EUROPEAN RECOMMENDATIONS FOR IMPROVING OVERALL ACCESS TO MEDICINES FOR PATIENTS WITH RARE DISEASES ACROSS THE EU

Nordic Rare Diseases Summit 2021, April 13th

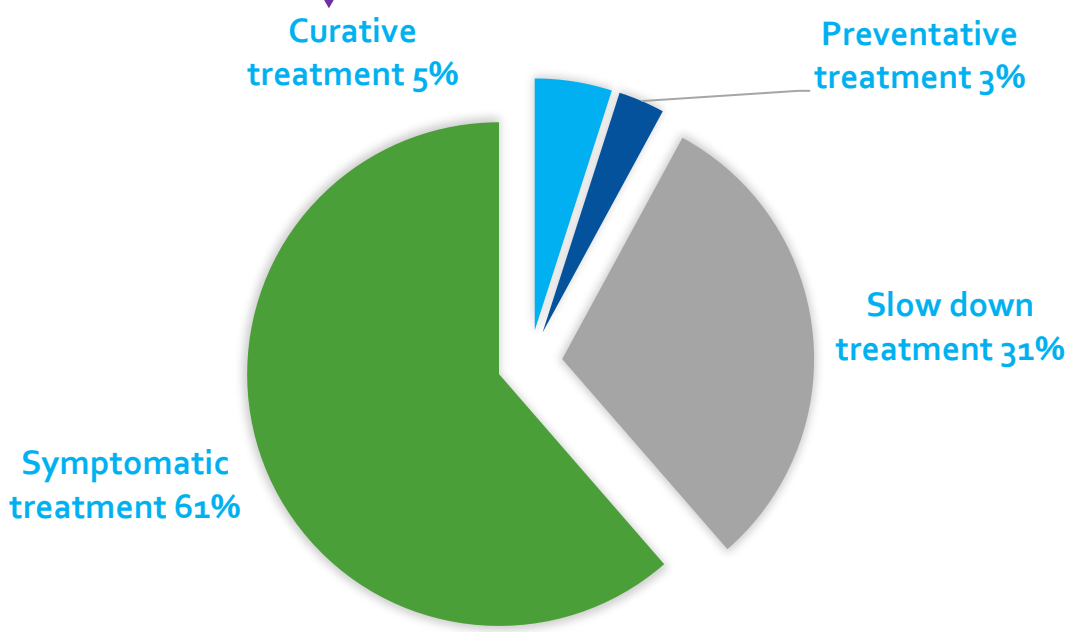
Yann Le Cam, Chief Executive Officer, EURORDIS

EURORDIS.ORG

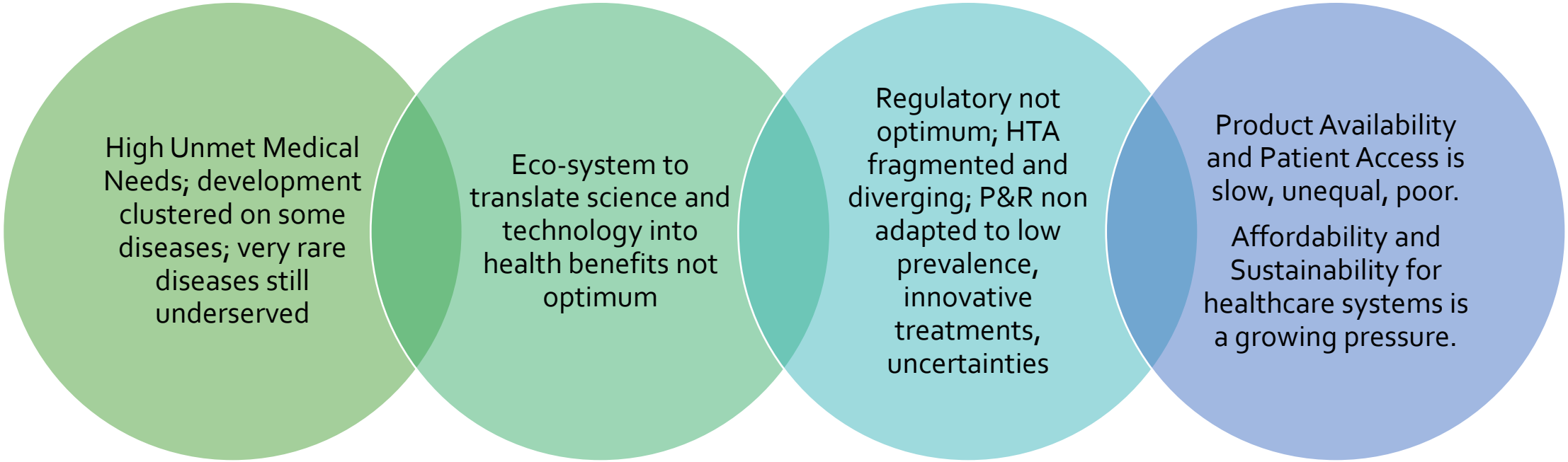
Unmet needs as perceived by people living with a rare disease?

69% have already experienced a treatment

31% have never experienced any treatment



Challenges


High Unmet Medical Needs; development clustered on some diseases; very rare diseases still underserved
Eco-system to translate science and technology into health benefits not optimum
Regulatory not optimum; HTA fragmented and diverging; P&R non adapted to low prevalence, innovative treatments, uncertainties
Product Availability and Patient Access is slow, unequal, poor.
Affordability and Sustainability for healthcare systems is a growing pressure.

Rare 2030 Recommendation for Available, Accessible and Affordable Treatments

Establish streamlined regulatory, pricing and reimbursement policies.

These policies should encourage a continuum of evidence generation along the full life cycle of a product or technology as well as the patient journey from diagnosis to treatment access.

A European eco-system able to attract investment in areas of unmet need, foster innovation, and address the challenges of healthcare sustainability.

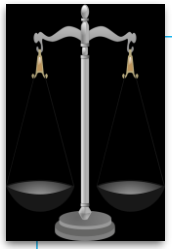
Ultimately improve the health outcomes and quality of life of people living with a rare disease.

Rare 2030
Foresight in Rare Disease Policy

Specifically recommends…

early-stage multi-stakeholder identification of unmet needs and subsequent priorities and investments

a threshold of eligibility that includes incidence in addition to prevalence of 5/10000 individuals and avoids artificial breakdown of non-rare diseases;



a graduated system of incentives, rewarding earliest dialogue and areas with no therapeutic options yet;

a strengthened mandate for the Committee on Orphan Medicinal Products at the European Medicines Agency (EMA);

a functional and efficient EU Health Technology Assessment (HTA) Framework and in the interim increased uptake of joint EMA/HTA assessment at the European level;

the introduction of a common European Table of Negotiations to allow for structured collaboration amongst Member

a continuum of comparative evidence generation throughout the patient journey and product/technology lifecycle collected in disease registries, supported by a European fund.

