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# The global burden, trends, and inequalities of individuals with developmental and intellectual disabilities attributable to iodine deficiency from 1990 to 2019 and its prediction up to 2030

Xuesong Yang<sup>1,#</sup>, Cheng Liu<sup>1,#</sup>, Yanbo Liu<sup>1</sup>, Zhigang He<sup>1</sup>, Juan Li<sup>1</sup>, Yijing Li<sup>1</sup>, Yanqiong Wu<sup>1</sup>, Anne Manyande<sup>2</sup>, Hongbing Xiang<sup>1,3</sup>

<sup>1</sup> Department of Anesthesiology and Pain Medicine, Hubei Key Laboratory of Geriatric Anesthesia and Perioperative Brain Health, Wuhan Clinical Research Center for Geriatric Anesthesia, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China <sup>2</sup> School of Human and Social Sciences, University of West London, London, UK

<sup>3</sup> Key Laboratory of Anesthesiology and Resuscitation (Huazhong University of Science and Technology), Ministry of Education, China

# These authors contributed equally

Address correspondence to: Hongbing Xiang, E-mail: hbxiang@tjh.tjmu.edu.cn

#### Abstract

Using data from the Global Burden of Disease (GBD) 2019, we conducted a cross-country inequity analysis to examine the worldwide burden of developmental and intellectual disabilities caused by the re-emerging issue of iodine deficiency from 1990 to 2019. After summarizing the latest evidence, we also made predictions up until the year 2030. According to our results, we observed a significant decline in age-standardized prevalence and annual Years Lived with Disability (YLD) rates during this period. Data analysis indicates that females are more susceptible, with adolescents being particularly vulnerable. Geographic distribution also suggests that areas with lower Socio-Demographic Index (SDI) are most severely affected. A correlation emerged between higher SDI and lower prevalence rates, highlighting the role of economic and social factors in the disease's incidence. The cross-national inequity analysis demonstrates that despite improvements in health inequalities, disparities still exist. Projections, in addition, show that the burden of disease is likely to head into a decline until 2030. This research underscores the necessity for targeted interventions, such as enhancing iodine supplementation and nutritional education, especially in areas with lower SDI. We aim to provide a foundation for policymakers to further research effective preventative and potential alternative treatment strategies.

**Keywords**: developmental and intellectual disabilities, iodine deficiency, systematic analysis, Global Burden of Disease

#### Introduction

Iodine deficiency, a significant contributor to the global burden of disease, affects the synthesis of thyroid hormones, leading to many diseases related to metabolism and growth, that threaten people's physical health and development[1, 2]. Thyroid hormones are iodine-containing compounds, representing a combination of  $T_3$ ,  $T_4$ , and  $rT_3$ [3]. Among these,  $T_4$  is the most abundantly secreted[4], while  $T_3$  the most biologically active, and is approximately five times more potent than the former[5-8]. The synthesis of thyroid hormones is dependent on the intake of iodine, which serves as an essential raw material for thyroid hormone production[9]. Approximately 80-90% of the required iodine comes from iodide compounds found in food, primarily iodized sodium and potassium[10]. The World Health Organization (WHO) recommends a daily iodine intake of 150 micrograms for adults[11]. However, the physiological iodine requirements increase during pregnancy and lactation, but the daily dose should not exceed 200 micrograms[11]. In addition to obtaining iodine from external sources, the iodine needed for thyroid hormone synthesis can also be recycled from iodine-containing compounds within the thyroid gland[12].

Thyroid hormones act on nearly all tissues in the body and play a crucial role in regulating various stages of promoting and maintaining growth, development, and metabolism[13; 14], with a wide range of biological effects. During the embryonic and neonatal stages, thyroid hormones facilitate the proliferation and differentiation of neurons as well as the formation of synapses[15]. Therefore, thyroid hormone deficiency during early childhood can lead to irreversible developmental disorders of the nervous system, known as cretinism[16]. This condition is characterized by delayed intellectual development, stunted growth, and incomplete tooth development. Compared to the general population, individuals with intellectual disabilities are more likely to face challenges in accessing equitable healthcare and experience premature mortality[17]. A study conducted in the United States by Gaylord et al. reported that the difference in cost attributed to intellectual disabilities (from 2001 to 2016) would continue to yield ongoing benefits of \$38 billion[18]. Therefore, it is essential for us to comprehend the epidemiological characteristics of this disease. In humans, throughout the first three months of fetal development, the fetus is unable to synthesize thyroid hormones on its own[19]. During this period, the thyroid hormones required for fetal growth and development are entirely supplied by the mother[20]. Therefore, pregnant women with a history of iodine deficiency particularly need iodine supplementation to reduce the risk of cretinism[20].

