EuRREB
European Registries for Rare Endocrine and Bone conditions

e-REC
Annual Activity Report

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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 6.5-year period from July 2018 to December 2024 inclusive.

Methods

The e-REC platform issued invitations to clinicians who had registered to participate in e-REC from July 2018 to December 2024 to complete a monthly return. Participants can create a bespoke reporting setup and report any newly encountered cases of any of the conditions that have been included in Endo-ERN and ERN BOND.

Results

By December 2024, a total of 113 centres from 32 countries had reported 56573 new cases of rare endocrine or bone conditions in e-REC. Since January 2024, two new countries and 12 new centres have joined the platform. Among those 32 countries, 29 are located in Europe. Of these 113 centres, 62 are in Endo-ERN only, 29 are in Endo-ERN and ERN-BOND, three are in ERN-BOND only, and 19 are not related to ERNs. The total number of e-REC users reached 346.

The total amount of participating in e-REC centres in different countries is shown on the map in figure 1. The biggest number of centres have been noted in Italy with 22 centres, followed by Germany (14 centres), the Netherlands and Spain (8 centres in each). Currently, 86 paediatric centres and 92 adult centres have actively participated in e-REC.

Since 2018, three important events have prompted the increase in e-REC participation (both for the number of cases and number of participating centres): the launch of the EuRR-Bone project (April 2020), the initiative to make participation in the e-REC registry mandatory for their members in 2023 for Endo-ERN and in 2024 for ERN BOND (as part of a continuous monitoring program).

This resulted in the increase of reported cases more than 3 times by the end of 2023. Figure 2 clearly demonstrates this trend. A total of 41933 new cases in adults and 14640 new cases in children have now been reported. Both age groups continue to show a growing trend.

The reporters can report in 10 different MTGs (Main Thematic Groups) in children (<18 years old) and adults (≥18 years old). The distribution of cases within MTGs differs between children and adults. Conditions within the 'Sex Development', 'Growth & Obesity' and 'Thyroid' condition groups were most commonly reported in children (figure 3), whereas in adults the most commonly reported were conditions within the 'Hypothalamic and Pituitary', 'Thyroid' and 'Adrenal' condition groups (figure 4). In 2024, the 'Growth & Obesity', 'Bone Dysplasia' and 'Calcium & Phosphate' MTGs showed an impressive increase in numbers in children's group in comparison to 2023. In adults during the last year, we still register the tendency in the increasing number of new cases in 'Hypothalamic and Pituitary', 'Thyroid' and 'Adrenal' condition groups, but also a meaningful peak was noticed in the 'Bone Dysplasia' and 'Genetic Endocrine Tumour Syndrome' MTGs.

The detailed results according by Main Thematic Group will be described below.