With measurable goals

More and better quality curative, stabilising, palliative, assistive, rehabilitative and preventive technologies and therapies available, accessible and affordable

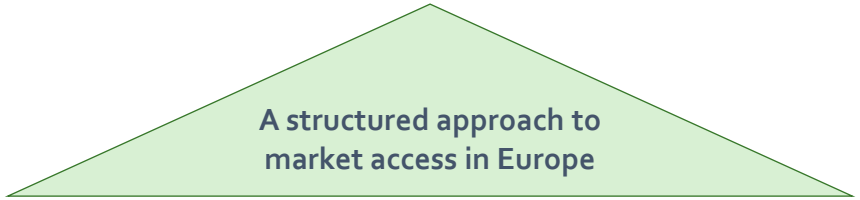
A European competitive ecosystem in the development of RD therapies and a more robust pharma and biotech manufacturing presence

1000 new therapies available

3 to 5 time more therapies approved every year, 3 to 5 times more affordable than current available treatments

EURORDIS suggested approach (2018)

The ambition of EURORDIS is to have 3 to 5 times more new rare disease therapies approved per year, 3 to 5 times cheaper than today by 2025



Structured voluntary cooperation between healthcare systems in the European Union

PILLAR 1

A new blueprint to cut costs and fast-track R&D

PILLAR 2

Early dialogue and European cooperation on the determination of value

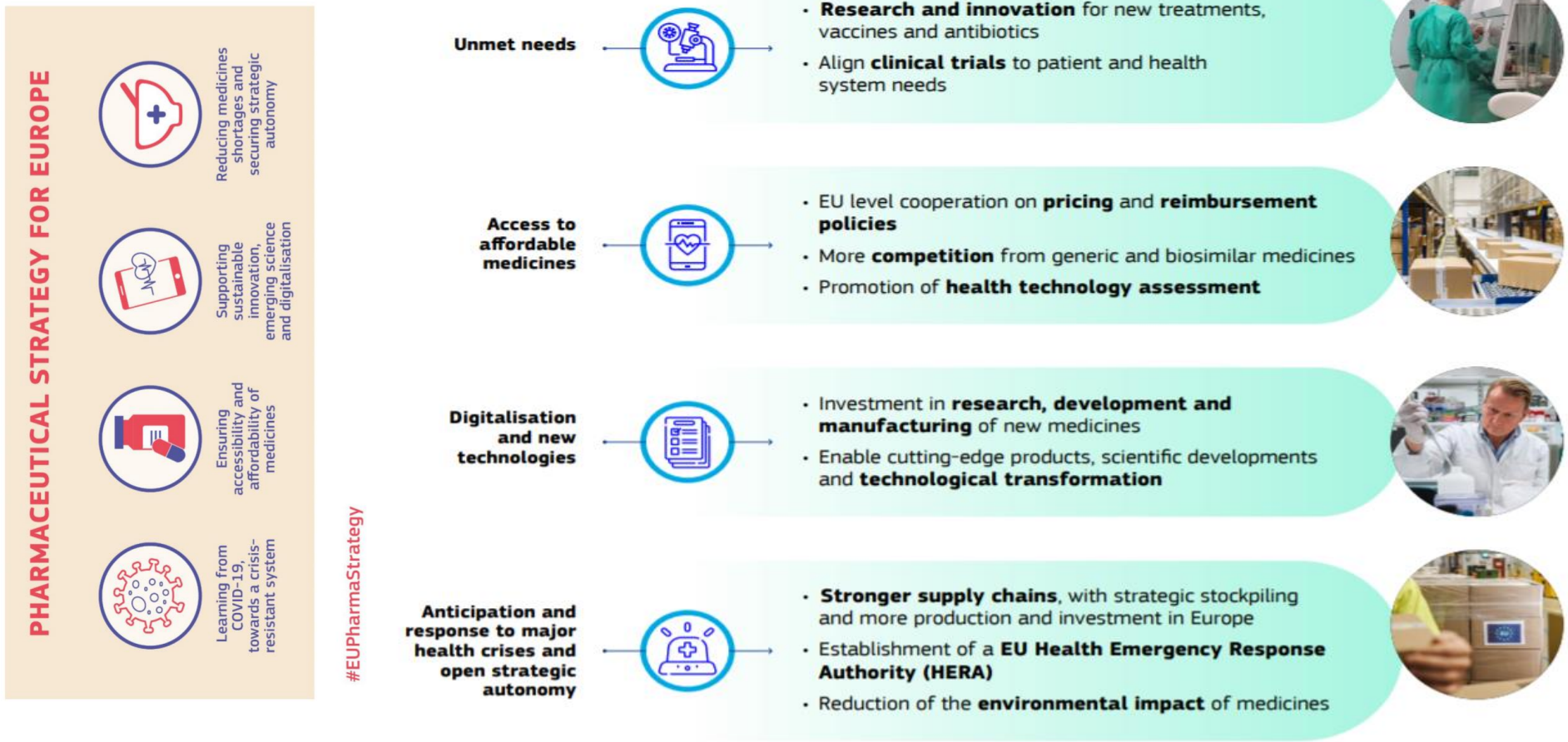
PILLAR 3

A European cooperation framework for fair prices and sustainable healthcare budgets

