United in One Voice

ICOSEP

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Dear Dr. Petrič,

Your attention is requested on behalf of the millions of growth impacted children. Our member medical societies and patient organizations thank you for your review of this "fixable" health concern.

Children's Growth Irregularities Incidence Rate

There is global concern about the health of children which is consistently overlooked. It is perhaps such a simple health marker that people assume it will resolve itself. Therefore, it is often ignored.

What is this issue?

Children's growth.

All physicians are taught about the important diagnostic value of monitoring children's growth. It begins even before we are born and continues at each doctor's visit as we mature. This natural event of children's growth is of such importance that the World Health Organization initiated a Multicenter Growth Reference Study. Following their study, they released data defining healthy growth curves for growth charts allowing medical professionals to quickly assess this major signal of a child's health and development.

Parents are rarely aware that scribbles on the wall marking the height of their child and annual physicals contain critical information for physicians. Therefore, if children do not have have a serious injury or illness, parents may rarely take them to see a medical specialist throughout their developmental years.

Why is this important?

A child's irregular growth rate can alert physicians to a possible underlying and potentially life alerting problem in development. Early identification may increase the potential for successful medical intervention and hope for each child's future good health.

If your child's growth was failing due to a treatable brain tumor, wouldn't you want to know as soon as possible? Or if the problem was a simple hormone issue such as a thyroid problem which can be corrected by a daily pill....how upsetting would it be to know that the one medication was not authorized? What would you do?

As parents and medical professionals who assist with this issue, our question is...why is children's growth not one of the top priorities for medical awareness and authorized care?

This following report outlines specific examples of how many children this issue affects.

Jamie Harvey

Jamie Harvey, CEO ICOSEP, MAGIC Foundation Co-founder

Children's Growth Irregularities- A Global Challenge

There were 139.822 million projected births in 2021. (1)

Utilizing the incidence rates (detailed below) of children born in 2021, we can closely estimate the number of children impacted by only a few of the hundreds of growth impacting medical conditions.

Incidence Rates

Hypopituitarism (Hypopit) is diagnosed at a frequency of 300:1,000,000 to 455:1,000,000. (9) This statistically yields the number of children born with Hypopit as between 41,947 and 63,619 each year.

Isolated Hypothyroidism (Hypothy) occurs in 1:3,000 to 1:4,000 (10). The number of new children identified with Isolated Hypothyroidism ranges from 34,956 and 46,607 each year.

Isolated Growth Hormone Deficiency (GHD) has an incidence rate of between 1:3,000 to 1:4,000 children. (6) This frequency reveals that between 34,956 and 46,607 children were born with GHD in 2021.

Turner Syndrome (TS) occurs 1:2,500 female live births. (2) Using global data of male to female annual birth ratios, showing that the number of males to females averages between 103 to 107 males born to every 100 females (3) we can report a global birth rate of TS girls for the year 2021 to be approximately 22,371.

Noonan syndrome: (NS) Untreated, the mortality rate of NS is 3x higher than average for children. (4) The incidence of Noonan Syndrome is reported to be between 1:1,000 and 1:2,500. This gives us an annual birth rate of between 55,929 and 139,822 born with Noonan Syndrome in 2021.

Russell Silver Syndrome also known as Silver Russell Syndrome (RSS) occurs 1:30,000 to 1:100,000 (5). This reveals that globally between 1,389 and 4,661 children were born with RSS in 2021.

Achondroplasia/Hypochondroplasia (Achon) occurs 1:20,000 to 1:30,000 live births. (12) This statistic places the birthrate of children with Achon to be between 4,614 and 6,991 each year.

Small for Gestational Age (SGA) is a bit more challenging to report. 10% of all live births in developed countries are reported as SGA (7). And an alarming 20% (32.4 million) of live births in low or less developed countries are referenced as SGA, according to a 2015 abstract which was based on the number of births in 2010. (8) When SGA is defined as a birth weight and/or birth length < -2 SDS (about 2.5% of all newborns), approximately 90% will catch-up in length and weight in the first 2 years of life (Hokken-Koelega A. et al. Pediatric Research 1995). This percentage is estimated as approximately 80% in the low or less developed countries. Thus 10% to 20% of the SGA born children each year remain lacking in normal height development after their first 2 years of life. The number of affected children is "approximately" between 180,200 and 360,400 accounting for the current declining birth rate. (9) Short stature after SGA birth represents one of the largest groups among those with growth disorders.

