**European Registries for Rare Endocrine and Bone Conditions (EuRREB): Results from the Platform for e-Reporting of Rare Conditions (e-REC) March 2024**

## Introduction

e-REC (e-Reporting of Rare Endocrine Conditions) is an electronic reporting platform that captures activity and allows for a better understanding of the occurrence of a wide range of rare endocrine and bone conditions. For clinical networks such as Endo-ERN and ERN-BOND, the e-REC platform allows continuous reporting of core indicators of activity and enables these clinical networks to objectively map the conditions and related activity. However, the platform is open to all centres that look after people with such conditions and not just limited to reference centres within ERNs.

## Aim

This report has been developed to describe the current activity in e-REC over a 5.5-year period from July 2018 to December 2023 inclusive.

## Methods

The e-REC platform issued invitations to clinicians who had registered to participate in e-REC from July 2018 to December 2023 to complete a monthly return. Participants can create a bespoke reporting set up and report any newly encountered cases of any of the conditions that have been included in Endo-ERN and ERN-BOND.

## Results

By December 2023, a total of 101 centres from 30 countries had reported on the e-REC 36914 new cases. Of these 101 centres, 50 are in Endo-ERN only, 28 are in Endo-ERN and ERN-BOND, three are in ERN-BOND only and 20 are not related to ERN's.