PILLAR 4

A continuum of evidence generation linked to healthcare budget spending

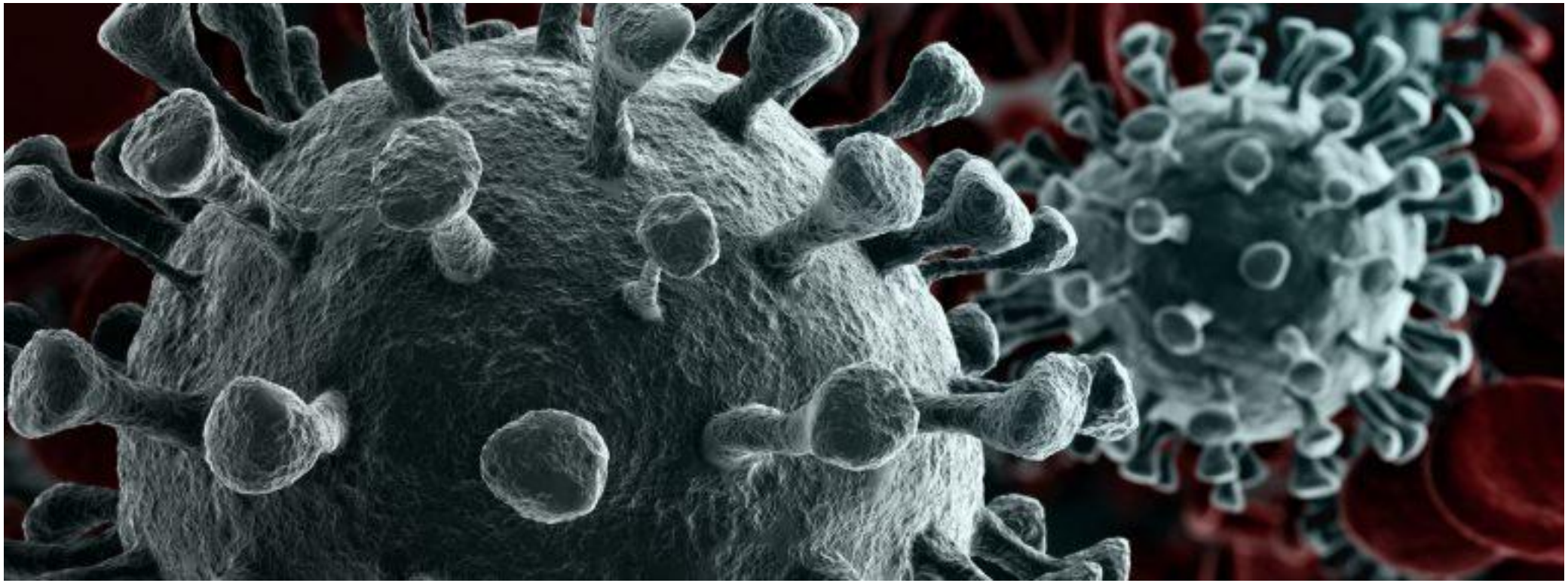
The (policy) opportunity



A strategic, coordinated approach to development & access to treatment to rare diseases in Europe reconciling unmet needs and innovation

Source: European Commission

A word about COVID



Some learning lessons

Collaboration before competition	Maturing of genome sequencing system	Massive use of data and computing to identify suitable candidate	Regulatory flexibility (namely, rolling data review)
Growing acceptance of other type of clinical trials	Procurement to match innovation with unmet need(s)	Mature scientific knowledge stemming from rare disease research	Investments (public, private and both)!

EURORDIS
RARE DISEASES EUROPE

THANK YOU

EURORDIS.ORG

How the Nordic countries align with the European ORPH-VAL principles for assessing medicines for rare diseases

Lieven Annemans

Ghent University, Brussels University (VUB)

Copenhagen (virtually) April 13 2021

Lieven.annemans@ugent.be
https://www.linkedin.com/in/lieven-annemans-3376b46/

GHENT UNIVERSITY

Content

- Values, Value and Value for Money in Healthcare
- How valuable is the value assessment in the highly valued Nordics?
- Takeaways

No-one should be left behind

- ✓ "Ensuring **universal access to quality care** demands greater efforts to improve the effectiveness, accessibility and resilience of health systems in all EU countries."
- ✓ **"More should be done to improve the health of populations in EU countries** and, in particular, to **reduce inequalities in access and quality of services**."
- ✓ "This is necessary to achieve more inclusive economic growth and to ensure healthy lives and promote well-being for all at all ages."
- ✓ **"This is necessary from an ethical point of view. Every citizen has the right to receive the best possible healthcare" (added myself)**

OECD/EU (2016), *Health at a Glance: Europe 2016 – State of Health in the EU Cycle*, OECD Publishing, Paris.
http://dx.doi.org/10.1787/9789264265592-en

"The aim of healthcare policy is to **optimize the health of the population within the limits of the available resources,** and within an **ethical framework** built on equity and solidarity principles."

EU Council of Ministers of Health Dec 2010, based on the text of the Belgian Presidency

It’s about adding value

OXFORD DICTIONARY

[val-yoo]

Spell Syllables

Synonyms Examples Word Origin

See more synonyms on Thesaurus.com

noun

1. relative worth, merit, or importance:
   the value of a college education; the value of a queen in chess.

2. monetary or material worth, as in commerce or trade:
   This piece of land has greatly increased in value.

3. the worth of something in terms of the amount of other things for which it can be exchanged or in terms of some medium of exchange.

What is the value of an orphan medicine?

Annemans *et al. Orphanet Journal of Rare Diseases* (2017) 12:50
DOI 10.1186/s13023-017-0601-9

Orphanet Journal of Rare Diseases

POSITION STATEMENT Open Access

Recommendations from the European Working Group for Value Assessment and Funding Processes in Rare Diseases (ORPH-VAL)

Lieven Annemans[1], Ségolène Aymé[2], Yann Le Cam[3], Karen Facey[4], Penilla Gunther[5], Elena Nicod[6], Michele Reni[7], Jean-Louis Roux[8], Michael Schlander[9,10,11], David Taylor[12], Carlo Tomino[13], Josep Torrent-Farnell[14], Sheela Upadhyaya[15], Adam Hutchings[16*] and Lugdivine Le Dez[17]

