European Registries for Rare Endocrine Conditions (EuRRECa): Results from the Platform for e-Reporting of Rare Conditions (e-REC)

Introduction

e-REC (e-Reporting of Rare Endocrine Conditions) is an electronic reporting platform which acts as a registry 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. The e-REC platform also assisted the Rare Disease Committee of the ESE in mapping the occurrence of COVID-19 infection in people with rare conditions.

Aim

This report has been developed to describe the current activity in e-REC over a 3.5-year period from July 2018 to December 2021 inclusive.

Methods

The e-REC platform issued invitations to clinicians who had registered to participate in e-REC from July 2018 to December 2021 to ask them to complete a monthly return. Participants can create a bespoke reporting set up and can report any newly encountered cases of any of the conditions that have been included in Endo-ERN, ERN-BOND and more recently, COVID-19 infections.

Results

By December 2021, a total of 61 centres from 22 countries had reported on the e-REC. Of these 61 centres, 28 are in Endo-ERN only, 16 are in Endo-ERN and ERN-BOND, 3 are in ERN-BOND only and 14 are in no ERNs.

Country	Centres	Country2	Centres3
Austria	5	Israel	1
Belgium	7	Italy	9
Croatia	1	Latvia	1
Czechia	1	Lithuania	1
Egypt	1	Luxembourg	1
Estonia	1	Netherlands	6
Finland	1	Portugal	1
France	2	Romania	1
Germany	9	Spain	3
Greece	2	Sweden	2
Hungary	1	UK	4

Table 1 – Number of centres in each country that are active (i.e. have submitted 1 or more returns between July 2018 and December 2021).

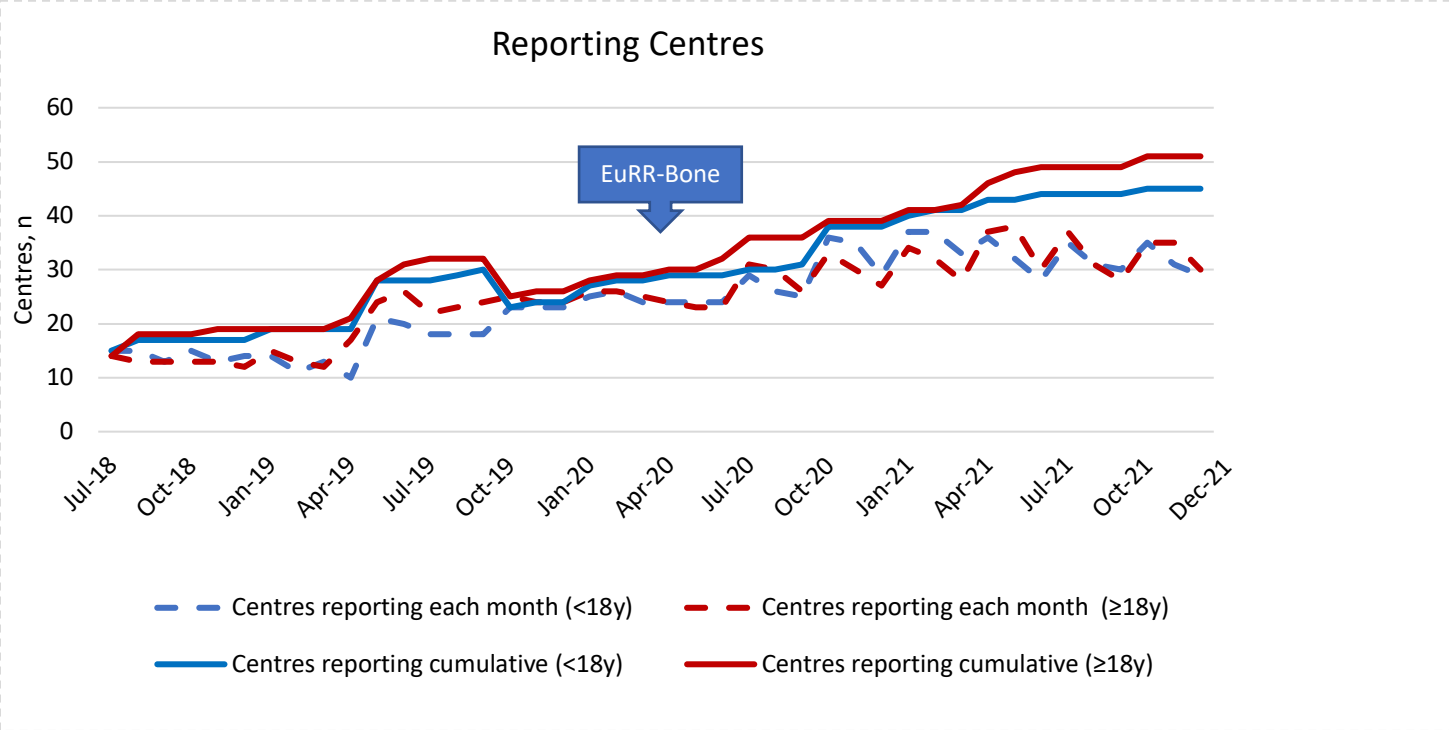


Fig.1 – Change in the number of centres that have been actively reporting between July 2018 and December 2021. Currently, 45 paediatric centres and 51 adult centres have actively participated in e-REC. The arrow indicates the launch of the EuRR-Bone project (April 2020).

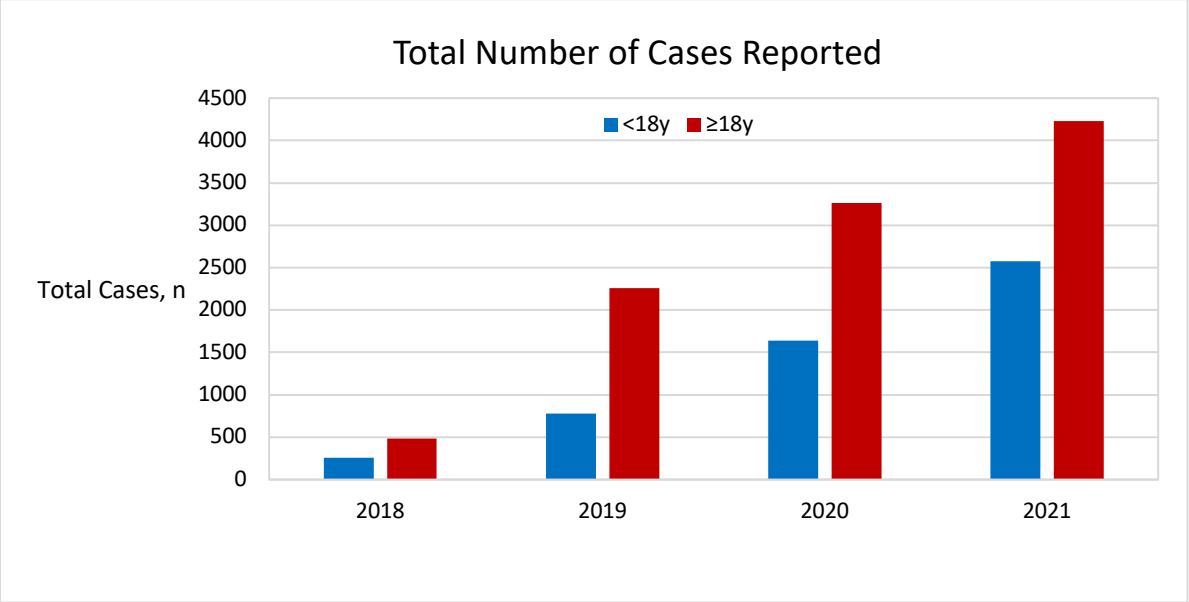
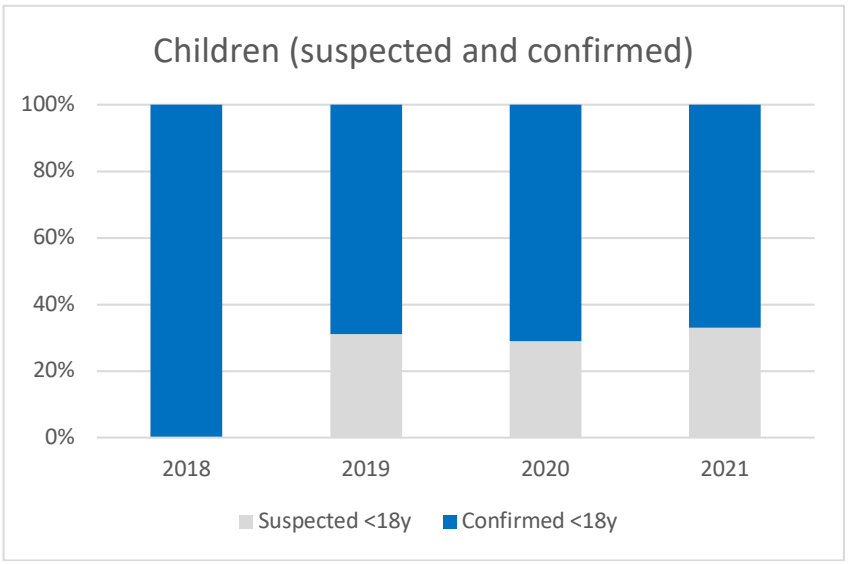


Fig. 2 – The change in cases reported between July 2018 and December 2021. A total of 10,230 new cases in adults and 5252 new cases in children have now been reported.



