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‘The Rare Hypophosphatemia module’

EuRREB
European Registries for Rare
Endocrine and Bone conditions

The rare hypophosphatemia module

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France

EuRREB
European Registries for Rare
Endocrine and Bone conditions

Development of Rare Hypophosphataemia module

Study Group:

Study Group: Rare Hypophosphataemia

Name(s)	Expertise / Role	Organisation
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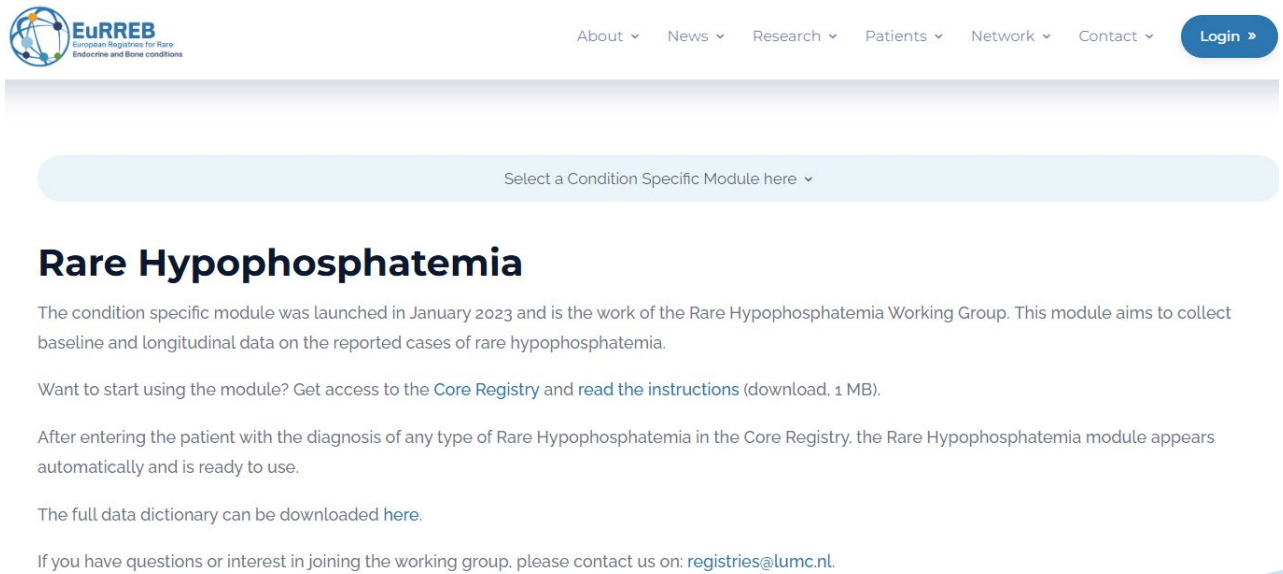
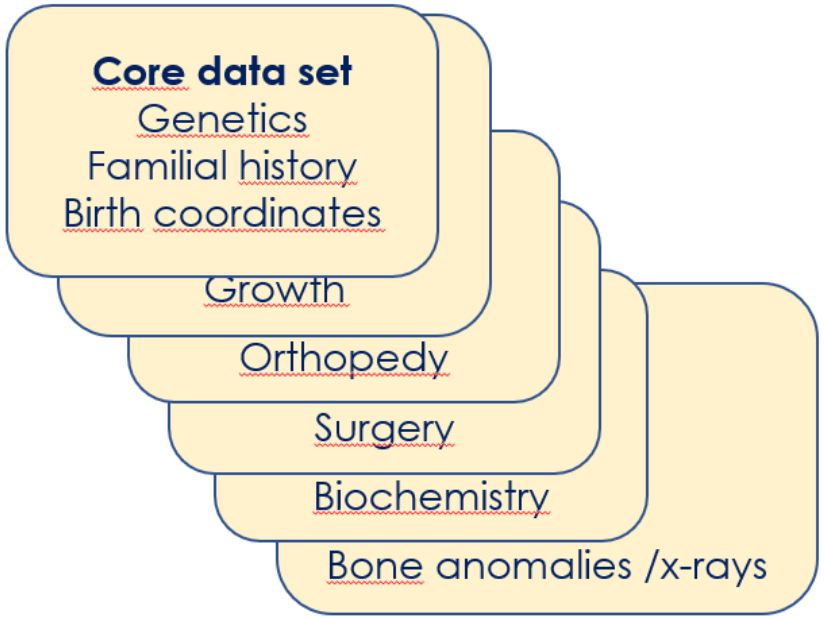
Ola Nilsson	pediatric endocrinologist	Karolinska Institute, Sweden

- Module launched since January 2023
- Data dictionary available online at www.eurreb.eu