Although iodine deficiency stands as the most prevalent and preventable cause of mental disorders globally[21],nevertheless, there exists a shortage of research, based on the Global Burden of Disease (GBD) data, concerning the intellectual and developmental disabilities due to iodine deficiency. The purpose of this review is to analyze the global burden of intellectual disabilities resulting from iodine deficiency worldwide, provide a reference for scholars in the field and promote the prevention of this condition.

#### Method

#### **Definitions and data source**

In the GBD study, developmental and intellectual disabilities refer to situations where an individual's intellectual abilities are below the average. The severity of intellectual disabilities is categorized into five levels based on IQ test scores (standardized with a mean of 100), including borderline (IQ scores of 70-85), mild (IQ scores of 50-69), moderate (IQ scores of 35-49), severe (IQ scores of 20-34), and profound (IQ scores of 0-19)[22]. The nonfatal iodine deficiency burden includes estimates for visible goiter (grade 2) and its associated consequences such as thyroid dysfunction, heart failure, and intellectual disability but excludes estimates for subclinical iodine deficiency.[23].

We conducted an extensive analysis to extract data on the prevalence and Years Lived with Disability (YLD) associated with developmental and intellectual disabilities resulting from iodine deficiency. This analysis encompasses a global perspective and further dissects the data by region, income group, and sex, spanning the years from 1990 to 2019. Our estimates are presented in both raw values and age-standardized rates. YLD serves as a crucial metric in gauging the impact of this condition on individuals' and societies' quality of life. It relies on standardized disability weights assigned to each health state. YLD is calculated by multiplying the number of incident cases in the population by the 'disability' weight specific to the condition, taking into account the average duration of cases until remission or death. Therefore, mortality plays a pivotal role in estimating disability. To compile this data, we leveraged the Global Burden of Disease (GBD) study, which aggregates clinical informatic data from various sources, including hospital records, ambulatory care (such as general practitioner visits), and health insurance claims. For each GBD cause (disease), we computed ratios of non-primary to primary diagnosis rates and ratios of outpatient to inpatient

care across multiple regions. In our modeling process, we employed DisMod-MR. The strategy allowed us to generate precise estimates for each metric of interest, including prevalence and YLD, while accounting for variables such as age, sex, location, and year of analysis. We estimated the developmental and intellectual disabilities of two extended categories: severe intellectual disability and profound intellectual disability from the GBD 2019. The classification information of developmental and intellectual disabilities came from a 2008 systematic review[24]. We conducted all statistical analyses and generated visualizations using R statistical software (version 4.2.3). Statistical significance was determined with a p-value < 0.05.

#### Socio-economic status

Our estimates are categorized according to the Socio-Demographic Index (SDI), determined by factors such as income per capita, educational attainment, and the total fertility rate among women under the age of 25 years. SDI is classified into five categories: low (<0.46), low-middle (0.46–0.61), middle (0.61–0.69), high-middle (0.69–0.80), and high (>0.80)[25, 26].

#### Health inequalities

In this study, we used the concentration index (CI) and the slope index to quantify the health inequalities. The slope index of inequality and concentration index, are the two standard indicators of absolute inequality and relative inequality, respectively[27]. The slope index of inequality is calculated by regressing the national DLYs ratio for all age groups on a relative positional scale associated with SDI, and defined as the midpoint of the population cumulative range ranked by the SDI[28]. Heteroscedasticity is explained by a weighted regression model. The concentration index is calculated by numerically integrating the area under the Lorenz concentration curve, which is fitted using the cumulative scores of DALYs and the cumulative relative distribution of the population based on SDI[29].

#### Projections till the year 2030

We used Bayesian age-period-cohort (BAPC) models to assess and project the prevalence and YLDs rates till 2030[30]. The BAPC model relies on an integrated nested Laplacian approximation to estimate marginal posterior distributions, helping circumvent some of the mixing and convergence issues associated with the traditional Bayesian method of Markov Chain Monte Carlo sampling[31]. The BAPC and INLA packages in R statistical software (version 4.2.3) were used for BAPC analyses.

