

2021



ANNUAL REPORT | 2021

Care4BrittleBones Foundation



OI | IN NUMBERS

Some children break one of their bones

500.000 PEOPLE

Worldwide have OI

Germany: 5,000; UK, France and Italy: 4,000 each;
Netherlands: 1,000; Belgium: 700; Switzerland: 500

10 TIMES A YEAR

People most affected with OI break over

200 TIMES IN A LIFETIME

OI IN THE WORLD

0 MEDICATIONS

Have been developed specially for OI,
but two in progress

OI is one of

7.000 RARE DISEASES

Together rare diseases are the 4th largest
disease classification in the world.

8.500 BABIES

Worldwide are born each year with OI

100 VOLUNTEERS

92.390/66.890 EUR

13.5 %

Overhead

Excluding / including exceptional items: Spent and/or allocated to
our goals (research, information sharing, collaboration/
knowledge exchange for OI, including conference)

REACHING OUT IN 2021

90.410 EUR

Of funds raised in 2021 for much needed research for OI

5.6 %

Fundraising Cost

26 WORKSHOPS AND EVENTS

Organised in 2021 by Care4BrittleBones and its network



CONTENTS |

OI IN NUMBERS	2
2021 Anchoring improvements for quality of life with OI	4
What is Osteogenesis Imperfecta (OI)?	5
Care4BrittleBones Organisation	7
Strategy Ways of working.....	133
Operational delivery 2021	177
Research.....	17
Fundraising	24
Collaboration and reach.....	25
IT Our Systems and Tools	27
Communications Networks	28
OI Community Networks.....	28
Scientific Networks.....	29
Communication.....	30
Financial Report.....	32
Thank you!.....	48



2021 | ANCHORING IMPROVEMENTS FOR QUALITY OF LIFE WITH OI

We started the year with great uncertainty due to the COVID-19 Corona pandemic. The pandemic weight heavily on us in several ways:

1. It impacted first and foremost our OI community in many very sever ways. Pneumonia is the leading cause of early death of people with OI. As a consequence, many people were “hiding” out from Corona, anxious that the virus would “find them”, often deprived from their help infrastructure, that could also (unintendedly) transport infection. Also people were often not able to get their standard medical treatment or surgeries due to the pressure on healthcare providers and hospital practice being affected due to the pandemic. The Corona pandemic led to many people being more anxious than ever.
2. It also impacted the income generation for our Foundation. As in the year before, fundraising events through running or concerts etc was not possible.

Under these challenging circumstances a lot has been achieved we can take pride of. The year 2021 was used very effectively to anchor various improvements. This applies to two areas:

- We have reconfirmed and matured our operating model and new way of working which has been initiated end of 2020, when the CARE4BONES foundation was established. We have updated our board, our Multi Year Plan and our Advisory Board.
- Most research projects continued throughout the year, as many of them are based on virtual collaboration. The highlight was the publication and implementation of first global Outcome Measurement Set for the multidisciplinary treatment of OI (www.key4oi.org) which was published and implemented in 6 different hospitals in 2021. Key4OI will lead to improved clinical care for people with OI on an individual level as well as a boost of research related to quality of life for OI.

Overall we look back on 2021 as a year which has brought many unique challenges, but also some special opportunities. We have worked tirelessly to sustain our momentum and ensure we move into 2022 as a vital and sustainable Charity. We are encouraged by what we continue to achieve with our partners throughout the OI world, and feel real gratitude for the encouragement, support and trust placed in us. We will continue to work with all our dedication and focus to make a difference to the quality of life for people with OI.

On behalf of the whole foundation Care4BrittleBones, thank you!

Andreas Matsangos **Dagmar Mekking**
Chairman CEO (Directeur-Bestuurder)





*“We have a single goal:
to enable scientific
research that improves
the quality of life
of people with OI.”*

*We want the best
possible health for
everyone with OI and to
find a cure.”*

WHAT IS OSTEOGENESIS IMPERFECTA (OI)?

Brittle Bone Disease, also called OI, is a genetic bone condition that affects the connective tissue of the body. It is caused by insufficient production of collagen that normally ensures strong, healthy bones.

The main characteristic of OI is the fragility of the bones. People with OI can experience anything from “a few more fractures than normal” to more than 200 fractures in a lifetime. A small incident can have big consequences for people with OI. Other symptoms include physical deformities, chronic pain, scoliosis, short stature, hearing and dental problems as well as severe breathing and heart issues.

OI is a purely physical disorder but has broader consequences. People with OI have the same needs and hopes for their lives as everyone else but they need to realise their dreams with a very fragile body. Often OI-related physical challenges also lead to significant psychosocial challenges, like exclusion and the fear of experiencing yet another fracture. This can lead to people with OI feeling left out and alone.

There are five main types of OI. People with the disorder are affected in very different ways – those with a less severe form of OI are able to work and participate fully in study and social activities. Many people with OI, however, have to deal with frequent pain and mobility issues, which heavily influence how they live their lives. Some people with OI can have a significantly reduced life expectancy.

Children are the most affected group. Some children will have a fracture every few weeks, undergo 20 surgeries or more at a young age and spend half their childhood wearing a cast. This has a big impact on the child as well as the family around him/her.

Generally, the most important symptoms of OI we are looking to improve are:

| Fractures | Pain | Anxiety | Isolation





| STATUS OF RESEARCH FOR OI TODAY

OI has been recognised for more than 100 years; however, there is no treatment that fundamentally addresses the condition. The key approaches used today are 'hand-me-down medications' from other related conditions such as Osteoporosis. These medications treat some of the symptoms for example, bisphosphonates which make bones harder. Whilst these medications clearly have benefits, they also come with potential adverse side effects. Moreover, their long-term effects are unclear. Most striking of all is that they don't address the root cause. Simply put: this is not good enough.

Research for OI patients is not providing the right solutions today because it is a **rare disease** affecting relatively few people. There are about 500,000 people worldwide with this disorder (1 person out of 15,000 has OI). Like many other rare diseases, hardly any research funding is available to change the status quo.

It is time to address what is holding back progress. We are keen to put urgently-needed support in place to address the challenges of OI in a strategic way. The key reasons for pushing forward now are:

1. **Promising new technologies** have become available, such as gene therapy or stem cell therapy, new medical treatment options, innovative materials and techniques for surgeries.
2. Modern **communication technology** is enabling collaboration and knowledge sharing between the world's top experts for rare diseases. Distributed around the world, they previously worked mostly in isolation.
3. **Big data** for small diseases is coming within reach. Genetic testing has become widely accessible and is cheaper than ever before. Over time this will allow us to look at 'scientific mysteries' like the discrepancy between genotype and phenotype. The largest research project ever completed in people with OI included fewer than 3,000 people. Significantly larger cohorts will soon be possible. This will enable new insights into patterns and stronger research as long as researchers are willing to work together and share data and/or patient organisations work together to collect data themselves.
4. There are significant questions to be addressed regarding bone metabolism, which is still, broadly speaking, unknown territory. A new trend in the last 2-3 years is to **look across related rare bone diseases** to understand the underlying biochemical processes. This has led to the formation of the European Reference Network for Rare Bone Diseases and the US-Canadian Brittle Bone Diseases Consortium. OI within both of these groups is standing out as the top priority research area amongst the nearly 450 rare bone diseases that exist.

These circumstances create new opportunities for OI research. Care4BrittleBones has identified various short, mid and long-term opportunities that have the potential to improve the quality of life of people with Osteogenesis Imperfecta and eventually to lead to a breakthrough therapy for OI.



CARE4BRITTLEBONES | ORGANISATION

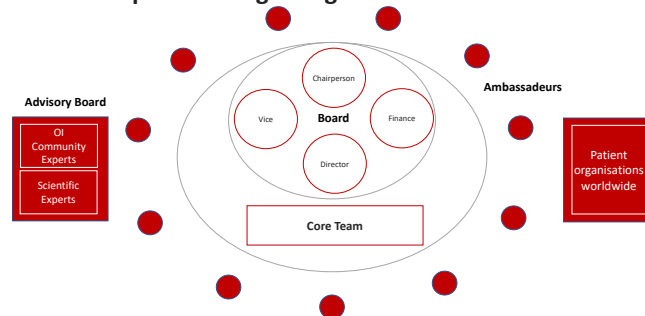
Care4BrittleBones consists of the board of the foundation and connects regularly with the following key stakeholders / stakeholder groups:

1. The Board
2. The Core Team
3. Two Advisory Boards
4. Our Ambassadors
5. Patient Organisations

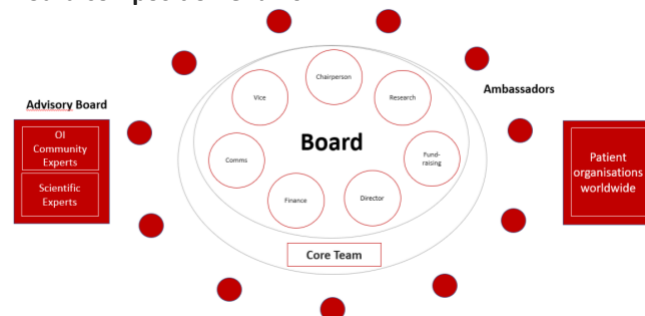
In 2021 we decided to increase the number of board members from originally 4 to 7, which was possible without a change of the statutes. This was decided in order to allocate the different areas of accountabilities more clearly with one board member each and share the workload amongst them. Resourcing the right talent from the OI community into the new board positions was one of the most important tasks we had to accomplish in 2021. It was progressed in collaboration between all members of the Core Team and has led to a harmonious transition and a new lead team with strong potential to lead Care4BrittleBones into the future. We are very pleased with the following 3 new board members: Starting May 2021 [Andreas Matsangos](#) has taken on the role as chairman following up Graham Marshall. Graham had to step down from his role, as he started a new position in a pharmaceutical company starting May 2021. We were in firm alignment, that a conflict of interest or a perceived conflict of interest would need to be avoided at any cost. He has led the foundation very successfully for 4 years and we are very thankful for his inspiring and effective leadership. He will remain affiliated with our foundation and will be regularly called upon, if he can support the foundation in ways that are appropriate.

Also we have newly added [Lida Zhvtnik](#) to the team for research and [Nicklas Teicke](#) has taken on the role of fundraising. The communications role has been temporarily filled in 2021 by [Amy Hassett](#). Due to competing priorities on her agenda she regrettably decided to step down again. The role of communications is currently not filled and covered temporarily by the director of the foundation.

Board composition beginning 2021



Board composition end 2021





1. | THE BOARD

At the end of the year 2021 Care4BrittleBones was formally led by its Board of 6 team members:



Andreas Matsangos
Chairman/Secretary



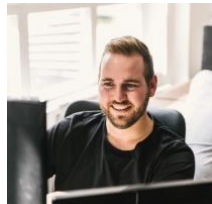
Celine Disch
Vicepresident



Dagmar Mekking
Director



Dirk-Jan Stegink
Treasurer



Nicklas Teicke
Fundraising



Lidiia Zhytnik
Research

The Board is ultimately accountable for all aspects of the foundation, with a strong focus on strategy, finance, risk and governance.

Governance of the foundation by the Board is organised as follows:

The Board meets on an ad hoc basis and approves the annual budget, operational plan, strategy document and (re)appointment of the director and monitors the performance against the plans. We also meet on a monthly basis together with the Core Team to discuss all matters both strategic and operational. The chairman and director meet weekly to consult on key topics. The Board formally reviews the performance of the director annually.