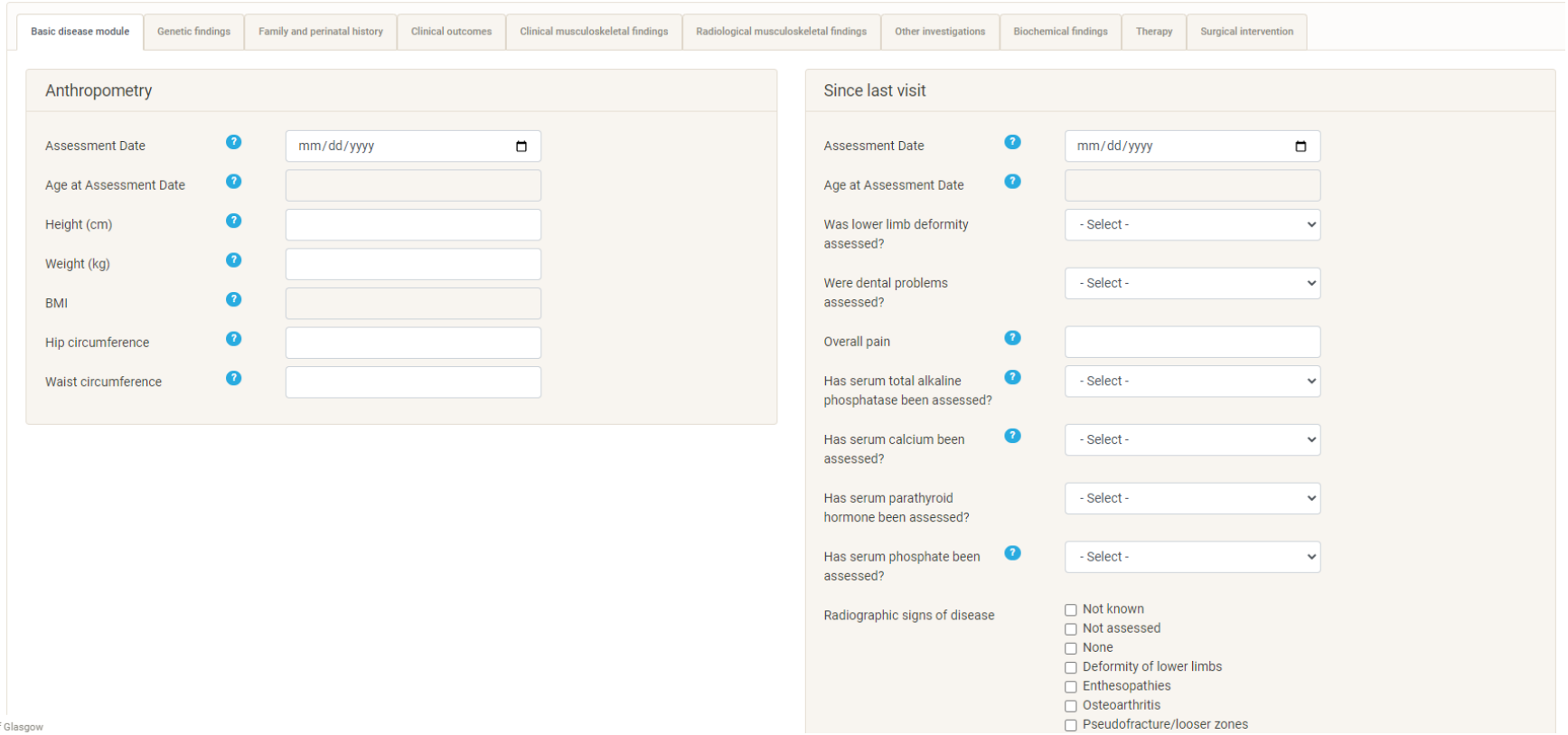
RH module – Dataset

Phosphopenic rickets and/or osteomalacia with renal tubular phosphate wasting due to elevated FGF23 levels and/or signalling												
X-linked hypophosphataemia (XLH; OMIM#307800)	*PHEX* (Xp22.1)	N	↓	↑, ↑↑	↓	↑	↓	↑, N	N, ↑[c]	N	N[d]	↑ FGF23 expression in bone and impaired FGF23 cleavage
Autosomal dominant hypophosphataemic rickets (ADHR; OMIM#193100)	*FGF23* (12p13.3)	N	↓	↑, ↑↑	↓	↑	↓	↑, N	N, ↑[c]	N	N[d]	FGF23 protein resistant to degradation
Autosomal recessive hypophosphataemic rickets 1 (ARHR1; OMIM#241520)	*DMP1* (4q22.1)	N	↓	↑, ↑↑	↓	↑	↓	↑, N	N, ↑[c]	N	N[d]	↑ FGF23 expression in bone
Autosomal recessive hypophosphataemic rickets 2 (ARHR2; OMIM#613312)	ENPP1 (6q23.2)	N	↓	↑, ↑↑	↓	↑	↓	↑, N	N, ↑[c]	N	N[d]	↑ FGF23 expression in bone
Raine syndrome associated (ARHR3; OMIM#259775)	*FAM20C* (7q22.3)	N	↓	↑, ↑↑	?	↑	↓	↑, N	N, ↑[c]	N	N[d]	↑ FGF23 expression in bone
Fibrous dysplasia (FD; OMIM#174800)	*GNAS* (20q13.3)	N, ↓	↓	↑, ↑↑	↓	↑	↓	N, ↑	N, ↑[c]	N	N[d]	↑ FGF23 expression in bone
Tumour-induced osteomalacia (TIO)	NA	N, ↓	↓	↑, ↑↑	↓	↑	↓	N, ↑	N, ↑[c]	N	N[d]	↑ FGF23 expression in tumoural cells
Phosphopenic rickets and/or osteomalacia due to primary renal tubular phosphate wasting												