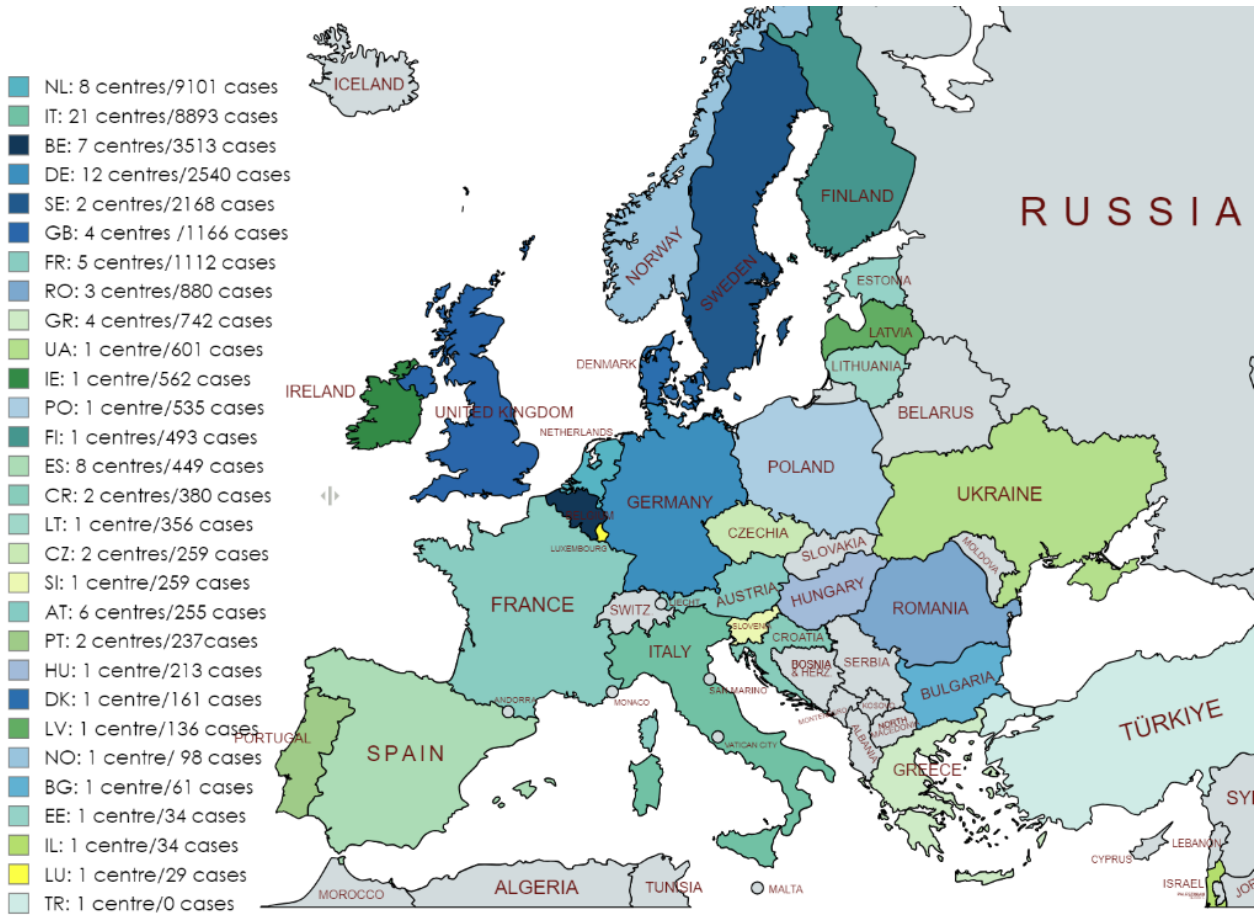



*Fig. 1 – Number of centres and reported cases in each country that are active (i.e. have submitted 1 or more returns between July 2018 and December 2023).*