#### Results

# The Global burden of developmental and intellectual disabilities due to iodine deficiency by year and age

After controlling the effect of population and age structure, age-standardized prevalence rates for developmental and intellectual disabilities due to iodine deficiency fell by 58.54%, from 54.37(95 % UI 38.57 to 67.63) per 100 000 population in 1990 to 22.54 (95 % UI 14.47 to 29.23) per 100 000 population in 2019 (Table 1).

Similarly, global age-standardized YLD rates decreased by 57.08 %, from 9.6 (95 % UI 5.61 to 14.39) per 100 000 population in 1990 to 4.12 (95 % UI 2.25 to 6.4) per 100 000 population in 2017. From1990, the age-standardized prevalence and YLD rates showed a downward trend (Figure 1A and 1B). In 2019, the prevalence and YLD rates of developmental and intellectual disabilities gradually increased with age, and all reached a peak in the 15-19 age group (Figure 1C and 1D). Then, the prevalence and YLD rates by age declined rapidly in the 15-19 age group and slowly in those above the age of 20 to 24. For each age group, profound intellectual disability levels were higher than severe intellectual disability in 2019. Regardless of age, year, or degree of developmental and intellectual disabilities, the age-standardized prevalence and YLD rates were consistently higher in females than in males.

#### Developmental and intellectual disabilities burden due to iodine deficiency based on Global

#### Burden of Disease regions.

These heatmaps illustrate the distributional situation of sex and developmental and intellectual disabilities of burden due to iodine deficiency in GBD regions in 2019 (Figure 2 and 1S). The shade of color of each block in the heatmap represents the size of the numerical value, and the figure inside, the absolute number of the age-standardized prevalence and YLD rates. The Low SDI region had the highest total age-standardized prevalence rates and YLD rates in both sexes, followed by South Asia and Central Sub–Saharan Africa. Profound intellectual disability accounted for the majority of the age-standardized prevalence rates of all GBD regions and the Low SDI region had the highest age-standardized prevalence rates and YLD rates for profound intellectual disability. But the lowest age-standardized prevalence rates and YLD rates were seen in South Asia.

#### Geographical distribution, socio-economic disparities, and health inequalities in

#### developmental and intellectual disabilities due to iodine deficiency

Figure 3 maps the distribution of the health burden of developmental and intellectual disabilities due to iodine deficiency worldwide in 2019. The age-standardized prevalence rate (Figure 3A) was highest in Somalia [162.42 (95 % UI 99.59 to 216.34) per 100 000 population], followed by Yemen [121.68 (95 % UI (65.61 to 174.69) per 100 000 population] and Afghanistan [117.09 (95 % UI (78.01 to 146.97) per 100 000 population] (Fig. 3A and Table 1S). The highest age-standardized YLD rate was also found in Somalia [28.74 (95 % UI 15.49 to 45.61) per 100 000 population], followed by Yemen [21.9 (95 % UI 10.71 to 35.69) per 100 000 population] and Afghanistan [20.54 (95 % UI 12.11 to 31.52) per 100 000 population] (Fig. 3B and Table 1S). HDI data in 2019 were available for 204 countries and territories, including thirty three in the low HDI group, forty two in low-middle SDI, forty one in middle SDI group, forty two in high-middle SDI group.

In terms of the number of intellectual disabilities due to iodine deficiency in different SDI regions, in 1990, the low-middle SDI region had the largest number of prevalence and YLDs, accounting for 48.5% and 49.1%, followed by Middle SDI and Low SDI regions (Figure 5A and 5C). The high SDI region had the smallest number of prevalence and YLDs, accounting for only 0.02%. But in 2019, the proportion of the number of prevalence and YLDs cases with low SDI region increased and exceeded that of the number of cases with middle SDI region, and the other regions proportion was about the same as 1990 (Figure 5B and 5D).

Significant absolute and relative SDI-related inequalities in the burden of developmental and intellectual disabilities due to iodine deficiency were observed, with a disproportionately higher burden shouldered by countries with lower SDI. As illustrated by the slope index of inequality, the gap in YLDs rate between the highest and the lowest SDI country decreased from -9.7 (95% CI - 10.7 to -8.7) in 1990 to -4.9 (95% CI -5.4 to -4.3) in 2019 (Figure 5E and Table 3). The results of the concentration index indicates that the between-country inequality in the distribution of the developmental and intellectual disabilities due to iodine deficiency burden declined, from -48.0 (95% CI -60.0 to -36.0) in 1990 to -45.5 (95% CI -56.8 to -34.2) in 2019 (Figure 5F and Table 3).