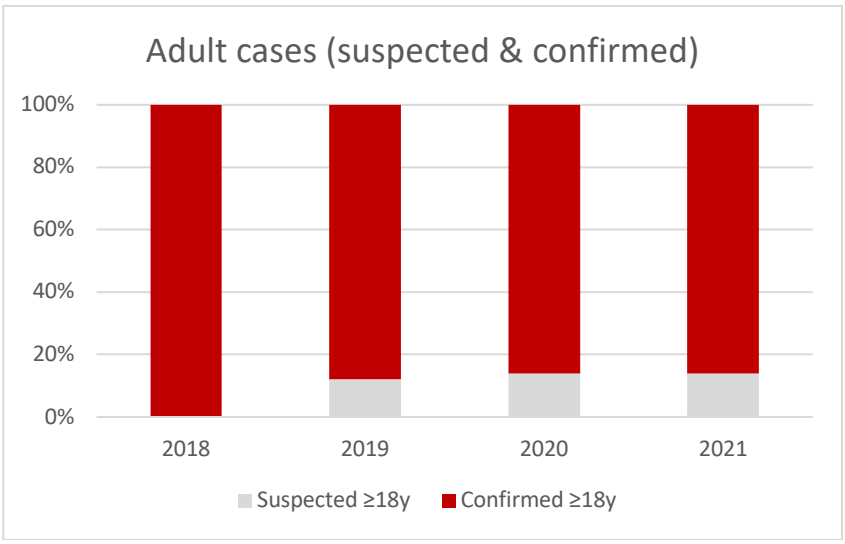
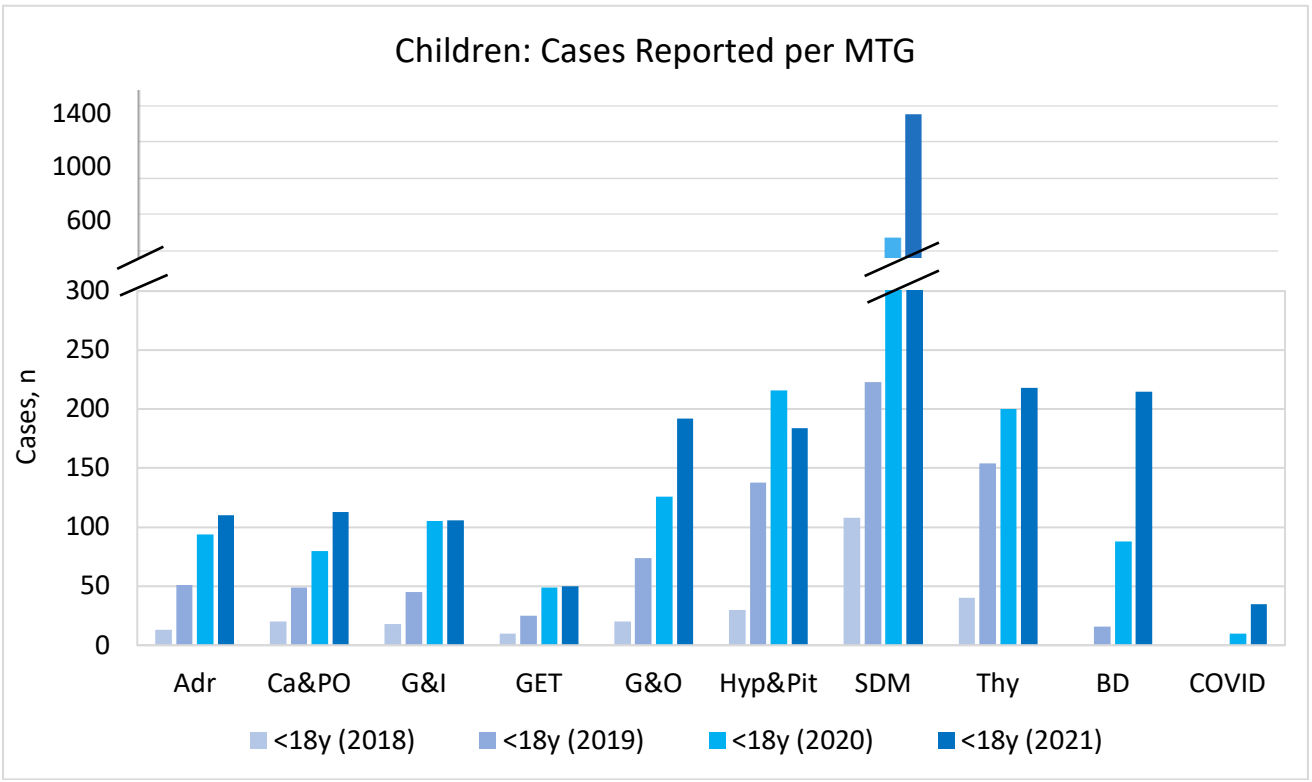


Fig 3. Since the last quarter of 2019, the platform collects information on the proportion of cases that are considered to be 'suspected' and the proportion that are considered to be 'confirmed'. Suspected cases (in grey) are shown as a percentage of total cases for children (blue) and adults (red). The platform also allows updating of previously reported suspected cases to either confirmed or excluded.