Hereditary hypophosphataemic rickets with hypercalciuria (HHRH; OMIM#241530)	*SLC34A3* (9q34.3)	N	↓	↑(↑↑)	N, ↑	↑	↓	↓	Low N, ↓	N	↑↑	Loss of function of NaPi2c in the proximal tubule
X-linked recessive hypophosphataemic rickets (OMIM#300554)	*CLCN5* (Xp11.23)	N	↓	↑(↑↑)	N, ↑	↑	↓	Varies	Varies	N	↑	Loss of function of CLCN5 in the proximal tubule
Hypophosphataemia and nephrocalcinosis (NPHLOP1; OMIM#612286) and Fanconi reno-tubular syndrome 2 (FRTS2; OMIM#613388)	*SLC34A1* (5q35.3)	N	↓	↑(↑↑)	↑	↑	↓	↓	Varies	N	↑	Loss of function of NaPi2a in the proximal tubule



RH module – CROs

Variables (CRO/PRO)	Pediatric and adult patients	PROMs
Ped 95 (95/0*) Adult 84 (84/0*) *PROMs	Yes	EQ-5D, BPI-SF, MSK-QL, OHIP-14 BFI, PedsQL fatigue



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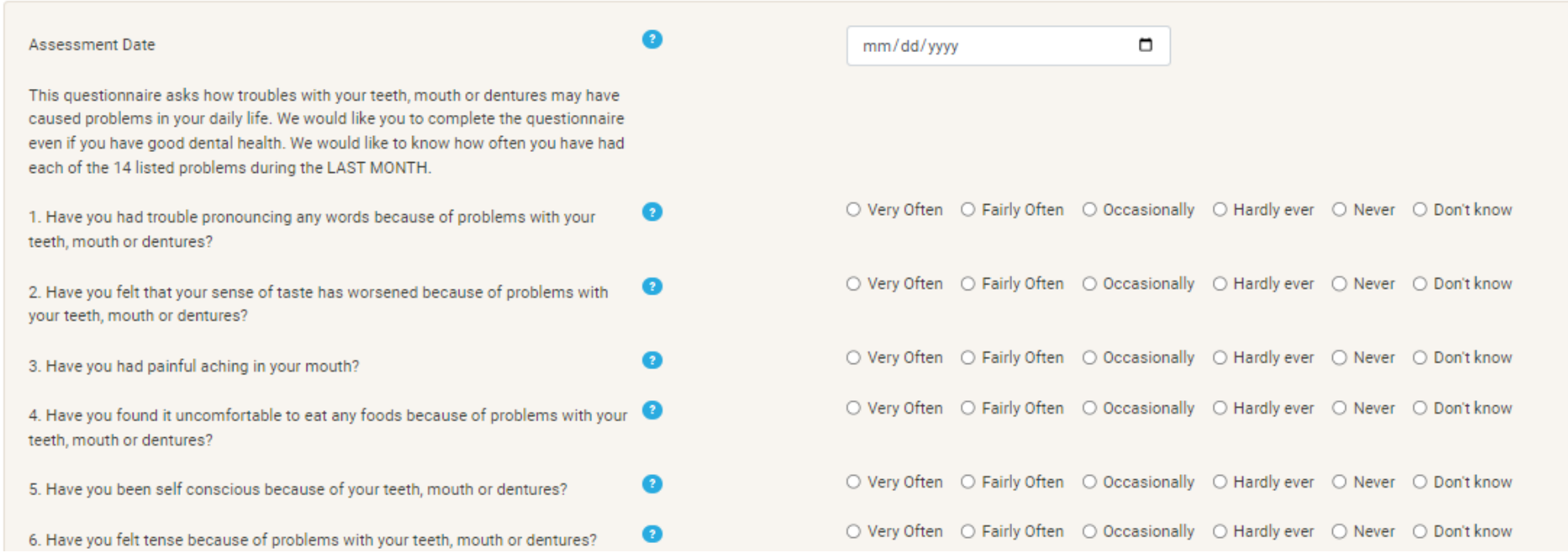
RH module – CROs

Variables (CRO/PRO)	Pediatric and adult patients	PROMs
Ped 95 (95/0*) Adult 84 (84/0*) *PROMs	Yes	EQ-5D, BPI-SF, MSK-QL, OHIP-14 BFI, PedsQL fatigue

Oral health questionnaire OHIP-14



Assessment Date — mm/dd/yyyy

This questionnaire asks how troubles with your teeth, mouth or dentures may have caused problems in your daily life. We would like you to complete the questionnaire even if you have good dental health. We would like to know how often you have had each of the 14 listed problems during the LAST MONTH.