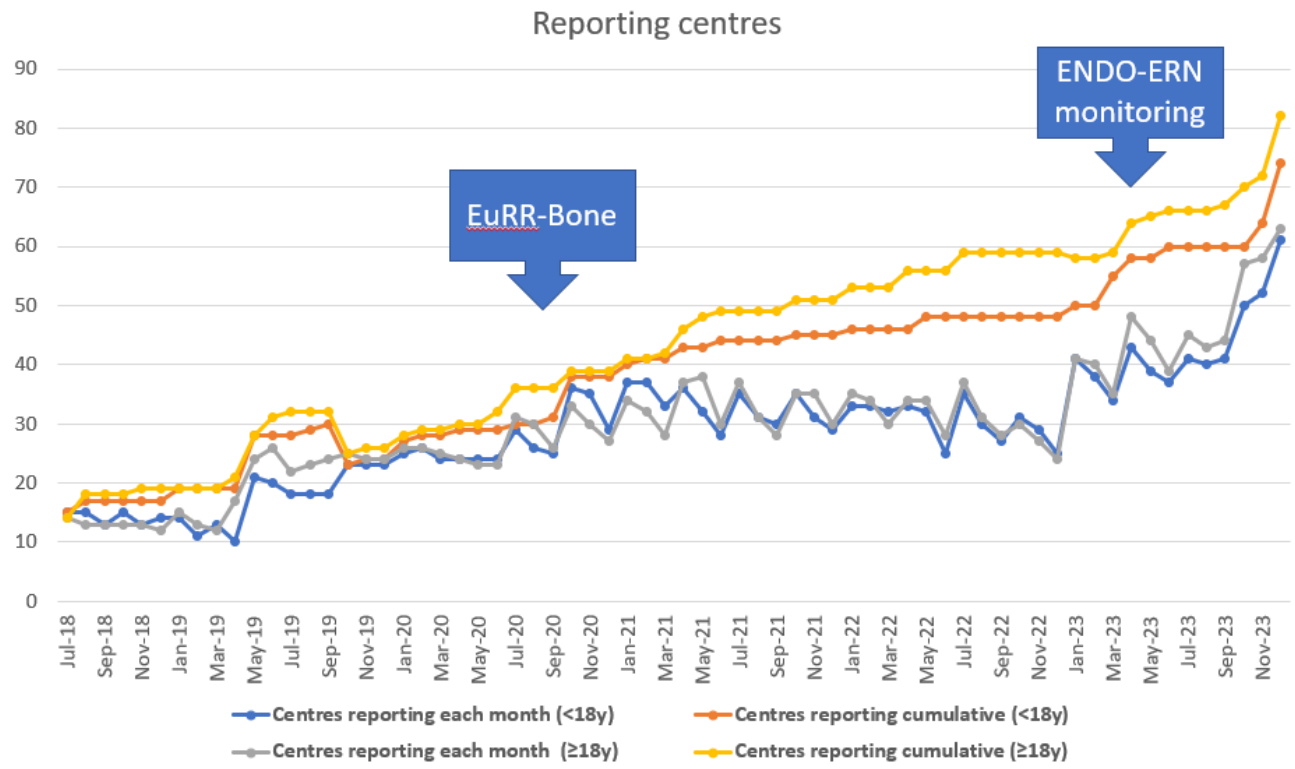



*Fig. 2 – Change in the number of centres that have been actively reporting between July 2018 and December 2023. Currently, 74 paediatric centres and 82 adult centres have actively participated in e-REC. The