to collect updated information.
Are you planning to use Key4OI in your new registry?
Yes, we will use/collect most of the data from Key4OI, like the variables about the diagnostic process, fractures, surgery, treatment, function in daily life etc. We will also try to use the same PROMS (patient reported outcome measures) as described in Key4OI (for example for pain, fatigue and social functioning) among other things to avoid duplication of work – both for professionals and for those who have the diagnosis.

You once said that "everything is connected" - outcome measures, registries, clinical work and guidelines - what did you mean by that?
I think I mean exactly that. Everything is, or should be, connected. One decision should always be based on another. I see the ideal follow-up of people with OI as a circle, or maybe more like a spiral, which begins and ends with the person who have the diagnosis. In other words. If you see several patients with a specific diagnosis at your clinic, do the clinical examinations and treatment systematically! Collect the information in a registry and use this information for research and quality improvement. Then update the treatment protocols and guidelines based on your findings. After that you go back to your patients and use the updated version. Then you have gone through the circle. But every time you do it, you start on a higher level – hence the spiral.

Will the new Norwegian registry be connected to any international registries?
Yes, as we said earlier, we do hope to connect with EuRR-Bone. We will also look into more diagnosis specific registries internationally and see whether it is relevant to compare data or do projects together.

What are the biggest knowledge gaps in OI today?
Compared to what we knew 10-15 years ago, we have much better knowledge regarding several areas concerning OI today. However, there is still a way to go to get enough and systematically collected data, which may form a basis for creating the best guidelines for treatment and follow-up across borders. I think some of the biggest knowledge gaps today are knowledge about soft tissue problems, women’s health and sexual challenges for people with OI. Another gap is more unified treatment protocols for both adults and children.

Any messages for the readers of the OIFE Magazine?
Dear friends, if the registries are to be as good and useful as possible, then both professionals and people who have the diagnosis must pull the workload together. We all have to contribute to new, systematic and important knowledge.

Link to the new registry: https://bit.ly/3wgrqEU
The RUDY study

RUDY is a study in rare diseases. Headed up by a research team at the University of Oxford in the UK, RUDY aims to transform clinical care for participants through patient-driven research. A secure web-based database is used to collect and store data, and is the primary mode of interaction with study participants. The study continues to expand including more rare disease. There are currently 286 individuals registered in the study who have OI, as well as other bone conditions such as XLH and HPP. They are very interested in getting more (UK only)!

The Primary Objectives of the Study are:
- To describe in detail how a rare disease affects individuals
- To describe the differences between individuals with the same rare disease diagnosis

And the Secondary Objectives are:
- To determine the personal burden and impact of rare diseases using quality of life and functional outcomes
- To determine the family burden and impact of rare diseases using quality of life and functional outcomes
- To generally increase our understanding of individuals with rare diseases
- To find the genetic basis for rare diseases that affect individuals and families
- To provide a research cohort of patients with rare diseases that can then be approached for further sub-studies.

For more information about the study – go to [https://research.ndorms.ox.ac.uk/rudy/](https://research.ndorms.ox.ac.uk/rudy/)

New home for the OI Variant Database

After 6 months of coordinating and networking efforts from OIFE, it has succeeded to find a new home for the OI Variant Database. This is a database mostly used by clinical geneticists when diagnosing a person with OI. All the data have now been moved from Leicester to Leiden University (LOVD), where it will be hosted after professor Dalgleish retirement. The directors of the Amsterdam UMC Genome diagnostics laboratory have agreed to take responsibility for the long term curation of the database. The laboratory participates in the NFU-accredited OI expert center of AUMC/VUmc and is the national reference center for OI diagnostic testing: [https://genomediagnostics.amsterdamumc.nl](https://genomediagnostics.amsterdamumc.nl). Information about all the OI-genes can now be accessed here: [https://databases.lovd.nl/shared/genes](https://databases.lovd.nl/shared/genes)
Mobile Rehabilitation Project in Russia

Interview with Nadezhda Epishina, M.D.
and physical therapist Charitable Fund „Fragile people“, Moscow, Russia

Who are you and what is your relationship to OI? My name is Nadezhda Epishina. I am a doctor and a physical therapist. I have been engaged in the project “Mobile rehabilitation service“ of the Charitable foundation “Khrupkiye Lyudi” (Fragile people) since 2018. Before my work here I practiced rehabilitation with children who had different musculoskeletal conditions. Since 2018 I have been working only with children and adults who have OI. I like my work very much and feel a great admiration for OI patients. I am inspired by their high intelligence, sense of humor, firmness of purpose and persistence as well as incredible cheerfulness in spite of all difficulties that they need to overcome. We motivate each other and work in one team.

