Unmet Medical Need: Case studies from those directly affected

INTRODUCTION

The European Commission's stated objective for the revision of the pharmaceutical legislation is to better direct innovation towards areas of Unmet Medical Need (UMN) while addressing availability, access, affordability, and fostering innovation. The Commission intends to establish a shared understanding of UMN through a definition and a set of criteria to be classified as meeting UMN. This would be reflected in regulatory pathways to stimulate Research & Development (R&D) in those areas, and to frame intellectual property incentives and rewards.

To understand better the patients' perspective on UMN, a small study was commissioned by EFPIA which explores the perspectives of patient leaders in 7 different disease areas. These are allergies and airways diseases, Alzheimer's disease, cardiovascular disease (CVD), diabetes, mental health (depression), multiple sclerosis (MS) and rare diseases.

Patient communities across these disease areas want a fair and inclusive approach to defining UMN that captures their breadth and complexity, rather than a narrow definition as such. They also wish to avoid pitching one disease against another, which undermines solidarity, and to have an ethical approach to addressing this topic.

UMN in several of these areas are wide-ranging, from accessing quality information about a therapy or treatment, delayed or non-diagnosis, lack of appropriate treatment and/or cure, lack of specialist and ongoing care and support throughout the patient pathway, and addressing the fundamental psychological quality of life impact of a serious condition. Several representatives also identified prevention as an unmet need.

They underlined that these are closely related to lack of access, inequalities, and in some cases, stigma and discrimination. For patients, their unmet needs often go beyond treatment per se and include issues around social care, peer support, continued education, employment and job retention, and relationships, family, and community life.

In addition to this study, a roundtable took place on 5 October bringing together patient representative and healthcare professionals to look at this in further detail.

It was also addressed in a session of the **EFPIA Patient Think Tank** in September 2022. Some additional key points emerging from the discussion in the Think Tank were:

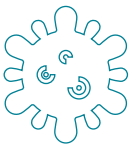
The importance of ensuring all actors, including industry, are involved in discussions on the definition and criteria around UMN

The lack of involvement of women in research and identifying the specific UMN of women in, for example, cardiovascular health

Rather than talking about UMN we should discuss unmet patient needs. We should investigate better the pain points during the patients journey to define these

It is important to acknowledge the specific needs of children, and paediatric unmet medical needs

The MS Barometer underlines systems failure to address UMN



In many disease areas we should look at Unmet Social Needs as well as UMN

We should also think about the UMN of the citizen as well as the patient, through the lens of prevention

A perspective from people living with depression

Based on an interview with Hilkka Karkkainen, Board member of Gamian Europe

EFFECTIVE PERSONALISED TREATMENTS NEEDED

Depression is a complex condition, often very interwoven with physical health. People living with depression have a feeling that they are not good enough. They feel a constant pressure in the chest. They do not want to socialise, preferring to be alone, yet they are very lonely. There is a pretence that everything is fine, when in reality, it is not. Sleep is a major issue — either insomnia or extreme fatigue when you want to sleep all the time. Research has demonstrated that the social determinants of health play an instrumental role in depression, with people from lower socio-economic groups, with less education being more affected. Gender also plays a role, with men less likely than women to seek help. In extreme cases, depression can lead to suicide.

Typically, medication is prescribed without sufficient regard for patient preferences and other complementary treatment options such as psychotherapy or medical aids. Side effects are an issue, for example cognitive disfunction, weight gain, or negative impacts on sexual life, and there is limited discussion with General Practitioners (GPs) on the patient pathway. **There is a lack of specialists and psychotherapists across Europe and sometimes it takes several months to get an appointment.** Typically, medication takes a few weeks to have any effect, and during that period the depression can worsen.

The term Unmet Medical Need has been used in the context of depression, for example of novel medical devices for Transcranial Magnetic Stimulation (TMS), a non-invasive procedure that stimulates nerve cells to alleviate symptoms of depression.

KEY POINTS

- → Timely diagnosis and prescription of optimal treatment must be accelerated
- → Personalised approaches to care are needed
- → Lack of precision, novel and effective treatments that do not have side effects
- → Access to innovative non-invasive technologies is limited
- → Social determinants of health play an important role in depression
- → Non-clinical burden of disease is under-appreciated
- → More research needed on causes and triggers of depression, and on loneliness and financial burden of depression

HEAVY NON-CLINICAL BURDEN

The burden to the health system is enormous — it often takes a long time to get the right diagnosis

A main criterion applying to UMN should be the seriousness of the disease, and sufficient emphasis should be placed on the non-clinical burden. This is very heavy in depression, affecting the person, the carer, the family. In consequence, it impacts on society — one is often unable to work and relies on benefits. **The burden to the health system is enormous — it often takes a long time to get the right diagnosis, to identify the right medication, and during this period things can become even bleaker.** Treatment resistant depression often means the situation becomes hopeless, with no respite or recovery on the horizon.

We know little about the effectiveness of anti-depressant drugs on comorbid psychiatric and/or substance misuse disorders, or about the specific needs of key subpopulations (adolescents, expectant or new mothers, older people).

There should be better knowledge in healthcare centres and awareness among general practitioners in order to identify and treat depression at an early stage. As a society, we should focus more on building children's resilience at school and adopt a prevention approach. In Finland, for example, Mental Health Skills are part of the educational curriculum.

PERSONALISED APPROACHES NEEDED

For people living with depression, a major UMN is a personalised approach — accessing the right treatment at the right time. **There is a lack of precision, novel and effective treatments that do not have side effects.** More work is required in the area of psychedelics' assisted therapy, for example. **There is also a need to incentivise new research on the causal, neurological factors behind depression.**

Loneliness, isolation, financial problems are major challenges for people living with depression and point to wider unmet need. The shift towards digitalisation and on-line working, whilst important, a priori, can be problematic for some who cannot afford computers or smart phones.