arrow indicates the launch of the EuRR-Bone project (April 2020) and ENDO-ERN initiative to make participation in e-REC registry obligatory activity for their centres.*

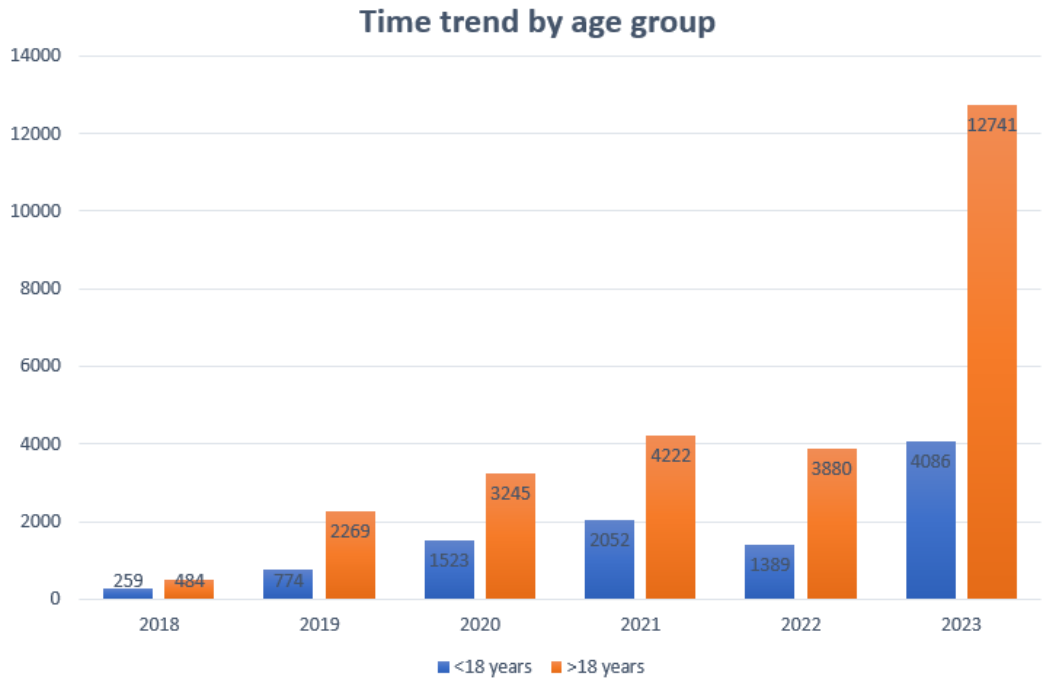
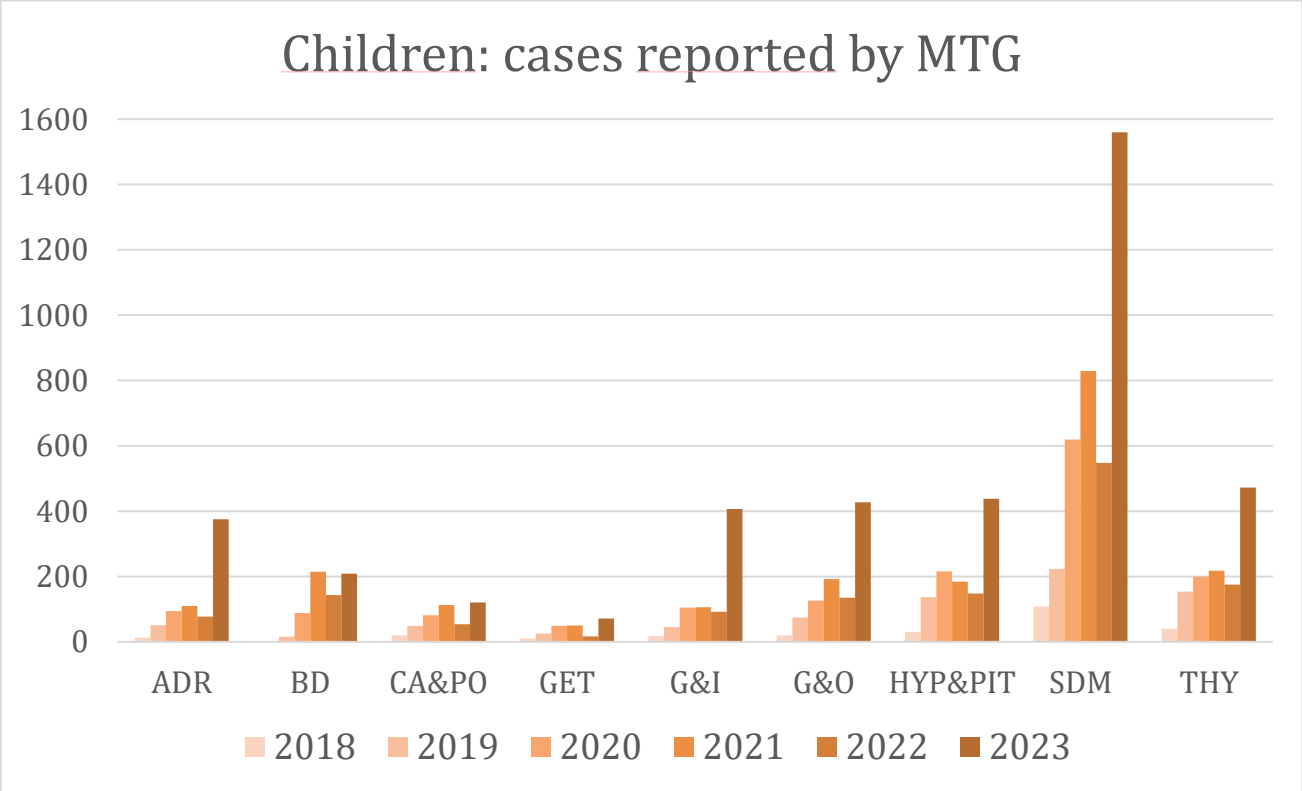