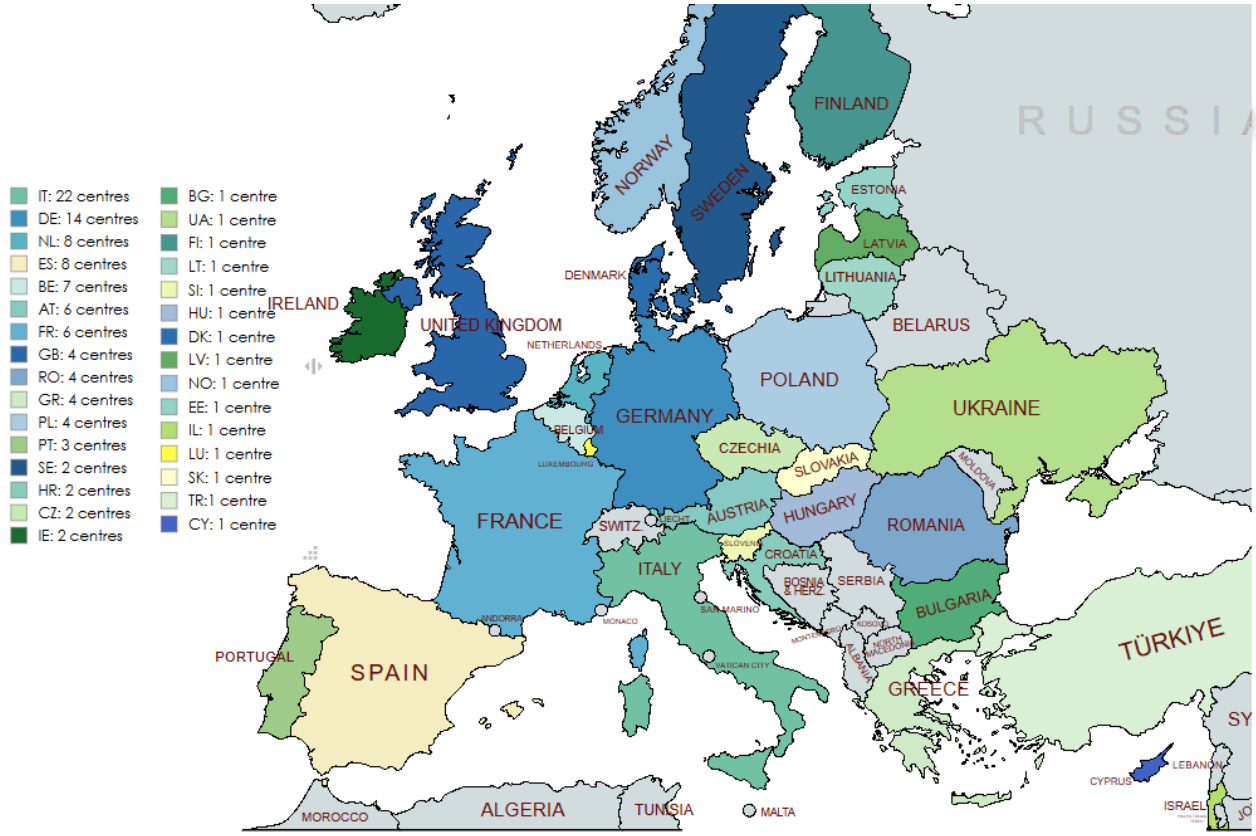

Fig. 1 – Number of centres in each country that are active (i.e. have submitted one or more returns between July 2018 and December 2024)