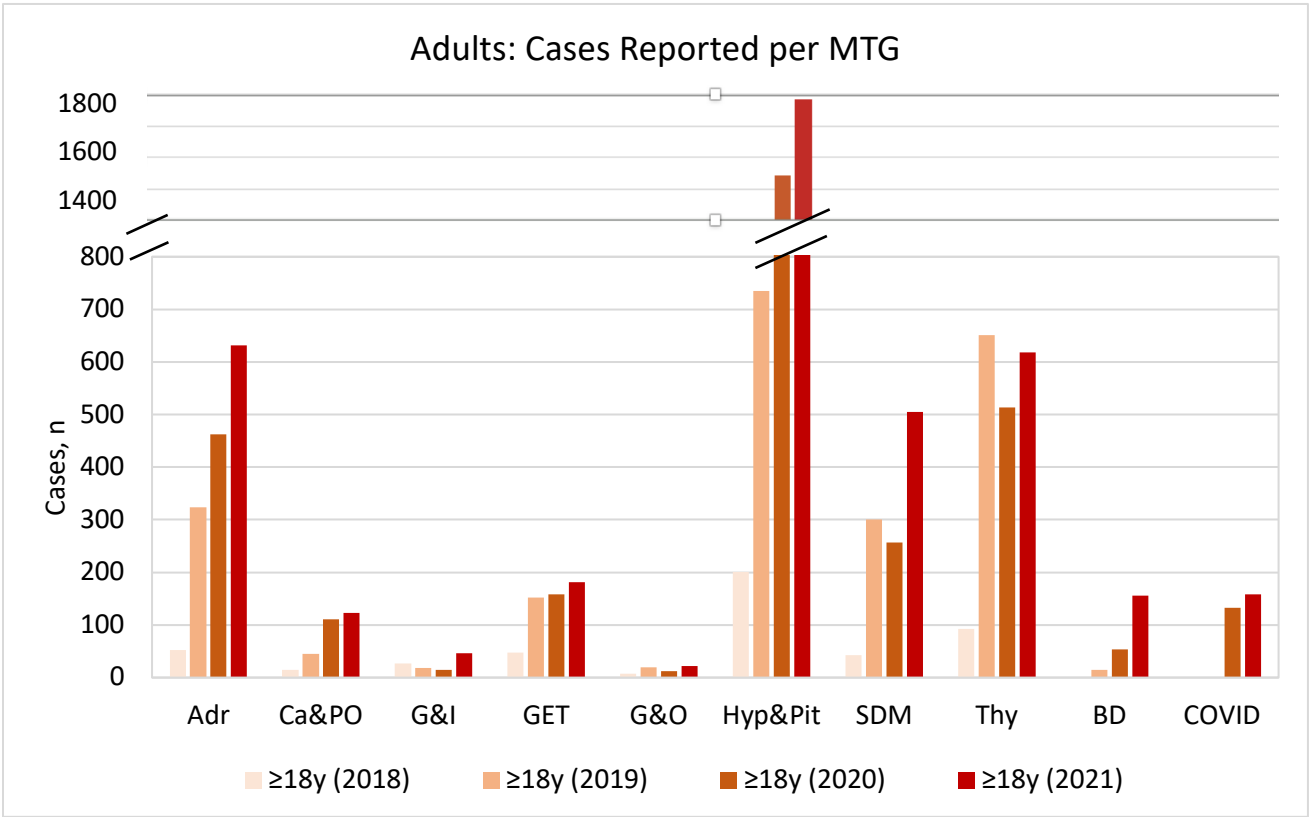


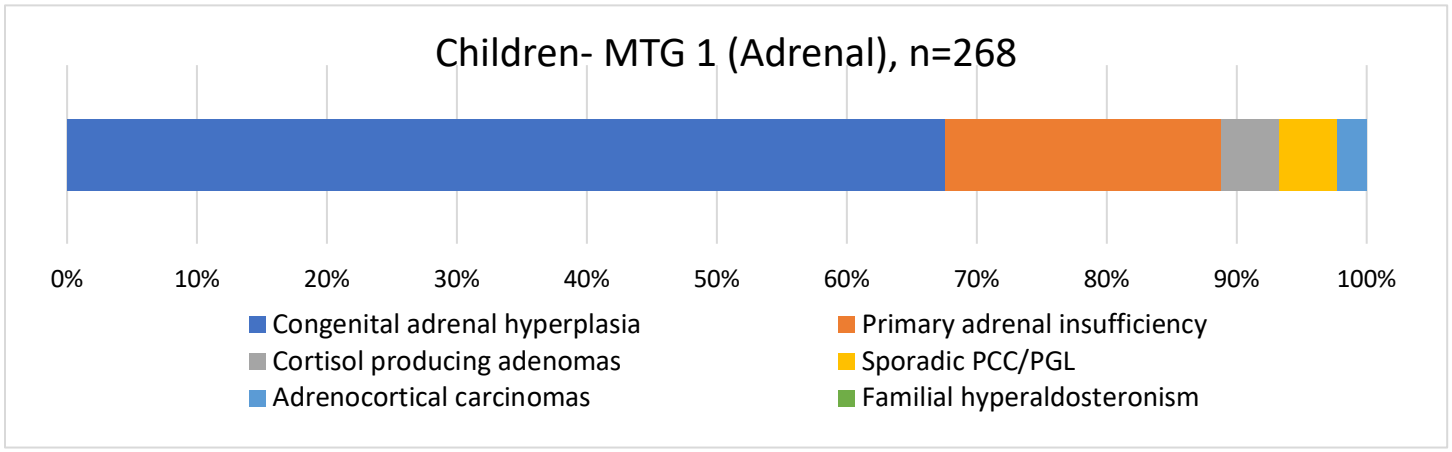
Fig.4 – Cases reported per Main Thematic Group (MTG) between July 2018 and December 2021. Conditions within the 'Sex Development' and 'Pituitary' condition groups were most commonly reported amongst children and adults, respectively. However, in general, the increase in reported conditions is across all MTGs.

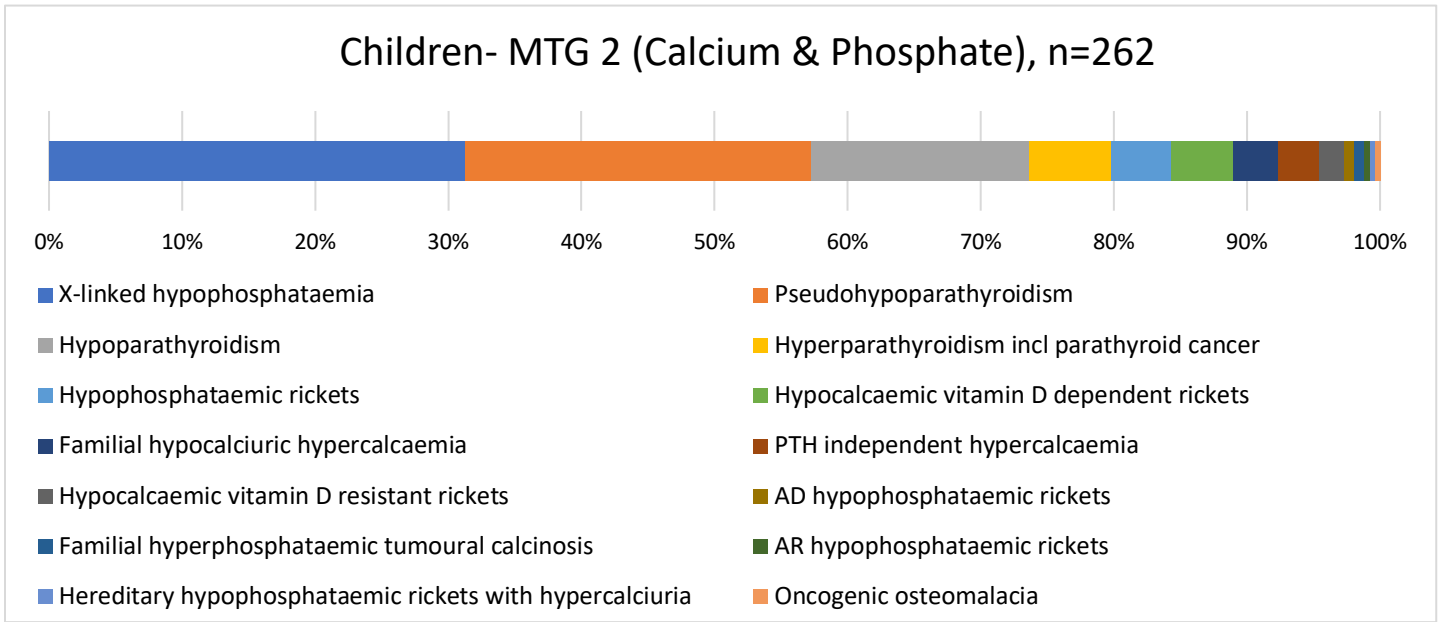
Cases per centre per MTG

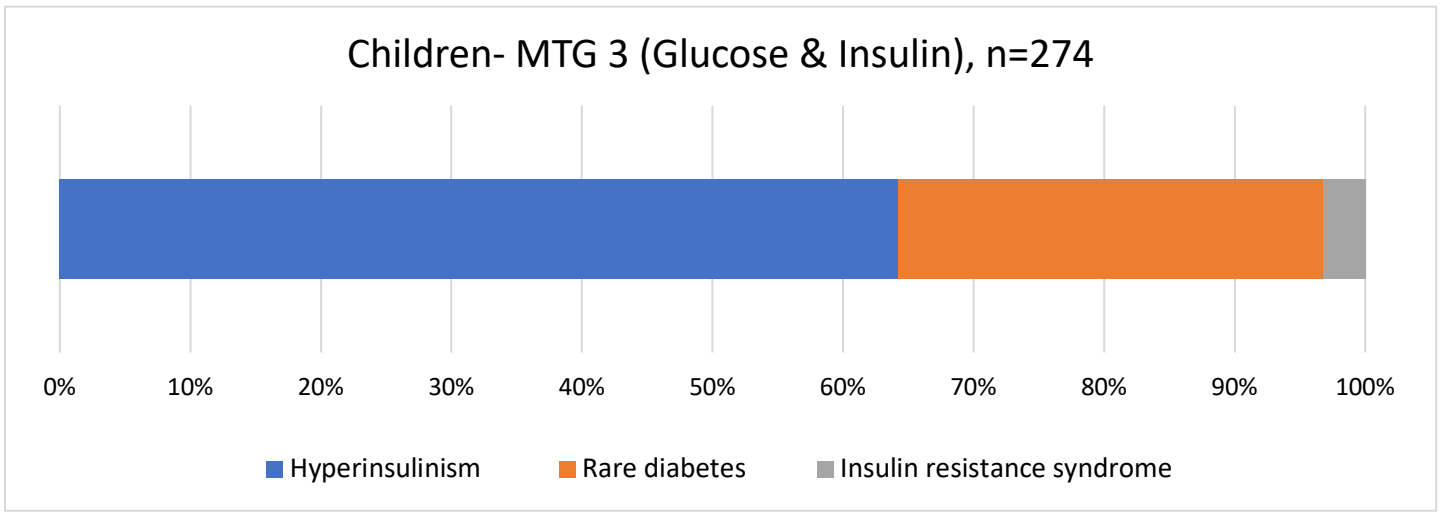
	<18y			≥18y		
Condition Group	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**
Adrenal	6	0	26	32	1	77
Ca & PO	5	0	31	5	1	28
Gluc & Ins	6	1	14	1	0	20
Gen Endocrine Tumours	3	0	11	13	4	25
Growth & Obesity	7	1	39	1	0	5
Hypothal & Pituitary	15	0	29	91	6	255
Sex Dev & Maturation	30	10	137	22	1	89
Thyroid	16	1	31	49	5	75
Bone Dysplasia	10	1	48	8	1	25
COVID-19	2	0	15	10	0	36