*Fig. 3 – The change in cases reported between July 2018 and December 2023. A total of 26836 new cases in adults and 10078 new cases in children have now been reported.*



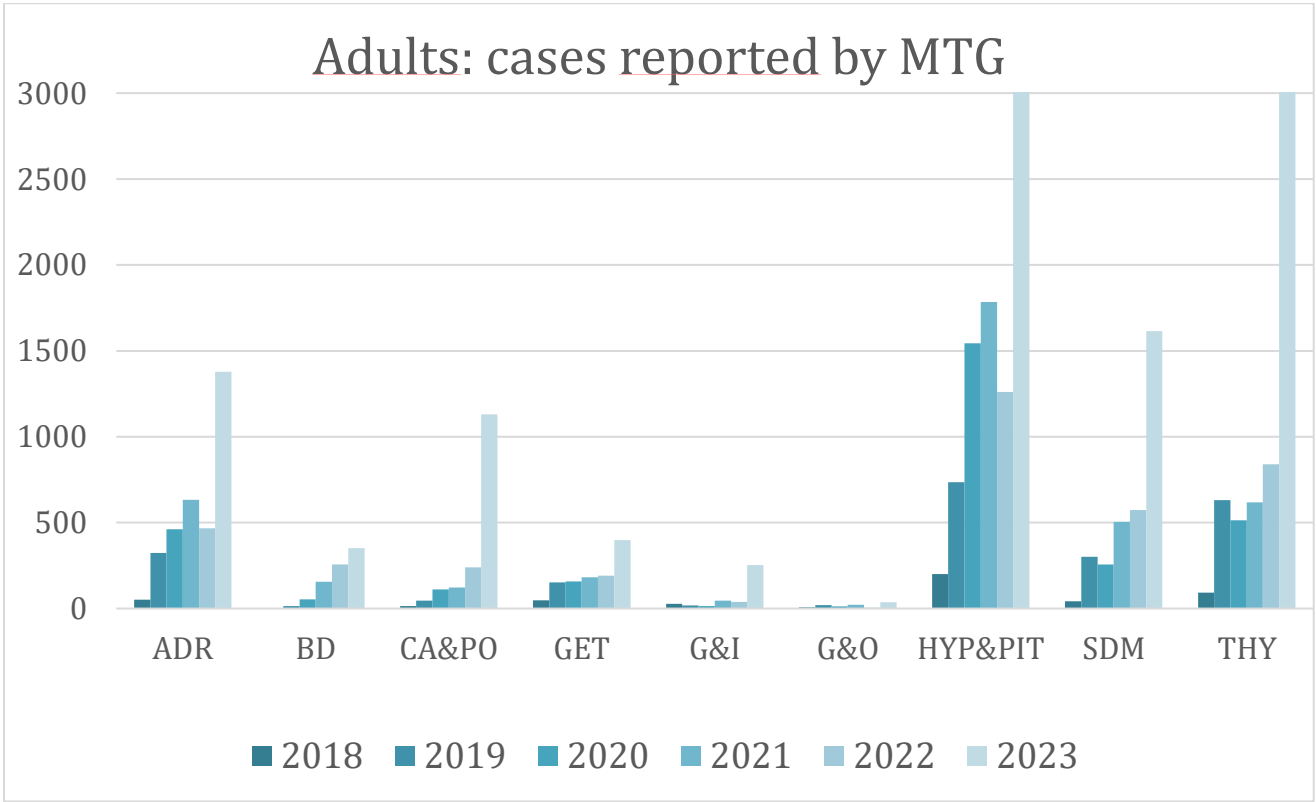




*Fig. 4 – Cases reported per Main Thematic Group (MTG) between July 2018 and December 2023. Conditions within the 'Sex Development', 'Pituitary' and 'Thyroid' condition groups were most commonly reported amongst children and adults, respectively. However, in general, the increase in reported conditions is across all MTGs.*

1. **MTG 1: Adrenal**

In total 4035 cases were reported by 59 centres from 22 countries, among them 720 paediatric cases and 3315 adult cases. In children the most reported condition was congenital adrenal hyperplasia (n=465, 65%), followed by primary adrenal insufficiency (n=151, 21%), cortisol producing adenomas (n=47, 6%), sporadic pheochromocytoma/paraganglioma (n=35, 5%), adrenocortical carcinomas (n=19, 3%) and familial hyperaldosteronism (n=3, 0%). The median of cases reported by centre was 9, with a maximum of 170 cases reported by one of the centres.
In adults the most reported cases were sporadic pheochromocytoma/paraganglioma (n=1209, 37%), followed by primary adrenal insufficiency (n=632, 19%), cortisol producing adenomas (n=612, 18%), congenital adrenal hyperplasia (n=427, 13%), adrenocortical carcinomas (n=363, 11%) and familial hyperaldosteronism (n=72, 2%). The median of cases reported by centre was 35, with a maximum of 674 cases reported by one of the centres.

2. **MTG 2: Calcium & Phosphate**

In total 2101 cases were reported by 55 centres from 21 countries, among them 438 paediatric cases and 1663 adult cases. In children the most reported condition was X-linked hypophosphatemia (n=121, 28%), followed by IPPSD/Pseudohypoparathyroidism (n=93, 21%), hypoparathyroidism (n=80, 18%), hypophosphataemic rickets (n=38, 9%), hyperparathyroidism including parathyroid cancer (n=30, 7%) and other conditions. The median of cases reported by centre was 4, with a maximum of 74 cases reported by one of the centres.
In adults the most reported cases were hyperparathyroidism including parathyroid cancer (n=914, 55%), followed by hypoparathyroidism (n=476, 28%), X-linked hypophosphatemia (n=77, 5%) and other conditions. The median of cases reported by centre was 15, with a maximum of 212 cases reported by one of the centres.