During Covid, many patients were unable to access therapy and their only recourse were patient organisations, which helped many people through peer support not to sink completely. **The added value of formal and informal support networks cannot be overestimated.**

The impact of addressing these UMN would be very high. It would impact positively on individuals, their families, and carers — enriching quality of life through the ability to work and socialise, to live life normally. It would also ease the burden of treatments and costs to the healthcare system and society at large.

People living with depression should be involved in planning research so that they can help to shape it and ensure it responds to the real needs and goals of patients.

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Gamian Europe has been successfully involved in EU research projects for the last 10 years, although we still see some tokenism. It is also important to work collaboratively with companies — how can they develop better medicines if patients are not engaged meaningfully?

Understanding of mental health and its importance has increased considerably over the last few years, in part because of COVID and the impact of war and conflicts. **The mental health community is hopeful that this should result in greater investment in research and innovation,** not only in therapies, although they are key, but also in our response as a society. It is clear that stigma of depression, while still prevalent, has diminished in recent years. People talk more openly about depression, especially young people. Mental illness is largely recognised today in the same way as physical illness, and this will create a new landscape for unmet needs to be addressed in the future.

A perspective from the Alzheimer's Disease community

Based on an interview with Jean Georges, Executive Director of Alzheimer Europe

NEEDED: DISEASE-MODIFYING THERAPIES

Knowledge about Alzheimer's Disease (AD) has evolved in the last 10 years: we now understand that brain changes can occur 10-20 years before symptoms begin. Early stages of the disease, such as mild cognitive impairment, can be diagnosed. As the disease progresses, other symptoms appear — more profound memory loss, reduced ability to manage daily life, difficulties getting dressed or maintaining personal hygiene. In later stages of the illness, people living with Alzheimer's may lose their independence, their mobility and are often placed in nursing homes or long-term residential care.

It is a hugely costly disease in both human and financial terms that has a major impact on the individual, the family, community, and society at large.

The only Alzheimer's Disease treatments available provide temporary symptom relief; **there is no disease-modifying treatment available in Europe to address its progression or deliver a cure.** With a rapidly ageing population, AD is a growing public health and societal concern worldwide. The term Unmet Medical Need is thus used a great deal in Alzheimer's Disease to advocate for more investment in research. The Innovative Medicines Initiative (IMI), for example, highlighted AD as a major priority, which resulted in several projects. It is an area of research suited to a public-private partnership because **it offers stakeholders a chance to pool the lessons they have learned through decades of research**, mistakes they have made, and data they have compiled from years of unsuccessful attempts to develop a disease-modifying treatment.

KEY POINTS

- → Dementia is a broad spectrum of conditions with a major impact
- → Disease-modifying treatments are needed to cure or halt progression
- → Currently no therapies available to prevent Alzheimer's Disease
- → Collaboration and data sharing is essential to advancing research
- → Diagnosis often comes late — and sometimes not at all
- → AD community provide support for patients & families, and help to tackle stigma

LACK OF PREVENTION AND EFFECTIVE TREATMENT

AD is life threatening and only symptomatic treatments that work for a limited period have been authorised.

There is no treatment that can cure or halt the underlying disease.

There also exists no promising treatment that could prevent the disease. Dementia is a very broad condition — there are other types of dementia beyond Alzheimer's, such as Lewy body Dementia, Vascular Dementia, Front-temporal dementias and Corticobasal syndrome (CBS), which are rarer but also have a huge impact on people's quality of life and that of their families. A wide definition of Unmet Needs would be very important to enable research advances in other forms of dementia and indeed in other disease areas, where the needs are broad and the burden is great.

Biomarkers to support diagnosis do exist in the area of Alzheimer's Disease but are not properly utilised due to the current absence of a disease-modifying treatment. There are also issues linked to the cost for imaging and patients' acceptance for lumbar punctures required for biomarkers. In addition, people are too often underdiagnosed or diagnosed late, without addressing the underlying cause of the disease.

The absence of a disease-modifying treatment creates many issues, including lack of timely diagnosis. ***"Healthcare professionals are sometimes nihilistic and loathe to diagnose if no treatment exists".**** It is frequent that diagnosis takes over two years after an individual notices that something is not quite right. This is a major problem as it delays the kind of human peer support that can make a major difference in quality of life — early intervention is critical. The long journey to diagnosis can have impact on relationships, with symptoms of Alzheimer's such as aggression repetition, being misconstrued, and initially not seen as caused purely by a medical condition.

"An early diagnosis can transform lives and enable couples and families to confront the disease together".

Stigma continues to be a major issue — which is why dementia friendly communities are so important where people can live as normal members of the family despite their disease, and carers can be supported and trained. As the disease progresses, there is more reliance on social care services; yet, unfortunately, there are significant differences across countries in Europe regarding the quality and affordability of these services.

*European Carers' Report 2018: Carers' experiences of diagnosis in five European countries. ISBN 978-999959-995-2-0, Luxembourg, Alzheimer Europe

NEW THERAPIES WOULD BE A GAME-CHANGER

If a disease-modifying treatment became available, the impact could be huge. The attitude towards the disease would shift, there would be more awareness, and GPs could diagnose, or refer, more swiftly. There would be fewer negative connotations, where people associate the disease with a painful and isolated end of life. **People would be able to live well for long periods of the disease** — the early stages might last longer. Costs to society would also be diminished. If the disease progressed more slowly, the demand on nursing care and residential homes, one of the costliest aspects of care, would reduce dramatically.