GHENT UNIVERSITY

NORDIC RARE DISEASE SUMMIT 2021

Guide to core elements of value

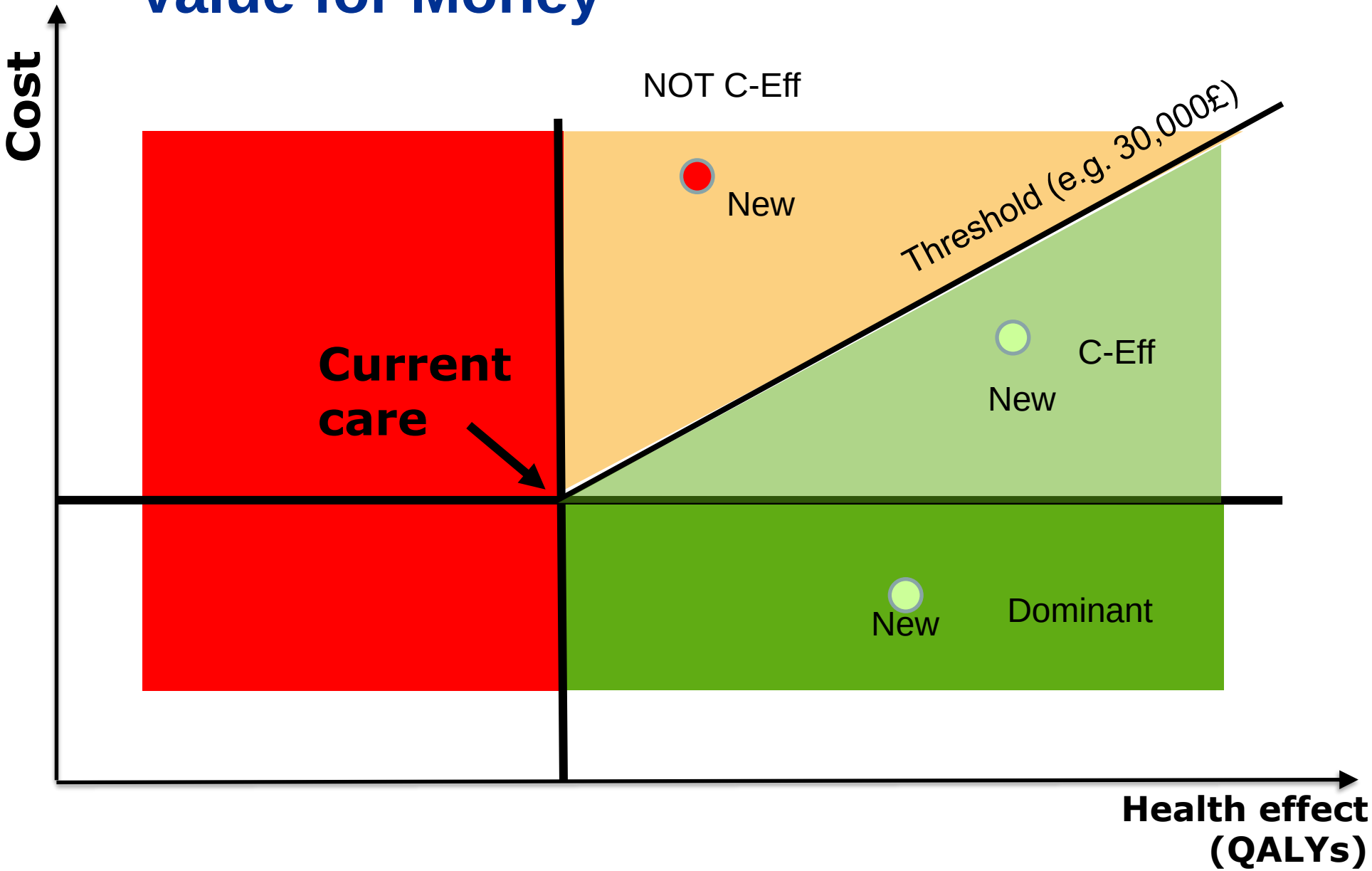
Value of an orphan medicine		
	Impact of DISEASE on	Impact of TREATMENT on
Patient level	Survival/life expectancy; Morbidity Patient experience and quality of life (QALYs) Patient economic burden	
Healthcare system level	Healthcare system resources and budget Healthcare system organisation	
Societal level	Family/Carer Quality of life Family/carer economic burden Societal economic burden	
Considerations beyond product value		
Societal preferences for rare diseases Sustainability of innovation in rare diseases		

Based on Annemans et al – ORPH-VAL – 2017

GHENT UNIVERSITY

NORDIC RARE DISEASE SUMMIT 2021

Value for Money



Annemans L. Health Economics for non-Economists. Pelckmans Pro 2017

Single Threshold? No way!

Policy & practice

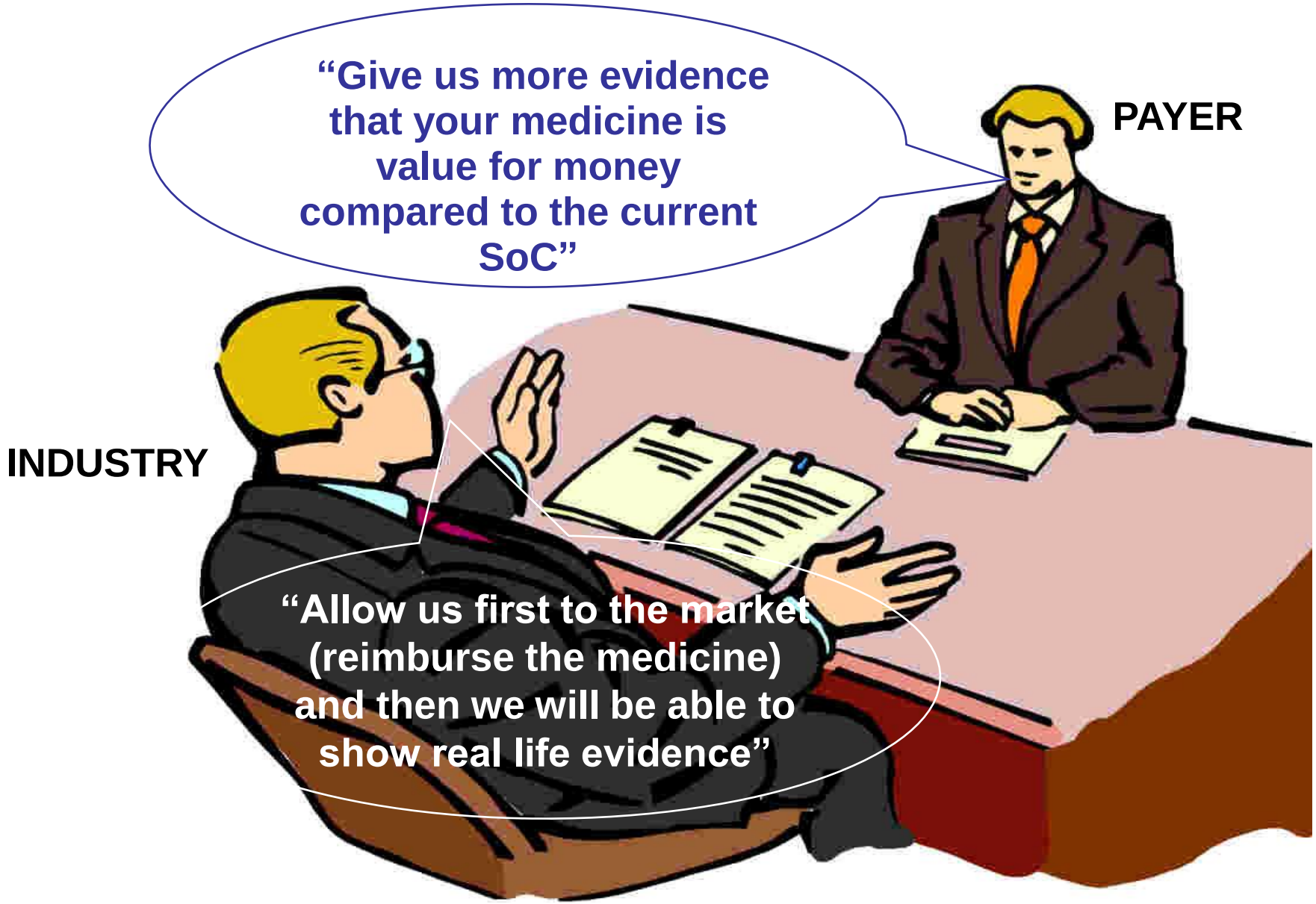
Cost–effectiveness thresholds: pros and cons