Please tell us about the rehabilitation project! The goal of our project is to help people with OI to develop and keep the maximum possible level of physical activity and independence skills. We look for the most important activities to increase their level of quality of life in general. In our work we apply the functional rehabilitation that is built into patient’s day-to-day life and is functionally significant for the child. We work by the following directions: physical therapy, ergotherapy and psychology. Our approaches are:

1 Life. All our clients, a child and an adult, is a very important person to us. That is why we set the rehabilitation purposes individually in each case. We do our best to align the rehabilitation purposes with those tasks that the person must do at his/her everyday activities, help in socialization and realization of his/her abilities and personal goals.

2 Partnership. We work in partnership with each client, his family and surroundings, project specialists and our colleagues. We set the goals, plan interventions and assess the results together. Every teammate takes an active part, and the shared responsibility helps to provide the all-round support.

3 Evidence methods. We rely on the methods with proven effectiveness in our work.

4 Integration and preplanning. We provide comprehensive care through physical therapy, ergotherapy, and psychological support. "Thoughtfulness of assistance" is important because it is considered within the framework of the international classification of functioning. We try to consider and take into account all spheres of a person’s life, as well as the goals and possibilities of each client.

5 Training. The families, OI patients and healthcare professionals are trained within the framework of the project. Our specialists are also continuously taught and upgrade the level of their competency.

6 Rehabilitation built into life. We believe that a better rehabilitation is one that is built into everyday life when it is functional and meaningful to the individual.
In 2018 when I started working with OI patients, there was almost no information on how to work with OI-people in Russia. I was gathering information bit by bit from foreign sources, and the methodological guidance taken from OIFE’s website helped me a lot. We also have translated several books and methodological guides on OI. This allowed us/me to start working and gradually build up experience and results. During a period from 2018 to 2020 I worked in the project at the direction of rehabilitation of the foundation on the basis of H. Turner National Medical Research Center (NMRC) for Children’s Orthopedics and Trauma Surgery in St. Petersburg as well as in a remote format. During this time approximately 200 juvenile patients with OI and other bone conditions and several adult OI-patients had received counseling and regular training. Properly selected individual recommendations help our patients to increase motor activity, overcome fear, become more confident and independent.

When the COVID pandemic started in 2020 our fund received the grant support for realization of the project in a remote (online) format. We started with three, but today, seven specialists are working on the project and two PTs are trained to work with OI adults. There are 74 children aged 0-18 in the project on a permanent basis now. OI adults are also periodically consulted.

We have an extensive geographical outreach. Project participants are from more than 20 regions of the Russian Federation, CIS (Post Soviet Republics) and other European countries. We consider the education of the OI patients and families a very important part of their rehabilitation. Therefore we constantly organize webinars, educational projects, publish useful materials and create a comprehensive knowledge base on issues of rare bone conditions. We also advise a medical staff.

What makes our project unique? Thanks to the opportunities of our online meetings, we meet and guide families regularly. Together with a family we think about how to organize everyday life and help OI patients to become more independent and strong. We help our clients at the very first stages after surgery or fracture. We can engage the family members and make rehabilitation a joyful process for all participants. Because the most important thing we can give our clients is to teach them to love the movement, not to fear it, to understand its importance and joy. We are seeking to find physical activity that a particular OI patient like and want to do regularly.
What were the biggest challenges?
We faced various difficulties. At the beginning of the work there was a serious lack of information on the rehabilitation of people with OI. The remote format of the work has caused new difficulties. For example, the technical problems such as accessibility to the Internet and skills to use IT technologies. There are also different level of awareness and knowledge about OI among parents of OI-children as well as differences in access to services. It was very difficult for me to create a team of specialists with the necessary knowledge and skills: to find such colleagues, to train them and to be their tutor. Of course, like all the foundations, we are constantly forced to think about financing of the project. All our clients are given free assistance.