Involving people living with Alzheimer's in research and policy is very important. Alzheimer Europe engages with them as advisors to the organisation, and pharmaceutical companies are involving people in early-stage research and clinical trials to understand what is meaningful to them — and to get insights on inclusive recruitment and how to organise site visits that really take on board the needs of people themselves.

People with experience of the disease also contribute to greater understanding of wider unmet needs in social and care services, which is vital in this area.

Due to the limited treatment options currently available, Alzheimer Europe has less experience than other organisations when it comes to inequities in access to medical treatment but even for symptomatic treatment, introduced 20 years ago it took four or five years before the medication was authorised and available; it took even longer for the treatment to be reimbursed.

Even today, symptomatic treatments are generic but in some countries are still not reimbursed — another UMN.

Further inequities, or UMN, prevail for ethnic minority groups with Alzheimer's Disease. Research and healthcare systems are still geared towards identifying people from a majority Caucasian population.

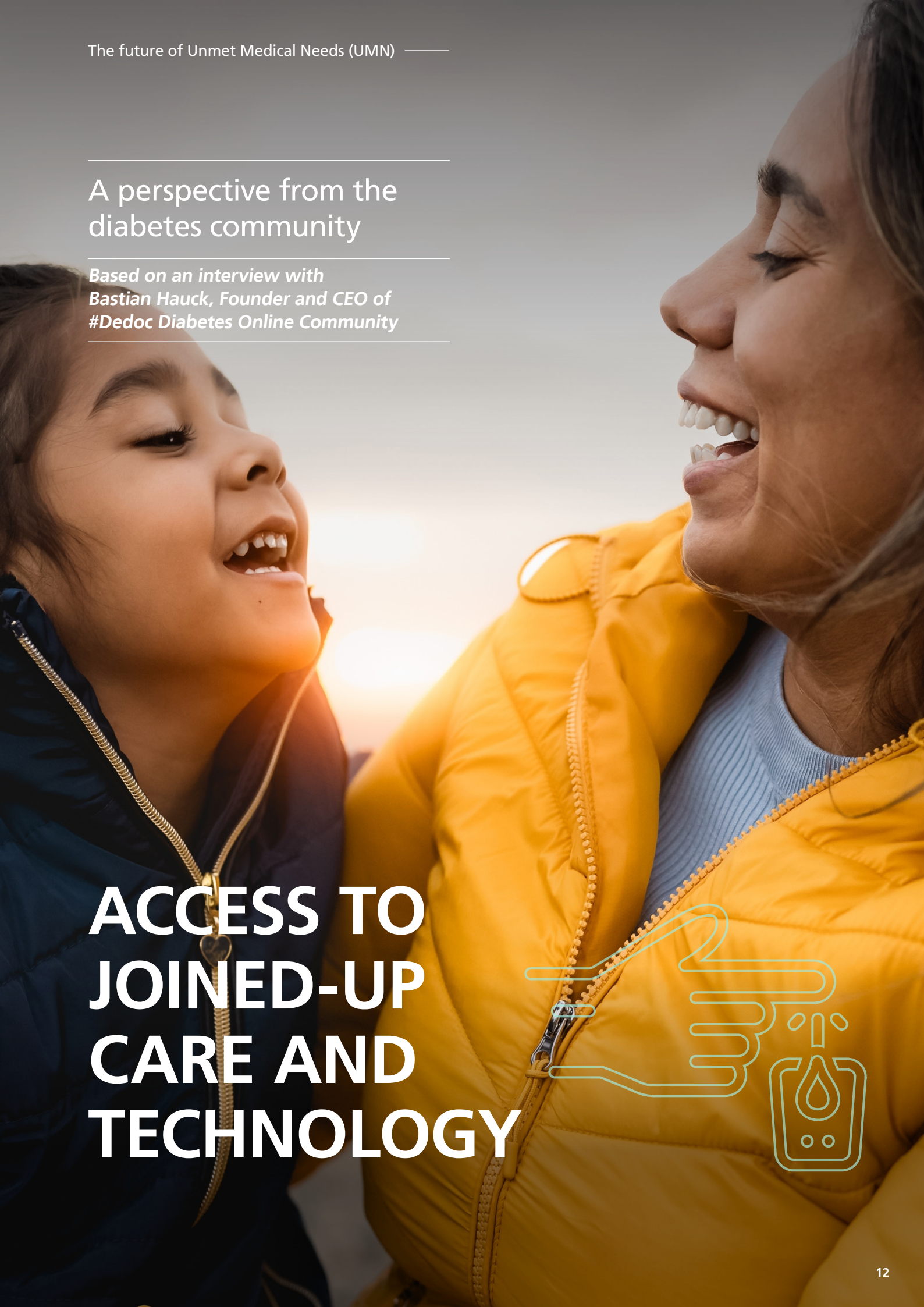
Socio-economic differences also play a role. Alzheimer organizations tend to be set up by people with a more comfortable socio-economic background and education, which can lead to challenges around inclusion and research bias.

After so many years with only symptomatic treatments available, the primary aspiration must be for a disease-modifying treatment. Further emphasis should also be placed on post diagnostic support in social care, beyond medical care per se. Optimal care services that help a person living with Alzheimer's Disease enjoy the best possible quality of life remain an unmet need and require more research and progressive policy making.