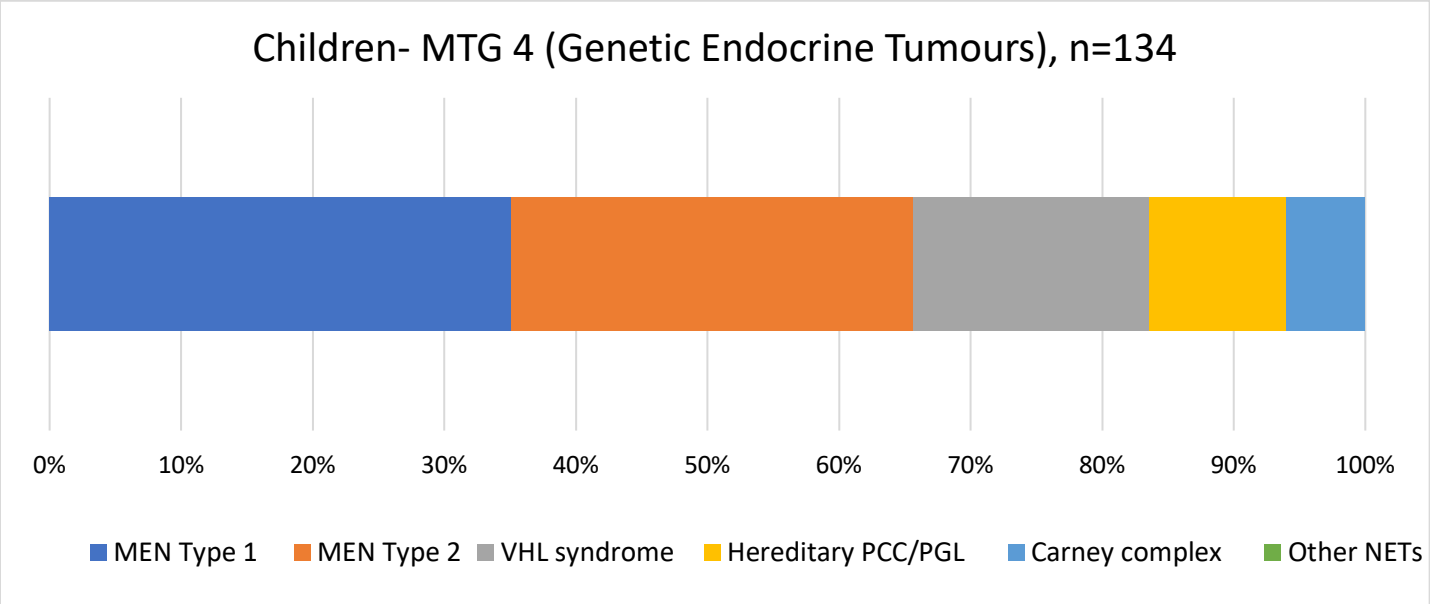
Table 2 – Cases reported per centre per MTG between July 2018 and December 2021.

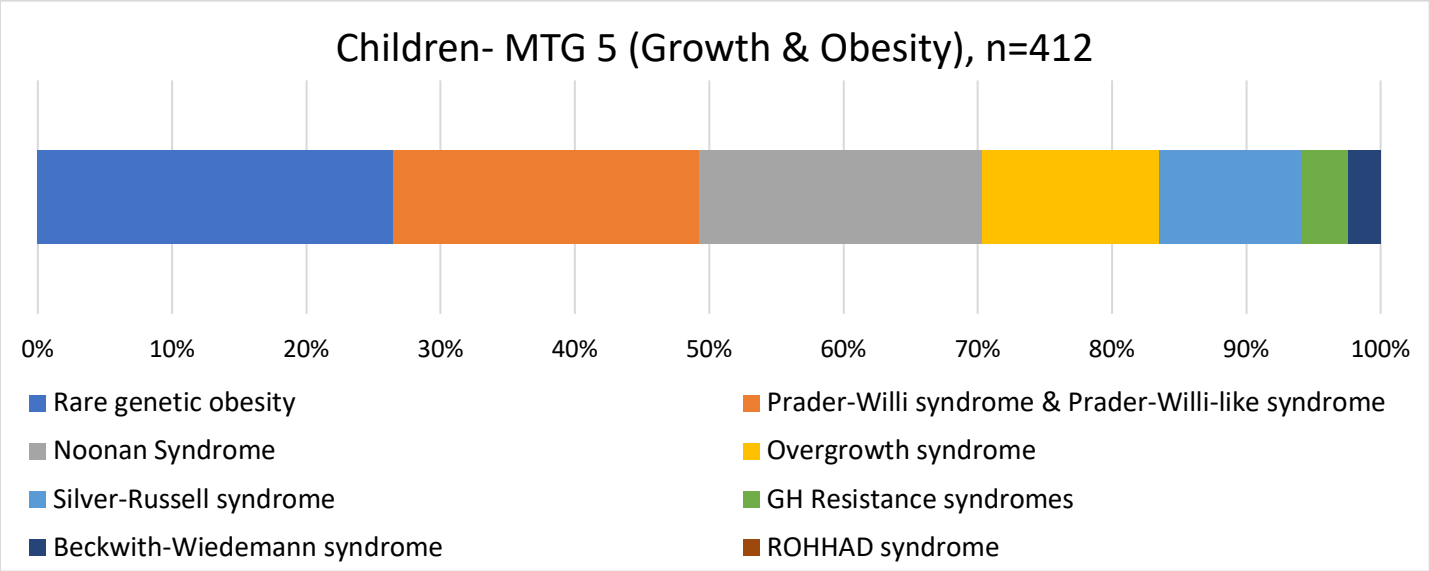
Fig.5a – Commonly reported conditions in children between July 2018 and December 2021; cases, n.