2. | THE CORE TEAM

The activities of the foundation are carried out by the Core Team, which acts as an extension of the Board. They define the strategy and operational plans, set and manage standards for fundraising and research, drive communications and PR, manage the financials and compliance, manage projects, develop relationships with funding institutions, support volunteers and manage the annual research proposal rounds.



The Core Team consists of highly skilled and motivated professionals from multiple industry sectors with significant experience working internationally and cross-culturally. They meet on a monthly basis to discuss all matters concerning the foundation. The Core Team has various subcommittees:

Finance	Dirk-Jan Stegink , Iwona Juzwa-Parfus,
Fundraising	Nicklas Teicke , Dagmar Mekking, Lieke Mekking,
Communications	vacancy , Celine Disch
IT / Data Privacy	Henk Latour , Kees Mezouar
Research	Lidiia Zhytnik , Dagmar Mekking, Lieke Mekking, Graham Marshall
Collaboration	Andreas Matsangos , Dagmar Mekking



As physical meetings were not possible in 2020/2021 due to the COVID – Pandemic, we are reusing a picture for the core team from 2019.



3. | ADVISORY BOARD

Advisory Board members are carefully chosen based on their expertise and reputation for collaboration. They are acting in the best interest of people with OI worldwide, irrespective of their own discipline or national background.

The **Scientific Advisory Board Members** have expertise in genetics, endocrinology, bone metabolism, pediatrics, orthopedics, and occupational health. All scientific advisory board members have an outstanding professional reputation and a proven track record of working closely with the OI-community over many years.

The Scientific Advisory Board has been updated in 2021. The update happened based on a (new) role description and the personal availability of members. In the context of the overall recommitment of all Advisory Board members, Lena Lande Wekre has decided to close out her role on the Advisory Board, based on the number of competing priorities on her agenda. She has been a highly valued Advisory Board member since the very beginning of Care4BrittleBones and we would like to express our sincere gratitude for her inspiring guidance and very valuable advice over many years. We continue our strong relationship on a project basis.

We are thrilled with the recommitment of all other members and we are equally pleased that we have been able to increase the level of expertise in our Scientific Advisory Board with 5 very strong new members: Richard Kruse, Kathleen Montpetit, Frank Rauch, Michael To, Frank Zaucke. The new advisory board members enable us to adopt a truly multidisciplinary perspective on OI for all matters. The 10 Advisory Board members are all extremely knowledgeable in their field and lifelong dedicated to quality of life for people with OI. The reform has also enabled a truly global representation, which is in line with the global focus of our foundation since the day we started.

All OI Advisory Board members have OI themselves and have good knowledge of the disorder and a broad network in the OI community. The OI Advisory Board members will have an opportunity to recommit in 2022, similar to the update on the Scientific Board members. The aim is to have 10 OI Advisory Board members to ensure balance between the 2 parts of the Advisory Board that act together as one.

The Advisory Board advises on which research projects we should prioritise and steer on research strategy and communication.

THE OI ADVISORY BOARD MEMBERS



**Margriet
Crezee**
Netherlands



**Ute
Wallentin**
Germany



**Eero Neva-
lainen**
Finland



**Kevin Van-
antwerpen**
Belgium



**Therese Stutz
-Steiger**
Switzerland



**Leonardo
Panzeri**
Italy



**Benedicte
Alliot**
France



THE SCIENTIFIC ADVISORY BOARD MEMBERS



Lars Folkestad
Endocrinology
Denmark



Antonella Forlino
Research
Italy



Richard Kruse
Orthopaedics
USA



Kathleen Montpetit
Occupational
Therapist (retired)
Canada



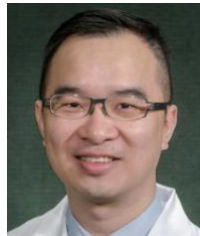
Frank Rauch
Pediatrics
Canada



Marianne Rohrbach
Endocrinology
Switzerland



Oliver Semler
Pediatrics
Germany



Michael To
Orthopedics
HongKong SAR /
Shenzhen China



Fleur van Dijk
Genetics
UK



Frank Zaucke
Research
Germany

4. | OUR AMBASSADORS

Our ambassadors are dedicated to networking and fundraising for OI research. Most of them either have OI themselves or have a relative with OI. We encourage anyone around the world who would like to support Care4BrittleBones by raising awareness and fundraising to get in touch (e-mail to dagmar.mekking@care4brittlebones).



Andrea Kiel



Annemarie
Visser & Kris
Koenis



Danielle de
Bakker



Diana Lips



Erik Meinen



Harry
Vondenhoff



Leonie Rouweler



Irma van der
Hoek



Jeanette
Chedda



Jessy van de Pol



Karin Kragt-
Vermolen



Laura Marx



Marijke van
Liempt



Marina Gil



Melvin
Elderhorst



Michaël Roele



Mira Thompson



Rebecca Meijer



Rene van der
Rijst



Rick Brink



Roos Hoffmann



Rob & Rebecca
van Berkel



Welmoed
Santema



Zuhal Soyan



In addition, many children enthusiastically and effectively help us! They intuitively understand how difficult it is to be excluded from normal play and sports activities because their body is too fragile. They want to help and are very successful at involving their schools, sports clubs and friends to support Care4BrittleBones.



More information about the ambassadors and their stories can be found on the Care4BrittleBones website www.care4brittlebones.org

5. | PATIENT ORGANISATIONS

We work closely with various patient organisations in all of our activities. We believe that an active role for people with OI is an important aspect of a meaningful and impactful research agenda. Their willingness to advocate for research, articulate their needs and participate in research makes a major difference. We also maintain regular connections with OIFE (OI Federation Europe) and the OIF (OI Foundation based in the USA).

Overview Care4BrittleBones





STRATEGY | WAYS OF WORKING

1. | STATUTORY GOAL

The vision of our foundation as reflected in our statutes is unchanged. The foundation aims to promote scientific research into Osteogenesis Imperfecta with the intention of improving the quality of life of people with OI.

The Foundation seeks to achieve its objectives by:

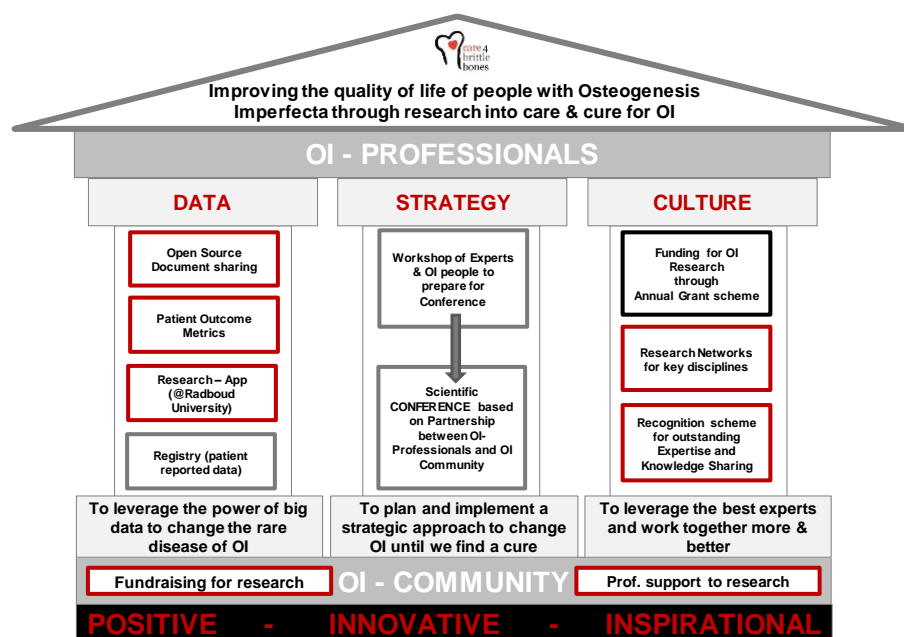
1. Raising funds;
2. Funding research and activities enabling research;
3. Contributing to impactful research by developing priorities and strategies for improving Osteogenesis Imperfecta, supporting collaboration and knowledge sharing regarding Osteogenesis Imperfecta and providing support to research in the widest sense;
4. Informing stakeholders.

As opposed to many other foundations, we are not only a fundraising organisation but also a coordinator, strategic partner and thought leader in research for OI.

2. | STRATEGY

We believe that a two-pronged approach is needed to improve the quality of life of people with OI. Our approach focuses on improving quality of life through short- and medium-term research, related to clinical interventions close to the patient (e.g. improved orthopaedic approach, physical rehabilitation, understanding scoliosis, etc.) and leveraging potential game-changing technologies, which may provide a cure for OI.

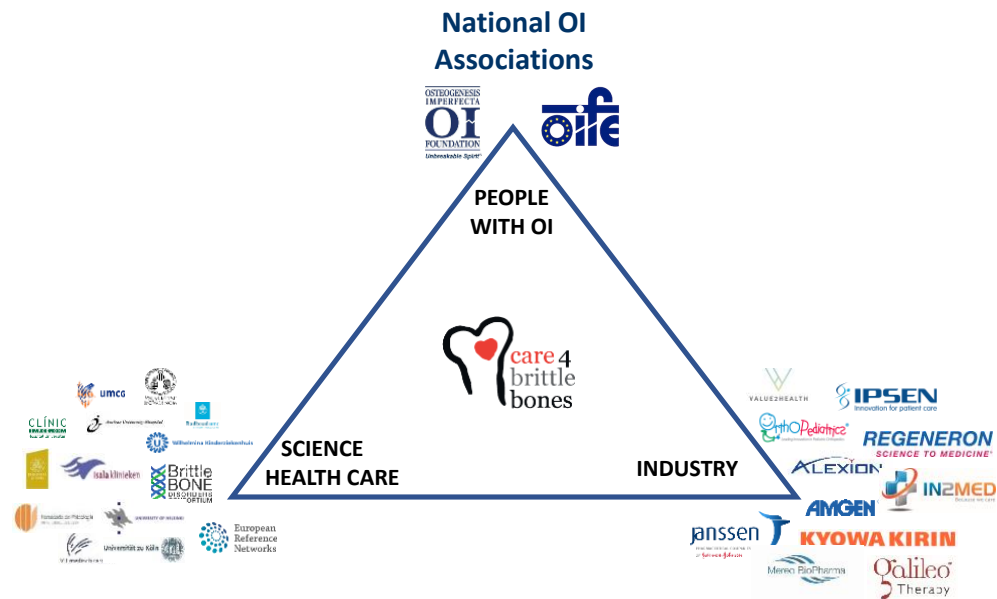
In 2021 Care4BrittleBones has continued to build on its research strategy, which is called "OIKOS". OIKOS is a holistic approach to driving change in research and improving the quality of life of people with OI. The three most important levers and associated strategic actions are: data, strategy and culture.





Care4BrittleBones strives to be a ‘bridge builder’ to connect the three main groups active in the field of OI Research: the OI patient community, healthcare providers/researchers and (pharmaceutical and other) industry. The [“QualityofLife4OI” Conferences](#) held in 2019 and in 2022 exemplify this aspiration.

We actively work together with all communities, providing professional experience, tools and bandwidth to accelerate OI research projects and strategies with a clear link to the quality of life of people with OI in the short-, mid- and long term. Our aim is to contribute to the development of an ecosystem that continuously drives positive change for OI. We realise that we must reach out beyond OI networks to support related rare bone diseases where we can. Bone metabolism still has many ‘blind spots’ that are unknown territory for researchers worldwide. Therefore, supporting the research of one rare bone disease can potentially provide insight into others such as OI. This is important for all of us.



Logos displayed are based on our current stakeholder relationships (2020).