A perspective from the diabetes community

Based on an interview with Bastian Hauck, Founder and CEO of #Dedoc Diabetes Online Community

ACCESS TO JOINED-UP CARE AND TECHNOLOGY



There are two main types of diabetes: type 1 diabetes, where the body's immune system attacks and destroys the cells that produce insulin, and type 2 diabetes, where the body does not produce enough insulin or the body's cells do not react to insulin. Type 2 is much more prevalent, affecting more than 90% of people living with diabetes. Both are chronic diseases and, at more advanced stages of type 2, medical needs are quite similar.

Treatment for diabetes has evolved significantly since the discovery of insulin one hundred years ago, with extended and rapidly acting insulin increasingly available. There have also been major advances in insulin delivery and monitoring devices, including better syringes, pulmonary insulin, insulin pumps, closed-loop insulin delivery systems, and continuous glucose monitoring (CGM) which automatically tracks blood glucose levels.

This means that life expectancy for people living with diabetes can be close to normal, and there are individuals in their eighties who have lived through many changes in treatment and self-management that have resulted in a lower individual burden. "The disease is quite well managed — you can almost live a normal life."

For anyone dealing with the condition, it is a 24/7 preoccupation — it means hundreds of decisions on disease management every single day, without respite.

This also affects the people close to you as there is **a constant, underlying fear of a hypoglycaemia attack which is life threatening.**

KEY POINTS

- → Access to integrated care a top priority
- → Stem cell therapies hold potential cure
- → People with diabetes endure a significant burden in managing their condition
- → Variation in access to technology depending on patient location and whether they have type 1 or type 2 diabetes
- → Greater attention needed to infrastructure, urban planning and inclusion

IMPROVING PATIENT EXPERIENCE OF CARE

Unmet Medical Need is quite an abstract concept in the diabetes community, used largely in the political discourse.

The most important UMN are linked to access, and integrated care. There remain huge deficits in health systems which create a chasm in being able to live one's daily life — the more that this is addressed, the less the UMN.

"From a user perspective, it is about access in all its forms, and merging care into daily life".

An example is continuous glucose monitoring (CGM): the big discussion in Germany on access and reimbursement is now largely solved for type 1 diabetes. Studies show clear benefits of CGM for people living with type 2 diabetes, but it is not yet reimbursed.

There is a scarcity of diabetes specialists and a lack of specific knowledge among GPs, particularly when there are complications. **For people living with diabetes, access to foot care, eye screening or cardiovascular monitoring can be crucial but is rarely readily available for all, even in higher income countries.** *"When I see a spike in my CGM, I want the opportunity to speak to someone today, not to have to wait weeks for the next appointment".*

Another major lacuna is the fragmentation of the health system which wastes not just hours but many days. Despite a treatment regimen — essentially, insulin — being unchanged for sometimes many years, there remains the requirement to see the doctor every three months and visit the pharmacy regularly. **Precious time at the doctors is spent on the prescription, rather than discussing the issues that really matter to the individual. In many cases there is no opportunity to book online and patients face long waiting times even with appointments, therefore effective digitalisation and whole systems' thinking could make a huge difference.** Early-stage user involvement in rethinking health system and services design is key here. Inclusion is also critical — it is inconceivable in today's world to think of a digital solution that is not also accessible to blind people, for example.

The unmet medical need when it comes to treatment per se is not as high as in other disease areas. Therapies and technologies are quite advanced. There is of course always room for improvement, and this is in the pipeline — but the fundamental unmet medical needs lie elsewhere. **Today, only a small proportion of people can access new generation therapies and devices.** This, coupled with gaps in the health system in terms of training and an integrated approach, are the major hurdles.

A CURE ON THE HORIZON?

Of course, a big consideration is a cure for diabetes. There is important work happening in stem cell therapy — but we are still years' away.

There are many barriers and question marks, from research funding to safety, to negative perceptions. It is seen as far off in the diabetes community.

Another key topic is the disparity between how type 1 diabetes and type 2 diabetes are treated. In a progressed stage, the needs are very similar. Yet access to a CGM is not possible for most people living with type 2 despite the difference this could make. From a health economics perspective, this is perhaps understandable, but from a human perspective it is very difficult to justify.

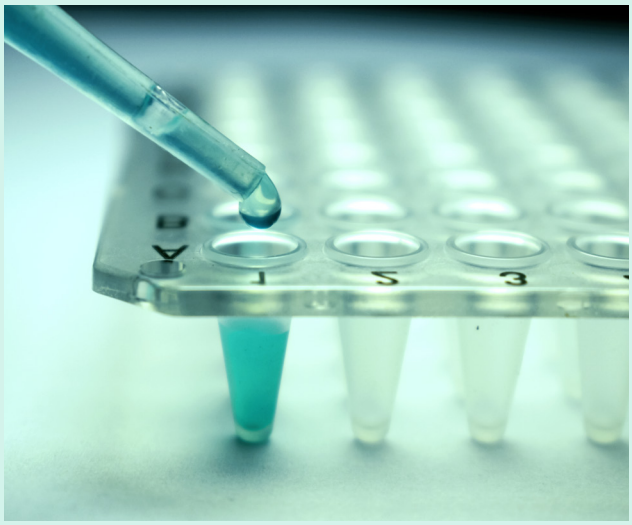
Addressing stigma is an unmet need that is also linked to access. Society has now largely understood and recognised type 1 diabetes as a serious disease and people living with the condition, with their daily struggles, are considered courageous, even heroic. **There is however much prejudice and bias associated with type 2 diabetes: people are considered ignorant, overweight, lazy.** This translates into the medical world, yet it is clearly much more complex than a doctor telling you to 'lose a bit of weight'. There are a whole range of social, psychological, even genetic determinants at play. There is a need for healthcare professionals to be more informed, empathetic and compassionate. **The social isolation of people living with type 2 diabetes should also not be underestimated, because it only reinforces the psychological burdens.**

When addressing unmet medical need, we also have to look at the bigger picture and consider infrastructure and urban planning, learning from cities that celebrate and enable movement and inclusion. And we also should focus on prevention, health promotion and general well-being.