What were the biggest successes?
The biggest successes are the successes of our mentees. That’s why there are so many requests to the project. For example, that a child with OI 3 type is already walking alone at 5 years of age, without support and has an active lifestyle. We build partnerships between families, children and professionals. Each of us is a full participant of the rehabilitation process.

What are the lessons learned from the project?
The main lesson learned is that through team working it is possible to achieve great results. Our rule is called 1+1=3. A positive experience and success of other people are motivators for the rest.

How was the collaboration with the Russian OI-organization?
Cooperation with the Russian OI-organization is one of the best happenings in my life. I work for a team of like-minded people who will always support and help. An active and positive life philosophy. Don’t give up and keep going, is something I have learned while working here.

Do you have any further plans/projects?
We will definitely continue to develop the project. We are going to start working on care for OI adults based on our work with younger people with OI. We want to create a methodological guide for health professionals with information on rehabilitation. We have established a line of psychological support for families. And the group format of work that is on-line training and on-line meetings is being actively developed.

Any messages to the OIFE Magazine?
The expression "fragile people, strong minds" I now know firsthand. This is true. How wonderful and important that OIFE supports people with OI from all over the world not only informatively but also psychologically, showing positive examples and drawing future prospects for life.
Welcome to Osteonopolis!
Russian Youth Camp for youth with OI

Camp participants landed in ancient Greece. They were divided into groups with different political parties and tried their best in creating social programs. Then political candidates would present their programs in the elections and the winner would run all of Greece.

Misha Kanashev, 13 years
I live in St. Petersburg and have type 4 OI. I have been to our camp 6 times. What I like most about the camps is the atmosphere, the organization of activities from which I can learn new things, the long-awaited meeting and fellowship with my friends and counselors. The highlight of Osteonopolis was that we learned a lot of new and interesting things about politics, worked as a team and supported each other in everything. I learned to be more independent and learned a little bit about politics. Other countries should have such camps as it would be very interesting for children from other countries to visit such interesting camps and make friends. It would be great to meet OI-people from other countries, so we can learn to communicate in a foreign language.

Zakhar Zverev, 15 years
I live in Balashikha, not far from Moscow. I have type I OI, so I have a neutral attitude towards it. It does not disturb me much in the daily life. I have been to OI camp seven times. The camp brought classes with people where I learned a lot of new things and communicated with old and new friends. This is the first camp about politics that I have attended. I also had met a lot of people that I was previously unfamiliar with. I began to understand politics better, began to assess the situation from all sides and made some conclusions to myself about the current state of affairs. Young people with OI in all countries should attend such events, make friends, learn new things, and realize that they are not alone.

Golovina Anastasia Alekseyevna, 20 years
I live in Moscow. The type of disease is unknown yet. I have been to OI Camp about 7 times. The best thing about OI Camp is the fact that everyone is equal. Everyone treats you the same as you do, understands you and your disease. Good program, great guys, really liked the team I was in. What I learned from OI Camp: Independence, that’s the first. And the second, to understand people better. It seems to me that in every country there should be such a thing. So that people and children with OI can feel better, get to know people like them and become more independent.

More testimonies and photos from Osteonopolis will be published on oife.org
Artists with OI: Erwin Aljukic

Erwin Aljukic is an actor, dancer, speaker and fashion journalist. Since 1998 he can be seen on TV, in the cinema and at the theater. In addition to acting, he studied fashion journalism and has been working as a freelancer ever since. In 2014 he devoted himself to contemporary dance. Aljukic has been a permanent member of the Münchener Kammerspiele since 2020.

Who are you and what do you do?
I am, you can say, one of Germany's most well known professional actors with a disability, working since 25 years continuously as an actor (TV, cinema, theater), dancer, voice artist and model.

A very important part of my work, since the very beginning of my career, has always been the work as ambassador for various organisations and/or as protagonist in numerous campaigns. I strive towards more equality of people with a disability, the LGBT- community but also immigrants, all aspects that do cover my own personality, as well.