3. **MTG 3: Genetic disorders of Glucose & Homeostasis**

In total 1170 cases were reported by 59 centres from 23 countries, among them 773 paediatric cases and 397 adult cases. In children the most reported condition was rare diabetes (n=366, 47%), followed by hyperinsulinism (n=354, 46%) and insulin resistance syndrome (27, 3%). Also 20 cases (3%) of genetic and 6 cases (1%) of acquired lipodystrophy were reported. The median of cases reported by centre was 6, with a maximum of 146 cases reported by one of the centres.
In adults the most reported cases were in rare diabetes group (n=225, 57%), followed by insulin resistance syndrome (100, 25%) and hyperinsulinism (n=42, 11%). Also 18 cases (4%) of genetic and 12 cases (3%) of acquired lipodystrophy were reported. The median of cases reported by centre was 3, with a maximum of 42 cases reported by one of the centres.

4. **MTG4: Genetic Endocrine Tumour Syndromes**

In total 1351 cases were reported by 59 centres from 17 countries, among them 223 paediatric cases and 1128 adult cases. In children the most reported condition was MEN Type 2 (n=81, 36%), followed by MEN Type 1 (n=70, 31%), Von Hippel Lindau syndrome (n=35, 16%), hereditary pheochromocytoma-paraganglioma (n=24, 11%), Carney complex (n=10, 5%) and other NETs (n=3, 1%). The median of cases reported by centre was 3, with a maximum of 43 cases reported by one of the centres.
In adults the most reported condition was hereditary pheochromocytoma-paraganglioma (n=445, 39%), followed by MEN Type 1 (n=262, 23%), MEN Type 2 (n=152, 14%), Von Hippel Lindau syndrome (n=113, 10%) and Carney complex (n=12, 1%). Other NETs were reported in 144 cases (13%). The median of cases reported by centre was 16.5, with a maximum of 161 cases reported by one of the centres.

5. **MTG5: Growth & Genetic Obesity Syndromes**

In total 1077 cases were reported by 43 centres from 18 countries, among them 974 paediatric cases and 103 adult cases. In children the most reported condition was Prader Willi Syndrome and Prader Willi-like Syndrome (n=234, 24%), followed by Noonan Syndrome (n=231, 24%), Rare Genetic Obesity (n=213, 22%), Silver Russell Syndrome (n=142, 15%), Overgrowth Syndrome (n=96, 10%), Beckwith-Wiedemann Syndrome (n=32, 3%), GH Resistance syndromes (n=25, 2%). Till now 1 case of ROHHAD

syndrome was reported. The median of cases reported by centre was 11, with a maximum of 229 cases reported by one of the centres.
In adults the most reported condition was also Prader Willi Syndrome and Prader Willi-like Syndrome (n=82, 79%). Other conditions were rarely reported in adults: Silver Russell Syndrome (n=8, 8%), Beckwith-Wiedemann Syndrome (n=5, 5%), Noonan Syndrome (n=4, 4%), Overgrowth Syndrome (n=2, 2%) and Rare Genetic Obesity (n=2, 2%). The median of cases reported by centre was 0, with a maximum of 46 cases reported by one of the centres.

**6. MTG6: Hypothalamic and Pituitary Conditions**

In total 11211 cases were reported by 63 centres from 25 countries, among them 1153 paediatric cases and 10058 adult cases. In children the most reported condition was congenital hypopituitarism (n=618, 54%), followed by acquired hypopituitarism (n=381, 33%) and pituitary adenoma (n=154, 13%). The median of cases reported by centre was 10, with a maximum of 277 cases reported by one of the centres.
In adults the most reported condition was pituitary adenoma (n=7762, 77%), followed by acquired hypopituitarism (n=2063, 21%) and congenital hypopituitarism (n=233, 2%). Since 2023 specific diagnoses of pituitary adenomas have been implemented in the e-REC registry. This led to more detailed reporting – 755 new cases of non-functioning pituitary adenoma (8%), 633 new cases of prolactinoma (6%), 333 new cases of acromegaly (3%), 235 new cases of Cushing disease (2%) and 130 new cases of craniopharyngioma (1%) were registered. The median of cases reported by centre was 101, with a maximum of 1211 cases reported by one of the centres.