Another critical aspect is peer support. Its enormous value is underestimated, and more recognition is needed for its role in supporting people to manage a complex condition every single day. **Referral by GPs and nurses to local support groups does not occur as it should.**

The impact of addressing Unmet Medical Need in the diabetes community is two-fold. First, the medical outcomes will be better, and secondly, a profound impact on daily life — friends, family, work, and quality of life — could be achieved.

When it comes to fairness and equity, basic principles and values should apply and we should focus on small steps that can really make a difference, mobilise patient leaders who will motivate their communities to cascade and create change. The maxim 'Think globally, Act locally' really resonates here.



A perspective from the Allergies and Airways Diseases Community

Based on an Interview with Susanna Palkonen, Executive Director, the European Federation of Allergies and Airways Diseases Association (EFA)

A DIVERSE POPULATION OF PATIENTS WITH INDIVIDUAL NEEDS

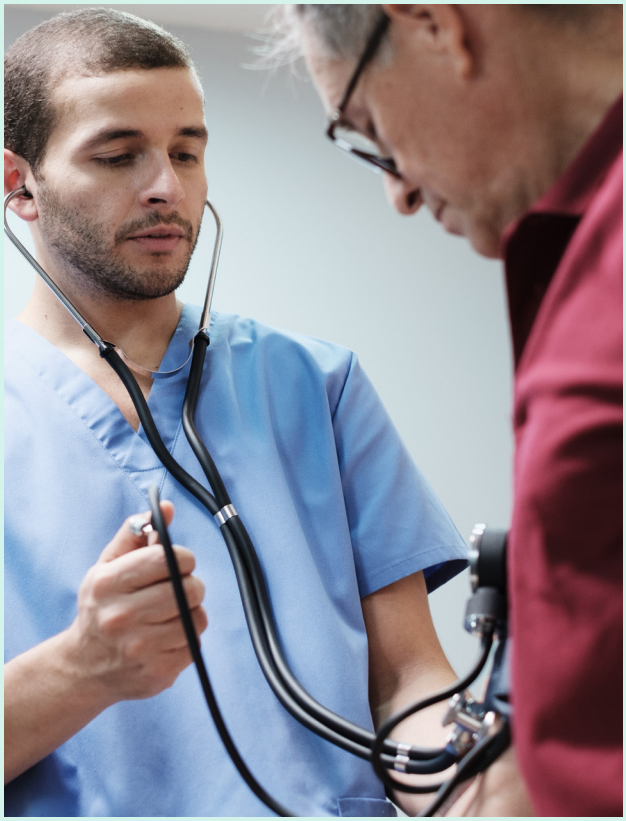
EFA unites allergy, asthma, and chronic obstructive pulmonary disease (COPD) patients' associations and each specific disease area has its own challenges.

In COPD, early diagnosis is key, but it is often overlooked, leading to severe consequences. People living with COPD tend to be older and quite frail, with co-morbidities such as cardiovascular disease, diabetes or mental health problems. **Very often, a multi-disciplinary, person-centred approach is missing.** There is a strong case for better end-of-life treatment, embracing the whole patient pathway. Stigma is prevalent, even from health care professionals, since the disease is caused largely by smoking.

In the area of asthma, diagnosis is not a problem, it is rather that the same standard treatment (steroids) tend to be prescribed for all asthmas, whether mild, moderate or severe. For moderate to severe asthma there are health system barriers in accessing targeted treatments that have recently been approved. Biologics do exist for extreme asthma, but these are very hard to get without fighting the system.

This is also the case with atopic dermatitis (eczema). The daily burden on people living with this condition includes following a rigorous, time-consuming daily routine of preventative treatments, which are often in themselves skin damaging.

Medical expertise is unevenly distributed in the allergies field and understanding the environmental, causal factors, such as mould in the home, is very complex.



KEY POINTS

- → Currently no treatment for food allergies
- → Access to biologics a challenge for people with eczema
- → New therapies needed for COPD
- → Uneven use of targeted asthma therapies leading to inequalities
- → Patients endure isolation, stress and, in some diseases, little expectation of improvement

PUTTING PATIENTS' NEEDS FIRST

UMN cannot start purely from a healthcare system perspective. Patients' needs should be defined by them, together with their healthcare professionals, based on their experiences of symptoms, their goals, and the outcomes that matter to them. For a patient living with COPD, it might be being able to walk 200m rather than 100m, without gasping for breath. This is extremely important for patients' lives.

The term "satisfactory" is too complacent when you are a patient living with a chronic disease. If the definition of UMN is too restrictive, the real needs of individuals will not be met.

In this case, asthma will be treated the same as it always was, with no ambition for more. **The burden or the seriousness of the disease is often based on who shouts loudest.** We need to think about the 'sacred needs' of patients — how serious it is for them as individuals and the kind of daily barriers they endure.

The term UMN is very intuitively understood by the patient community although it has not been used so much in the past — the focus was more on quality of life and burden of disease. **There are, however, many UMN in the allergies and airways disease field. If we take food allergy, for instance, there is no treatment as such. It is based purely on avoidance measures and if there is a serious incident and you are not carrying an adrenalin injector, you can die. This is clearly a very big unmet need.**

In the area of eczema, biologics are more targeted; however the UMN revolve around who can access these. Similarly with respiratory allergies, more cure related treatment, such as immunotherapy is not mainstreamed.