1. Have you had trouble pronouncing any words because of problems with your teeth, mouth or dentures?
2. Have you felt that your sense of taste has worsened because of problems with your teeth, mouth or dentures?
3. Have you had painful aching in your mouth?
4. Have you found it uncomfortable to eat any foods because of problems with your teeth, mouth or dentures?
5. Have you been self conscious because of your teeth, mouth or dentures?
6. Have you felt tense because of problems with your teeth, mouth or dentures?

Very Often | Fairly Often | Occasionally | Hardly ever | Never | Don't know

Updates in rare hypophosphatemia

Rare hypophosphatemia in e-REC

- **3749 new cases of Mineral disorders (Oct 2019 - Aug 2025)**

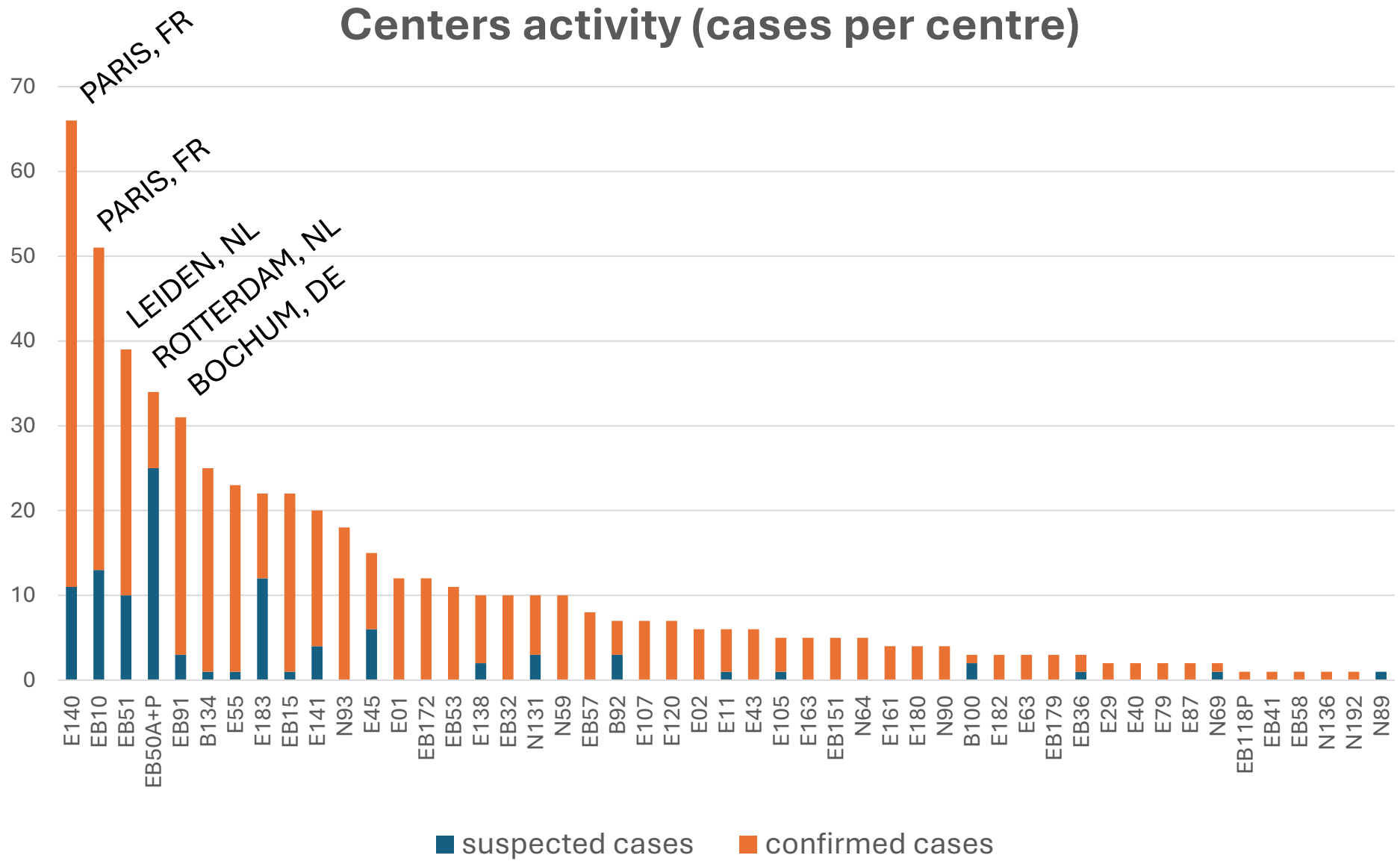
551 new case – rare hypophosphatemia (15%)