Multi Year Plan 2021 - 2026

In the first 5 years of its existence Care4BrittleBones worked based on annual plans only. In 2017, when Care4BrittleBones has moved from a volunteer-based organisation to a professionalised organisation, it developed a first “Multi Year Plan 2018 – 2020”. It was a document that proved extremely valuable for our foundation. We delivered more than 90% of the plan, with the main “underperforming area”: the area of fundraising. Reflecting on our past performance, we see that our strength has been the

- the ability to orchestrate and support large scale research and healthcare improvement projects, working across many expertise centers in the world
- the trusted partnerships we have established across the entire ecosystem, resulting in collaboration of dedicated experts dedicated to improving quality of life for people with OI: healthcare providers, researchers, industry and people with OI
- innovative edge and future oriented way of working.
- our strong reputation which has grown over almost 10 years. The foundation will celebrate its 10-year anniversary on 12 February 2022.

In 2021 we worked on the next Multi Year Plan which covers the period 2021 – 2026.



The plan covers again all areas required to “move the needle” on quality of life 4 OI: Research, Fundraising, Networks & Reach, Communications and Fundamentals. Each of the areas is underpinned by a more detailed document, defining ways of working to further long-term ambitions and operations. All main stakeholders (eg Advisory Board, OIFE, OIF, ERN BOND) have been able to feedback and contribute to the document. Once again, the discussions have proven very valuable to sharpen the priorities, we need to focus on to make impact. We are embarking on the next chapter towards improving quality of life with OI.

3. | WAYS OF WORKING (COMPLIANCE AND TRANSPARENCY)

Foundation Care4BrittleBones is recognised as a charitable organisation in the Netherlands (**ANBI** status, Algemene Nut Beoogende Instelling).

As a charitable organisation, we are firmly committed to the highest standards of operation. This relates to every single process, but in particular to **compliance** with all applicable rules and procedures (including data privacy) and **transparency** (e.g., time writing of the CEO/directeur-bestuurder, regularly reviewing our performance against the goals and sharing our reflections on strengths and weaknesses with our stakeholders).

To demonstrate our standards and ensure we stay up to date on the latest developments in the charity sector we are a member/accredited by the following organisations:

- **Goede Doelen Nederland** – sector organisation for charities in The Netherlands. Through Goede Doelen Nederland we are participating in discussions with other stakeholders in the sector regarding topics relevant to all charities in the Netherlands. As a member, we are aligning with their standards and recommendations.
- **CBF** – Centraal Beheer Fondsenwerving. CBF will annually review all key processes of a foundation and carry out testing to decide if they are robust with regards to governance standards and transparency. This provides extra assurance to our donors that we are operating according with strong internal standards.

In 2021 we continued to adhere to the **EU-General Data Privacy Guideline** (GDPR). All relevant information including a complaints procedure have been published on our website and the changes have been implemented.

Key to our work are the values we have adopted when setting up Care4BrittleBones in 2012: three simple words guide everything we do: **positive, inspiring and innovative**. This applies to our research, fundraising activities and to the way we interact with each other and our stakeholders.





4. | FINANCIAL COMPENSATION

In 2021, none of the board members, core team or volunteers, ambassadors and advisory board members received financial or other compensation except for the director and funding in relation to project roles (eg in Key4OI Compass project).

The director's remuneration is explained in more detail in the financial report.










OPERATIONAL DELIVERY | 2021

The year 2021 has been highly unusual again for everyone, including Foundation Care4BrittleBones, due to the impact of the COVID-19 Pandemic. Whilst our **fundraising** was strongly negatively impacted (again), most **research** activities were delivered as planned. In the area of **Collaboration, Education and Communication**, our activities have changed, due to the existence of the Foundation CARE4BONES, founded in December 2020. The initiation of CARE4BONES and the associated platform has fundamentally transform how we work together with researchers and with the OI community for improving quality of life for people with OI.

Color coding:

GREEN:	Accomplished fully
AMBER:	Mixed delivery
RED:	Below plans
GREY:	Hold

1. RESEARCH 	<ul style="list-style-type: none"> • Key4OI <ul style="list-style-type: none"> • Implemented in NL Expertise Centra • Key4OI Article • Patient tools / ZIN Nr. 2 project delivered with positive evaluation • Key4OI international Pilots motivated and starting to implement • Key4OI Plus for Hearing, Teeth & Jaw, Cardiovasc and Pulmonary delivered, incl ca. 100 OI adults involved and 30 experts • Physical wellbeing Network Survey and action plan delivered and 2 webinars (1 webinar) • Psychosocial network Expertise finder survey and 2 webinars (1 webinar, cancelled med.) • Pilot Blockchain technology – delivered -> Not delivered. Outside of our control. • Proposal Round – hold and wait for further developments/ funding >> Remained on hold. • Support ongoing research projects Vitamin K, Eat Breathe Sleep, Towards Therapy, OI Variant database (tbc) • 3 publications: Key4OI, Roadmap, Eat, Breathe, Sleep
2. COLLABORATION 	<ul style="list-style-type: none"> • Researchers: Mostly through Care4Bones. Prepare for virtual Quality of Life for OI Conference • OI Community (handled by CARE4BONES). • OIFE and OIF relationship. More collaboration to make more impact together is possible and desirable.
3. FUNDRAISING 	<ul style="list-style-type: none"> • Explore professional support for fundraising • Funding from Non Profit: 70.000 -> result 2.000 • Funding from Companies 10.000 -> result 30.000 • Funding from individuals 20.000 -> result 60.000 <p style="text-align: right;">Ca. € 90.000</p>
4. COMMUNICATION 	<ul style="list-style-type: none"> • Sustainable resourcing • Social Media impact • Engage OI Community and Professional community through Care4Bones
5. OPERATIONS 	<ul style="list-style-type: none"> • Multiyear plan development 2026 • Continue operational excellence in Finance and IT • Board succession + Team building + Nicklas / Lida • Advisory board 2021 reviewed and regularly engaged (min. 2x year).

RESEARCH

Summary

Given the extremely challenging circumstances healthcare providers and researchers found themselves in during the COVID-19 pandemic, the delivery on the research side was very strong.

a. Research projects status update

Foundation Care4BrittleBones has been involved in 10 research related activities in 2021. Our role varies per project:

1. The goal of this research is to assess whether vitamin K levels in children with O.I. are lower than in healthy children. Given that Vitamin K is required in the normal bone metabolism and the bone metabolism of children with OI is higher than normal, more Vitamin K may be needed for optimal bone



formation. If this proves to be true, the next step will be starting vitamin K supplementation therapy in a clinical trial. This is a potential very easy treatment option to achieve better bone health and growth in children with O.I. Whilst it would not eliminate OI, it would lead to improvements with no side effects. Analyses of the OI and control blood samples have been initiated, the full data are expected in 2022, and will be analysed and published thereafter. The project has been delayed due to Corona and some project-specific adverse events and it will be continued by WKZ, in cooperation with Maastricht University, coordinated by dr. Bea Zoer.

2. The project **Eat, Breathe, Sleep** by Dr. Antonella LoMauro has been supported by the Care4BrittleBones Foundation as well as the Italian patient organisation As.It.O.I. It has been successfully completed in 2021 and published open source in the Orphanet Journal of Rare Diseases. We congratulate the Dr. LoMauro and her team for her wonderful and important work!

Orphanet (LoMauro et al. Orphanet J Rare Dis (2021) 16:435 <https://doi.org/10.1186/s13023-021-02058-y>)

Abstract

Background: Although Osteogenesis Imperfecta (OI) affects the connective tissue causing extremely brittle bones with consequent skeletal deformities, it is important to go beyond bones. Indeed, the quality of life in OI does not only depend on bones status, as OI might affect also other important functions. We have therefore implemented a multidisciplinary study to assess lung function, breathing pattern, sleep quality and nutritional status in 27 adult OI type III and IV patients (median age: 34.6 years; 19 women; 14 type III).

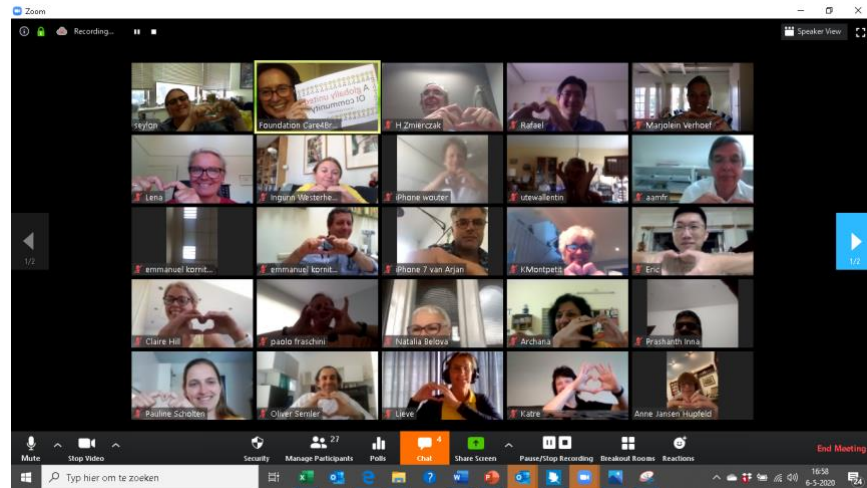
Results: According to nocturnal oxygen desaturation, two groups were identified: 13 patients with (OI_OSA, incidence: 48.2%) and 14 without (no_OSA) obstructive sleep apnea. The former was characterized by higher spinal and ribcage deformity, by more restrictive lung function, by paradoxical thoracic breathing in supine position, by rapid and shallow breathing, by higher body mass index, by longer neck and waist circumferences; by higher abdominal volume and by greater percentage of body fat mass, particularly localized in the trunk. The best predictor of OI_OSA was the negative value of the supine ribcage contribution to tidal volume, followed by the ratio between the neck and the waist circumferences with body height and the supine thoraco-abdominal volumes phase shift angle.

Conclusions: The pathophysiology of OI ensued a dangerous vicious circle, in which breathing, sleep and nutritional status are tightly linked, and they might all end up in negatively affecting the quality of life. The vicious circle is fed by some intrinsic characteristics of the disease (thoracic, cranial and mandibular deformities) and some bad daily habits of the patients (i.e., physical inactivity and low dietary quality). The former impacts on restricting the respiratory function, the latter makes OIers more prone to experience overweight or obesity. The main consequence is a high incidence of obstructive sleep apnea, which remains an underdiagnosed disorder in individuals with severe OI who are obese, with a neck to height ratio over than 31.6%, and characterized by paradoxical breathing in supine position. A multidisciplinary approach, including evaluations of breathing, sleep and nutrition, is required to better manage the disease and maximizing well-being of OI patients.

3. The **Blockchain project** remained on hold in 2021. The project is led by consortium with Care4BrittleBones only playing a relatively minor role. A decision will be taken in 2022, if the project will actually be started or stopped.
4. The very innovative project **"Towards a therapy for OI"** of Fleur van Dijk (UMC Groningen/NHS North West London Hospital NHS Trust) is looking into the use of induced pluripotent stem cells for OI Therapy using CRISPR-Cas technology. Due to COVID-19, the project had to be put on hold. The plan is to continue with the next stage of the project (testing on OIM mice) as soon as the pandemic allows this. It remained on hold in 2021 due to the pandemic. Our support to the research project remains strong.



5. In 2021 we made great progress in relation to **Key4OI**, our ambitious project to develop and implement consistent outcome measures for OI. (For more information, see the chapter: Highlights / Research). Many healthcare providers and scientists are following the project and are highly motivated to use Key4OI.