In what way has OI affected your art?
OI specifically has never been a topic in one of my works but my special physical situation with its very own possibilities and limitations do of course influence what kind of roles, stories I am offered and playing. In some movies, TV-shows, theatre pieces or dance performances the disability is in fact a topic. In others it's not.
When we’re talking about OI, it is more a very personal estimation of how far I can go or where and when I have to be careful. Even if things do look very dangerous or spectacular from the outside, this is no problem for me as long as I have the control. This includes control over whatever is happening right now on stage and in that moment. That means that with my colleagues I have to make very concrete arrangements. If I notice that my partner on stage has no good body awareness or if one part of the show or the rehearsal things are not clear, I don’t go further.

**What projects are you currently working on?**
The current piece is about care, called "WHO CARES?". I noticed very quickly how useful all my hospital experiences were and what it means to be dependent in certain situations. We OI'ers know how it is when from one moment to the other things change from being possible to not being possible anymore. Suddenly you depend on somebody. I saw how difficult it was for my non-disabled colleagues to really go into these situations.

**Why do you do what you do?**
In my work as an artist, I do see a way to bring in all my experiences - the good but also the bad ones. Personally, I am convinced that a good artist always sees himself/herself as a source - otherwise what you see on stage stays empty and superficial.

OI and all my other experiences forced me to confront myself with many topics in life - to cope with them and to overcome them. I am sure that this way I can be a role model for some persons. The true satisfaction in whatever you do MUST be something that is bigger than life....

**What themes do you pursue?**
As I mentioned before, this can be topics which are related to me and my personality but even much more exciting it is to be confronted with topics which are absolutely new to me. This lets me grow professionally but also personally.

**What’s your scariest experience related to your work?**
As I mentioned before, I feel very scared if I lose control on stage. This happened to me several times in the dance piece EVERY BODY ELECTRIC by Austrian choreographer Doris Uhlich we were playing all over the world. In that piece there is an 8 minutes solo with techno beats which starts very, very slowly and gets faster and faster until I get into a kind of trance and a completely physical climax.
Several times I was so much in the situation that I literally forgot to breathe. In one moment I had the feeling that my heart stopped to beat. Literally I wouldn't be able to shout for help and it felt like I would die on stage! I completely lost control over what I was doing. These were really traumatic experiences and each time I am scared of that solo.

**What role does the artist have in society?**

It's what I mentioned before in a way. I personally don't find it that interesting just to entertain an audience. But it makes me happy and satisfied if what I am doing, can lead people to think about certain things. With these new impulses they will hopefully change their lives and question things.

**What is your dream project?**

I am a very big fan of director Lars von Trier. In his movies he's questioning human behaviour. Actors like Nicole Kidman or Björk stated that they reached their limits in their professional lives. Maybe to understand my wish better; for 13 years I was playing in one of Germany's most famous daily soaps. The stories were all about normal, daily life. Now for 7 years I have the very big fortune to be part of pieces and projects where I can discover much more about me and the world I am living in. This is each time a very satisfying journey...

**Do you have any messages for readers of OIFE Magazine or for OIFE?**

I noticed very often how strong and courageous many Ol'ers are. This is indeed a phenomenon among many other "disabled groups" as well. But when I see how much the LGBT-community has managed to change over the years when it comes to more equality in many fields, this is something we should learn from. Too often due to the lack of opportunities we’re too passive or too thankful as soon as we get a chance. But we forget how much we invest ourselves. I wish that we get much more self-confident. Don’t wait until others offer a chance to us! But fight actively for your rights - full of pride, courage, and joy!
Research announcements & updates

The TOPaZ trial restarts recruitment after an 18-month pause due to Covid19

After more than 18 months, the TOPaZ trial has started to recruit patients once again. The trial is designed to determine if anabolic therapy with Teriparatide (TPTD) followed by a single infusion of zoledronic acid (ZA) is superior to standard care in adult patients with osteogenesis imperfecta (OI). The trial is open to anyone over 18 years with OI whether or not they have previously been treated. The only exception is people who have received anabolic therapies in the past two years.

Professor Stuart H Ralston, the Chief investigator said “We are delighted that recruitment has recommenced once again into this ground breaking study which is the only trial that has been designed to address the question of whether any treatment can prevent fractures in OI. We are very confident that we can bring this trial to a successful conclusion and determine if anabolic therapy is beneficial in OI.”