# Developmental and intellectual disabilities due to iodine deficiency projections till the year 2030

The ASPR and ASYR for both sexes are projected to see a gradual decline from 2020 to 2030, as depicted in Figures 6A, B, C, and D. It is worth noting that the trend for age-specific prevalence rate for both sexes will fall across all age groups and the highest level is found in the 5-19 years age group (Figures 2S, 3S). The pattern of age-specific YLDs rate closely aligns with the global age-

specific prevalence rate trend (Figures 4S, 5S). It is anticipated that from 2020 to 2030, both mortality cases and YLDs will diminish annually, with the numbers for females significantly outweighing those of males (Figures 6E, F).

#### Discussion

This review presents a comprehensive analysis of the global burden of developmental and intellectual disabilities due to iodine deficiency from 1990 to 2019, and uncovered a promising decline in age-standardized prevalence and YLD rates over this period. It also exhibited age and sex patterns, which suggest the importance of addressing iodine deficiency during adolescence and recognizing sex-specific vulnerabilities. Geographical distribution analysis underscores the need for targeted interventions in regions with limited access to iodine-rich foods and low socio-economic status. Surprisingly, we also found correlations between SDI and lower prevalence rates. These results show that economic and social factors also affect the incidence of such a disease. Developed countries with a high level of socio-economic development have already taken effective interventions to alleviate the health burdens arising from iodine deficiency. While health inequalities show improvement, a framework for action is needed to facilitate equitable distribution.

In our study, the highest burden of developmental and intellectual disabilities due to iodine deficiency was observed in regions with low-middle SDI in 2019. Between 1999 and 2000, the global prevalence, however, sharply decreased. This could likely be attributed to the proportion of the population consuming iodized salt increasing from less than 20% in 1990 to 70% in 2000[32, 33]. More importantly, the United Nations Children's Fund (UNICEF) set a goal in 1990 to eliminate Iodine Deficiency Disorders (IDD) as a public health issue by 2000 and promoted USI worldwide [34]. Although progress has been made in the elimination of iodine deficiency, over two billion people worldwide still face the risk of insufficient iodine intake [35, 36]. The burden is high in sub-Saharan Africa and South Asia, consistent with previous studies [37]. This might be due to limited dietary diversity, poor sanitary conditions, and interactions with infectious diseases [38]. We also found that the declining trend in ASPR at the global and regional levels aligns with a similar trend in ASYR.

Iodine deficiency has adverse effects on people of all age groups as the highest age-standardized prevalence rate of developmental and intellectual disabilities caused by iodine deficiency was

observed in the 10-19 age group. This could be due to the increased demand for iodine during adolescence, and its decreased content derived from food and salt[39]. Even a mild iodine deficiency during pregnancy can result in a lowered IQ and inferior academic performance in primary school when compared to peers[40, 41]. In adults, iodine deficiency can impair cognitive functions, resulting in emotional apathy, reduced learning capacity, and decreased productivity, which in turn has adverse effects on the country's population and economy[21]. The substantial expenditures associated with providing extra resources to address intellectual disabilities place a significant burden on society, not to mention the accompanying shame and the various mental and physical illnesses and their associated complications[42]. This suggests that in future research, we should conduct a thorough assessment of the costs imposed on society by intellectual disabilities resulting from iodine deficiency is greater in females than in males, potentially because male hormones stimulate thyroid growth while female hormones have an inhibitory effect[43]. Hence, the increasing trend of iodine deficiency in females is indeed a matter of concern.

In short, although we have made significant progress in reducing the burden of diseases caused by iodine deficiency, continued efforts are essential, especially in low-SDI regions. To further alleviate this burden, it is imperative to strengthen public health strategies, promote health education, and optimize the supply of essential nutrients.

The study serves as a vital resource for scholars and policymakers in guiding prevention efforts, with a focus on improving iodine supplementation, nutritional education, and sex-specific health initiatives in at-risk regions, while encouraging further research into effective interventions and treatments. However, our review does have some limitations. The data source of this review is generated from a GBD database, which may be subject to variations in reporting and recording across different organizations, potentially affecting data accuracy. The study also primarily focuses on the prevalence and YLD rates of developmental and intellectual disabilities due to iodine deficiency and does not delve into specific interventions and treatments. Future research should, therefore, explore effective actionable strategies for prevention and management.