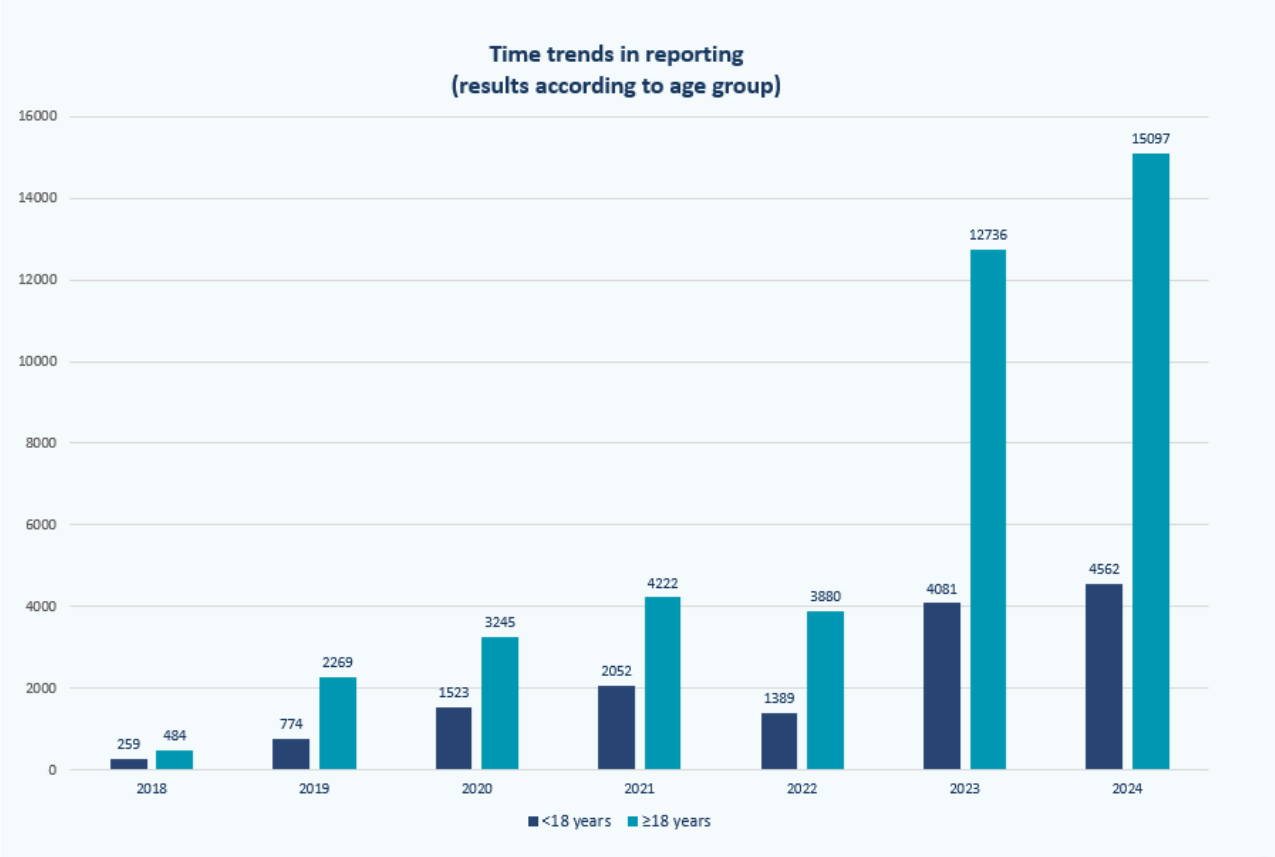

Fig. 2 – The trends in cases reported between July 2018 and December 2024