At the present time recruitment has already recommenced across the UK. Several sites in the EU are also about to start recruitment including the VUMC in Amsterdam, led by Dr Marelise Eekhof, the Hopital Lariboisière in Paris, led by Prof Martine Cohen-Solal and the University of Aarhus led by Prof Bente Langdahl. The TOPaZ study team are currently applying to the Efficacy and Mechanisms Evaluation board of the NIHR who are supporting the study, to request additional funds to bring the study to a successful conclusion. The study team are hopeful that the request for further funding will be approved given than 251 participants have already been recruited to the study. The team are hoping to enroll 380 participants with OI which would make it the largest clinical trial ever performed in this area. If you are interested in taking part in the study please feel free to email the study team on topaz.trial@ed.ac.uk or Professor Stuart H Ralston, the Chief Investigator on stuart.ralston@ed.ac.uk for further information.

BOOSTB4 update

The Swedish university Karolinska Institutet and the Karolinska University Hospital leads the academic clinical trial BOOSTB4 to study the safety (the primary outcome) and efficacy of the investigational drug BOOST cells (fetal mesenchymal stem cells) on fracture occurrence, growth, bone mineral density, biochemical bone turnover and quality of life in children who have OI.

The BOOSTB4 trial includes 2 groups of children (the postnatal and prenatal groups) who will receive 4 doses of BOOST cells. Currently, 6 children from different countries in Europe have received between 1 and 4 doses of the BOOST cells. No significant side effects have been detected.

The postnatal group is open to children up to 18 months of age who have a diagnosis of OI Type III or severe Type IV with a collagen mutation (glycine substitution in COL1A1 or COL1A2). All 15 participants receive 4 doses of BOOST cells 4 months apart. In June 2021, the prenatal group will open. In this group 1 dose of BOOST cells will be administered to affected fetuses before birth, followed by 3 doses of BOOST cells four months apart after birth.

The trial welcomes children and pregnant women from within Europe to Karolinska University Hospital in Stockholm in Sweden. Dr Eva Åström is the Principal Investigator for the clinical trial. For more information like inclusion and exclusion criteria, please visit the website www.BOOSTB4.eu. If you have any additional questions, please contact us via the email address BOOSTB4@clintec.ki.se.
Get in touch!

Professionals interested in pain & OI
OIFE is interested in getting in touch with professionals (PTs, OTs, psychologists, medical doctors, researchers, pain specialists etc) who have experience/knowledge about pain & pain management in OI (or related bone diseases). We are considering a mini conference and/or project related to pain & OI and we are interested in getting in touch with people who could contribute. So far we have 22 professionals from 11 different countries. It is still possible to join by sending an email to president@oife.org

Patient representatives for another pain project
A group of students are seeking patient advocates living with bone pain to co-create the BonePain Patient Ambassador Group in order to perform outreach work that bridges the gap between patients and researchers. The idea is to define the goals and the strategy for the outreach activities together with patients. Please note that all correspondence is conducted in English. Their information can be found on the flyer below and if you have any questions, please do not hesitate to contact them through the email in cc: pag@bonepain.eu

Hello! We are the Patient Ambassador Group (PAG), a team of PhD students from all over the world (you can see our pictures below).

As part of the European BonePainll consortual, we work to better understand the causes of bone pain in different diseases (e.g. bone cancer and osteoarthritis) and aid in developing novel analgesics.

PAG is a voluntary group with a people-first mission: we want to act as a bridge between the science within the BonePainll network and patients.

Do you live with bone pain?
PAG wants to hear from you! Contact us if you live in Europe and are interested in co-creating solutions to bridge the gap between scientists and patients.
News in brief

NEWS FROM BONE RESEARCH
Researchers at the University of Virginia School of Medicine have taken a new approach to understanding how our genes determine the strength of our bones, allowing them to identify several genes not previously known to influence bone density and, ultimately, our risk of fracture. The researcher collected information on 55 different skeletal characteristics in hundreds of mice, and then used an approach called systems genetics to analyze the data. The analysis identified a total of 66 genes that contribute to bone mineral density, including 19 not previously linked to it. The researchers believe that this information generated from mice can be used in the future to evaluate these newly identified genes as potential drug targets for OI, osteoporosis and other bone conditions. Read more in this article: https://bit.ly/36mITB5