6. Three new research projects under the overarching name **“Key4OI PLUS”** were started, building on the Key4OI methodology focussing on **Lung, Hearing and Teeth & Jaw in OI** (See chapter: Highlights / Research for more information). All three of them have been concluded in terms of the scientific work. All projects are working on a publication to share the insights and help to implement the results.
7. In Q3 2020, we had decided to newly fund the project or Ruud Bank / Ralph Sakkers **“Sweet Bones. Targeting collagen glycosylation to improve bone quality in osteogenesis imperfecta”**. The work was planned to start in 2021, but has been postponed to start only in 2022. The preclinical project is looking into the root causes why bones are so brittle, developing the fundamental thinking how to address brittleness in a completely new way.

b. Professional networks

- The **Psychosocial Network** held one webinar 2021. The main work was the preparation of the expertise finder survey ahead of the Conference Quality of Life 4 OI planned for 2022. The network was led by Kara Ayers, Ute Wallentin and Claire Hill.



- The **Physical Wellbeing Network** is led by Kathleen Montpetit, Lena Lande Wekre and Marjolein Verhoef. Thanks to a project subsidy, they conducted a major survey amongst the adolescents and adult OI community (16 years and older) in relation to physical wellbeing, movement and sleeping habits). The survey will inform various activities in this area in 2022 and beyond.

Abstract “Understanding the Physical Wellbeing of Adults with Osteogenesis Imperfecta”

Objectives

In 2020 the World Health Organization (WHO) formulated guidelines on physical activity, an important aspect of one’s physical well-being. To understand the needs of adults with OI regarding physical activity (active living, sport, fitness and exercise) a subcommittee of the Care4Brittle Bones Foundation decided to explore this need.

Methodology

A team of 3 health care professionals and a person with OI (with input from their various networks) developed a survey on physical well-being and OI. The survey was distributed in May - June 2021 through the media platforms of the OIF, OIFE, Care4BrittleBones, and generic social media platforms and word of mouth.

Preliminary results

273 persons with OI responded and provided important insights into their experience with, and feelings about, physical activity. The respondents were mainly female (72%) aged 16 to 65+ years with an overall high level of independence in self-care. Their usual level of mobility was independent walking and one third used a wheelchair.

Half of the respondents participated in exercise or sports on a weekly basis at low to moderate intensity. More than half was less active than previously. Factors helping to be physically active were (customized) exercise programs, knowledge of local facilities and access to equipment or assistance.

They described succinctly the health benefits of an active lifestyle. Challenges faced when active were pain management, cost and fear of fractures.

Sleep issues were present in 25% of respondents and 40% were often or always feeling tired during the day.

Conclusion

People with OI encounter challenges in being physically active yet many respondents succeeded in finding ways to be active. More than half stated they are less active than previously. Further analysis of motivating factors, challenges, knowledge of sleep issues, and nutrition is necessary to support people with OI to be physically active.

The ultimate goal is to use the feedback from this survey to develop guidelines and material in accordance with WHO’s recommendations for physical activity and adapted to people with OI. These “tool kits” will be developed using a holistic perspective about physical activity, nutrition, sleep, and co-created in collaboration with professionals, training experts and the OI community.



c. Conference QUALITYOFLIFE4OI 2022

In 2021 we intended to prepare for a next face2face Conference “Quality of Life 4 OI” in 2022 following the successful first event in 2019. Due to the continuing pandemic, the decision was taken to conduct a virtual event.

d. Contract Management

We actively managed our research contracts. The status of all running contracts is part of a regular review process.

e. Research Spent

Excluding extraordinary income items, we spent EUR 92.390 (EUR 66.890 after special items, see financial report below) on our statutory goals: research, information sharing and collaboration for knowledge exchange. In both cases, this is a decrease from 2020. The lower spend on these goals was necessary to keep our finances in balance.

Improvement opportunities, risks and uncertainties in this area:

It remains more necessary than ever to connect experts to learn from each other and build on each other’s work. The speed of innovation seems to accelerate, and the number of opportunities seem to increase which is great news for people with OI. For many OI professionals, interacting with people with OI forms only a minor part of their professional responsibilities, which makes projects vulnerable to delays and can lead to a lack of sharing of valuable lessons learned.

The start of the CARE4BONES foundation 2021 is applauded by the Care4BrittleBones foundation as THE way for people with OI and professionals to collaborate and share knowledge enabled by the www.care4bones.org platform. Due to the new foundation, the Care4BrittleBones Foundation is significantly less active in operational matters and focusses on large projects such as Key4OI as well as fundraising.





SPECIAL HIGHLIGHTS | MULTI YEAR RESEARCH

1. | KEY4OI – OUTCOME MEASURES SET

2021 was an important year to “road test” the Key4OI concept. Key4OI is the name of a set of Outcome measures for multidisciplinary care for children and adults with OI applicable to all different types of OI. The concept had been developed in 2018 and 2019 in a unique worldwide collaborative effort of many experts around the globe and many patient organisations. The results of this work have been published in the [OrphaNet Journal of Rare diseases](#).

Professional participants:



OI Community Representation:



In 2021 we have continued the pilots in the following locations:

- (1) Shriners Hospitals for Children, Montreal / Canada,
- (2) Alfred I duPont Children's Hospital, Delaware / USA
- (3) Norway
- (4) HongKong SAR / China
- (5) NL (lead by Isala, Utrecht UMC)

Every quarter we update for researchers, clinicians and the OI community around the world to keep them updated about the implementation of Key4OI with the so-called Key4OI Affiliate video conferences. In 2021 we established a dedicated website which brings all patient tools and healthcare provider tools together: www.key4oi.org



KEY4OI
«COMPASS»

NAME _____ DATE _____

EXPERTISE CENTER _____ **NAVIGATING TOGETHER»**

KEY4OI «COMPASS»

I'd like to _____

QUALITY OF LIFE

PAIN, FATIGUE, EMOTIONAL WELLBEING, PARTICIPATION, SOCIAL CONTACTS, SELF-CARE, ACTIVE LIVING

MAJOR EVENTS

SURGERIES, FRACTURES, GROWTH & WEIGHT, BONE MINERAL DENSITY, HYPER MOBILITY, MY BODY

1 MY GOALS

2 HOW WE WILL WORK TOWARDS MY GOALS

3 PLAN > WHO DOES WHAT WHEN AND WHERE

4 TO DO

✓check!

NEXT APPOINTMENT

DATE _____

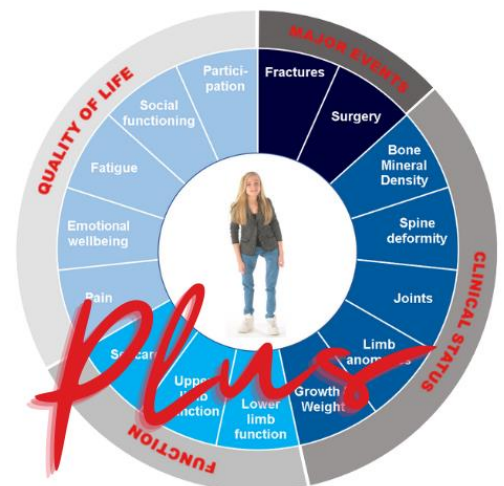
2. | KEY4OI PLUS

Given our experience with Key4OI and the importance of specific topics for the OI community many stakeholders suggested that we should continue to develop recommended outcome measures for clinical care. The priority was given to the following 3 topics due to their impact on quality of life:

- Teeth & Jaw
- Hearing
- Lung

Again, we used our networks to seek out the best expertise that is available for the three topics. We are most grateful for the collaboration from so many clinicians and researchers as well as highly qualified “OI patient experts”.

All of them are contributing on a pro-bono basis. In 2021 the project teams conducted many focus groups with adults with OI. The teams met on a bi-weekly or monthly basis to discuss outcome measures in the three areas. The projects will finish in 2022 with a publication and handover to practitioners who want to use the outcome measurement set.

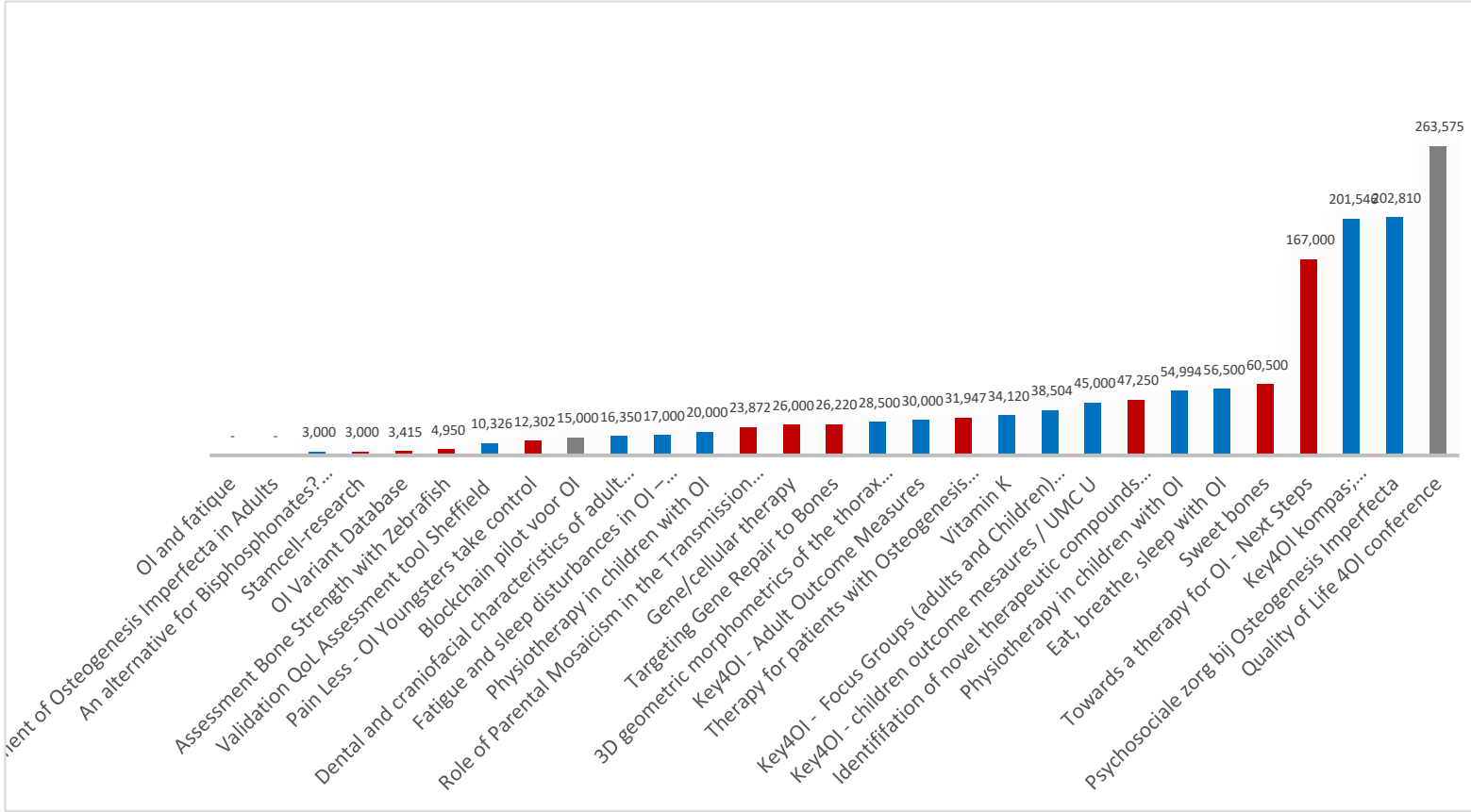




3. | LONG TERM OVERVIEW OF RESEARCH SUPPORTED BY CARE4BRITTLEBONES (2012 – 2021)

Over the past 9 years Care4BrittleBones has enabled 32 research projects, which are clearly linked to the quality of life of people with OI. These projects are a mix of basic research (focusing on the long term and potential game changing technologies) and clinical research (focusing on areas that bring potentially immediate benefit for people with OI in the short or mid-term). Many of them are still ongoing, as they often take longer than 2 years to complete due to their complexity and comprehensiveness. An overview of the research and research collaboration projects supported from 2012 – 2021 is displayed below.