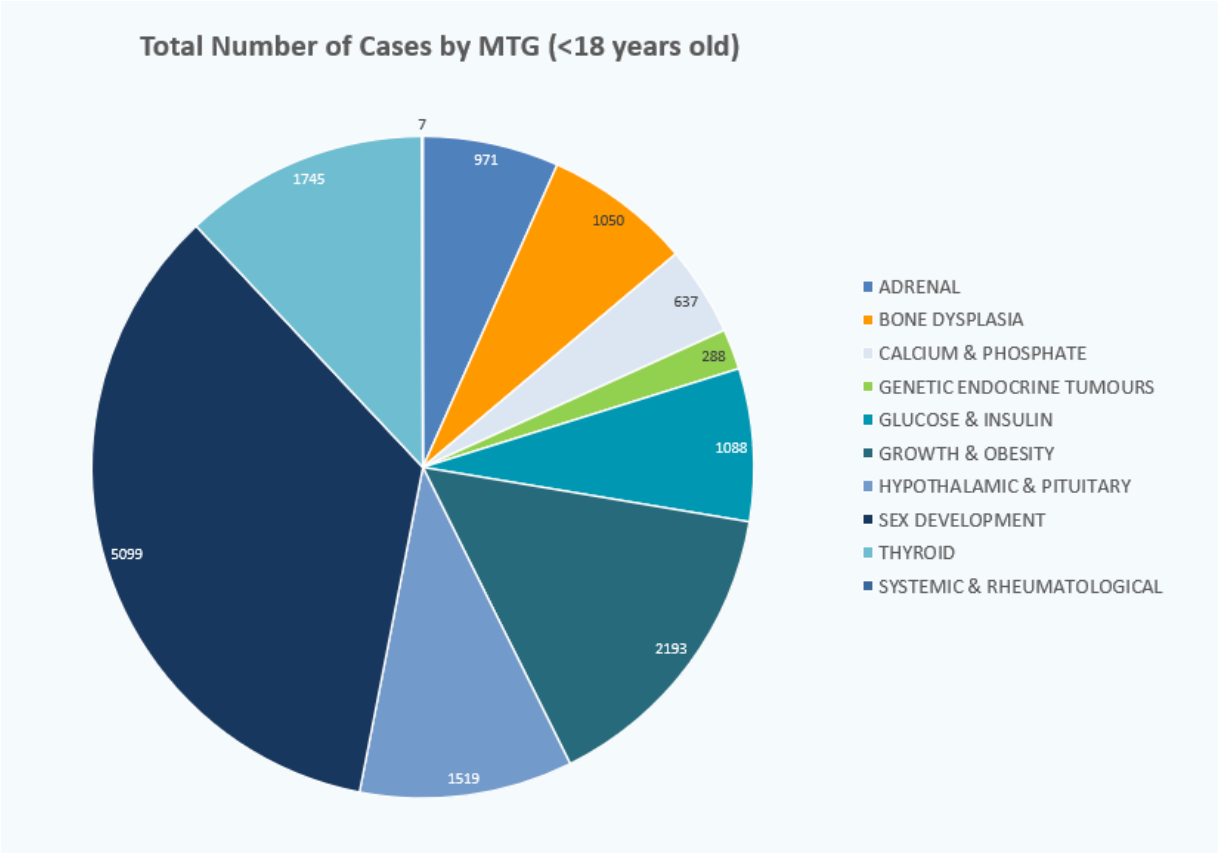

Fig. 3 – Distribution of cases between different MTGs (Main Thematic Groups) in children.