- 234 – children (suspected – 49, confirmed – 185)
- 317 – adults (suspected – 53, confirmed – 264)

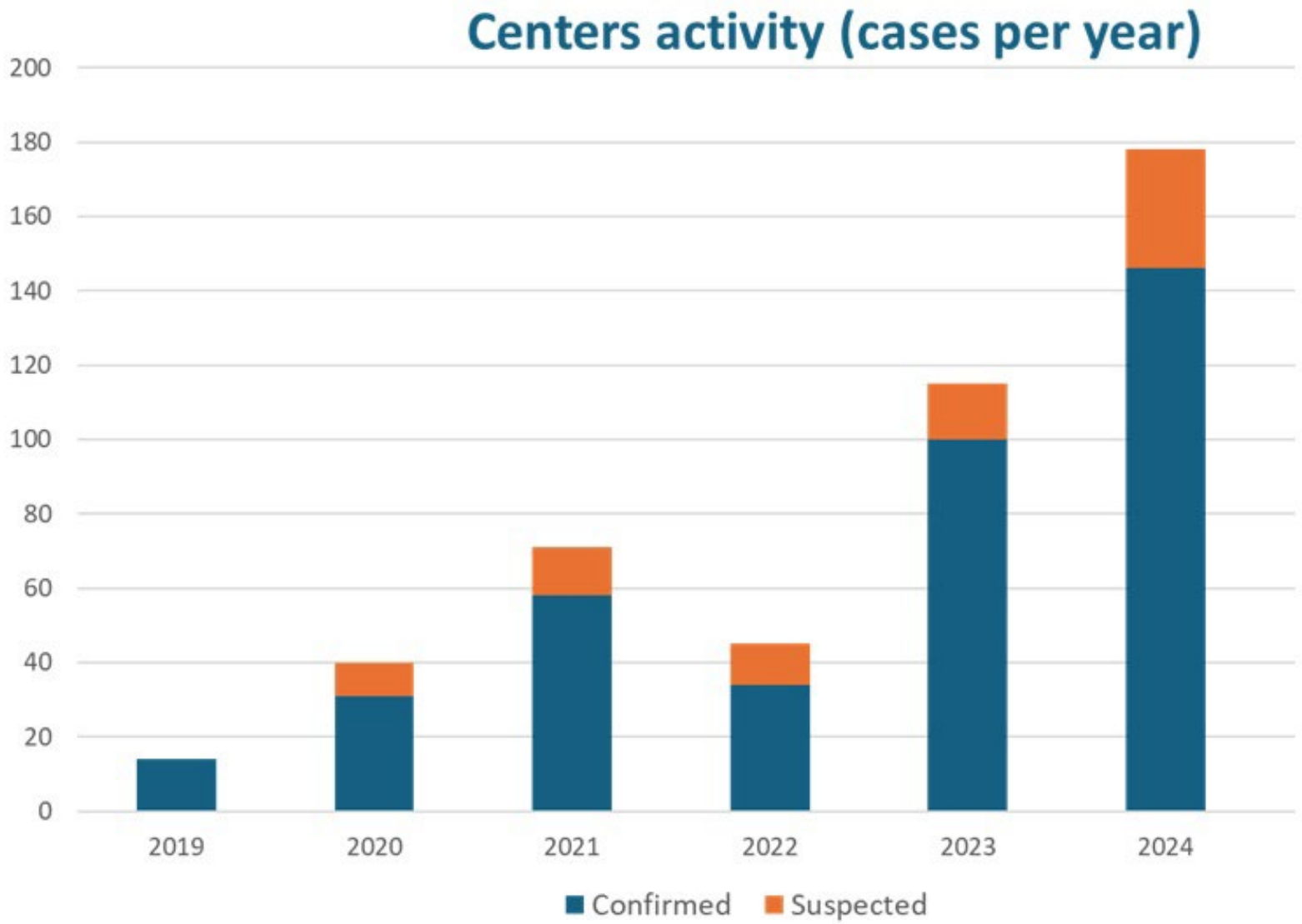
38 centers from 22 countries have reported cases

Row Labels	Sum of Suspected Cases	Sum of Confirmed Cases
Autosomal dominant hypophosphataemic rickets	11	53
Autosomal recessive hypophosphataemic rickets	1	6
Hereditary hypophosphataemic rickets with hypercalciuria	3	26
Hypophosphataemic rickets	19	60
Oncogenic osteomalacia	22	43
X-linked hypophosphataemia	46	261
Grand Total	**102**	**449**