In the area of COPD, there is very little treatment**, only one form of treatment is specifically developed for addressing the symptoms of COPD. As it is a progressive disease, better treatments are needed.**

With asthma, first-line options are now targeted therapies, but these tend to be restricted to the most severe cases. Very often access is a result of highly knowledgeable and supportive healthcare professionals or effective patient advocacy to fight the system. There are major inequalities in access across and within regions. In Sweden, for example, there is a huge variance in the availability of pulmonology specialists.

A key impact of UMN on people living with these conditions is a sense of isolation and resignation. Many have simply become accustomed to a poor quality of life. Frequent hospitalisation is a significant issue for people living with COPD or severe asthma, followed by months of recovery and permanent decline. Late COPD diagnosis is a death sentence.

When you have children with atopic eczema or food allergies, it affects the entire family, as much energy goes into protecting and controlling a child's daily life. **The psychological consequences on children who grow up constantly itching has never been investigated. These 'life-erasing' factors are not given priority.**

Were such UMN met, it would change people's lives and the quality of those lives completely across all disease areas.

NEW TOOLS AND PEER SUPPORT CAN ADD VALUE FOR PATIENTS

There is no miracle solution for patients' involvement in research prioritisation and their input in the lifecycle of medicines. There is a lack of patient experts, despite programmes like EUPATI. Patient organisations can play a key role if they have the resources to coordinate and pool responsibilities.

We need to look at how medical and social services are constructed around the person. **Specific approaches are essential for hard-to-reach communities, e.g., undocumented migrants and homeless people.**

There are many additional out-of-pocket costs linked to allergies and airways diseases that are rarely factored in — investment in special hygiene products, clothes, specific food. **Pulmonary rehabilitation is also extremely beneficial but rarely made available.**

A basic minimum right for patients from this community is a self-management plan, as much is dependent on the patients' own management of the disease, making adjustments as needed, in accordance with symptoms. Digital technology can play an enormous role here. Similarly, peer support can be strongly supported by digital technology and Artificial Intelligence (AI) — not as a replacement for human qualities but as an additional enhancer.

Health systems should use peer support much more as a vital resource.

Ultimately, we need to ask what the reasonable burden is that we can expect a person living with a chronic disease to bear. If we saw UMN through this lens, we would think differently about terms like 'seriousness' or 'satisfactory treatment'.

A perspective from the Cardiovascular Disease (CVD) Community

Based on an Interview with Neil Johnson, Chief Executive of the Global Heart Hub

Global Heart Hub

GETTING TO THE HEART OF WHAT PATIENTS NEED

Cardiovascular disease (CVD) is a general term for conditions affecting the heart or blood vessels. It is usually associated with a build-up of fatty deposits inside the arteries (atherosclerosis) and an increased risk of blood clots. It can also be associated with damage to arteries in organs such as the brain, heart, kidneys, and eyes, and often linked to other conditions such as diabetes and obesity.

A key challenge is the low level of awareness of cardiac symptoms among the public, which leads to delays in presentation. Another big issue is diagnosis and early detection. When a diagnosis is made, important barriers to optimal care include navigating a fragmented health system, healthcare professionals' lack of time and limited one-to-one support. Access to medication, post-hospital rehabilitation, and ongoing care can be problematic in some countries. Due to this complex environment, much work remains to optimise outcomes for the many people living with CVD across Europe.

UMN relate to clear medical or psychological needs pertaining to one's illness. An UMN exists when best practice guidelines have been published for treatments and therapies, yet the patient is unable to access these for whatever reason. **There are recurring gaps in the care pathway for the many people living with CVD.** The social determinants of health come into play with risk factors often affecting groups vulnerable to social exclusion. It is difficult to divorce UMN from the wider environment.

Although the concept of UMN has been used in the CVD patient community, we are not as advanced as other disease areas — you hear more about it in the rare diseases' environment, yet there are significant unmet needs in CVD. **If we look at Familial Hypercholesterolaemia (FH) for instance, there are UMN around screening and early detection. In an Irish context, it starts from having no CVD strategy, no clear care pathway, and insufficient specialists. There is limited access to appropriate medication; this is despite knowing what best practice looks like and the vast burden for many individuals, their families and society at large.**

KEY POINTS

- → Focus on disease management and quality of life rather than survival only
- → Address the full impact of disease, including psychological and financial burden
- → Innovation needed in heart failure, stroke, heart attack and heart valve disease
- → Personalised medicines, genetics and regeneration therapy have a role to play
- → Screening and early detection of familial hypercholesterolaemia is lacking
- → A forum is needed where patients and stakeholders can discuss UMN

DEFINING UNMET NEED — WITH PATIENTS

Reflecting on a definition of UMN, we must define 'life threatening' — is it life support, is it life and death threatening or is it quality-of-life threatening? With chronic diseases, we are looking at longer term implications. A heart attack is, of course, life threatening but afterwards it is life-limiting, quality-of-life limiting. In CVD there are no cures, it is about disease management. If, in defining UMN, we apply criteria purely linked to the life-threatening nature of the disease, and cure, this rules everything out and is too limited.

It is very important to get the CVD patient's voice into any conversation around UMN to underline this. **In CVD we need wider criteria that reflect the burden of disease, including the financial burden — this presents an enormous weight on individuals, on families, on health systems and on societies. That said, there is also the need for greater innovation in the search for a cure for CVD**. Currently statins are the only treatment response to unhealthily high levels of cholesterol.