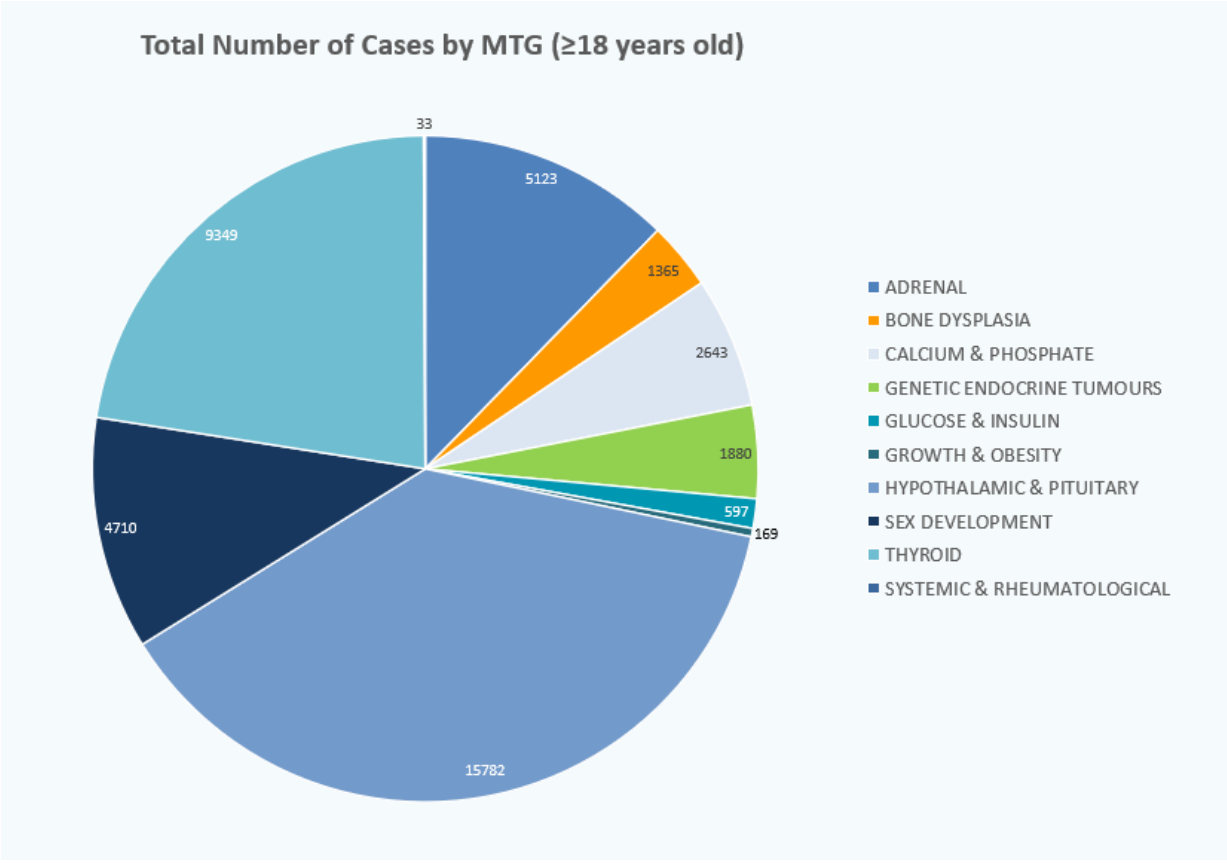

Fig. 4 – Distribution of cases between different MTGs (Main Thematic Groups) in adults.

Results according by Main Thematic Group

1. **MTG 1: Adrenal**

In total, 6094 cases were reported by 71 centres from 25 countries. Among these, 921 were paediatric cases and 5123 were adult cases.

In children the most reported condition was congenital adrenal hyperplasia (n=614, 63%), followed by primary adrenal insufficiency (n=229, 24%), adrenal Cushing syndrome (n=57, 6%), sporadic pheochromocytoma/paraganglioma (n=42, 4%), adrenocortical carcinomas (n=20, 2%) and familial hyperaldosteronism (n=9, 1%). The median of cases reported by centre was 9, with a maximum of 172 cases reported by one of the centres.

In adults the most reported cases were sporadic pheochromocytoma/paraganglioma (n=1698, 33%), followed by primary adrenal insufficiency (n=1024, 20%), adrenal Cushing syndrome (n=990, 19%), congenital adrenal hyperplasia (n=632, 12%), adrenocortical carcinomas (n=540, 11%) and familial hyperaldosteronism (n=239, 5%). The median of cases reported by centre was 45, with a maximum of 868 cases reported by one of the centres since 2019.

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

In total, 3280 cases were reported by 74 centres from 29 countries, among them 637 paediatric cases and 2643 adult cases.

In children the most reported condition was X-linked hypophosphatemia (n=179, 28%), followed by IPPSD/Pseudohypoparathyroidism (n=130, 20%), hypoparathyroidism (n=113, 18%), hyperparathyroidism including parathyroid cancer (n=45, 7%), hypophosphataemic rickets (n=38, 6%), familial hypocalciuric hypercalcaemia (n=38, 6%), and other conditions. The median of cases reported by centre was 5.5, with a maximum of 102 cases reported by one of the centres.

In adults the most reported cases were hyperparathyroidism including parathyroid cancer (n=1382, 52%), followed by hypoparathyroidism (n=667, 25%), PTH independent hypercalcaemia (n=156, 6%),
X-linked hypophosphatemia (n=125, 5%) and other conditions. The median of cases reported by centre was 23, with a maximum of 212 cases reported by one of the centres.

3. **MTG 3: Genetic Disorders of Glucose & Insulin Homeostasis**

In total, 1685 cases were reported by 55 centres from 25 countries, including 1088 paediatric cases and 597 adult cases.

In children the most reported condition was rare diabetes (n=544, 50%), followed by hyperinsulinism (n=459, 42%) and insulin resistance syndrome (47, 4%). Also 28 cases (3%) of genetic and 10 cases (1%) of acquired lipodystrophy were reported. The median of cases reported by centre was 8, with a maximum of 177 cases reported by one of the centres.

In adults the most reported cases were in rare diabetes group (n=349, 59%), followed by insulin resistance syndrome (114, 19%) and hyperinsulinism (n=47, 8%). Also 67 cases (11%) of genetic and 20 cases (3%) of acquired lipodystrophy were reported. The median of cases reported by centre was 4.5, with a maximum of 82 cases reported by one of the centres.