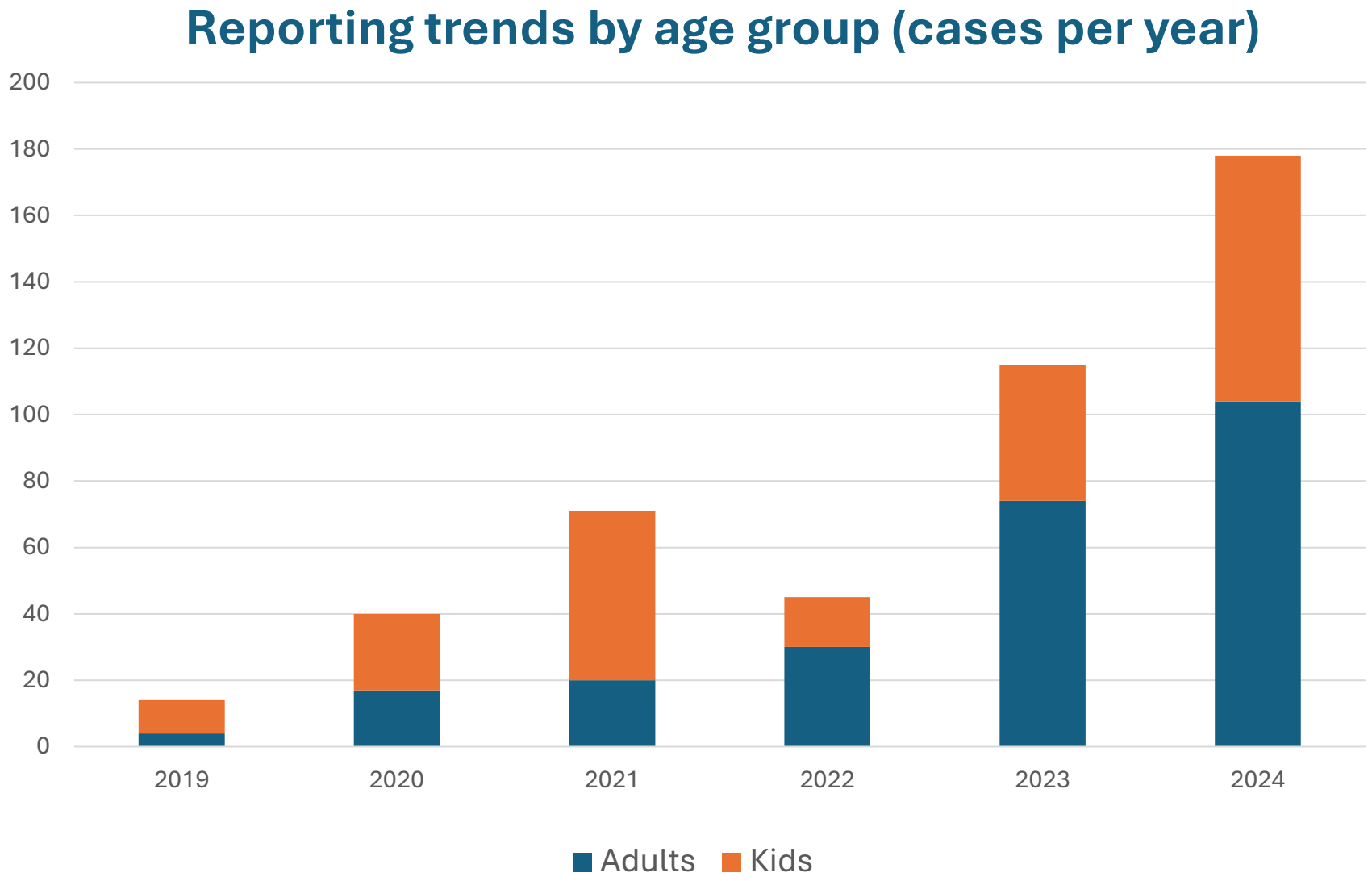
RH in e-Rec


Centers activity (cases per centre)
PARIS, FR
PARIS, FR
LEIDEN, NL
ROTTERDAM, NL
BOCHUM, DE
70
60
50
40
30
20
10
0
E140
EB10
EB51
EB50A+P
EB91
B134
E55
E183
EB15
E141
N93
E45
E01
EB172
EB53
E138
EB32
N131
N59
EB57
B92
E107
E120
E02
E11
E43
E105
E163
EB151
N64
E161
E180
N90
B100
E182
E63
EB179
EB36
E29
E40
E79
E87
N69
EB118P
EB41
EB58
N136
N192
N89
suspected cases
confirmed cases