Melanie Y Bertram,[a] Jeremy A Lauer,[a] Kees De Joncheere,[a] Tessa Edejer,[a] Raymond Hutubessy,[a] Marie-Paule Kieny[a] & Suzanne R Hill[a]

Bull World Health Organ 2016;94:925–930

Cost–effectiveness information should be used alongside other considerations in a transparent decision-making process, rather than in isolation based on a single threshold value.

A key challenge for OMPs: Evidence Gaps



GHENT UNIVERSITY

NORDIC RARE DISEASE SUMMIT 2021

Types of Evidence Gaps

Treatment related uncertainties

- Exact magnitude of treatment effect, variability in effect
- Long term effect
- Adverse events and safety

Disease related uncertainties

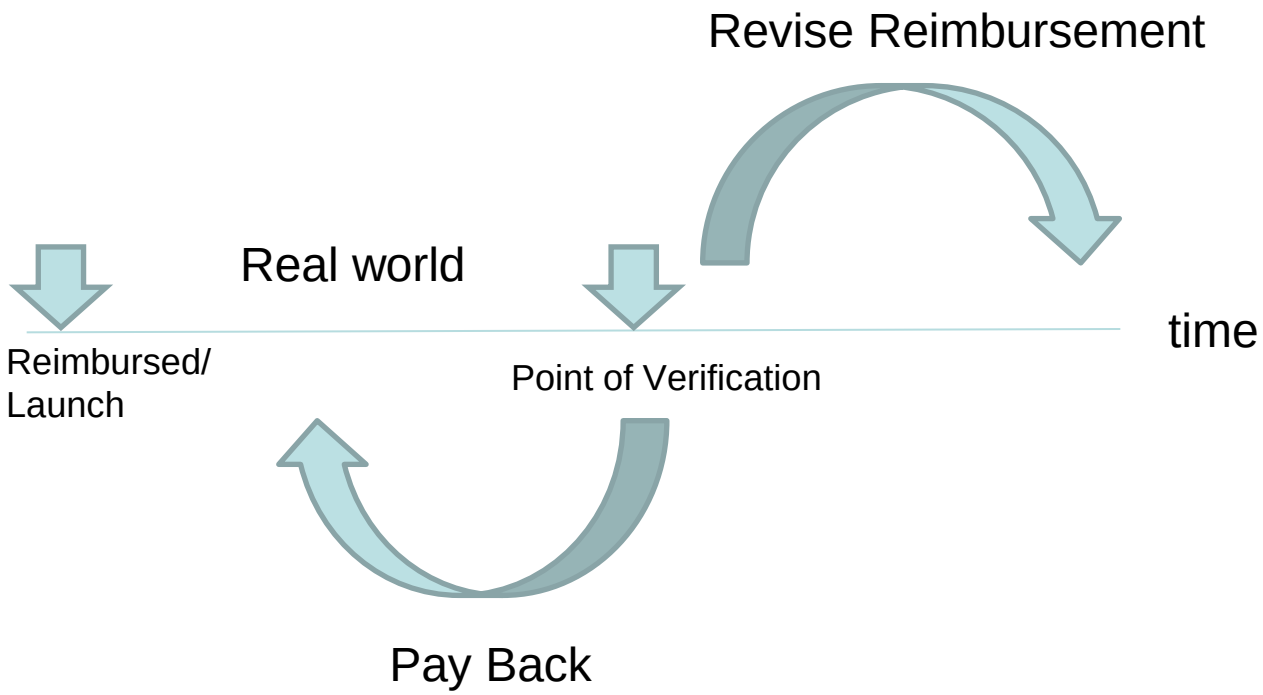
- Natural course of the disease
- Relation between surrogate and hard endpoint
- Incidence and prevalence

Healthcare system related uncertainties

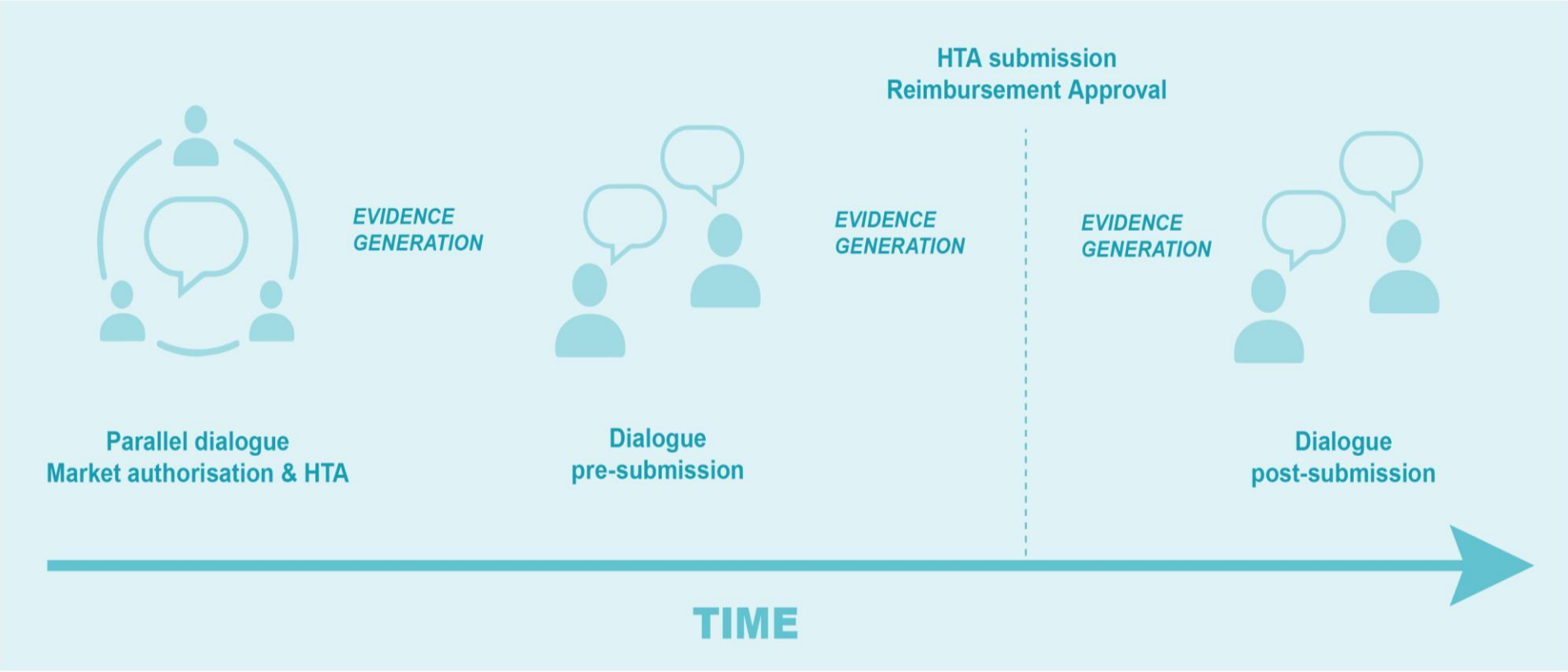
- Patient adherence and acceptability
- Provider use patterns
- Consequences to the health care system (e.g. avoided re-admissions)
- …