RED = Basic research. **BLUE** = Clinical research. **GREY** = both



FUNDRAISING

Summary

In 2021 fundraising was impacted strongly (again) by the COVID-19 pandemic. In the past we held various events for fundraising, such as running events or concerts. All of that was not possible. We really appreciate the continued support from our private donors who have loyally continued their support.

- a. **Trust funds:** We submitted ca. 200.000 Euros worth of proposals into various trust funds. Unfortunately, the success rate was disappointing this year. We believe that the



reason was the general “uncertainty in relation to COVID-19” causing trust funds to also act more cautiously.

- b. **Public funding:** We continue to have a very strong reputation in the Dutch public Health care system, namely Zorginstituut Nederland and the Dutch Ministry of Health. Given our very good relationship with the Dutch Patient organisation (VOI) and the Dutch Expertise centers it is possible to implement tangible improvement in the Dutch Healthcare system which benefit everyone with OI in the country. We have one large project funded with public subsidies: The Key4OI approach is being implemented with a public subsidy from the Dutch government which was already awarded in 2019. The implementation takes 2 years and has been extended slightly due to COVID-19 (project close Jan 2022)
- c. **Fundraising event:** In 2021 given the COVID-19 constraints we were only able to organise a single fundraiser. It was a Seasonal fundraiser and took place 2 weeks before Christmas. The event featured a colourful programme with various virtual performances, including 2 songs performed by a worldwide Choir of people from the OI community. The operational delivery was in the capable hands of the CARE4BONES Foundation to support research through the Care4BrittleBones Foundation.
- d. **Crowdfunding:** In 2021 we raised ca. 55.000 Euros in various ways from individuals, often involving our crowdfunding platforms research4oi.org, or facebook. The most important achievement in this area was the “[Initiative Einzigartig](#)”, which continues also into 2022. In 2021 we have changed our crowdfunding platform to a free version with less functionality in order to save costs.
- e. **Long term donors:** We have a small group of ca 10 long term donors. They all continued to support us in 2021 and we are extremely grateful for their loyalty.

Improvement opportunities, risks and uncertainties in this area:

Improving quality of life 4 OI requires long-term thinking and long term delivery. The reduction of income to the foundation throughout this pandemic exposed the vulnerability of our foundation in relation to a continuous income stream. We have mainly worked from project to project. A key challenge for 2021, is ensuring that more robust, continuous income streams be made available to ensure the sustainability of the foundation.

| COLLABORATION AND REACH

Summary:

Collaboration within the Care4BrittleBones Core team remained strong in 2021. Whilst everyone individually wrestled with the impact of COVID-19 to their personal life and the team underwent a significant update (see chapter Care4BrittleBones Board), the commitment to support the foundation and the trust amongst the team has remained a strength of Care4BrittleBones.

Collaboration with stakeholders outside of the foundation varied. We maintain strong positive relationships with most national patient organisations. Very few national patient organisations are a bit reserved. We are mindful to respect their lead role in the country. The collaboration between Care4BrittleBones, OIFE and OIF continues to be constructive. Whenever there is a need, the organisations will support each other. Care4BrittleBones continues to lobby for a stronger collaboration as it is in everyone’s interest to not duplicate and use the volunteer time and resources in the research and healthcare space as efficiently and effectively as possible. We will need to continue to building trust and collaboration also in 2022.



- a. **Core Team:** In 2021 we continued to deliver our work with support of the dedicated Care4BrittleBones Core Team. It meets every month. Due to COVID-19 all meetings have been virtual in 2020 and 2021. This has helped us to improve the international representation in the Core Team. Whilst previously all members of the Core Team were based in the Netherlands, the Core Team now is able to leverage talent from different countries. This has many upsides for the global engagement and having “eyes and ears” to pick up trends from many places. Each volunteer in the core team has strong professional acumen and expertise. The Core team discusses strategic topics relevant to everyone and important operational items. A robust infrastructure of collaboration tools are enabling us to work seamlessly together.
- b. **Ambassadors:** Ambassadors are people who believe with us in the importance of research for quality of life for people with OI. They can help to spot and access opportunities for fundraising and are often actively engaged in research projects or fundraising activities.
- c. **Engagement:** Due to COVID-19, it was particularly important to engage virtually on an individual and group level, through social media and with virtual engagements using zoom and teams. These engagements would have happened in the past in Care4BrittleBones. Since January 2021 they are handled by the CARE4BONES foundation, which has intensified and deepened engagements with all stakeholders.
 - We have grown the number of people who receive our **newsletter**, the number of posts on social media has increased tremendously, underpinned by a very active communications team. Currently, our newsletter is sent out to 1,700 individuals, which is similar to 2020 levels. New connections are usually connecting into CARE4BONES.
 - **Website:** The website has been kept up to date. It provides comprehensive and user-friendly access to a wide range of resources which help professionals and people with OI to have a better quality of life.

Improvement opportunities, risks and uncertainties in this area:

With the establishment of CARE4BONES the operational activities in this area have ramped down. Our focus is on strengthening the relationships with the big OI umbrella organisations OIF and OIFE as everyone will benefit from a friendly and mutually supportive relationship with maximum synergy and minimum overlap or other “noise”.



IT | OUR SYSTEMS AND TOOLS

Foundation Care4BrittleBones believes in innovation and technology. We therefore need to lead by example, ensuring we work to the highest standards with regards to the data we process. We make use of the following systems and tools:

- **e-bookkeeping tool**
- **Dropbox**
- **Website Care4BrittleBones.** All key information about Care4BrittleBones is available on our website which is updated on a regular basis
- **Website Conference QualityofLife4OI** We are keeping the 2019 conference website live as we will use it again for a next conference in 2022.
- **Policies and procedures:** We developed a data management plan in line with the new GDPR rules introduced in 2019, published our approach on data privacy and implemented a complaints policy and procedure. No complaints have been raised through this policy in 2021.
- **Formdesk for surveys:** We conducted several anonymous Delphi surveys, facilitated by ourselves, supported by a user-friendly web based tool, which fully protects the privacy of people participating in our surveys.
- **Mailchimp:** Our newsletter provider is Mailchimp. We continue to watch the data privacy compliance.
- We are working with various **social media channels and other platforms such as YouTube and SoundCloud, where we have dedicated channels** (see also the chapter on communications)
- **Crowdfunding platform www.research4OI.org** continued to run in 2021. Whilst it works technically well, we are currently reviewing our approach to crowdfunding and have decided to not continue with a paid account in 2021..





COMMUNICATIONS | NETWORKS

| OI COMMUNITY NETWORKS

In 2021, more than 100 people have been involved as volunteers of Foundation Care4BrittleBones. They are active in raising awareness (e.g. our ambassadors), in supporting research (e.g. researchers and OI community in Key4OI plus and many other projects), in raising funds and last - but not least – running the activities of our foundation (e.g. our Core Team). We connect with our volunteers individually in webinars and video conferences. Also, we interact with patient organisations in various countries and work together with them to achieve shared objectives. Our OI-world is a small world. We strongly believe we need to work together to improve quality of life for people with OI.

VOI – Dutch OI Association

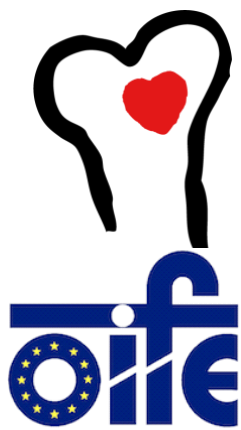


Foundation Care4BrittleBones originally started due to a call of the Dutch OI organisation VOI (Vereniging OI). In 2011, the VOI urged its members to consider what they could personally do to improve the lives of people with OI. The founders of Care4BrittleBones, parents of a daughter with OI and members of the VOI, volunteered to support research. Quickly it turned out that the VOI's statutory objectives did not include research. The VOI therefore suggested setting up a separate organisation and working together! And this is exactly what happened: The VOI and Foundation Care4BrittleBones serve complementary goals and support each other in various ways. While the VOI focuses on "making the best of today" by working with the healthcare providers in the Netherlands and organising meetings between people with OI, Care4BrittleBones aims to contribute to a better quality of life "tomorrow" by enabling research and working around the globe. Care4BrittleBones is present at all formal meetings of the VOI and is regularly invited to address VOI members during plenary meetings with a presentation about the activities of the foundation. Likewise, the VOI is kept up to date about the foundation and they are invited to attend the monthly meetings of Care4BrittleBones whenever they want. The connection is positive and strong and we will continue to support each other in topics of shared interest.

In 2021 Foundation Care4BrittleBones and VOI worked together successfully on several projects, especially on the Key4OI Compass project, the Key4OI Plus project and the "Living with OI" project. A collaboration agreement has been drafted which will be submitted for a vote to the VOI members to provide further transparency and strengthen the impact we can make together.

National Patient organisations internationally

We continue to engage with many national Patient organisations and with representatives in countries where there is no patient organisation yet.



OIFE

For many years Foundation Care4BrittleBones has been a supporting member of the **OIFE** (OI Federation of Europe). The OIFE is an umbrella association for organizations dealing with OI in Europe and beyond. They were established in 1993 and have 20 European member organisations (with voting rights) and various associated and supporting members (both not entitled to a vote). Foundation Care4BrittleBones and the OIFE work together on specific projects, such as the conference QualityofLife4OI (the OIFE was part of the Steering Committee). Also, the foundation frequently connects to president Ingunn Westerheim as a sounding board and advisor for strategic initiatives of the Foundation.



OIF Osteogenesis Imperfecta Foundation

The Osteogenesis Imperfecta Foundation is the most important OI association in the USA and is strongly linked to the Canadian COIS. With a very successful track record of 50 years of dedicated work by volunteers and strong support from their healthcare providers and researchers, they are a thriving and empowering network that we learn a lot from. Foundation Care4BrittleBones and the OIF work together on specific projects, such as the conference QualityofLife4OI (the OIF was part of the Steering Committee and sponsored many speakers with a US/Canadian background). Also, the foundation frequently connects to CEO Tracy Hart as a sounding board and advisor for strategic initiatives of the Foundation.

| SCIENTIFIC NETWORKS

Collaboration in the medical world is paramount for achieving progress in OI research and ultimately a better quality of life for people with OI. In 2021, Care4BrittleBones engaged with the following scientific professional contacts:

1. **ERN-BOND:** The European Reference Networks, coordinated by the European Union, advocate for increased collaboration across the 26 member states to support and address rare diseases. In 2021, they continued to develop their network and mature their working processes. 24 networks have been established, each of them focusing on a cluster of rare diseases. OI is part of the ERN-BOND, which covers more than 400 rare bone diseases. OI is one of the most important rare bone diseases, which is why it has been selected as one of the key focus areas of ERN-BOND. We are supporting the ERN-BOND EuRRBone database project which started in 2021 and are participating in a related working group. More information can be found on <http://ernbond.eu/>.
2. **BBDC:** The BrittleBonesDiseases Consortium is one of the most important networks in the US/Canadian region for research into OI. More information can be found on <https://www.rarediseasesnetwork.org/cms/BBDC>
3. **Dutch OI Group:** We are informally connected to the Dutch OI Group, a group of medical specialists who support OI in the Netherlands. The experts of this group are associated with the Wilhelmina Children's Hospital Utrecht (specialising in children with OI), Isala Hospital Zwolle (specialising in adults with IO), the University Medical Center of Amsterdam and several other hospitals. Together they ensure that they regularly share knowledge with each other and relevant stakeholders, including Care4BrittleBones.