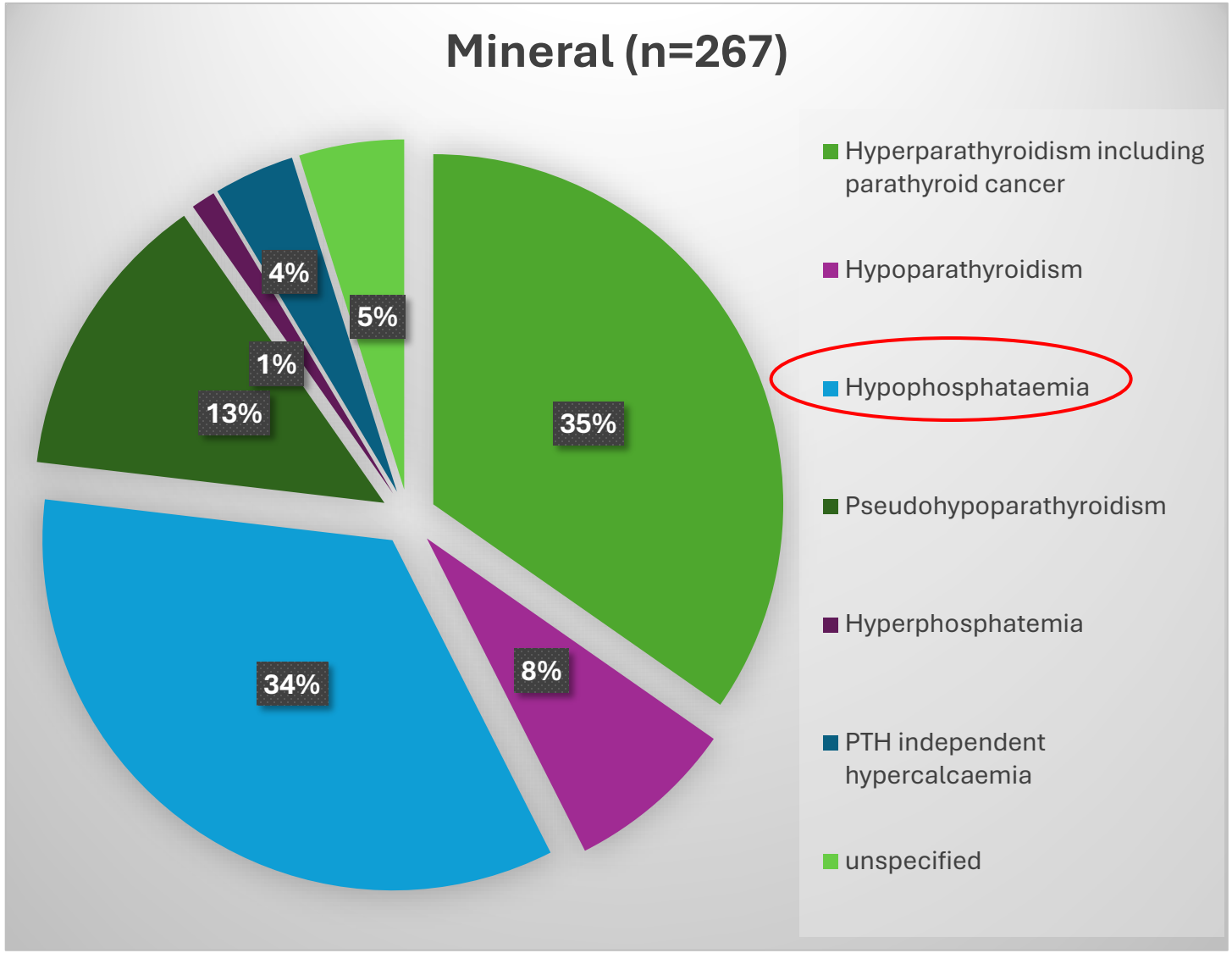
RH in e-REC


Centers activity (cases per year)
200
180
160
140
120
100
80
60
40
20
0
2019
2020
2021
2022
2023
2024
Confirmed
Suspected