Applying the global births reported for 2020 (9), this estimate that between 1,800,200 and 3.600.000 live SGA births will have growth challenges.

Congenital Adrenal Hyperplasia (CAH) occurs 1:15,000 (13). Based upon the 2021 total number of births reported, this frequency reveals that 9,328 children were born with CAH.

Idiopathic Short Stature (ISS) occurs 1:161. With a total global births reported to Unicef as 140,000,000 in 2021, the total number of ISS children born that year is 869,565. This number is based on the definition of ISS to be <-2.5 SDS (<0.62 percentile) growth.

Intrauterine Growth Restriction (IUGR). IUGR has undoubtedly important consequences for perinatal and long-term mortality and morbidity, and IUGR children born SGA who remain short will have a growth disorder for which treatment can be given. In developing countries, IUGR is seen in approximately 24% of newborns. (11) Sharing that

same statistic globally would quite conservatively put the number of IUGR children born in 2021 at 1,125,000.

The total number of children impacted by only 10 of the growth impacting conditions we sampled for 2021 is:

a. Using the low ratios: 2,875,255 million children were born with growth impacting medical conditions or,
b. Using the high ratios: 4,809,571 million children are born with growth impacting medical conditions each year.

This report does **not include** the 1,000+ potential additional rare causes of children's growth disruptions. (15) It is important to note, with regards to these specific diagnoses, and due to variations in reporting for SGA and IUGR births, (in some countries IUGR is listed as a subset of SGA) terminology and diagnosis listings throughout the world, an overlap may be reflected. Therefore, we did not include calculated totals of IUGR children. However, this population is significant.

These statistical facts offer a glimpse into the vast number of children who may be visually identifiable and helped via children's growth pattern awareness. Undiagnosed children with treatable underlying conditions are potentially more of a global catastrophe than previously realized. In particular, if the number one cause of growth challenges, poor nutrition, is included, the number of impacted children increases by millions.

Sharing awareness about the importance of monitoring children's growth is crucial. A simple annual checkup by medical professionals and referring those failing to grow in "normal ranges" to pediatric endocrinologists may literally save the lives of children impacted.

Members of ICOSEP, the international division of The MAGIC Foundation, strongly encourage parents to have their children evaluated every year. Additionally, we encourage physicians to monitor each child's growth with a keen eye for any irregularities and refer children who experience irregular growth to specialists. Irregular growth is the visual sign that the heart, lungs, bones and all cells in a child's body may be experiencing life altering issues which are not cosmetic at the source.

To review a list of specialists in your area for interviews, refer to http://icosep.org and click on the tabs for either the known patient groups or medical specialists.

Resources

1. https://ourworldindata.org/grapher/births-and-deaths-projected-to-2100
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6290843/
3. https://ourworldindata.org/sex-ratio-at-birth
   the averages we estimate the number of boys born in 2021 to be 83,893,200 / girls=55,928,000
4. https://www.epainassist.com/noonan-syndrome/what-is-the-prognosis-for-noonan-syndrome
5. https://medlineplus.gov/genetics/condition/russell-silver-syndrome/#frequency
6. https://www.pediatriconcall.com/articles/pediatric-endocrinology/growth-hormone-deficiency/growth-hormone-deficiency-introduction
7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3177763/
8. https://pubmed.ncbi.nlm.nih.gov/26111558/
9. https://www.theworldcounts.com/populations/world/births
10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4722397/
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14. https://pubmed.ncbi.nlm.nih.gov/11577925/
15. https://pubmed.ncbi.nlm.nih.gov/23640309/ 108,688
16. Causes of Growth Disorders download on this page https://icosep.org/resources/