4. **Meetings and Conferences:** In 2021 all physical gatherings were cancelled due to the COVID-19 Pandemic. Meetings were held virtually and this was experienced as efficient and effective.
5. Over the course of the last 9 years, we have established a worldwide **database of about 1100 OI researchers and health care providers across all disciplines** supporting people with OI. This includes, for example, orthopaedics, endocrinologists, geneticists, physiotherapists, and dental, hearing and breathing experts. We are in contact with **all leading researchers** in the world. We know them and they know us.



| COMMUNICATION

Starting 2021 the engagement of the OI community and professional community is increasingly left to CARE4BONES to handle as they think is best. Care4BrittleBones continues to communicate on research projects, eg Key4OI and the upcoming QUALITYOFLIFE4OI CONFERENCE which will take place again in 2022.

Website C4BB <http://www.care4brittlebones.org/en/>

Our website contains information about OI, provides an overview of the projects we are conducting and provides information on the foundation and its processes. On top of this “internal” information, it also supports an information platform catering for the needs of researchers, clinicians, healthcare professionals, OI communities and industry supporting OI. There is the facility to make a donation to support research and show various opportunities to help in other (non-monetary) ways. Our website is updated regularly with new events and is used as an archive.

Newsletter

During 2021 we have sent out 6 newsletters, mostly in relation to the QUALITYOFLIFE4OI Conference. They reach 1.600 healthcare providers, researchers and people in the OI community. The number of newsletters is about 50% of what has been sent out in 2020. This is to avoid overload of the respective audiences, since the CARE4BONES Foundation has also started to engage these communities.



Instagram & Facebook

Thanks for a dedicated volunteer, we are regularly communicating on various social media channels at least once a week. By sharing our Instagram posts directly to Facebook, we reach an even bigger audience. Facebook remains a separate channel for less visual messages and communication within (closed) groups such as “Ouders met OI” or “Parents with OI”.

Twitter

Care4BrittleBones also has a twitter account, from which information that is posted from Instagram/Facebook is also shared.

LinkedIn

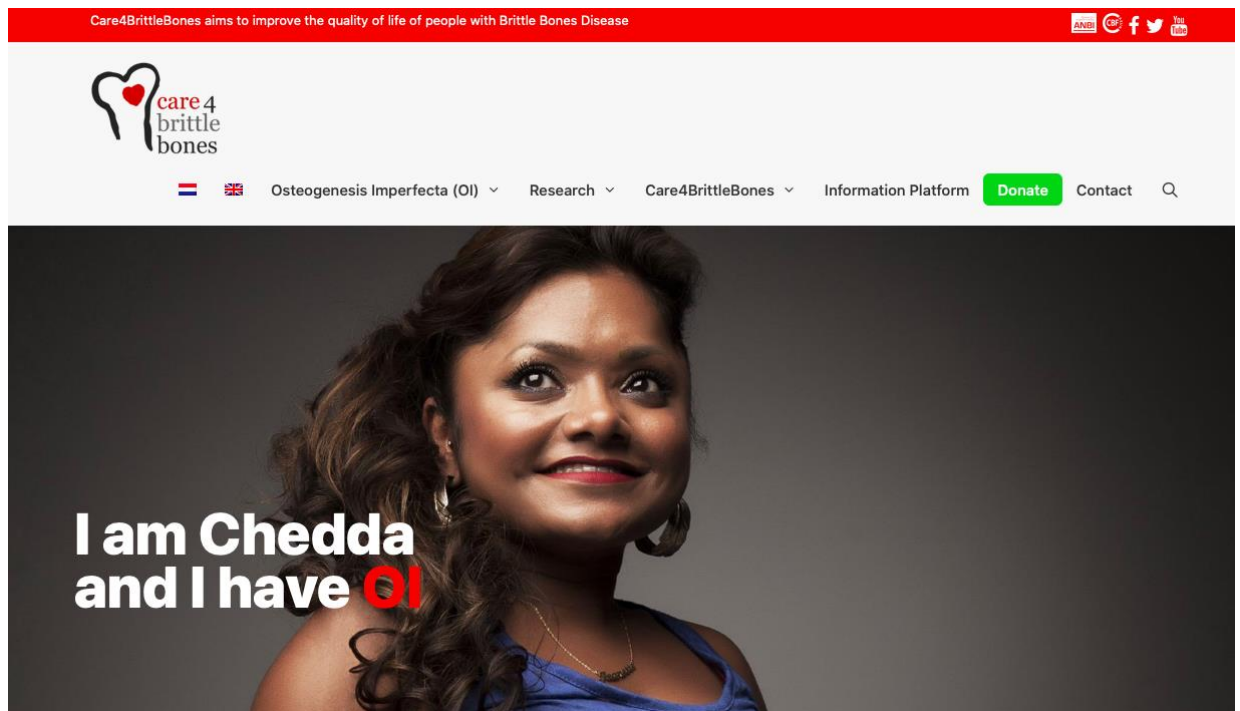
The variety in channels gives us the opportunity to target different audiences. We use LinkedIn for professional messages in the widest sense.

YouTube & Webinars

We use YouTube as an archive for our webinars and other video material.

Soundcloud

We have ca. 10 podcasts available on soundcloud at the moment.





FINANCIAL REPORT

SUMMARY OF FINANCIAL RESULTS INCLUDING EXPLANATION

Overall, our financial results were in line with our expectations for 2021. There were however unexpected once off adjustments that significantly influenced our year-end results: the Vitamin K project that had been on our planning and balance sheet for several years was cancelled at the end of 2021; the Eat, Breathe, Sleep project was successfully closed-out at the end of 2021 with a positive balance due to travel restrictions, i.e. lower costs than planned and included in our Earmarked Funds; the Sweet bones project indicated a change in setup, resulting in a lower funding need, reducing the amount we need to hold in our Earmarked Reserves.

In line with the rules and guidance for charitable foundations in The Netherlands we cannot simply transfer these budgets to our Other Reserves. Rather, we also need to adjust our expenses. As mentioned below, we charge costs in the year in which a project contribution is unconditionally contractually agreed. This accounting rule means we also need to adjust our expenses when we end up not fully spending the committed amount. If we wouldn't do this, the same funds might end up in our expenses twice.

This rather technical explanation ultimately means our expenses and hence our spend on goals are lower by EUR 25.500 due to these extraordinary expense items. This reduction in costs of course also significantly influences our annual balance of income & expenses, pushing it out of the planned negative space to a positive result of EUR 7.705.

As stated, our other financial results remained largely in line with our expectations. Our ability to raise funds continued to be heavily impacted by the Covid-19 situation. Slightly lower than budgeted income was balanced by lower spend on both overheads and research.

Thanks to an uptake in income from individuals in the last quarter of the year and the once off extraordinary items, our contingent reserves levels increased to EUR 113.211 (from EUR 46.717 end 2020). This provides a strong financial position going into 2022, though our organisation still faces many uncertainties.

As in previous years, we continued to ensure that most of our (financial) resources were spent on research support and research projects.

By significantly reducing our absolute spend on Fundraising and Management costs compared to 2020, we also managed to slightly reduce the total 'overhead' ratio (combining these two categories). While both categories were lower in absolute terms, the share of total spend for Fundraising decreased and the share of Management costs increased slightly against 2020: Fundraising and Management expenditures were 6% and 13% respectively of total spend in 2021, compared to 11% and 9% in 2020. This means that our overhead costs continue to be consistently and considerably lower than the recommended threshold of 25% for charities in the Netherlands.

Income

We continued to struggle to find new sources of income. From the feedback we received, this was largely due to the continued uncertainties created by Covid-19, in particular when it comes to income from trust funds and from charity events. Thanks to a significant uptake in funding from individuals in the last quarter (approx. half of the cash related to



income from this source came in during Q4) our total income was EUR 90.410 against a 2021 budget of EUR 100.000.

We were very happy to have the continued support from individual contributions to our foundation. We would like to emphasise that we continue to receive strong support from our governmental and non-profit partners through previously committed funding (not recognised as income in 2021, but reflected on the balance sheet and in the cash flow statement)

Spend on Purpose

The ratio of spend on purpose (including extraordinary items) vs total expenses increased to 81% from 79% in 2020. Including extraordinary items, spend was EUR 66.890. Excluding extraordinary items, (underlying) spend on Research projects and other purpose-related activities (e.g. providing information about research and supporting knowledge sharing) was slightly above budget by EUR 5.311, dropping to EUR 92.390 from EUR 134.068 in 2020. None of these extraordinary items impacted our delivery in 2021.

Fundraising

The cost of fundraising of EUR 4.634 is both significantly lower than the 2021 budget of EUR 32,500 as well as previous year spend of EUR 19.166. This was fully due to the effects of COVID-19 which didn't allow any in person fundraising events. The costs for the seasonal fundraiser were minimal. Most fundraising costs consisted of director time invested in driving and supporting application for funding.

Management & Admin

The 2021 budget of EUR 13.335 has been underspent by EUR 2.153 thanks to further small savings across the board. Lower spend was again helped COVID-19 restrictions, e.g. limiting key conferences (and hence our attendance). We are convinced we are working as efficiently as possible and have very little room to lower this spend further.

Financial Position

The financial position of the Foundation remains strong. Thanks to the extraordinary items that materialised in the last quarter of 2021, our Contingent Reserve showed a significant increase. The drivers for this increase are reallocations from Earmarked Funds and Earmarked Reserves, in other words previously committed funding that has been released to our 'general reserve'.

For a complete overview, the following items contributed to this increase, and all only (finally) materialised in the last quarter of 2021:

Extraordinary expenses (impacting balance sheet and income and expense account):

- An adjustment in the contractual setup of the Sweet Bones project (EUR 10.500 impact; recent developments in 2022 indicate we'll need to readjust to previous budget);
- The cancelation of the Vitamin K project (EUR 10.000 impact);
- The successful close-out of the Eat, Breathe, Sleep project with lower than committed spend. The project saw scope changes due to COVID and was reduced to a national project instead of a collaboration



between two countries requiring travel. This led to cost reduction. The project was delivered fully except for the international aspect.

Reduction of other Earmarked Funds, not fully committed, hence only balance sheet:

- Close out of the long-running Key4OI project with lower than anticipated spend (EUR 48.289 impact).