TRUST4RD, Orphanet Journal of rare diseases 2019

The need for adaptive processes



The Need for Iterative Dialogues



TRUST4RD, Orphanet Journal of rare diseases 2019

Content

- Values, Value and Value for Money in Healthcare
- How valuable is the value assessment in the highly valued Nordics?
- Takeaways

The ORPH-VAL principles

9 ORPH-VAL PRINCIPLES for OMPs	
1. The assessment should consider **all relevant elements of product value** in a multi-dimensional framework	CRITERIA
2. Pricing & reimbursement (P&R) decisions should be founded on the assessment of **value for money** and adjusted to **reflect other considerations**	
3. All **official regulatory and health technology assessments** of OMPs undertaken at the European level should be acknowledged by national health authorities	
4. The assessment and appraisal of OMPs in Europe should incorporate **rare disease expertise including both the healthcare professionals' and patients' perspectives**	PROCESSES
5. To accommodate uncertainty, value assessment and P&R decisions should be **adaptive** subject to the need and availability of information over time.	
6. All **eligible patients** within the **authorized label** of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations	
7. Funding should be provided at the **national level** to ensure patient access to OMPs	GOVERNANCE
8. Evidence-based funding mechanisms should be developed to guarantee **long-term sustainability**	
9. There should be **greater co-ordination** of OMP value assessment processes at a European level	

The Dolon report for the Nordics

- **Purpose**: Dolon was given the assignment to assess alignment of P&R systems in the Nordics applying the ORPH-VAL Principles, providing the possibility to generate a discussion on opportunities to improve access
- **Content**: The assessment highlights where the different countries could adjust their assessment methods to apply better for orphan drugs processes
- **Process**: The results have been validated by internal and external experts and are presented here at the summit for the first time

The ORPH-VAL principles – key areas for improvement

9 ORPH-VAL PRINCIPLES for OMPs	
1. The assessment should consider **all relevant elements of product value** in a multi-dimensional framework	✓- ✓✓
2. Pricing & reimbursement (P&R) decisions should be founded on the assessment of **value for money** and adjusted to **reflect other considerations**	✓✓
3. All **official regulatory and health technology assessments** of OMPs undertaken at the European level should be acknowledged by national health authorities	✓✓✓
4. The assessment and appraisal of OMPs in Europe should incorporate **rare disease expertise including both the healthcare professionals' and patients' perspectives**	✓✓
5. To accommodate uncertainty, value assessment and P&R decisions should be **adaptive** subject to the need and availability of information over time.	✓- ✓✓
6. All **eligible patients** within the **authorized label** of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations	✓✓✓
7. Funding should be provided at the **national level** to ensure patient access to OMPs	✓- ✓✓✓
8. Evidence-based funding mechanisms should be developed to guarantee **long-term sustainability**	✓- ✓✓✓
9. There should be **greater co-ordination** of OMP value assessment processes at a European level	✓- ✓✓

Key areas for improvements in the Nordic countries

1-2

Value assessment processes should consider all RDT specificities in a consistent way

- More comprehensive decision-making framework **including all relevant criteria for RDTs**
- More **formalised and consistent consideration of these criteria** through separate RDT pathways or special criteria, including better guidance on weight of criteria on decisions
- **Better documentation including reasons for decisions** (weight of criteria on decisions, deliberative processes)

4

More consistent disease-specific expertise should be incorporated in current processes

- Involvement of **disease-specific expertise** to provide knowledge on clinical data and pathways, and **patient experiences, preferences, needs and values**
- **More formal and consistent integration of clinician and patient perspectives** in the appraisal and decision-making

5

RDT assessment processes should be adaptive and subject to the need and availability of information over time

- Processes should **allow review of decisions over time**
- Decisions should be able to **move up and down** with new evidence
- Use of **real-world evidence** when reviewing decisions, preferably via supra-national registries
- Clarity around **roles and responsibilities of all parties involved** in the pathway

Content

- Values, Value and Value for Money in Healthcare
- How valuable is the value assessment in the highly valued Nordics?
- Takeaways

Takeaways

- The importance of investing in health
- Value has many faces
- Value for Money also needed for OMPs
- Evidence Gaps as Key Challenge
- Nordics perform generally well on the ORPH-VAL assessment principles
- Room for improvement: more formalized, balanced, adaptive and collaborative approach

GHENT UNIVERSITY

To access the Dolon report visit: nordicrarediseasesummit2021.com

NORDIC RARE DISEASE SUMMIT 2021

“Everything will be ok in the end.
If it’s not ok, it’s not the end.”