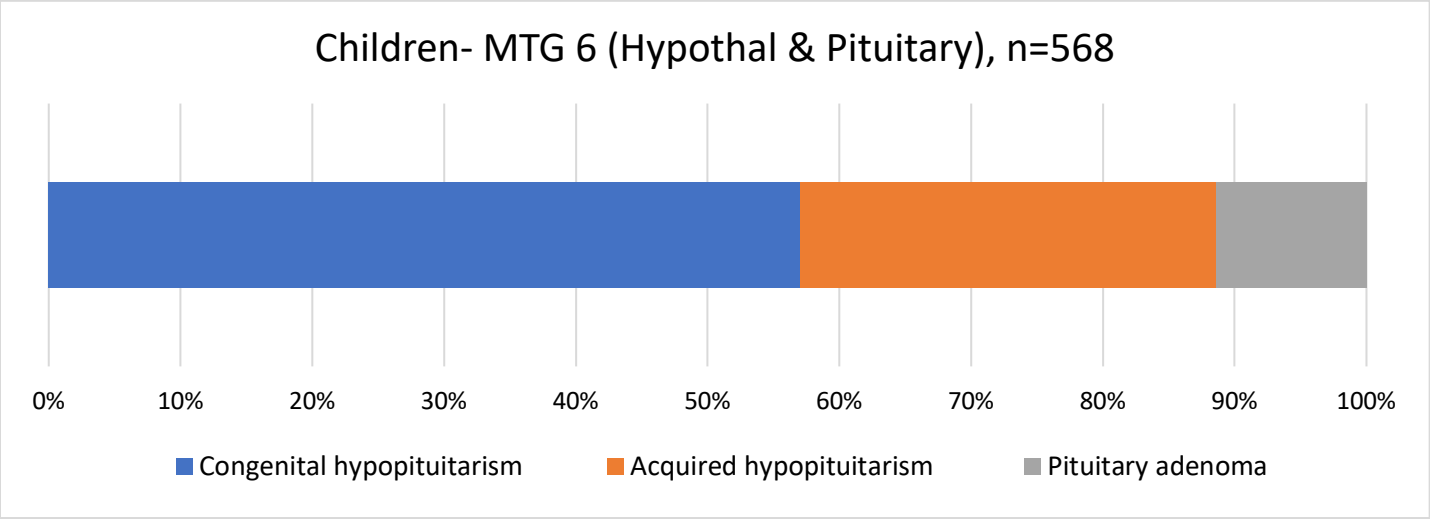


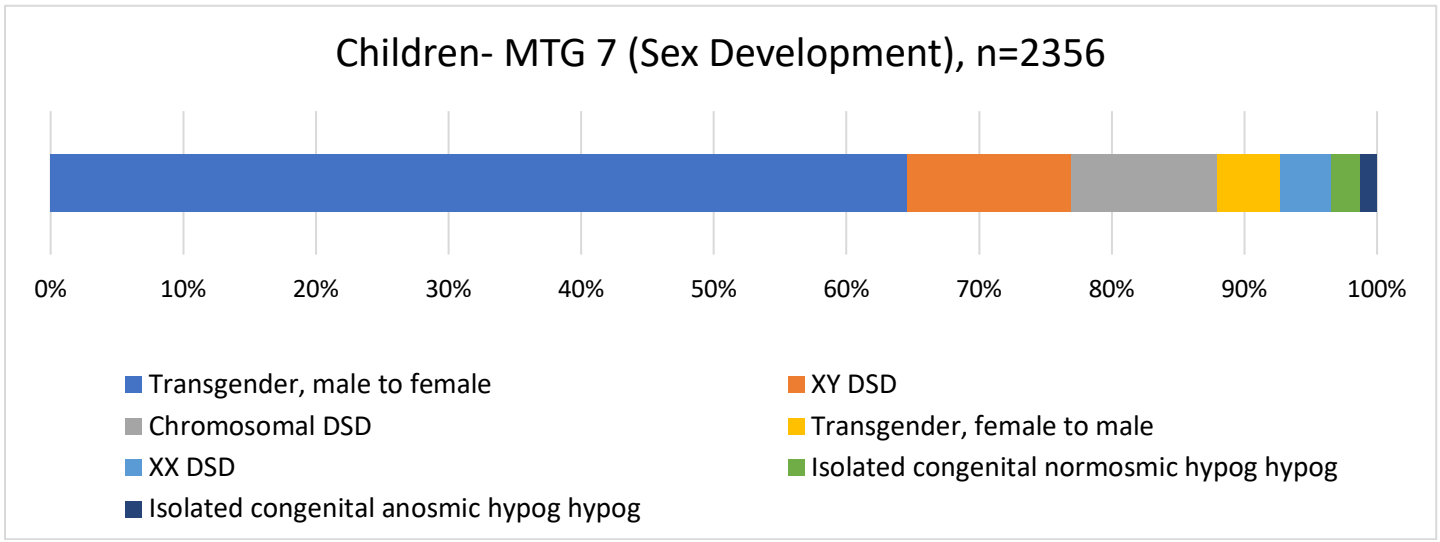


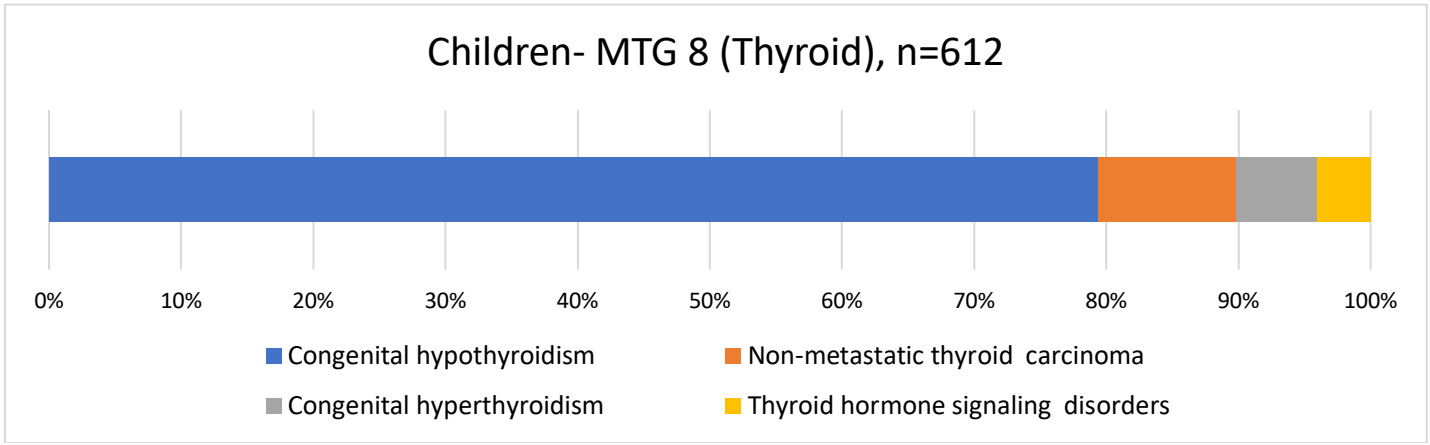



Children- MTG 4 (Genetic Endocrine Tumours), n=134
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
MEN Type 1
MEN Type 2
VHL syndrome
Hereditary PCC/PGL
Carney complex
Other NETs


Children- MTG 5 (Growth & Obesity), n=412
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Rare genetic obesity
Prader-Willi syndrome & Prader-Willi-like syndrome
Noonan Syndrome
Overgrowth syndrome
Silver-Russell syndrome
GH Resistance syndromes
Beckwith-Wiedemann syndrome
ROHHAD syndrome


Children- MTG 6 (Hypothal & Pituitary), n=568
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Congenital hypopituitarism
Acquired hypopituitarism
Pituitary adenoma


Children- MTG 7 (Sex Development), n=2356
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Transgender, male to female
XY DSD
Chromosomal DSD
Transgender, female to male
XX DSD
Isolated congenital normosmic hypog hypog
Isolated congenital anosmic hypog hypog


Children- MTG 8 (Thyroid), n=612
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Congenital hypothyroidism
Non-metastatic thyroid carcinoma
Congenital hyperthyroidism
Thyroid hormone signaling disorders