#### Conclusion

From 1990 to 2019, the global burden of developmental and intellectual disabilities caused by iodine deficiency has decreased, especially in regions with a high Socio-Demographic Index (SDI). However, its burden remains high in children and adolescents, as well as in low and middle-income countries, with females experiencing a higher level than males. The findings of this study are valuable for policymakers in assessing current intervention measures and guiding future nutritional supplementation strategies to alleviate the burden of intellectual and developmental disorders caused by iodine deficiency.

#### References

- 1. Brent, G.A., *Mechanisms of thyroid hormone action*. The Journal of clinical investigation, 2012. **122**(9): p. 3035-3043.
- 2. Zimmermann, M.B., P.L. Jooste, and C.S. Pandav, *Iodine-deficiency disorders*. The Lancet, 2008. **372**(9645): p. 1251-1262.
- 3. Cheng, S.Y., J.L. Leonard, and P.J. Davis, *Molecular aspects of thyroid hormone actions*. Endocr Rev, 2010. **31**(2): p. 139-70.
- 4. Wu, S.Y., et al., *Alternate pathways of thyroid hormone metabolism*. Thyroid, 2005. **15**(8): p. 943-58.
- 5. Gross, J. and R. Pitt-Rivers, *Physiological activity of 3:5:3'-Ltriiodothyronine*. Lancet, 1952. **1**(6708): p. 593-4.
- Pitt-Rivers, R., Metabolic effects of compounds structurally related to thyroxine in vivo: thyroxine derivatives. J Clin Endocrinol Metab, 1954. 14(11): p. 1444-50.
- 7. Mussett, M.V. and R. Pitt-Rivers, *The thyroid-like activity of triiodothyronine analogues*. Lancet, 1954. **267**(6850): p. 1212-3.
- 8. Lerman, J., *The contribution of triiodothyronine to thyroid physiology*. J Clin Endocrinol Metab, 1954. **14**(6): p. 690-3.
- 9. Leung, A., E.N. Pearce, and L.E. Braverman, *Role of iodine in thyroid physiology*. Expert Rev Endocrinol Metab, 2010. **5**(4): p. 593-602.
- 10. Sorrenti, S., et al., *Iodine: Its Role in Thyroid Hormone Biosynthesis and Beyond*. Nutrients, 2021. **13**(12).
- 11. Organization, W.H., Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers. 2007.
- Bianco, A.C. and R.R. da Conceição, *The deiodinase trio and thyroid hormone signaling*. Thyroid Hormone Nuclear Receptor: Methods and Protocols, 2018: p. 67-83.
- 13. Shahid MA, A.M., Sharma S., Physiology, Thyroid Hormone. 2023
- 14. Zimmermann, M.B., *Iodine deficiency*. Endocr Rev, 2009. **30**(4): p. 376-408.