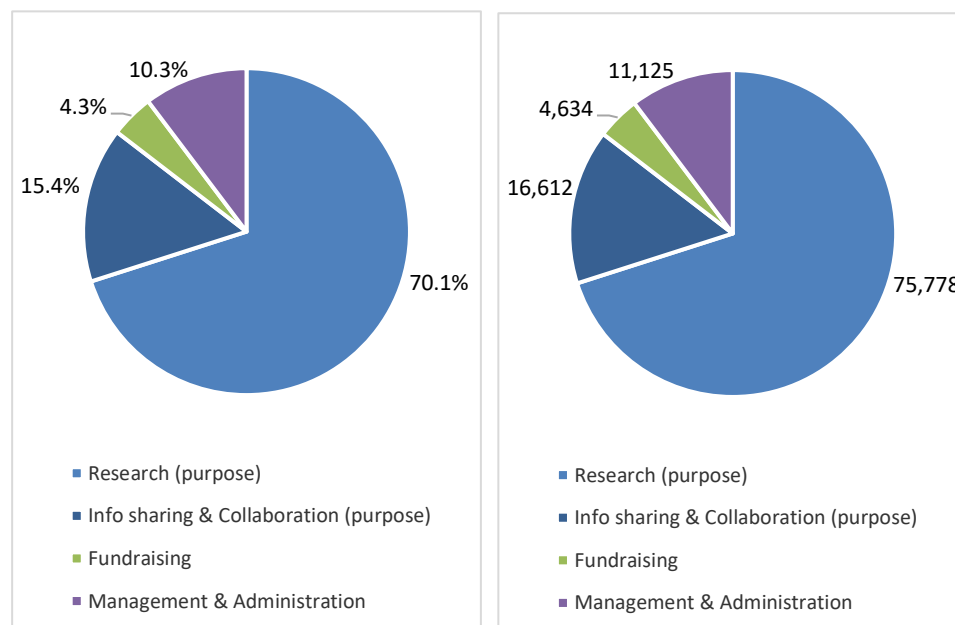
Combined with an uptake in income from individuals in the last quarter of the year, this led to an unexpected large increase in the Contingent Reserves levels to EUR 113.211 (from EUR 46.717 end 2020). This provides a strong financial position going into 2022, though our organisation still faces many uncertainties.

While this increase in Contingent Reserves provides a solid financial basis for our Foundation in uncertain times, it also means that we exceed the standard set by the Board for the reserve for Care4BrittleBones. This is set at a maximum of 1 times the annual costs of the organization. This standard stems from the Financial Management Guidelines for Charities of Goede Doelen Nederland. Using this standard, the maximum amount of contingent reserves is EUR 89.544. As described above, this surplus is largely due to unexpected events in the last quarter of 2021 and in our outlook for 2022 we have budgeted for higher spend on purpose (mainly research related) to ensure we bring our contingent reserves back in line with the standard.

KEY NUMBERS

How did we spend your contribution?

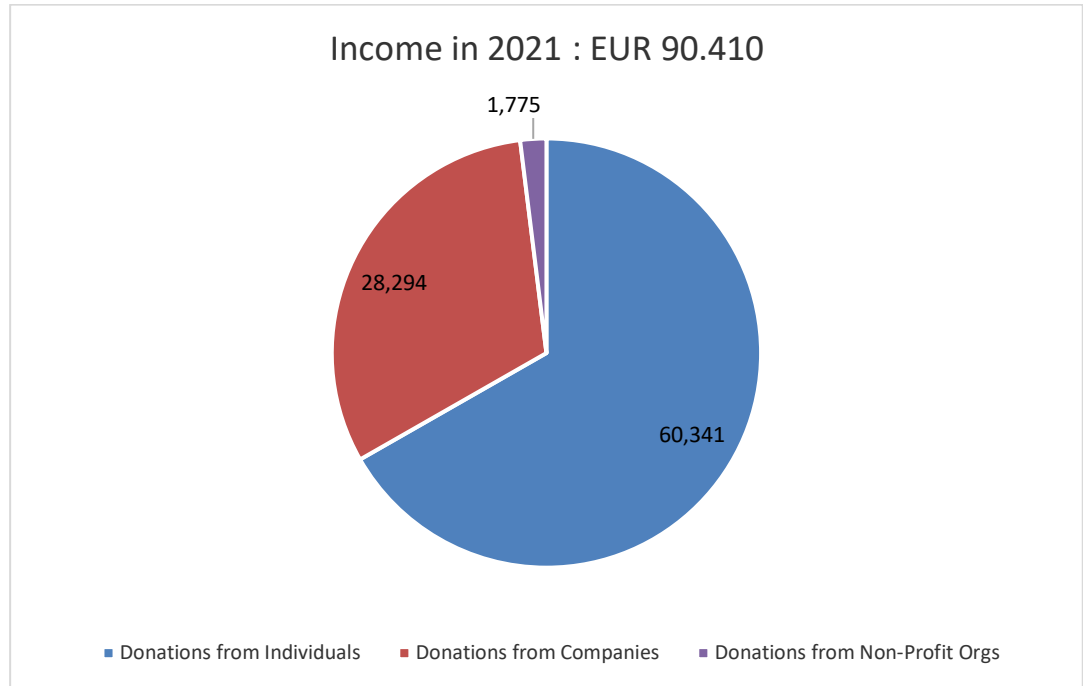
Spent in 2021: € 82.649; graphs show spend excluding extraordinary expenses €108.149



Note: excludes extraordinary expenses as these are negative expenses and cannot be shown as separate category. This makes %s deviate from %s in text above



What are the sources of income to fund research for OI?





BUDGET 2022

The Care4BrittleBones budget for the following year is approved annually by the Board. Normally, this is based on a balanced operation, i.e. with a change of the Contingent Reserve of zero. There could be balances on designated reserves and funds. These are actually balance sheet transactions that arise from timing differences in income and expenses. Often the Foundation first receives the benefits and then only spends the funds and / or incurs them. Given that we exceeded the standard for contingent reserves by the end of 2021, the Foundation has budgeted to spend more than in 2021 and planned a sizable negative result of EUR -25.044.

Income

For 2022 we have not projected a return to pre-COVID-19 days. Given the uncertain outlook, we projected the same level of income as that of the 2021 budget. This would mean exceeding actual 2021 income by roughly EUR 10.000. We feel confident this level is achievable given our strong income generation at the end of 2021. Should we be able to generate more income, there are several research related priorities that we would eagerly fund and start.

Expenses

Foundation Goals

Given the limited availability of funds, we do not aim to launch a new research proposal round in 2022. We do intend to fund additional activities, such as further Key4OI related work and enhancing support to ongoing research that has no or limited funding. Compared to 2021 we intend to spend roughly the same amount on information sharing. This relates mainly to our participation in key external research fora and conferences. This means the percentage of spend on Foundation Goals is expected to in line with be 80%. This is a slight decrease from 2021 (81%), which is mainly due to a slightly higher fundraising budget compared to 2021 actuals.

Fundraising

The absolute level of fundraising costs is expected to almost double against 2021 actuals. This mainly relates to our intention to start organising fundraising events again. Even with these intentions, we manage to keep the share of fundraising costs as part of our total costs at 7%, flat against 2021 budget and slightly higher than 2021 actuals (6%). If we can free up additional funding, we might spend more time on fundraising, since we believe this will have a positive contribution to our income levels.

Management & Admin

The cost of Management & Admin is expected to increase slightly against 2021 actuals in absolute terms. This is mainly due to our intention to organise the first face-to-face team event since the start of COVID-19. Due to fixed costs for memberships, IT, communications, insurance, etc. there is hardly any room to accommodate this increase. As a share of total costs, Management & Admin costs are however expected to stay flat against 2021 actuals at 13%.



Budget 2022 (continued)

Income & Expenses	Budget 2022		Actuals 2021		Budget 2021	
	EURO	EURO	EURO	EURO	EURO	EURO
Income						
Income from Individuals		40.000		60.341		20.000
Income from Companies		20.000		28.294		10.000
Income from Lottery Organizations						
Income from Grants from Government						
Income from Associated (international) Organizations						
Income from other Non-Profit Organizations		40.000		1.775		70.000
Total Acquired Income		100.000		90.410		100.000
Income as compensation for the delivery of:						
- Products and/or Services						
- Other income						
Total Income		100.000		90.410		100.000
Expenses						
Spent on Goals						
- Research	76.500		75.778		70.180	
- Information sharing & Collaboration	23.325		16.612		16.899	
- Other			(25.500)		0	
		99.825		66.890		87.079
Fundraising costs		8.451		4.634		7.856
Management & Administration costs		16.767		11.125		13.335
Total Expenses		125.044		82.649		108.270
Balance before Financial Income & Expenses		(25.044)		7.761		(8.270)
Balance Financial Income & Expenses				(56)		
Balance Income & Expenses		(25.044)		7.705		(8.270)



FINANCIAL STATEMENTS 2021

Income Statement

Income & Expenses	Actual 2021		Budget 2021	
	EURO	EURO	EURO	EURO
Income				
Income from Individuals		60.341		20.000
Income from Companies		28.294		10.000
Income from Lottery Organizations				0
Income from Grants from Government				0
Income from Associated (international) Organizations				0
Income from other Non-Profit Organizations		1.775		70.000
Total Acquired Income		90.410		100.000
Income as compensation for the delivery of:				
- Products and/or Services				0
- Other income		0		
Total Income		90.410		100.000
Expenses				
Spent on Goals				
- Research		75.778		70.180
- Information sharing & Collaboration		16.612		16.899
- Other		(25.500)		0
		66.890		87.079
Fundraising costs		4.634		7.856
Management & Administration costs		11.125		13.335
Total Expenses		82.649		108.270
Balance before Financial Income & Expenses		7.761		(8.270)
Balance Financial Income & Expenses		(56)		0
Balance Income & Expenses		7.705		(8.270)
Assignment Balance Income & Expenses				
Addition to / Withdrawal from:				
- Other Reserves		66.495		
- Earmarked Reserves		(10.500)		
- Earmarked Funds		(48.289)		
		7.705		



Balance Sheet

	Notes	31-dec-21		31-dec-20	
		EURO	EURO	EURO	EURO
Assets					
Receivables & Accrued Assets	1	34.070		108.716	
Cash & Cash Equivalents	2	250.856		267.618	
			284.926		376.334
			284.926		376.334
Liabilities					
Reserves & Funds					
- Reserves					
- Earmarked Reserves	3	50.000		60.500	
- Other Reserves	4	113.211		46.717	
			163.211		107.217
- Funds					
- Earmarked Funds	5		31.642		79.931
			194.853		187.148
Long Term Debt	6		0		22.100
Short Term Debt	7		90.073		167.086
			284.926		376.334

Cashflow statement

	2021	2020
Cash collected from:		
Donations	78.635	102.668
Income from Grants from Government	84.646	100.776
Income from other Non-Profit Organizations	1.775	54.246
Products & Services	0	0
Interest received	0	50
Total cash collected	165.057	257.740
Cash paid for:		
Research projects	166.003	207.720
Sponsoring events		
Governance costs	11.125	23.166
Fundraising activities	4.634	19.166
Interest paid	56	
Total cash paid	181.819	250.052
Net cash from operations	(16.762)	7.688
Cash Balance:	2021	2020
Opening balance ABN AMRO, SNS & Paypal	267.618	259.930
Closing balance ABN AMRO, SNS & Paypal	250.856	267.618
Net cash from operations	(16.762)	7.688



| NOTES TO THE ACCOUNTS

General

The consolidated financial statements for 2021 have been prepared in accordance with Part 9, Book 2 of the Netherlands Civil Code and in particular the regulations of the Guideline 650 Fundraising Organizations (RJ650). The purpose of this annual account is to provide insight into income and expenditure, and in the financial position of Care4BrittleBones.

Accounting policies for valuation and determination of results

Unless stated otherwise, the assets and liabilities are valued at the acquisition price, the manufacturing price or the current value. If no specific valuation principle is stated, valuation takes place at the acquisition price.

The accounting policies used for valuation and determination of results have remained unchanged compared to the previous year.

In order to be able to apply the principles and rules for the preparation of the annual accounts, it is necessary for the management of Care4BrittleBones to form an opinion on various matters, and to make the directives that can be essential for the amounts included in the financial statements. If it is necessary to provide the insight required in article 2: 362 paragraph 1 of the Dutch Civil Code, the nature of these judgments and assessments, including the associated assumptions, has been included in the notes to the relevant financial statements.