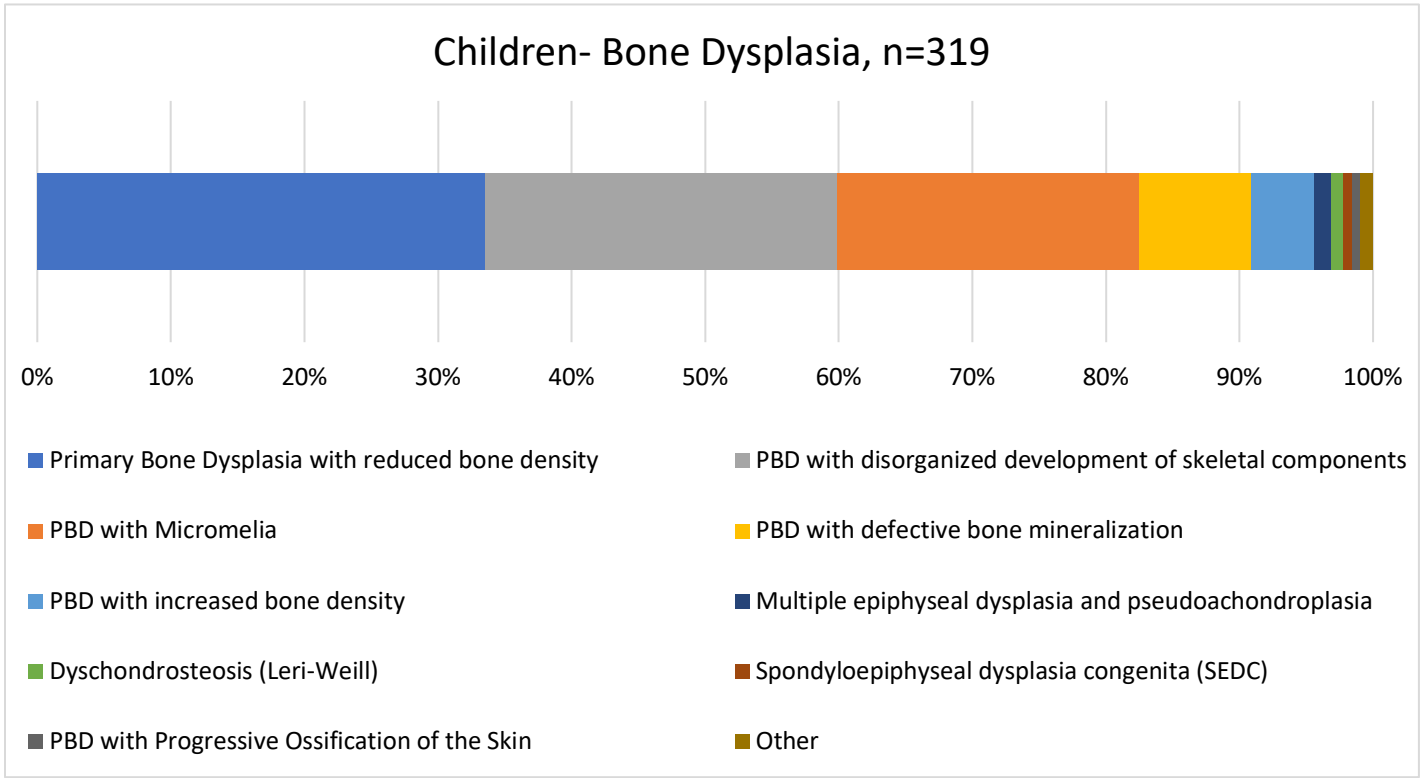
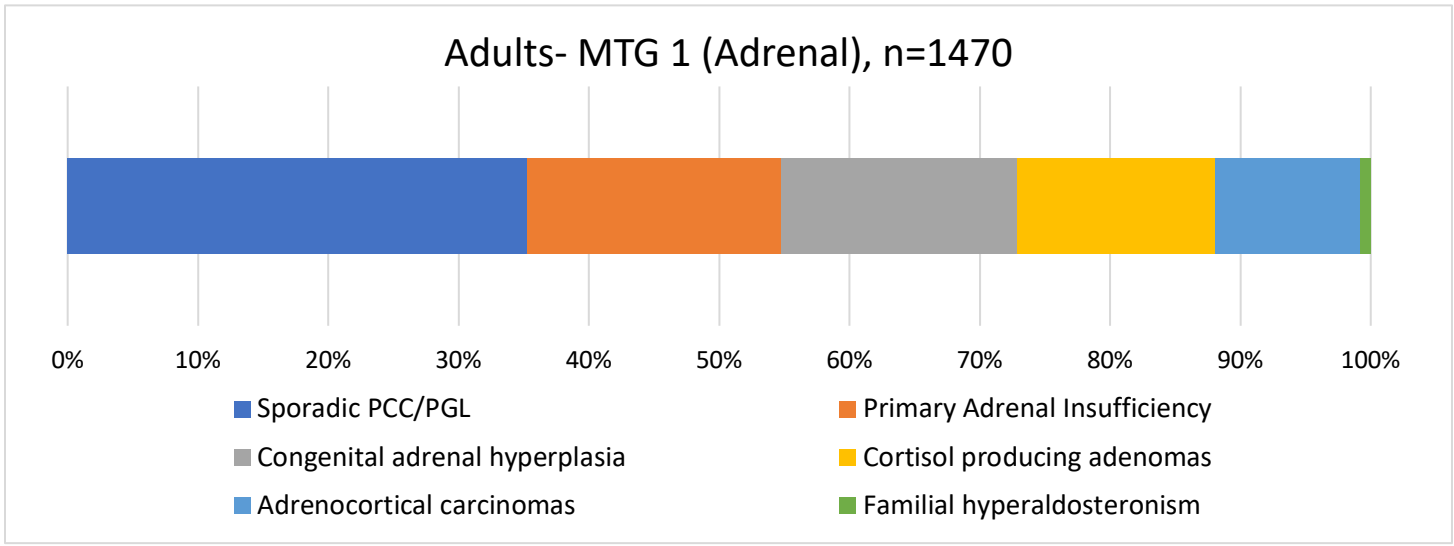
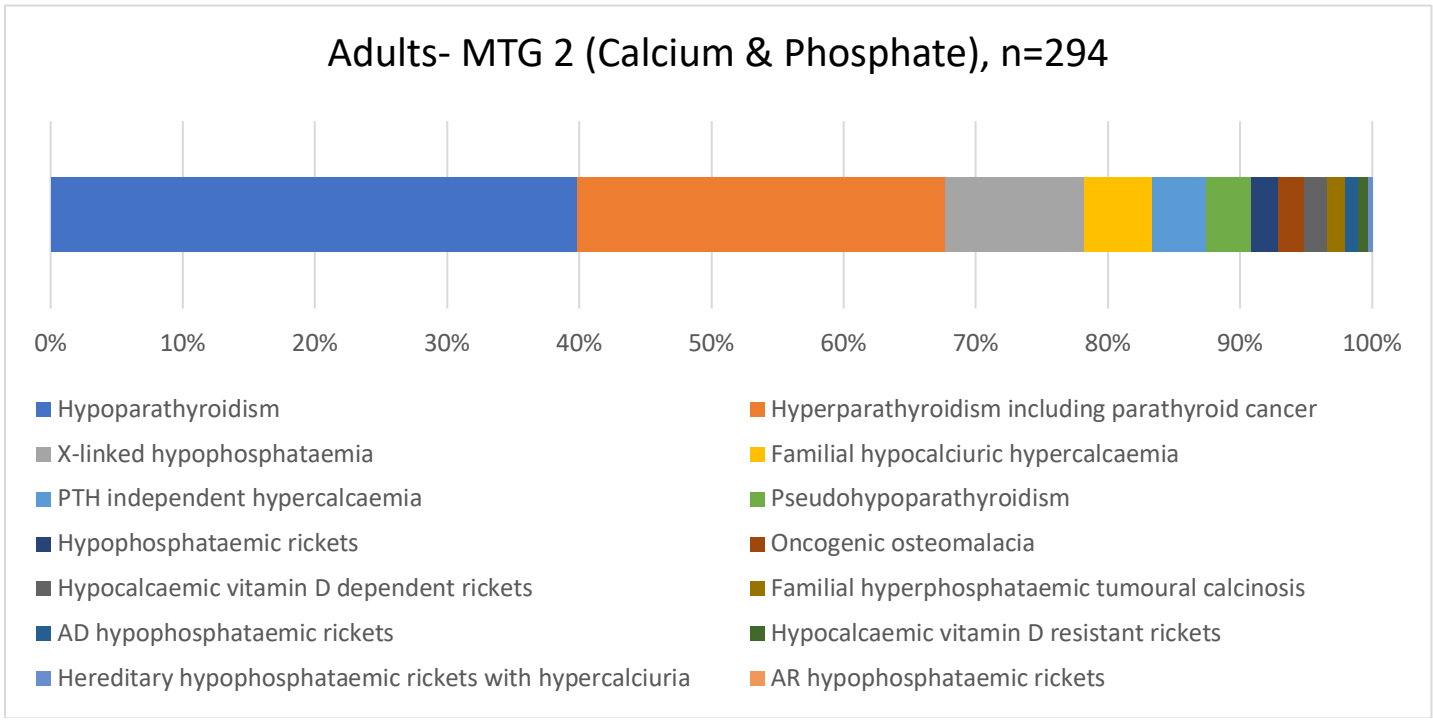
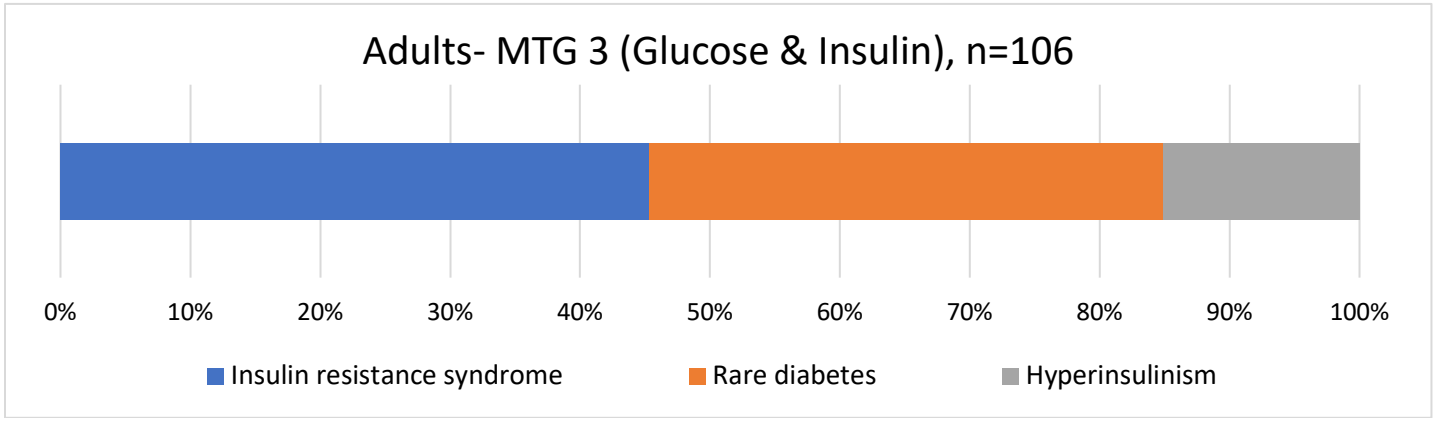
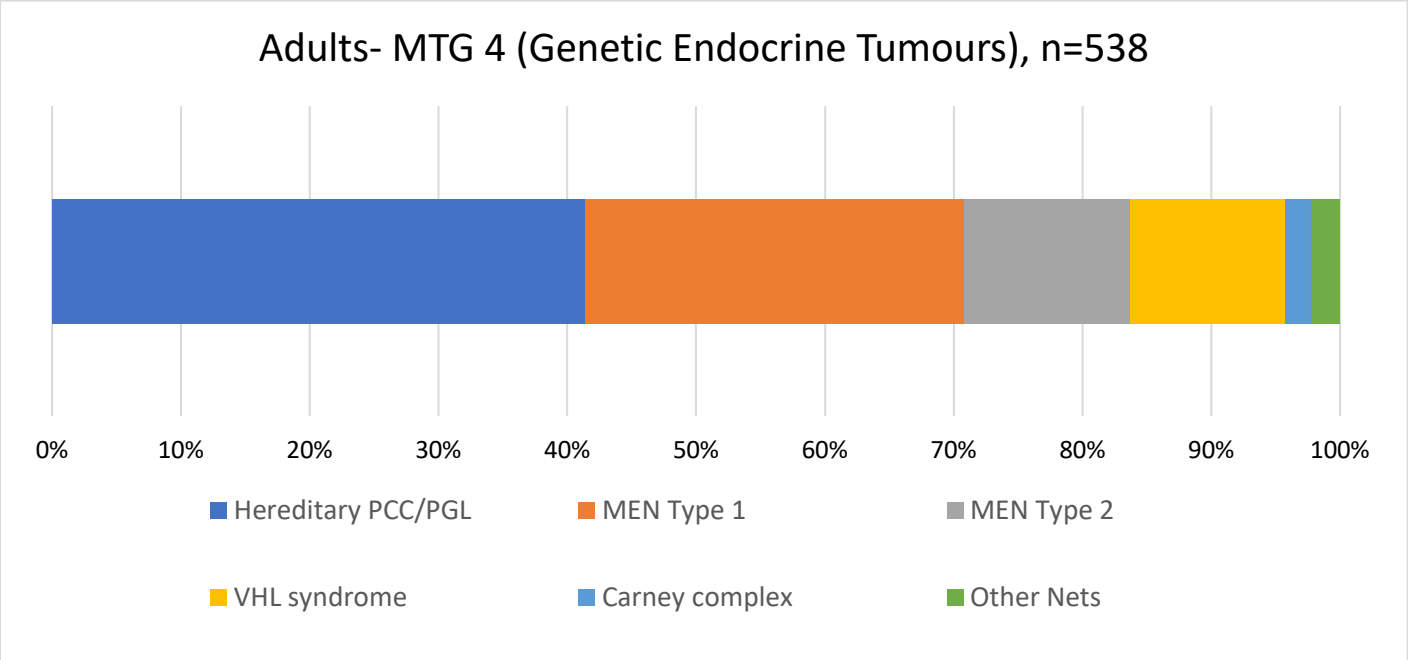