- Hetzel, B.S., *Iodine and neuropsychological development*. J Nutr, 2000.
   130(2S Suppl): p. 493s-495s.
- 16. Delange, F., *Iodine deficiency as a cause of brain damage*. Postgrad Med J, 2001. **77**(906): p. 217-20.
- 17. Liao, P., et al., *Prevalence and incidence of physical health conditions in people with intellectual disability–a systematic review.* PloS one, 2021. 16(8): p. e0256294.
- Gaylord, A., et al., *Trends in neurodevelopmental disability burden due to* early life chemical exposure in the USA from 2001 to 2016: A populationbased disease burden and cost analysis. Molecular and cellular endocrinology, 2020. 502: p. 110666.
- Glinoer, D., *The regulation of thyroid function during normal pregnancy: importance of the iodine nutrition status.* Best Pract Res Clin Endocrinol Metab, 2004. 18(2): p. 133-52.
- 20. Moleti, M., et al., *Maternal thyroid function in different conditions of iodine nutrition in pregnant women exposed to mild-moderate iodine deficiency: an observational study.* Clin Endocrinol (Oxf), 2011. **74**(6): p. 762-8.
- 21. Zimmermann, M.B., P.L. Jooste, and C.S. Pandav, *Iodine-deficiency disorders*. Lancet, 2008. **372**(9645): p. 1251-62.
- 22. Vos, T., et al., *Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019.* The Lancet, 2020. **396**(10258): p. 1204-1222.
- 23. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet, 2020. **396**(10258): p. 1204-1222.
- 24. Katz, G. and E. Lazcano-Ponce, *Intellectual disability: definition, etiological factors, classification, diagnosis, treatment and prognosis.* Salud Publica Mex, 2008. **50 Suppl 2**: p. s132-41.
- 25. Wang, H., et al., *Global magnitude of encephalitis burden and its evolving pattern over the past 30 years.* J Infect, 2022. **84**(6): p. 777-787.
- 26. Zhao, S., et al., *Global magnitude and long-term trend of ischemic heart disease burden attributed to household air pollution from solid fuels in 204 countries and territories, 1990-2019.* Indoor Air, 2022. **32**(2): p. e12981.
- 27. Organization, W.H., *Handbook on health inequality monitoring: With a special focus on low-and middle-income countries.* 2023.
- 28. Peng, J., H. Xu, and X. Tang, *Global inequalities in the burden of digestive diseases from 1990 to 2019: findings from the Global Burden of Disease Study 2019.* Gastroenterology, 2023.
- 29. Ordunez, P., et al., *Rheumatic heart disease burden, trends, and inequalities in the Americas, 1990-2017: a population-based study.* Lancet Glob Health, 2019. **7**(10): p. e1388-e1397.
- 30. Riebler, A. and L. Held, *Projecting the future burden of cancer: Bayesian ageperiod-cohort analysis with integrated nested Laplace approximations.* Biometrical Journal, 2017. **59**(3): p. 531-549.

- 31. Huang, J., et al., *The comparative burden of brain and central nervous system cancers from 1990 to 2019 between China and the United States and predicting the future burden.* Frontiers in public health, 2022. **10**: p. 1018836.
- 32. UNICEF., et al., Sustainable elimination of iodine deficiency: Progress since the 1990 World Summit for Children. 2008: UNICEF.
- 33. Delange, F., et al., *World status of monitoring of iodine deficiency disorders control programs*. Thyroid, 2002. **12**(10): p. 915-924.
- 34. Wei, R., et al., *Burden and trends of iodine deficiency in Asia from 1990 to 2019*. Public Health, 2023. **222**: p. 75-84.
- 35. De Benoist, B., et al., *Iodine deficiency in 2007: global progress since 2003.* Food and nutrition bulletin, 2008. **29**(3): p. 195-202.
- Andersson, M., B. de Benoist, and L. Rogers, *Epidemiology of iodine deficiency: salt iodisation and iodine status*. Best practice & research Clinical endocrinology & metabolism, 2010. 24(1): p. 1-11.
- 37. Han, X., et al., Global, regional, and national burdens of common micronutrient deficiencies from 1990 to 2019: A secondary trend analysis based on the Global Burden of Disease 2019 study. EClinicalMedicine, 2022. 44: p. 101299.
- Hassen, H.Y., et al., National incidence, prevalence and disability-adjusted life years (DALYs) of common micronutrient deficiencies in Ethiopia from 1990 to 2017: estimates from the global burden of diseases study. Global health action, 2020. 13(1): p. 1776507.
- 39. Dodd, N. and A. Samuel, *Iodine deficiency in adolescents from Bombay slums*. The National Medical Journal of India, 1993. **6**(3): p. 110-113.
- 40. Qian, M., et al., *The effects of iodine on intelligence in children: a metaanalysis of studies conducted in China*. Asia Pac J Clin Nutr, 2005. **14**(1): p. 32-42.
- 41. Hynes, K.L., et al., *Mild iodine deficiency during pregnancy is associated with reduced educational outcomes in the offspring: 9-year follow-up of the gestational iodine cohort.* J Clin Endocrinol Metab, 2013. **98**(5): p. 1954-62.
- 42. Maulik, P.K., et al., *Prevalence of intellectual disability: a meta-analysis of population-based studies.* Res Dev Disabil, 2011. **32**(2): p. 419-36.
- 43. Rossi, R., et al., *Evidence for androgen receptor gene expression and growth inhibitory effect of dihydrotestosterone on human adrenocortical cells.* J Endocrinol, 1998. **159**(3): p. 373-80.