Cash flow statement

The cash flow statement has been prepared according to the direct method. The cash in the cash flow statement consists of cash and cash equivalents.

Receivables and Accrued Assets

Debtors and other receivables are initially valued at fair value. Subsequently, these receivables are valued at the amortized cost price subject to a deferral of provisions deemed necessary.

Cash & Cash Equivalents

Cash and cash equivalents consist of current - and saving account bank balances and Paypal balance. Cash and cash equivalents are valued at nominal value.

Project obligations

Contractually committed contributions to third parties are recognized as project obligations, split into long-term and short-term obligations. These are defined obligations, which are therefore recognized as expenses, but not yet implemented or for which no reports have yet been received.



Statement of income and expenses

Accounting principles for the determination of the result.

Income is recognized for the amounts received or promised without deducting the costs incurred by the own organization. Income is in principle recognized in the year in which it is unconditionally committed to or, when the former is not possible, when it is ultimately received.

Charges

Projects are often carried out together with research institutions. Defined contributions in the context of research projects are charged to the year in which the contribution was unconditionally contractually agreed. Other expenses are allocated to the year to which they relate.

Cost allocation

The recommendation 'Costs of allocation of Management and Administration' of Goede Doelen Nederland is followed.

By making use of projects in the administration, which are categorized according to the objectives (Research and Information & Collaboration), costs are recorded as much as possible directly.

The remuneration costs of the director are allocated to the goals, fundraising and management and administration on the basis of time writing.

Reserves and funds

The Care4BrittleBones's assets must be subdivided into reserves and funds on the basis of the Reporting on Fundraising Institutions. The Reserves include the contingent reserve and part of the reserves that are further earmarked by the association's board for special spending purposes (so-called "Earmarked Reserves"). Funds include those funds that have been given a specific destination by a third party, called "Earmarked Funds", as a result of which Care4BrittleBones can only spend these funds on this specific project.

The contingent reserve, reported under "Other Reserves", is intended as a buffer for disappointing income or unexpected expenses. With this reserve, Care4BrittleBones can continue its activities in financially difficult times.

As a CBF (Centraal Bureau Fondsenwerving) accredited organisation, Care4BrittleBones is bound by the rules for holding or building up reserves by fundraising institutions, as well as the instructions for how the asset management policy should be accounted for in the annual report. In accordance with the Financial Management Guidelines for Charities of Goede Doelen Nederland, the Association Board of Care4BrittleBones decided to set the standard for the reserve for Care4BrittleBones as a whole at a maximum of 1 times the annual costs of the organization. Based on the 2022 budget, a contingent reserve of a maximum of EUR 89.544 will follow as of 31 December 2021. The realized balance Other Reserves of EUR 113.211 is significantly above this threshold set by the Association Board. The plan for 2022 aims to bring these reserves back in line with the standard, as described above.



Short-term debts have a duration of less than 1 year. The project obligations and commitments to (research) organizations to the financing of projects have a remaining duration of less than 1 year

NOTES TO THE BALANCE SHEET

Note 1

	2021	2020
Receivables & Accrued Assets	EURO	EURO
Receivables from Individuals	-	-
Receivables from Companies	18.700	-
Grants from Government	-	-
Interest		
Receivables from Non-Profit Organizations	15.370	108.716
Total	34.070	108.716

Note 2

	2021	2020
Cash & Cash Equivalents	EURO	EURO
ABN AMRO Current Account	39.005	22.922
ABN AMRO Savings Account	98.952	143.951
SNS Bank Savings Account	99.950	99.950
PayPal	12.949	795
Total	250.856	267.618

Note 3

	2021	2020
Earmarked Reserves	EURO	EURO
Balance 1/1	60.500	20.415
Additions		60.500
Withdrawals	(10.500)	(20.415)
Balance 31/12	50.000	60.500

Note 4

	2021	2020
Other Reserves	EURO	EURO
Balance 1/1	46.717	121.533
Additions	66.495	41.943
Withdrawals	0	(116.759)
Balance 31/12	113.211	46.717

The Additions relate to the closing of obligations for closed and cancelled projects.



Note 5

	2021	2020
Earmarked Funds	EURO	EURO
Balance 1/1	79.931	101.459
Additions	0	0
Withdrawals	(48.289)	(21.528)
Balance 31/12	31.642	79.931

The withdrawals are related to movements in commitments for the Key4OI Kompas.

Note 6

	2021	2020
Long Term Debt	EURO	EURO
Project Commitments	0	22.100

The project commitments concern commitments to research organizations for the funding of projects with a remaining duration of more than 1 year. The reduction is fully a move to short term debt.

Note 7

	2021	2020
Short Term Debt	EURO	EURO
Project Commitments	70.278	167.086
Creditors	19.795	0
Total	90.073	167.086

The project commitments concern commitments to research organizations for the funding of projects with a remaining duration of less than 1 year.



NOTES TO THE INCOME STATEMENT

Explanation of Spending

	Spent on objectives		Management & Admin	Total Actual 2021	Budget 2021	Total Actual 2020
	Research	Information sharing & Collaboration				
Project contributions	14,091	1,662		15,754	5,815	3,010
Outsourced work	15,982	0	86	16,068	2,000	74,034
Remuneration of director	45,704	14,950	5,849	71,051	87,120	87,120
Office and general costs			5,276	5,276	13,335	4,976
Extraordinary expenses	-25,500			-25,500		
Total	50,278	16,612	11,125	82,649	108,270	169,140



PROJECT OVERVIEW– SPENT ON GOALS

	Year	Project Title	Category	Lead Country	Institution	Lead researcher	Status	Project Committed 1/1/2021	Movement in commitment 2021	Total Commitment 31/12/2021	PY Paid/reserved	Outstanding 1/1/2021	CY Paid/reserved	Directors' remuneration 2021	Total actual to date	Outstanding to be paid 31/12/2021
2016	No contract	Vitamin K	Clinical research	Netherlands	Wilhelmina Kinderziekenhuis	Bea Zier and Attilie van Dijk	Cancelled	10.000	-10.000	0	0	0	0	0	0	0
2017	2017-0011	Towards a therapy for OI - Next Steps	Basic science	Netherlands	Isala / UMC Groningen	Fleur van Dijk	committed	156.600	0	156.600	100.000	56.600	40.000	0	140.000	16.600
2017	2017-0012	Eat, breathe, sleep with OI	Clinical research	Italy	Politecnico di Milano Dipartimento di Elettronica	Antonella Lo Mauro	Completed	35.000	-5.000	30.000	15.000	15.000	15.000	0	30.000	0
2019	2019-021	Key4OI Kompas;		NL	Care488		committed	201.546	0	201.546	73.228	128.318	84.270	17.428	174.926	26.620
2019	2019-022	Blockchain pilot voor OI		Netherlands			committed	15.000	-6.300	8.700	927	7.773	0	1.913	2.840	5.860
2020	2020-023	Sweet bones			UMCG	Ruud Bank	committed	60.500	-10.500	50.000	0	0	0	0	0	50.000
		Other Projects		Netherlands			Ongoing	0	0	0	0	0	0	0	41.313	0
		Related Expenses														
Total Projects		Total Projects						478.646	-31.800	446.846	189.155	207.691	139.270	60.654	388.079	99.080
Overall Total		Overall Total						478.646	-31.800	446.846	189.155	207.691	139.270	60.654	388.079	99.080



NOTES ON THE ROLE AND REMUNERATION OF THE DIRECTOR

Notes on the role and remuneration of Management

Name	Dagmar Mekking
Position	Director
Line of work	Contract
Hours	32,6
Parttime percentage	82%
Period	1/1/2021-31/12/2021

Annual remuneration (gross)	71.051 *
Vacation payment	-
Year-end payment	-
Compensation holidays not utilised	-
Total	71.051
Taxable reimbursement	-
Pension payments (Foundation)	-
Pension compensation	-
Other long term remuneration	-
End of Service payment	-
Total	71.051

In setting the remuneration policy and the actual director's remuneration Care4BrittleBones follows the "Regeling beloning directeuren van goededoelenorganisaties" (ref. www.goededoelennederland.nl). This guideline provides maximum thresholds for the director's annual income based on specific weighing criteria.

The assessment of the circumstances of C4BB is done annually by the Board. The assessment over 2021 led to a so-called BSD-score of 310 points with a maximum annual income of EUR 88.928,- for our director. On a self-employed basis, i.e. including pension payments that would otherwise fall to the Foundation as an employer, this translates to a maximum of EUR 107.738 (1 FTE/12 months). The total remuneration of the Director (self employed) on a full-time basis of EUR 87.120 remains within this maximum. It should be noted that it also falls within the job grade D which was the outcome of previous assessments.

The allocation of remuneration costs of the director is based on time writing, see 'Explanation of spending' (page 59).

**including 21% VAT (is not recoverable as our foundation is exempt from VAT).*



ACCOUNTING CONTROL STATEMENT

2021 control statement:

Accounting Control Statement

The Auditing Committee in the person of Ms E.L. Koster and Mr. R. Le Grand have on Sunday 12th June 2020, in the presence of Treasurer Mr. D.J. Stegink and Mrs. I Juzwa-Parus checked the books of the Care4BrittleBones foundation for the financial year 2021.

The Committee states that:

- The Annuals Accounts give a correct representation of the income and expenses for the year 2021
- The balance sheet as at 31 December 2021 give a true and fair view of the Reserves.

Den Haag, June 25th 2021

The Auditing Committee

E.L. Koster

R. Le Grand



THANK YOU!

We would like to thank everyone who directly supported Care4BrittleBones in the last year – our generous donors, fundraisers and ambassadors and other volunteers. The achievements of Care4BrittleBones are enabled by this group of people, working relentlessly together to make a difference for people with OI. A wholehearted thank you to the core team for the numerous brainstorming sessions, discussions, challenges and huge effort committed to our cause. The power and passion of this team makes our organization move forward.

We also would like to thank our partners in the OI “ecosystem”: Our partners in universities and academic institutions, hospitals and other health related institutions and the life science and health industry. Your deep expertise and true dedication to improve the lives of people with OI and other rare bone diseases are an inspiration to us. We admire your innovative ideas and your courage to try out new approaches in responsible ways to take away pain and fractures. Your work gives us hope for a better future. Special thanks for persevering through another challenging pandemic year keeping things going as much as humanly possible. It is incredibly appreciated.

And of course – a big thank you everyone who support us and worked with us in the wider OI Community network, people with OI, their families and friends as well as the OI associations on a regional, national and international level! We are extremely proud to serve you all and thankful for the opportunity to work together to improve quality of life for people with OI!

We stand strong together!





CARE4BRITTLEBONES | FOUNDATION

Care4BrittleBones (statutory name 'Stichting Care4BrittleBones') is located in Wassenaar. It is registered as a foundation (Dutch: 'Stichting') at the Chamber of Commerce of The Hague Nr. 54665256.

Established as a foundation in February 2012, Care4BrittleBones is recognised as a charitable organisation in the Netherlands since 12 June 2012 (RSIN 851392854; www.kennisbankfilantropie.nl/anbi/care4brittlebones).

Based on a ruling of the European Court of Justice, the recognition as charitable institution in one member state is sufficient to establish beneficial tax treatment for donations from donors based in any country of the European Union.



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Internet	www.care4brittlebones.org
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 Twitter	@Care4BB
 YouTube	www.youtube.com/c/care4brittlebonesOrg070
 LinkedIn	www.linkedin.com/company/10639515