BONE FRAGILITY & EDS
According to the researchers from Boston, US, the case in the article in the link, demonstrates that there is at least one other genetic case for infantile fractures other than OI and child abuse that is associated with Ehler-Danlos Syndrome (EDS): https://bit.ly/3hRoR7e

PATIENTS IN PUBLICATIONS COURSE
The Patients in Publications course consists of four modules and should take about four to five hours to complete. In each module, you will work through a case study, learn about each step in the publication process, and gain valuable tips. The course is self-paced and open-access. No pre-registration is needed. Simply visit the wecanadvocate.eu website to start taking the course now. The course is for patient advocates who plan to publish their own research, or who have been in invited to be co-authors or peer-reviewers of journal articles. Read more and register here: https://wecanadvocate.eu/patients-in-publications/

FOUNDING MOTHERS & FATHERS
Did you know that three important people in the history of OI passed away in 2020? Read about our founding mothers & fathers in the article on OIFE’s webpage: https://oife.org/2021/04/16/founding-fathers-and-mothers/

EUROPEAN MEETING ON ORPHAN DRUGS
Representatives from OIFE attended the online meeting about the new EU legislation on orphan drugs (medicines for rare conditions).

A European Expert Group presented their report on which measures they think should be taken to make medicines for rare conditions more accessible for people with rare conditions in Europe. See the recording and download their recommendations: https://bit.ly/3zhm2UO
NEW HOSPITAL COVERING OI OPENED IN ZIMBABWE
The charity CURE International has opened their first hospital in Zimbabwe offering surgeries free to children under 18 regardless of race, religion, or gender. Conditions that the hospital treats include, but are not limited to, angular limb deformities, congenital upper and lower limb conditions such as clubfoot, bowed legs, knock knees, rickets, osteogenesis imperfecta, and cerebral palsy. More information in the video and news article below. CURE hospitals are now located in the following countries in Africa and Asia: Ethiopia, Kenya, Malawi, Niger, Philippines, Uganda, Zambia and Zimbabwe. Read more here: https://bit.ly/2VrPGHH

COIS EDUCATION FUND
The Canadian Osteogenesis Imperfecta Society (COIS) has announced the creation of the COIS Education Fund. The inaugural Research Fellowship will honor the lifetime work and achievements of Dr Francis Glorieux. His ground-breaking research into the treatment and care of OI patients and his commitment to the global OI community is world renowned. https://www.cois-scoi.ca/research-grants

The Francis Glorieux Fellowship for Medical Research will provide an opportunity for medical researchers to take his legacy forward and, like him, make important and far-reaching contributions to the OI family.

INDEPENDENT LIVING & OI
The Brittle Bone Society did a survey on independent living among their members this year. They made a really nice infographic about what they learned. Are you surprised by any of the findings?

LIFE AS A "SHADOW CHILD"
Often siblings of children with a chronic illness are called “shadow children” because they live in the blind spot of their parents. They are often alone with their grief and put their own needs aside for their siblings’ needs. Read the very nice blogpost from Kristine Holm Laursen (Krisser) from Denmark about her experiences with being a shadow child and running as a coping strategy: https://oife.org/2021/05/29/life-as-a-shadow-child/

#30MILLIONREASONS
OIFE completely agree with EURORDIS - European Rare Diseases Organisation that we need a new EU Action Plan for Rare Diseases to ensure a better future for people with rare diseases tomorrow.

Be sure to #ShareYourReason & let your voices be heard!

https://action.eurordis.org/
REGISTRATION IS OPEN FOR INTOI 2020+1

Registration is now open for the INTOI 2020+1: Virtual International OI Meeting Early-Stage Investigator Symposium on September 9, 2021, from 11:00 am-4:00 pm, EDT (GMT - 4:00). Meeting registration is free and open to scientific and medical professionals interested in OI research. The presentation focus is on engaging early-stage investigators working in the field of osteogenesis imperfecta. Registration is here: https://us02web.zoom.us/meeting/register/tZwuc-2trjgpH9Blfj3fNqNAxCiKB8-rf8S

Questions about this event? Please email bonelink@oif.org

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OIFE Calendar

For an updated list of events & conferences - see OIFE's web calendar: http://bit.ly/36A6mw8