**Figure 1** The ASYR (A) and ASPR (B) of developmental and intellectual disabilities attributable to iodine deficiency per 100,000 people from 1990 to 2019 and age-specific rates of YLDs (C) and prevalence (D) of developmental intellectual disability attributable to iodine deficiency by sex and type in 2019. ASPR = age-standardized prevalence rate; ASYR= age standardized YLDs rate.



Figure 2 These heatmaps show the ASPR of developmental intellectual disability attributable to iodine deficiency in GBD regions by sex and severity categories in 2019. The shade of color of each block in the heatmap represents the size of the numerical value, and the figure inside represents the absolute number of the age-standardized prevalence. ASPR = age-standardized prevalence rate.



**Figure 3** These maps show the ASPR (A) and ASYR (B) of developmental and intellectual disabilities attributable to iodine deficiency per 100,000 people in 2019. ASPR = age-standardized prevalence rate; ASYR= age standardized YLDs rate.

In 2019, countries with higher sociodemographic indexes tended to have lower prevalence rates than those with a low sociodemographic index (Figure 4). Spearman rank-order analysis revealed a strong, negative correlation between the age-standardized prevalence rate (rho = -0.689; p < 0.001) and sociodemographic index (Figure 4A), and likewise, a clear negative correlation was also seen between the age-standardized YLD rate and sociodemographic index (rho = -0.668; p < 0.001) (Figure 4B). The estimated annual percentage change of age-standardized prevalence and YLD rates from 1990 to 2019 showed weak correlations (rho = -0.186, P = 0.033;rho = -0.216, P = 0.013) with the sociodemographic index (Figure 4C and 4D).



**Figure 4** The correlation between global ASPR (A), ASYR (B), EAPC of ASPR (C), and EAPC of ASYR (D) and socio-demographic index (SDI) for developmental and intellectual disabilities attributable to iodine deficiency for both sexes. ASPR = age-standardized prevalence rate; ASYR= age standardized YLDs rate. EAPC = estimated annual percentage change.



**Figure 5** The proportion of the number of prevalence (A) and YLDs (C) in 1990 and 2019 (B, D) for different socio-demographic index (SDI) regions and income-related health inequality regression (E) and concentration curves (F) for YLDs of developmental and intellectual disabilities attributable to iodine deficiency across 204 counties and territories, 1990 vs 2019.



Figure 6 Projections of ASPR (A, B) and ASYR (C, D) in males and females from 2020

to 2030. The open dot represents the observed value, and the fan the predicted distribution between the 2.5 and 97.5% quantiles. The forecast average is shown as a solid line. The vertical dotted line indicates where the prediction begins. The projections of prevalence cases (E) and YLDs (F) by sexes of developmental and intellectual disabilities attributable to iodine deficiency from 2020 to 2030. The error bar denotes the 95% credible interval of the predictive value.

	Preval	YLDs				
mber in 1990	ASPR in 1990	Number in 2019	ASPR in 2019	Number in 1990	ASYR in 1990	
2955939	39       54.37       1751707       22.54         3677780)       (38.57 to 67.63)       (1124857 to 2271089)       (14.47 to 29.23)		522410	9.6		
946 to 3677780)			(306451 to 782379)	(5.61 to 14.39)		
583	0.07	345	0.03	116	0.01	(.
281 to 872)	(0.03 to 0.1)	(155 to 525)	(0.01 to 0.05)	(49 to 198)	(0.01 to 0.02)	
156717	13.38	53978	3.66	29319	2.5	
642 to 225218)	(7.79 to 19.2)	(28385 to 76706)	(1.87 to 5.23)	(14035 to 47695)	(1.2 to 4.06)	
809624	47.85	227321	9.21	145527	8.57	
957 to 1066429)	(30.69 to 63.33)	(136423 to 305283)	(5.54 to 12.33)	(79136 to 226511)	(4.67 to 13.33)	
1452236	131.81	776150	43.11	253294	22.92	(
087 to 1714400)	(100.43 to 155.87)	(496888 to 1011954)	(27.94 to 56.08)	(158121 to 370039)	(14.17 to 33.46)	
535979	107.77	693212	66.82	94008	18.85	(
370 to 662015)	(77.76 to 134.49)	(449796 to 908251)	(43.36 to 87.81)	(55716 to 140603)	(11.13 to 28.33)	
33952	59.79	63889	47.45	6304	11.05	
714 to 58511)	(24.55 to 102.24)	(26178 to 110615)	(20.33 to 82.03)	(2225 to 11575)	(4.15 to 20.14)	
221100	17.65	1113	0.07	41334	3.28	
212 to 339028)	(8.77 to 26.9)	(629 to 1836)	(0.04 to 0.11)	(17883 to 69847)	(1.47 to 5.55)	
18562	7.92	17841	8.14	3646	1.56	
192 to 26274)	(4.26 to 11.22)	(9696 to 25647)	(4.29 to 11.69)	(1660 to 5946)	(0.69 to 2.54)	
136468	75.55	130571	32.86	24167	13.38	
412 to 186866)	(45.61 to 105.13)	(72058 to 188494)	(17.56 to 48.59)	(12671 to 38795)	(6.96 to 21.47)	
367	1.15	345	0.54	67	0.21	
184 to 614)	(0.6 to 1.83)	(195 to 512)	(0.31 to 0.81)	(29 to 124)	(0.1 to 0.38)	
0	0	0	0	0	0	
(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	
0	0	0	0	0	0	
(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	
6448	18.65	7071	14.68	1261	3.64	
299 to 10000)	(7.08 to 28.68)	(2755 to 10372)	(5.67 to 21.51)	(391 to 2172)	(1.19 to 6.25)	