The UMN in CVD are wide ranging and apparent in all areas — heart failure, stroke, heart attack, heart valve diseases, etc.

Personalised medicines, genetics, regeneration therapy all have a role to play. If we look at only one area, FH, mentioned earlier, the absence of screening at a young age and early detection guarantees an early serious CVD event or even fatality.

SAVINGS FOR HEALTH AND SOCIAL SYSTEMS

Addressing these UMN would have a transformational impact; individuals affected would be able to participate in and contribute to family, work and to the community, all tremendously important for quality of life. It would also result in huge cost savings for health and social systems. Not addressing these UMN results in a very high financial burden.

Looking at research prioritisation, one important gap is a forum for collective discussion on UMN.

At disease level we know who all the relevant stakeholders are — we need a conversation on priorities based on UMN to incubate ideas. Alongside this, there remains the need for far greater patient and public involvement in medicines R&D more generally.

Wider inequalities, socio-economic and demographic considerations are strong drivers of UMN in the areas of CVD, from a social determinant / risk factor perspective. Evidence demonstrates that better off, well-educated individuals tend to be empowered and more able to adapt and be responsive to treatments.

Beyond UMN per se, a major unmet need is psychosocial. People living with CVD will have experienced a trauma, yet further down that patient journey they are largely on their own, which leads to isolation, loneliness, stress, depression, and low mood.

There needs to be much more emphasis on this impact of the condition. Peer support is vitally important, driven, in part, by the need for information and education on self-management, particularly in an era when time with health care professionals is so limited.

A perspective from the European Multiple Sclerosis Community

Based on an Interview with a representative of the European Multiple Sclerosis Platform (EMSP)

PREVENTING PROGRESSION, IMPROVING LIVES

Multiple Sclerosis (MS) is a neurogenerative autoimmune progressive disease. Signs and symptoms of MS vary widely and depend on the amount of nerve damage and on which nerves are affected. Some people with severe MS may lose the ability to walk independently or at all, while others may experience long periods of remission without any new symptoms.

In addition to mobility, MS can affect vision, cognition, sensation, bladder function, and others.

Primary progressive MS means few flares or relapses, but constant deterioration of functions. Nearly all relapsing-remitting MS (RRMS) can turn into secondary progressive MS. Regardless, **for people living with MS the neurodegenerative process is continuous. The disease gradually removes your ability to live your life independently and you become much more reliant on the people around you.**

No Evidence of Disease Activity (NEDA), also referred to as freedom from disease activity, is a goal that is emerging in multiple sclerosis treatment. The aim is to treat people with MS with disease-modifying drugs (DMDs) to reach a situation whereby they have no relapse and slow disease progression.

KEY POINTS

- → Quality of life (not only life-expectancy) should be the focus of disease management
- → Lack of options is a common concern for people with MS
- → Prevention, diagnostics, early intervention and halting progression are key
- → Cognition, fatigue and the burden of treatment are often overlooked
- → Patients must be included in conversations on research priorities, workplace relations and long-term care

PRIORITISING QUALITY TIME

UMN include any conditions with a negative impact on one's quality of life that are not adequately addressed in medical terms — hence unmet. This needs to be seen in the context of quality of life not only life expectancy. One can live for many years with MS but the quality of those years is important.

The term UMN has been used in the MS community in the context of access; people living with MS voicing their unmet medical needs during the drug approval and reimbursement process.

Regarding a definition of UMN, the criteria should not only focus on longevity or seriousness of the disease but on the devastating impact on quality of life and non–availability of options. Emphasis should also be placed on adequacy: treatments may exist, but they are not adequately addressing UMN. **We should not only focus on cure. We need to look at prevention, at diagnostics, at early intervention, and at stopping the progression of the disease.**

The UMN in MS are very pressing, from primary progression to secondary progression, the neurodegenerative process itself and indeed prevention. One key symptom, cognition, is not yet addressed sufficiently at all. Fatigue is also an enormously important issue and a stark example of some of the invisible symptoms that have an impact on people's functioning in a family or work environment. The burden of treatment is another core topic, particularly regarding side effects; the biggest issue is progressive multifocal leukoencephalopathy (PML).

Prevention is a new focus as there is now ground-breaking work in the Epstein- Barr virus (EBV).

Other UMN may not be considered as important unless you are part of the MS community. MS is a disease of young people and the ability to have children whilst on medication, questionable because of toxicity, is highly relevant to them. The impact of the disease on mental health is also a critical issue as it often causes depression.

The MS community, if asked, would have very clear ideas on prioritisation of UMN.

The impact of UMN in MS can be summed up as people steadily losing their lives through a gradual decline of their health. For some patients, they do not experience symptoms and there is not much effect on daily life, then suddenly a relapse will occur. The fear and uncertainty that patients experience are huge. It is of prime importance that people living with MS take care of themselves on an ongoing basis. As the disease becomes more dominant, people are forced to stop work, which results in a decreased social status and income and takes a big toll. If they have children, they need help in taking care of them.

Were the UMN fully addressed, people's quality of life and dignity would be restored or improved.

They would no longer feel like a burden to the family or to society. Some people living with MS may be high achievers — related stress can be a factor, and they would bring much in their productive years, were it not for MS.

There has been an evolution in how people living with MS are seen. Until quite recently, they were viewed as dependent people, with few work or family responsibilities. Now there is more understanding about reasonable accommodation and adjustments in the workplace to enable people to participate. In some countries, women with MS are now being actively supported to have children. This has largely been the result of second line treatments. **The challenge now is how to halt neurodegenerative decline.**

SETTING END POINTS, TOGETHER

Regarding research prioritisation, it would be important for patients to be involved in prioritising UMN and defining those that are most pressing.