Children- Bone Dysplasia, n=319
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Primary Bone Dysplasia with reduced bone density
PBD with disorganized development of skeletal components
PBD with Micromelia
PBD with defective bone mineralization
PBD with increased bone density
Multiple epiphyseal dysplasia and pseudoachondroplasia
Dyschondrosteosis (Leri-Weill)
Spondyloepiphyseal dysplasia congenita (SEDC)
PBD with Progressive Ossification of the Skin
Other

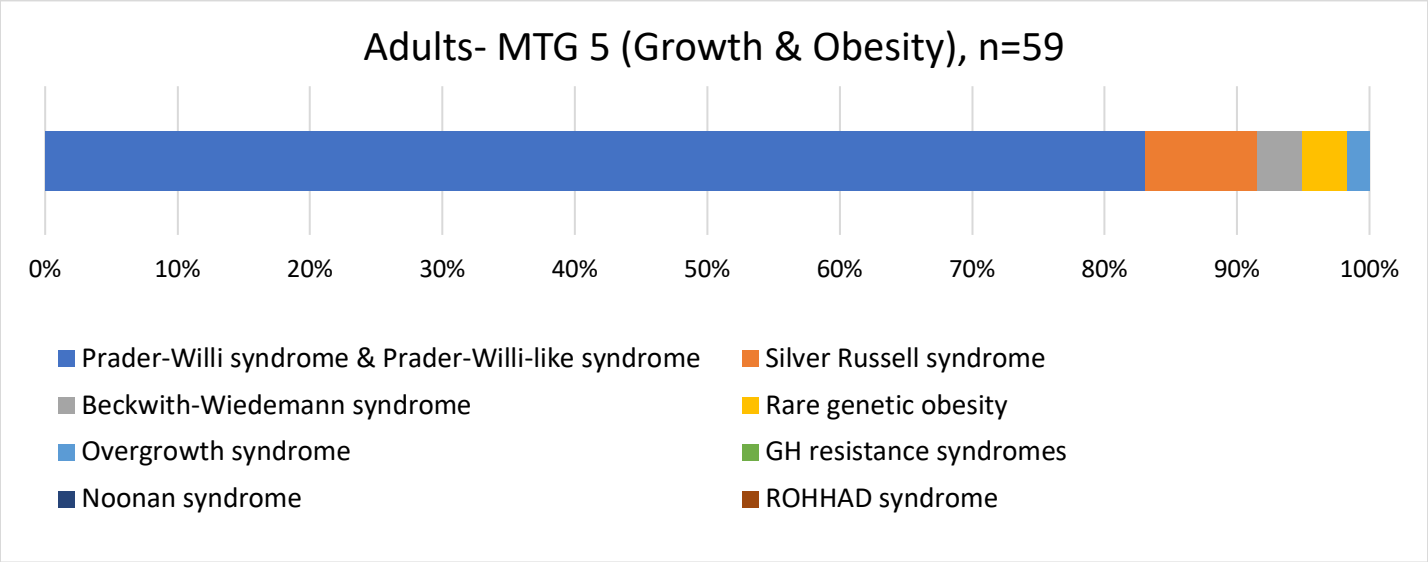
Fig.5b – Commonly reported conditions in adults between July 2018 and December 2021; cases, n.