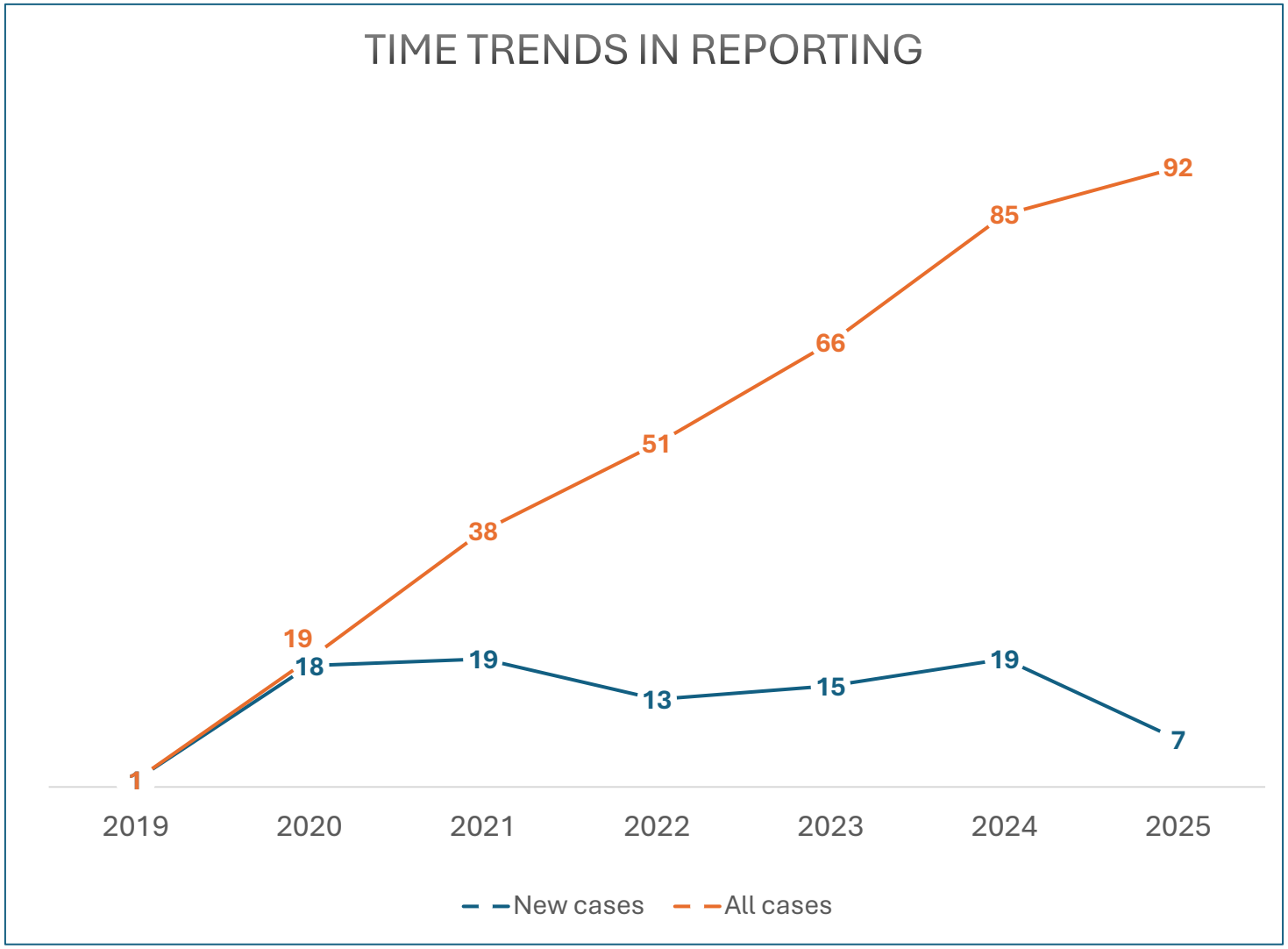
RH in e-REC


Reporting trends by age group (cases per year)
200
180
160
140
120
100
80
60
40
20
0
2019
2020
2021
2022
2023
2024
Adults
Kids

Calcium and phosphate group in the Core Registry



RH in the Core Registry



12 centers from 10 countries

RH in the Core Registry

Primary Condition	Hypophosphataemia
Row Labels	**Count of Patient ID**
	1
Autosomal dominant hypophosphataemic rickets	1
Autosomal recessive hypophosphataemic rickets	3
Hereditary hypophosphataemic rickets with hypercalciuria	1
Hypophosphataemic rickets	8
Oncogenic osteomalacia	6
X-linked hypophosphataemia	72
Grand Total	**92**

- **Children n=65**

-mean age – 7.5±3.3 years

- **Adults n= 27**

-mean age – 44.4±19.8 years

- Female n= 57 (62%)
- Male n= 35 (38%)

- 43 were diagnosed with XLH at the age 3,91±3,5 years
- 8 were diagnosed with XLH at the age 42±16 years
- Genetic confirmation - in 52 cases (72%)

RH module in the Core Registry

- Children version – completed – 53 times for 28 patients
- Adults version completed – 14 times for 11 patients

- 5 centers from 5 countries

Plans for future

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Plans for future

- Optimize the module and make it “user friendly”
  - Changes in the module: after a first analysis: many fields are left empty
  - **Main module specific to XLH, 2 versions: pediatric and adult “XLH Module”**
  - Additional tabs for pregnancy and fertility
  - Discuss the interest of other submodules in the RH: TIO etc
  - Changes will help to better fit future studies (e.g. complications, orthopedic evaluation, patient management)
- Module promotion/testing

Thank you

Funded by
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Ways to contact us:

eurreb.eu

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drop-in sessions via Zoom

European Registries for Rare Endocrine and Bone Conditions

EuRREB
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Endocrine and Bone conditions

Endo-ERN
European Reference Network on Rare Endocrine Conditions

ERN BOND
EUROPEAN REFERENCE NETWORK ON RARE BONE DISEASES