MS is a complex disease with many desirable possible end points: jointly with the MS community, priorities can be set in an inclusive way. And further down the life cycle, when it comes to regulatory and Health Technology Assessment, the patients' voice is vital.

Reflecting on equity, fairness, and population health, one fundamental issue is the sustainability of health systems. We cannot address UMN effectively unless we invest wisely in health systems to foster societal health.

People living with MS have other needs beyond UMN. Appropriate long-term social care for those who are strongly affected is a major issue in many countries. Patients are often placed in institutions with others who have very different psycho-social needs. Medication can be withdrawn when it is no longer considered effective on medical grounds, which can result in dramatic physical and psychological consequences.

In today's economic climate, particularly in Central and Eastern Europe (CEE), people living with MS often do not inform their employer out of fear of discrimination. This means there is no reasonable accommodation in the workplace. This has a high price, as they will then avoid listening and taking care of their body and rest when needed. The individual's MS may then relapse or worsen. Improving understanding of MS in society is in the interests of all.

A perspective from the Rare Diseases Community

Based on an interview with Dorica Dan, President of the Romanian National Association for Rare Diseases and Vice President of EURORDIS

PATIENTS STRUGGLE TO ACCESS DIAGNOSIS AND CARE

Over 6,000 rare diseases have been identified worldwide. In the European Union, a disease is considered rare when it affects 5 in 10,000 people or fewer. Rare diseases are complex, often lead to disability, and require interdisciplinary care. Yet most rare diseases are little known by healthcare professionals and the wider public. This lack of awareness and knowledge, though understandable, is a significant issue for patients.

For 95% of rare diseases no treatment exists. This is, obviously, a major UMN. Families and the rare disease community often rely only on social supports. There are UMNs at all stages in the care pathway, from accurate and timely diagnosis to continuity of care and case management.

A key criterion linked to UMN is access. Even in the 5% of rare diseases for which a treatment exists, patients often lack access: the treatment may be considered too expensive, or the 'market' considered too small. Yet availability is key.

Most rare diseases are complex and life threatening and this is an important consideration in relation to UMN. Another vital criterion is the role that treatment can play in improving quality of life. The question of 'cure' is generally not so present in discussions with the community — the most important and pressing aspect is quality of life and reducing the burden of disease, not only for the patient, but for the entire family.

KEY POINTS

- → For 95% of rare diseases, there is no treatment
- → Access to therapies, where they exist, is limited and uneven
- → Patients and families face major barriers in securing a diagnosis
- → Research and care should draw on the experiences of people with rare diseases
- → Education of doctors, nurses and social care workers can improve the care of patients with rare diseases, even in rural areas

ACCELERATE THE JOURNEY TO DIAGNOSIS AND TREATMENT

Genetic testing and screening are essential when it comes to diagnosis, but there are major barriers and UMN in this area. In Romania, the rare disease community is left behind — patient organisations are working to challenge this but it is a very hard process.

My own experience is telling. I am the mother of a young woman with Prader-Willi syndrome. It took 18 years from when my daughter was a baby to almost adulthood to get a diagnosis. We went to many, many doctors. There was no name for the condition she had. We accompanied her to rehabilitation to help her learn to walk and speak, and had to be present all the time to make sure she was able to attend kindergarten and school — and be integrated there. This was a 24-hour-a-day job, and not an easy one.

Eighteen years on, it was a relief to get the diagnosis, and to know it was not our fault, and not her fault. With the diagnosis, access to growth hormone therapy helped, but there is no other treatment addressing symptoms and no cure. My husband was very healthy until recently, until he too was diagnosed with a rare disease — scleroderma — for which there is little treatment and no cure. So, rare disease can affect anybody at any age, and it is vitally important to share knowledge, personal stories and experiences. In fact, this is invaluable for research to help address UMN.

Research should respond to the true needs of patients and they should be involved at all stages, including, of course, the very early stages. Patients and their families can contribute to research as they know best their own needs and can give vital feedback about their goals and what really affects their lives.

Were UMN to be addressed effectively in the rare diseases area, the impact on patients, families, community and society would be enormous. People would be able to live their lives as they choose, with their family and with their own resources, and be part of the wider community. Unless you live with rare diseases, it is hard to appreciate this but it is hugely important.

It is critical that the rare diseases community is not left behind. Health is not only an expense but an important investment in people. We have a duty to respect each other — to give opportunities to people to be as healthy as they can be and, where there is a treatment, to make this available to patients. We must create opportunities for all to benefit from medical and social services at the right time and place. Knowledge, communication and training are key.

KNOWLEDGE, COMMUNICATION AND TRAINING ARE KEY

Knowledge is critical — to better understand the disease — to be in close contact with peers, to share expectations and experience.

The social dimension and quality of life aspects of rare diseases are so important and yet there are some basic educational gaps. There are, for example, no curricula for rare diseases. This should change. Rare diseases should be part of university education and continuous professional development, not only for health care professionals but also for social workers and care workers.

Improved communication and dialogue are also key: empathy should be integral to education and professional development.

A good example is a project we completed in Romania on health education in isolated communities, training community nurses to become case managers to improve outcomes for people living with rare diseases and their families. We are now training nurses in centres of expertise. We all teach and we all learn through sharing best practice examples.

Out of 2,000 community nurses in Romania, we have trained 700 nurses since 2020. We reach out to all community nurses to ensure they are aware of rare diseases and to be able to connect them to the relevant centre of expertise or expert for the person they are supporting. I really believe this will improve the lives of patients living in Romania — and address UMN for people in rural areas.