John Lennon

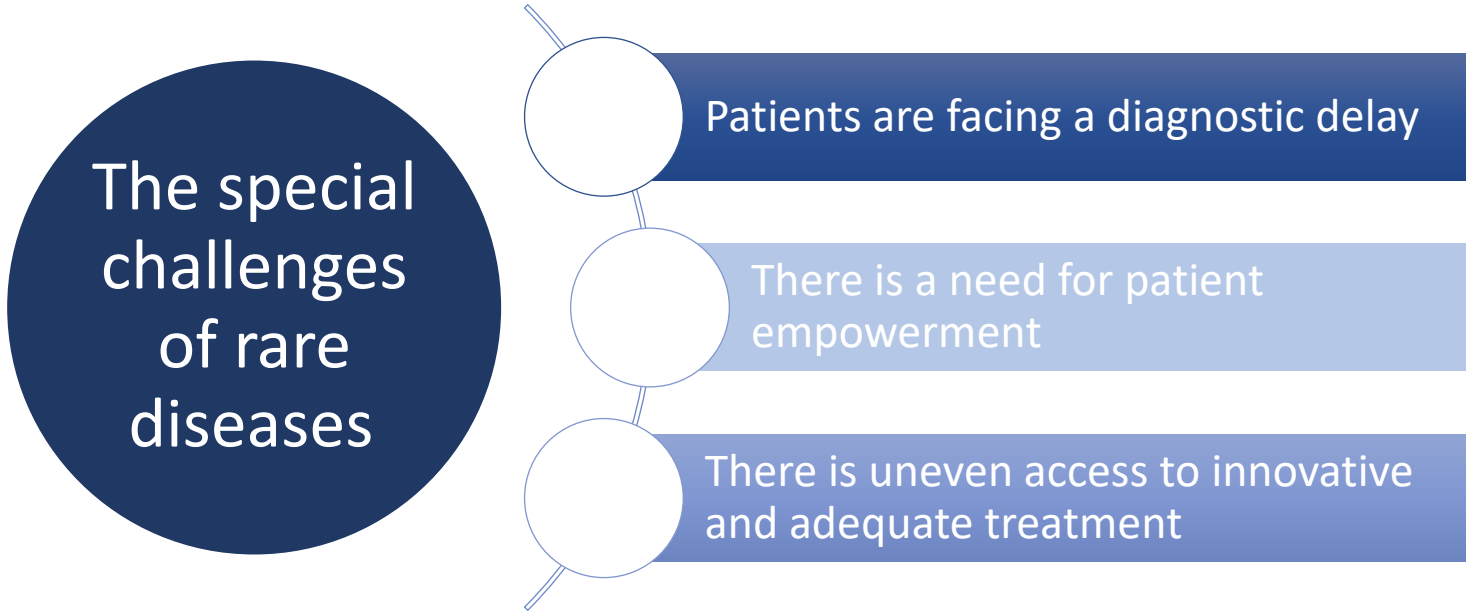
NORDIC
RARE DISEASE
SUMMIT 2021

Nordic Roadmap for Rare Diseases

by Birthe Byskov Holm, President, Rare Diseases Denmark

NORDIC RARE DISEASE SUMMIT 2021

The Nordic Roadmap for rare diseases



Diagnostic Delay

NORDIC RARE DISEASE SUMMIT 2021

Challenges

- On average it takes 6-8 years before a person with a rare disease receives the correct diagnosis
- 40% of rare disease patients are initially misdiagnosed
- Limited awareness and knowledge of the signs and symptoms of rare diseases
- Cooperation and pooling of knowledge is unsystematic making knowledge sharing difficult

Recommendations

- Investment in pioneering diagnostic platforms
- Increase the support to the European Reference Networks
- Harmonized coding systems for rare diseases across regional, national and international registries
- Implementation of innovative technologies and easily accessible information hotlines
- Systematic use of neo natal screening programs

Patient empowerment

NORDIC RARE DISEASE SUMMIT 2021

Challenges

- Empowerment needed due to low prevalence, lack of expertise and poor quality of life
- People living with a rare disease are facing a lack of involvement
- Patients and relatives hold unique knowledge, that should be recognized

Recommendations

- Putting empowerment on the agenda to promote patient empowerment at all levels
- Inclusion of patient representatives in decision making processes and sustainable support for patient organizations
- Ensure recognition of unique knowledge and involvement to contribute to development of sustainable healthcare systems

Patients' access to innovation

NORDIC RARE DISEASE SUMMIT 2021

Challenges

- Few or no treatment options
- Delayed or no access to treatment
- Assessment systems often take a narrow approach to assessing the value of new treatments

Recommendations

- Access to treatment should be supported by provision of funding at a national level
- Combining immediate access for patients with models that allows for controlled uptake, risk sharing and on-going assessment of added value
- Assessment systems across the Nordics should take into account the special conditions of rare diseases
- The perspective should reflect a holistic view of patient value when considering all relevant elements of product values

Going forward we promise each other

NORDIC RARE DISEASE SUMMIT 2021

To continue to collaborate across borders and expert fields

Given the rarity and high complexity, we need to recognize that people living with a rare disease must be treated differently to secure the same progress as we take for granted for people living with more common diseases

The Nordic countries will pave the way for enabling better lives for people living with rare diseases

We face the same challenges, we operate within similar ecosystems and have strong traditions for working together.
We are uniquely positioned to pave the way for future international collaboration to support the long-term vision of enabling better lives for people living with rare diseases

To recognize the unique challenges of patients with rare diseases

All countries need to commit themselves to set ambitious goals and monitor the implementation and effect of existing and future strategies

Read the Nordic Roadmap at nordicrarediseasesummit2021.com

ROADMAP FOR RARE DISEASES

The Nordic Rare Disease Summit, organized as a virtual meeting on 12th and 13th of April 2021, gathered a wide range of rare disease experts, decision- and policymakers as well as representatives from NGO's, patient organizations, academia and industry from across the Nordic countries. All coming together to debate how to best overcome the special challenges characterizing the rare disease area.

This Nordic Roadmap for Rare Diseases sums up key messages, discussions and new knowledge from the summit – with an aspiration to provide policy guidance relevant for the Nordic countries, recommendations for future co-operation and a shared call for action.

WHAT WE ARE FACING: The special challenges of rare diseases are…

The summit discussions revolved around three overarching themes "Diagnostic Delay", "Patient Empowerment" and "Patients' Access to Innovation". Despite progress in these areas, a stronger focus and an increased collaboration amongst all stakeholders is needed to enable better lives for people living with a rare disease. This need is reinforced by the COVID-19 pandemic which has negatively impacted quality of life and challenged access to necessary care.

Diagnostic Delay

The journey to diagnosis for people with rare diseases can often be long and uncertain. On average it takes six to eight years before a person with a rare disease receives the correct diagnosis and more than 40% of rare disease patients are misdiagnosed at initial presentation.[1,2,3]

Due to the rarity of the diseases there is limited awareness and knowledge of the signs and the symptoms of rare diseases. Most physicians will only see a small number of people with a rare disease, which makes it difficult to build up the necessary clinical knowledge and experience to recognize the symptoms.