 Table 1. Prevalence and YLDs of developmental and intellectual disabilities

 attributable to iodine deficiency in 1990 and 2019 for both sexes and all locations.

Prevalence					YLDs	
mber in 1990	ASPR in 1990	Number in 2019	ASPR in 2019	Number in 1990	ASYR in 1990 0	
0	0	0	0	0		
(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	
1641	1.32	0	0	323	0.26	
398 to 2328)	(0.72 to 1.87)	(0 to 0)	(0 to 0)	(151 to 538)	(0.12 to 0.43)	
15976	10.46	19456	7.59	3172	2.07	
197 to 25927)	(3.2 to 16.82)	(5346 to 31795)	(2.09 to 12.38)	(755 to 5697)	(0.55 to 3.65)	
10568	15.78	7448	7.88	2031	3.02	
261 to 17002)	(7.99 to 25.07)	(3681 to 10907)	(3.93 to 11.51)	(858 to 3613)	(1.29 to 5.29)	
219123	69.04	225931	36.97	39759	12.46	
683 to 298443)	(44.33 to 93.25)	(135265 to 304999)	(22.36 to 49.61)	(21393 to 62783)	(6.78 to 19.54)	(
467	8.64	435	3.87	83	1.54	
274 to 655)	(5.52 to 11.75)	(242 to 717)	(2.32 to 6.03)	(45 to 133)	(0.88 to 2.39)	
1999901	185.37	1136564	60.97	347729	32.13	
749 to 2356206)	(141.29 to 219.06)	(746286 to 1441295)	(40.28 to 77.26)	(217431 to 510003)	(19.87 to 47.08)	(1
232078	54.08	81186	11.52	41491	9.62	
630 to 293450)	(36.66 to 67.91)	(41907 to 114305)	(5.97 to 16.24)	(23681 to 62921)	(5.5 to 14.62)	
0	0	0	0	0	0	
(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	
3552	7.05	944	1.18	685	1.35	
383 to 5687)	(2.78 to 11.42)	(310 to 1545)	(0.4 to 1.93)	(229 to 1212)	(0.48 to 2.4)	
845	0.59	0	0	156	0.11	
457 to 1264)	(0.34 to 0.87)	(0 to 0)	(0 to 0)	(73 to 262)	(0.05 to 0.18)	
0	0	0	0	0	0	
(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	(0 to 0)	
54892	30.71	58912	14.29	10202	5.71	
861 to 84559)	(15.17 to 48.2)	(27622 to 89156)	(6.59 to 22.05)	(4415 to 17586)	(2.42 to 9.92)	

Diseases	Health inequality metrics	Year	Value	95% CI
	Slope index of inequality	1990	-9.7	-10.7 to -8.7
Developmental and		2019	-4.9	-5.4 to -4.3
intellectual disabilities attributable to iodine deficiency	Concentration index	1990	-48.0	-60.0 to - 36.0
		2019	-45.5	-56.8 to - 34.2

 Table 3. Summary measures for cross-country inequalities related to SDI in YLDs
 of developmental and intellectual disabilities attributable to iodine deficiency.