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

In total, 2168 cases were reported by 62 centres from 23 countries, including 288 paediatric cases and 1880 adult cases.

In children the most reported condition was MEN Type 2 (n=108, 38%), followed by MEN Type 1 (n=86, 30%), Von Hippel Lindau syndrome (n=41, 14%), hereditary pheochromocytoma-paraganglioma (n=27, 9%), Carney complex (n=15, 5%) and other NETs (n=11, 4%). The median of cases reported by centre was 3, with a maximum of 54 cases reported by one of the centres.

In adults the most reported condition was hereditary pheochromocytoma-paraganglioma (n=753, 40%), followed by MEN Type 1 (n=405, 22%), MEN Type 2 (n=258, 14%), Von Hippel Lindau syndrome (n=160, 9%) and Carney complex (n=23, 1%). Other NETs were reported in 279 cases (15%). The median of cases reported by centre was 17, with a maximum of 204 cases reported by one of the centres.

5. MTG5: Growth & Genetic Obesity Syndromes

In total, 2362 cases were reported by 59 centres from 24 countries, including 2193 paediatric cases and 169 adult cases.

In children the most reported condition was Rare Genetic Obesity (n=640, 29%), followed by Prader Willi Syndrome and Prader Willi-like Syndrome (n=400, 18%), Noonan Syndrome (n=398, 18%), Silver Russell Syndrome (n=277, 13%), Overgrowth Syndrome (n=225, 10%), Beckwith-Wiedemann Syndrome (n=215, 10%), GH Resistance syndromes (n=36, 2%). Till now 2 cases of ROHHAD syndrome were reported. The median of cases reported by centre was 15, with a maximum of 332 cases reported by one of the centres.

In adults the most reported condition was also Prader Willi Syndrome and Prader Willi-like Syndrome (n=106, 63%). Other conditions were rarely reported in adults: Silver Russell Syndrome (n=11, 6%), Beckwith-Wiedemann Syndrome (n=17, 10%), Noonan Syndrome (n=13, 8%), Overgrowth Syndrome (n=17, 10%), and Rare Genetic Obesity (n=4, 2%). The median of cases reported by centre was 1, with a maximum of 49 cases reported by one of the centres.

6. MTG6: Hypothalamic & Pituitary Conditions

In total, 17301 cases were reported by 78 centres from 29 countries, including 1519 paediatric cases and 15782 adult cases.

In children the most reported condition was congenital hypopituitarism (n=775, 51%), followed by acquired hypopituitarism (n=488, 32%), pituitary adenoma (n=222, 15%) and craniopharyngioma (n=34, 2%). The median of cases reported by centre was 13.5, with a maximum of 277 cases reported by one of the centres.

In adults the most reported condition was pituitary adenoma (n=12283, 78%), followed by acquired hypopituitarism (n=2870, 18%), congenital hypopituitarism (n=315, 2%) and craniopharyngioma (n=314, 2%). Since 2023 specific diagnoses of pituitary adenomas have been implemented in the e-REC registry. This led to more detailed reporting – 1901 new cases of non-functioning pituitary adenoma (12%), 1548 new cases of prolactinoma (10%), 838 new cases of acromegaly (5%), and 505 new cases of Cushing disease (3%) were registered. The median of cases reported by centre was 161, with a maximum of 1609 cases reported by one of the centres.

7. MTG7: Sex Development & Maturation

In total, 9809 cases were reported by 60 centres from 25 countries, among them 5099 paediatric cases and 4710 adult cases.

In children the most reported condition was gender incongruence (n=2286, 45%), followed by XY DSD (n=1045, 21%), chromosomal DSD (n=976, 19%), XX DSD (n=552, 11%), Isolated Congenital Normosmic Hypogonadotrophic Hypogonadism (n=142, 3%), Isolated Congenital Anosmic Hypogonadotrophic Hypogonadism (n=98, 2%). The median of cases reported by centre was 19, with a maximum of 1678 cases reported by one of the centres.