In addition, the cooperation and pooling of knowledge across expertise areas and across countries is unsystematic and therefore the potential for knowledge exchange between healthcare specialists remains untapped.

The issue of diagnostic delay and the need for better tools, knowledge and cooperation to secure earlier diagnosis of people with rare diseases was elaborated throughout the summit.

Need for patient empowerment

Due to low prevalence, lack of expertise and poor quality of life amongst many people living with a rare disease, empowerment plays a crucial role.

Patients and their relatives hold unique knowledge of living with a rare disease and should be involved and consulted on all levels.[4]. There is a need for empowerment on individual patient level in the form of personal skills and knowledge, on community level in the form of mutual support groups, information sharing and coalition building, and on policy level to improve the shaping, prioritization and implementation of policies targeted people with rare diseases.

These needs are far from met today. People living with rare diseases are facing a lack of involvement and empowerment, and more can be done to develop disease specific information, guidelines and tools to strengthen patient engagement.

Uneven access to innovative and adequate treatment Rare diseases typically have few – or no – treatment options, and too often people living with a rare disease have delayed or no access to the treatment they need.

In the Nordic region, the assessment systems are typically not designed for rare diseases, and they often take a narrow approach to assessing the value of new treatments[5]. The current approach lacks a holistic view, that in a consistent way includes patient experiences, preferences, needs and life quality when assessing the value and price. The populations are small, and rare disease trials often lack the large scale datasets, which are requested by the authorities to demonstrate treatment value. Consequently, some innovative treatments for rare diseases never make it to the patients, who need them most. At the summit, it was recognized that delays and failure to gain access to innovative treatments may root in insufficient assessment systems.

[1] Ronicke S, et al. Orphanet J Rare Dis 2019;14(1):69.
[2] Vandeborne L, et al. Orphanet J Rare Dis 2019;14(1):99.
[3] The Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease
[4] Marta De Santis, Clara Hervas, Ariane Weinman, Valentina Bottarelli, National Centre for Rare Diseases, Istituto Superiore di Sanità, Rome, Italy, EURORDIS – Rare Diseases Europe
[5] Nordic Rare Disease Summit – An Assessment of Alignment of P&R Systems with the ORPH-VAL Principles, DOLON March 2021

WHAT WE SHOULD STRIVE TO DO:

We can overcome the special challenges of rare diseases by…

At the summit leading experts shared best practices and reflected on potential solutions to the challenges of rare diseases.

Securing advanced diagnosing

The improvement of diagnosis relies on innovative approaches, where technology innovators, patient advocates, healthcare providers and researchers cooperate to tackle the challenge of rare disease diagnostics. This cooperation should be supported by European Reference Networks in EU as much as in wider Europe, which can provide doctors with a structure for sharing experiences and knowledge in an efficient way. ERNs can serve as databases where healthcare professionals can find the right information at the right time.[6]

To shorten the journey towards accurate and timely diagnosis it is necessary to invest in pioneering diagnostic platforms and exploit digital innovation to find new solutions. Timely diagnosis requires timely action, and we need to include and offer neo natal screening programs systematically in all Nordic countries. Further, all countries need to secure implementation of innovative technologies and easily accessible information hotlines for HCPs and patients. Finally, we need to implement internationally harmonised coding systems for rare diseases like OrphaCodes and establish registries on a national, regional and international level.

Empowering patients at all levels

Patients' knowledge and expertise should be recognized and promoted as a resource on all levels of the healthcare systems: At micro level, empowerment will serve as a resource for patients and their relatives to gain greater control over decisions and actions concerning their health and wellbeing. At community level, empowerment can improve social services and quality of health. Finally, at policy level, empowerment is important to allow patients to contribute as a resource in development of sustainable healthcare systems.

This requires development of health policies that acknowledges and focuses on patient empowerment, as well as sustainable financial support systems for patient organizations and education, employment and inclusion of patient representatives in decision processes.

We need to recognize chronic patients as experts of their own care by involving them as "co-managers" of their condition in partnership with HCPs. By putting empowerment on the agenda, health policies should guarantee education and training of all stakeholders, patients, HCPs and institutions, and thus contribute to a cultural change towards patient empowerment on all levels.

Securing access to innovative treatment

As part of addressing the unmet medical needs of people living with rare diseases, we need to break the access deadlock by recognizing value of treatment in a holistic way and paying for innovation that adds true value for patients, while securing financially sustainable healthcare systems.

The assessment processes across the Nordic region need to be more transparent and must take the often limited evidence of effect for medicines for rare diseases into account. Linked to this, a holistic view of patient value should be implemented considering all relevant elements of product value, e.g. quality of life, societal preferences, rarity, budget impact and sustainability of innovation in rare diseases. The expertise of health care professionals and patient groups should be systematically integrated.

Access to treatment could also be supported by provision of funding at national level and by combining immediate access for patients with models that allows for controlled uptake, risk-sharing and on-going assessment of added value through use of real world evidence.

National plans and strategies for rare diseases to secure progress and commitment in all areas

Despite an increased acknowledgement of the importance of a national strategy for rare diseases, the implementation, including the financial support and political willingness, still varies within the Nordic countries. To overcome the challenges, all countries need to commit themselves to set ambitious goals and monitor the implementation and effect of the existing and future plans and strategies, including any additional challenges resulting from the COVID-19 pandemic. Further, establishment of rare disease registries is an important step towards achieving sufficient data that can improve diagnostics and care.

In addition to this roadmap, the national plans and strategies can take inspiration from the Rare 2030 recommendations which sets out the need for a new European policy framework for rare diseases to guide the implementation of national plans for rare diseases with the same measurable objectives.[7]

Only with national strategies and cross-country cooperation - supported by the necessary political and economic ambition – can we make lasting progress within rare diseases.

WE PROMISE EACH OTHER….

Today, we promise each other to continue to work together across borders and expert fields to overcome the special challenges of rare diseases. Due to the rarity and high complexity, we need to recognize that rare diseases must be treated different in order to secure the same progress as we take for granted for people living with more common diseases. In the Nordic countries, we have taken the first steps, and will strive to pave the way for future international collaboration to support the long-term vision of enabling better lives for people living with rare disease.

6 The *EU Directive on Patients' Rights in Cross-Border Healthcare* requires the EU Commission to support the development of ERNs throughout Member States.
7 The Rare 2030 "Recommendations: The future of rare diseases starts today, http://www.rare2030.eu/recommendations