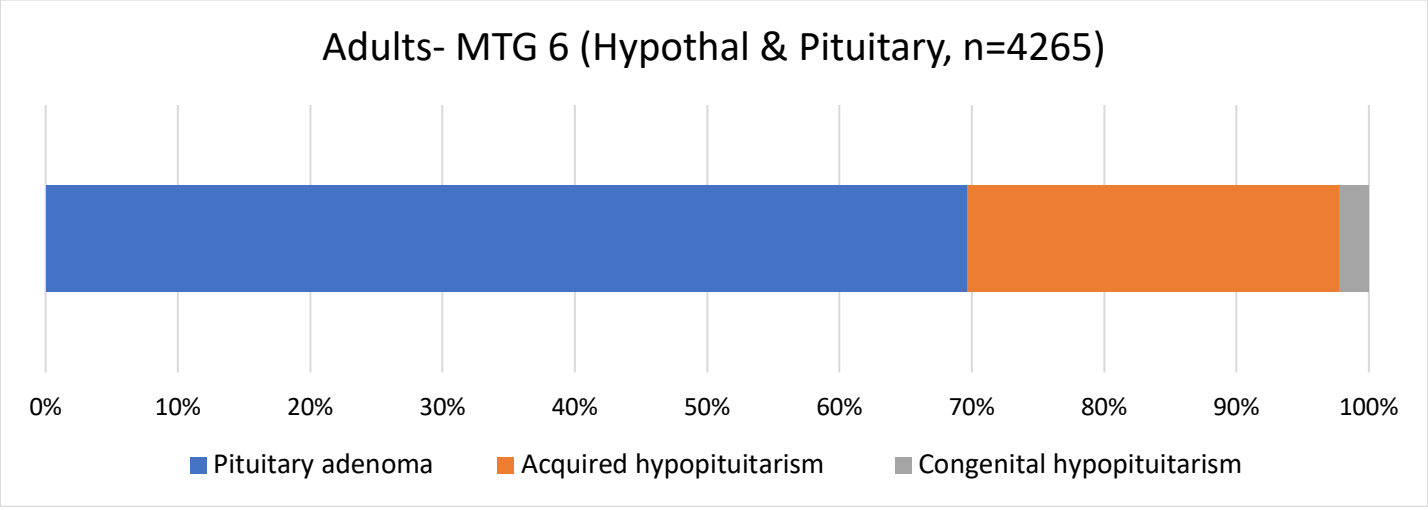


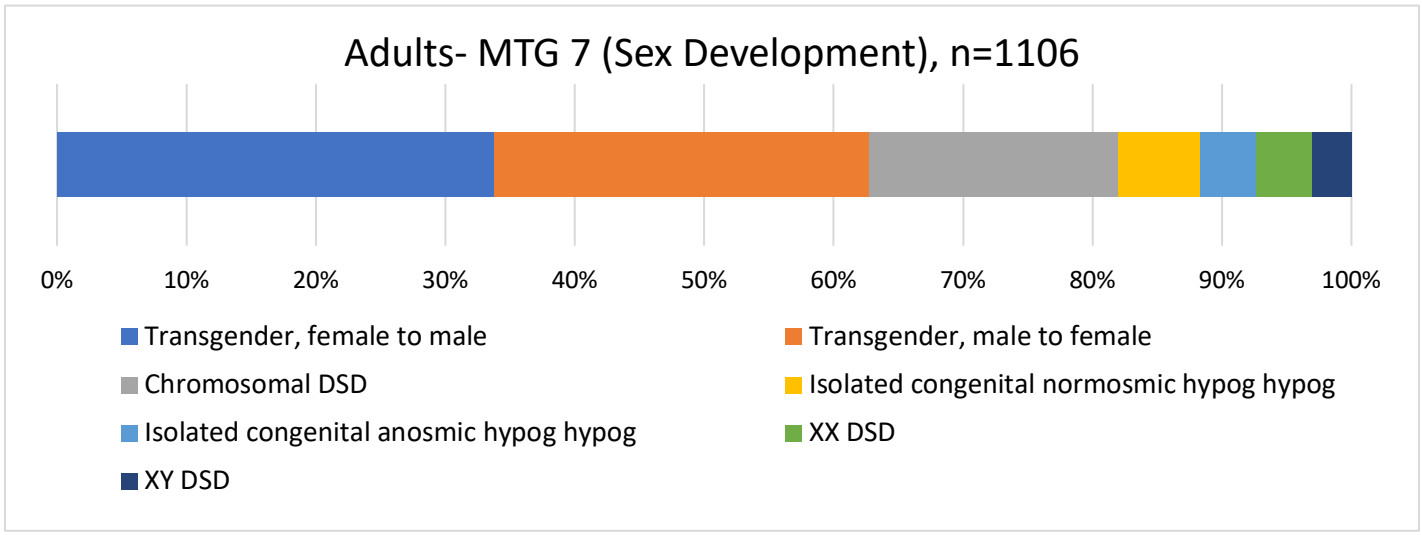


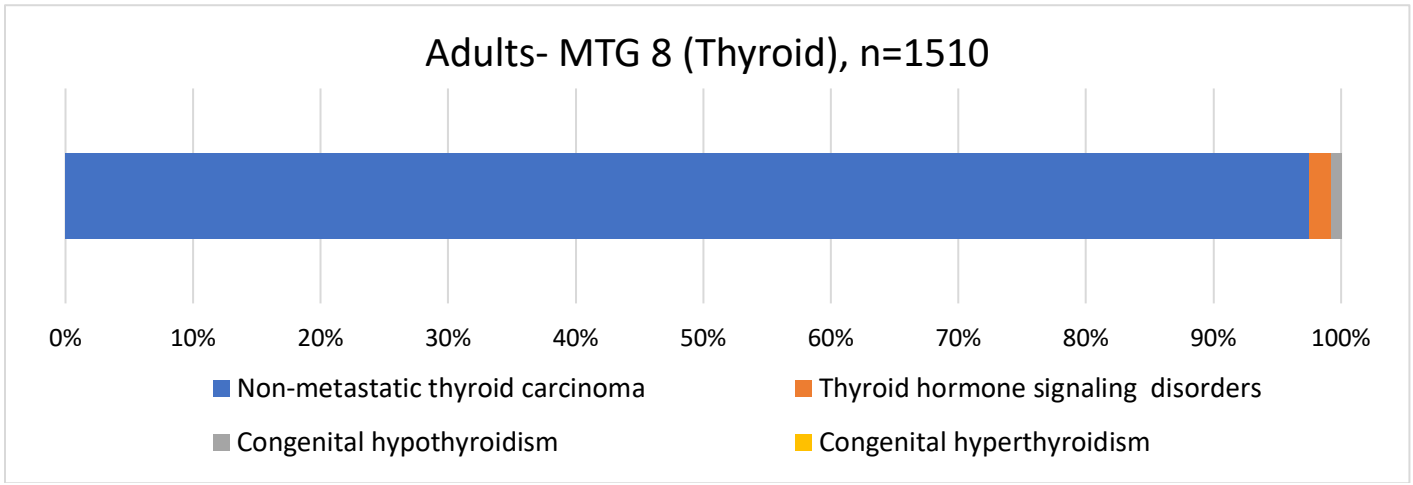


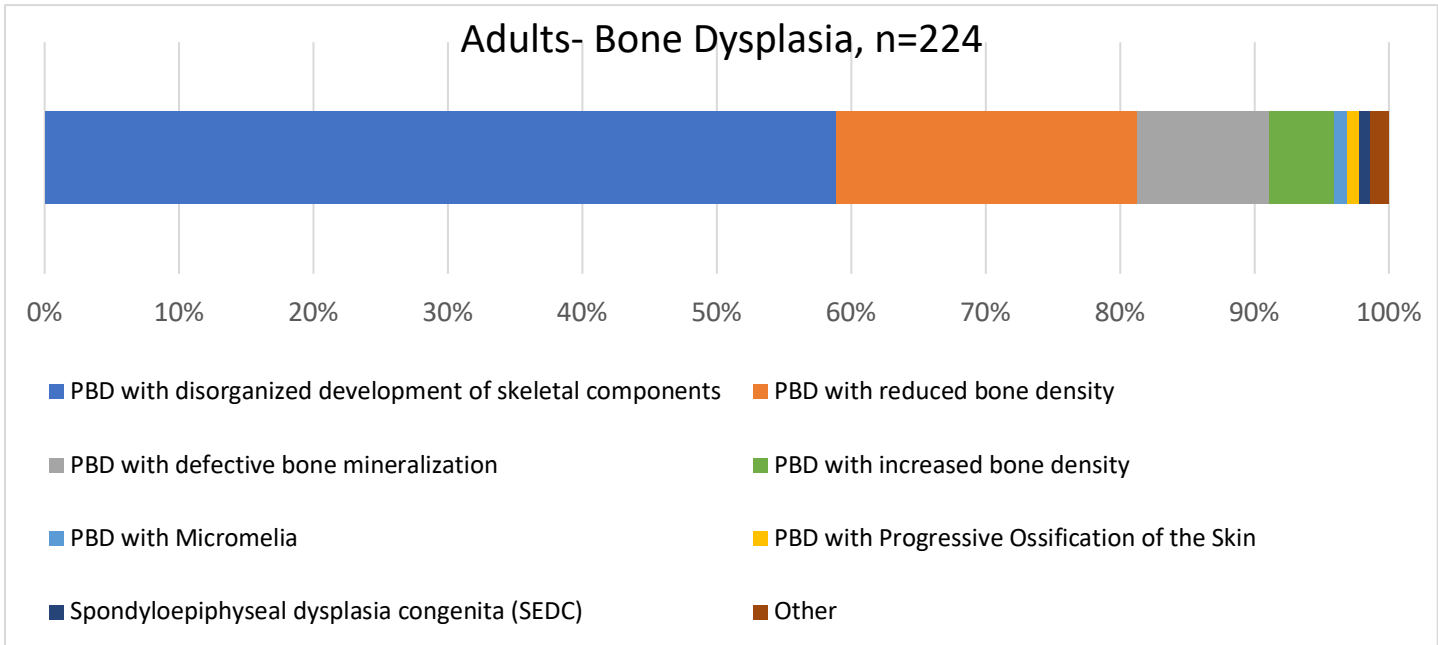

Adults- MTG 4 (Genetic Endocrine Tumours), n=538
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Hereditary PCC/PGL
MEN Type 1
MEN Type 2
VHL syndrome
Carney complex
Other Nets


Adults- MTG 5 (Growth & Obesity), n=59
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Prader-Willi syndrome & Prader-Willi-like syndrome
Silver Russell syndrome
Beckwith-Wiedemann syndrome
Rare genetic obesity
Overgrowth syndrome
GH resistance syndromes
Noonan syndrome
ROHHAD syndrome


Adults- MTG 6 (Hypothal & Pituitary, n=4265)
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Pituitary adenoma
Acquired hypopituitarism
Congenital hypopituitarism


Adults- MTG 7 (Sex Development), n=1106
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Transgender, female to male
Transgender, male to female
Chromosomal DSD
Isolated congenital normosmic hypog hypog
Isolated congenital anosmic hypog hypog
XX DSD
XY DSD


Adults- MTG 8 (Thyroid), n=1510
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Non-metastatic thyroid carcinoma
Thyroid hormone signaling disorders
Congenital hypothyroidism
Congenital hyperthyroidism


Adults- Bone Dysplasia, n=224
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
PBD with disorganized development of skeletal components
PBD with reduced bone density
PBD with defective bone mineralization
PBD with increased bone density
PBD with Micromelia
PBD with Progressive Ossification of the Skin
Spondyloepiphyseal dysplasia congenita (SEDC)
Other

Interpretation of Findings

- The e-REC platform is a simple registry platform that can be used to capture information on new encounters with patients with rare endocrine and bone conditions.
- Although the number of centres that have registered to use the platform continues to increase, the number of centres that are actively reporting cases remains steady.
- There is wide variability in the number of cases encountered for different conditions amongst different centres.
- The proportion of cases that have a suspected diagnosis are higher in children compared to adults and may reflect the groups of conditions that are reported more often in these two groups.

Recommendations

- The use of the platform should continue to be disseminated widely.
- Members of ERNs should be able to utilize the platform for continuous reporting.
- Data are now available to investigators for further analysis and research.

Salma Ali, Jillian Bryce, Ana Priego, Natasha Appelman-Dijkstra, Faisal Ahmed
EuRRECa Work Package 6
March 2022