**7. MTG7: Sex Development & Maturation**

In total 7118 cases were reported by 51 centres from 22 countries, among them 3824 paediatric cases and 3294 adult cases. In children the most reported condition was gender incongruence (n=1822, 48%), followed by XY DSD (n=747, 19%), chromosomal DSD (n=681, 18%), XX DSD (n=406, 11%), Isolated Congenital Normosmic Hypogonadotrophic Hypogonadism (n=98, 3%), Isolated Congenital Anosmic Hypogonadotrophic Hypogonadism (n=70, 2%). The median of cases reported by centre was 18, with a maximum of 1258 cases reported by one of the centres.
In adults the most reported condition also was gender incongruence (n=2181, 66%), followed by chromosomal DSD (n=461, 14%), XY DSD (n=170, 5%), XX DSD (n=163, 5%), Isolated Congenital Normosmic Hypogonadotrophic Hypogonadism (n=204, 3%), Isolated Congenital Anosmic Hypogonadotrophic Hypogonadism (n=115, 6%). The median of cases reported by centre was 22.5, with a maximum of 617 cases reported by one of the centres.

**8. MTG8: Thyroid**

In total 7023 cases were reported by 53 centres from 20 countries, among them 1259 paediatric cases and 5764 adult cases. In children the most reported condition was congenital hypothyroidism (n=911, 72%), followed by non-metastatic thyroid carcinoma (n=227, 18%), thyroid hormone signalling disorders (n=69, 6%), congenital hyperthyroidism (n=52, 4%). The median of cases reported by centre was 7, with a maximum of 192 cases reported by one of the centres.
In adults the most reported condition was non-metastatic thyroid carcinoma (n=5645, 98%), followed by thyroid hormone signalling disorders (n=86, 2%), congenital hypothyroidism (n=20, 0%), congenital hyperthyroidism (n=13, 0%). The median of cases reported by centre was 75.5, with a maximum of 540 cases reported by one of the centres.

**9. MTG9: Bone dysplasia**

In total 1486 cases were reported by 42 centres from 19 countries, among them 660 paediatric cases and 826 adult cases. In children the most reported condition was osteogenesis imperfecta (n=153, 23%), followed by primary bone dysplasia (PBD) with micromelia (n=139, 21%), PBD with disorganized development of skeletal components (n=71, 11%), PBD with defective bone mineralisation (n=45, 7%), PBD with reduced bone density (n=45, 7%), McCune-Albright syndrome (n=44, 7%), multiple osteochondroma (n=40, 6%), dysostosis (n=20, 3%), PBD with increased bone density (n=20, 3%). The median of cases reported by centre was 7, with a maximum of 116 cases reported by one of the centres.

In adults the most reported condition was PBD with disorganized development of skeletal components (n=264, 32%), followed by PBD with defective bone mineralisation (n=172, 21%), osteogenesis imperfecta (n=168, 20%), multiple osteochondroma (n=38, 5%), osteonecrosis (n=35, 4%), PBD with reduced bone density (n=33, 4%), McCune-Albright syndrome (n=26, 3%), osteopetrosis and related disorders (n=26, 3%). The median of cases reported by centre was 3, with a maximum of 271 cases reported by one of the centres.

**Conclusions**

- The number of centres that have registered to use the platform continues to increase as well as the number of centres that are actively reporting cases. The continuous monitoring program of Endo ERN was one of the most important drivers of this increase the past year.
- There is wide variability in the number of cases encountered for different conditions amongst different centres.
- The biggest number of centres reported in MTG6 (Hypothalamus & Pituitary), which is also reflected by the highest numbers of reported cases in this group.
- To date this provides a large dataset which is available for researchers upon request.

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