In adults the most reported condition also was gender incongruence (n=3191, 68%), followed by chromosomal DSD (n=636, 14%), XX DSD (n=248, 5%), XY DSD (n=227, 5%), Isolated Congenital Normosmic Hypogonadotrophic Hypogonadism (n=253, 5%), Isolated Congenital Anosmic Hypogonadotrophic Hypogonadism (n=155, 3%). The median of cases reported by centre was 36, with a maximum of 906 cases reported by one of the centres.

8. MTG8: Thyroid

In total, 11094 cases were reported by 69 centres from 27 countries, including 1745 paediatric cases and 9349 adult cases.

In children the most reported condition was congenital hypothyroidism (n=1229, 70%), followed by non-metastatic thyroid carcinoma (n=308, 18%), thyroid hormone signalling disorders (n=110, 6%), congenital hyperthyroidism (n=98, 6%). The median of cases reported by centre was 11, with a maximum of 192 cases reported by one of the centres.

In adults the most reported condition was non-metastatic thyroid carcinoma (n=9092, 97%), followed by thyroid hormone signalling disorders (n=185, 2%), congenital hypothyroidism (n=53, 0%), congenital

hyperthyroidism (n=19, 0%). The median of cases reported by centre was 102, with a maximum of 1399 cases reported by one of the centres.

9. MTG9: Bone Dysplasia

In total, 2415 cases were reported by 58 centres from 24 countries, including 1050 paediatric cases and 1365 adult cases.

In children the most reported condition was osteogenesis imperfecta (n=207, 20%), followed by achondroplasia (n=156, 15%), fibrous dysplasia/McCune-Albright syndrome (n=115, 11%), multiple osteochondroma (n=46, 4%), dysostosis (n=35, 3%), dyschondrosteosis/Leri-Weill (n=29, 3%), and spondyloepiphyseal dysplasia congenita/SEDC (n=28, 3%). Other groups of conditions reported frequently in this MTG are - rare bone disease related to a common gene or pathway defect (n=111, 11%), primary bone dysplasia (PBD) with disorganized development of skeletal components (n=51, 5%), PBD with defective bone mineralisation (n=50, 5%), PBD with reduced bone density (n=48, 5%), PBD with increased bone density (n=21, 1%). The median of cases reported by centre was nine, with a maximum of 170 cases reported by one of the centres.

In adults the most reported condition was fibrous dysplasia/McCune-Albright syndrome (n=472, 35%), followed by osteogenesis imperfecta (n=292, 21%), multiple osteochondroma (n=57, 4%) and osteonecrosis (n=46, 3%). Other groups of conditions reported frequently in this MTG are - PBD with defective bone mineralisation (n=222, 16%), PBD with reduced bone density (n=96, 7%), osteopetrosis and related disorders (n=36, 3%). The median of cases reported by centre was three, with a maximum of 340 cases reported by one of the centres.

10. MTG10: Systemic & Rheumatological

In the summer of 2024 this new MTG was added to platform to serve the needs of the reporters dealing with systemic and rheumatological conditions causing endocrine and bone complications. This MTG comprises now four conditions: Langerhans cell histiocytosis (LCH), chronic nonbacterial osteitis (CNO), isolated sternocostoclavicular hyperostosis (SCCH) and SAPHO syndrome.

Since then, 40 cases have been reported (seven in children and 33 in adults) by three centres from three countries. CNO was reported in 15 cases (45%), SCCH – 14 cases (42%), SAPHO syndrome in six (18%) and LCH – five cases (15%).

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 programmes of Endo-ERN and ERN BOND have been important drivers of this increase during the last years.
- There is wide variability in the number of cases encountered for different conditions amongst different centres.
- The condition group with the largest number of reporters is MTG6 (Hypothalamus & Pituitary) which also has the highest number of reported cases.
- To date, this provides a large dataset which is available for researchers upon request.

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