Global burden of Iodine Deficiency Disorders in the year 2000

Tanuja Rastogi, Colin Mathers

This draft was prepared in 2002, at a time where studies examining urinary iodine concentrations were still being analysed. It is desirable to describe iodine deficiency disorders using such studies, and efforts are under way at WHO to do so. This draft is to be superseded by the work in progress and will require updating.

1. Introduction

Iodine deficiency disorders (IDD) was estimated to be the 77th leading cause of disease burden in the world in 1990, accounting for 0.1% of total DALYs (Murray & Lopez, 1996). Iodine deficiency disorders constitute a wide range of clinical and subclinical manifestations of iodine deficiency ranging from goitre to cretinism (Hetzel, 1983, Bailey, 1995). The clinical indicators for IDD that are measured in the GBD 2000 are based on the classification recommended by the WHO/UNICEF/ICCIDD's *Consultation on IDD Indicators* (1992) and include:

1. Goitre (Grades 1-2)*:
    a. Grade 1 (G1): A mass in the neck consistent with an enlarged thyroid that is a palpable, but not visible when the neck is in the normal position.
    b. Grade 2 (G2): A swelling in the neck that is visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated. (palpable and visible)
2. Mild developmental disability (MDD): A condition characterized by bilateral hearing loss, delay of walking ability, and mild intellectual impairment.
3. Cretinism: A condition characterized by mental deficiency and neurological symptoms or hypothyroidism and stunting
4. Cretinoidism: A condition that has some but not all features of full cretinism

These are indicators for clinical IDD and reflect a burden of disease definition that is pertinent to the development of disease estimates and does not necessarily reflect an absolute nutritional definition where conditions can overlap across different categories.

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*Important Note: The estimates provided in GBD 1990 for goitre used labels for TGR *(G0, G1, G2)* that are no longer used in nutritional surveys of IDD. The nutritional label *'G0'* officially refers to 'not palpable or not visible goitre' (no goitre) and was, in fact, not measured in GBD 1990. Thus, to clarify: the *'GBD 1990 G0'* actually refers to G1 (palpable, not visible goitre), and *'GBD 1990 G1'* refers to G2 (visible and palpable), and last, *'GBD 1990 G2'* refers also to G2 (visible and palpable) but are the very large goitres which are no longer measured (which also had a higher disability weight of 0.025). At present for the GBD 2000, the 2 forms of goitre are assessed:

G1: Palpable, not visible goitres
G2: Visible and palpable goitres (including very large goitres)

The corresponding disabilities weights are: G1 = 0 and G2 =0.001

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2. Case and sequelae definitions

The case definition and sequelae used for VAD are given below.

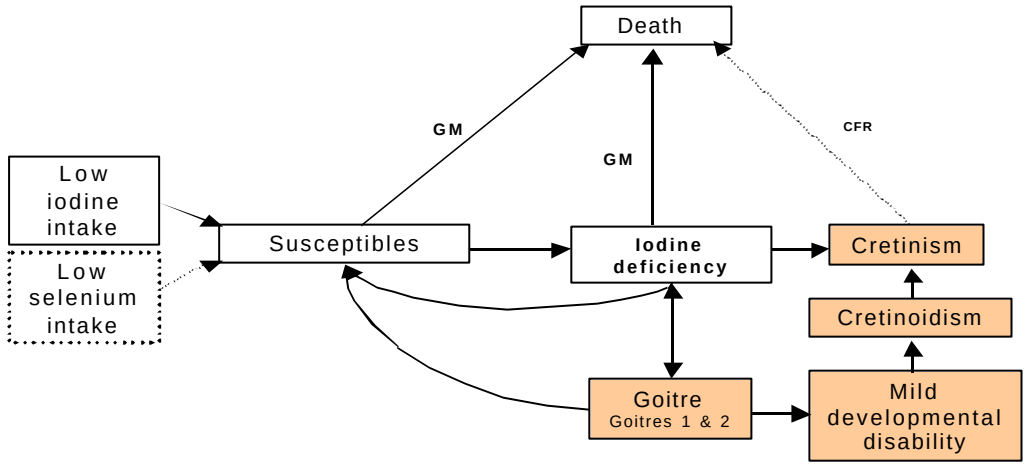
Table 1. Case and sequelae definitions for Vitamin A deficiency

Cause category	**GBD 2000 Code**	**ICD 9 codes**	**ICD 10 codes**
Iodine deficiency disorders	U055	243	E00-E02

Case/Sequelae	**Definition**
Iodine deficiency disorders:	
Goitre – grade 1	A mass in the neck consistent with an enlarged thyroid – grade 1 = Palpable but not visible
Goitre – grade 2	A mass in the neck consistent with an enlarged thyroid – grade 2 = Visible in neutral neck position
Mild developmental disability	Any of the following due to iodine deficiency: Bilateral hearing loss, delay of walking ability, mild intellectual impairment
Cretinism	Hypothyroid cretinism: Hypothyroidism and stunting as a RESULT of iodine deficiency. Neurological cretinism: Mental deficiency (IQ below 70), deaf-mutism, and spastic paralysis as a RESULT of iodine deficiency

3. Disease model

IODINE DEFICIENCY DISORDERS



YLD calculated for boxes with bold outline and orange shading.

4. Methods

Country-specific estimates were obtained and used to calculate regional estimates for TGR, cretinism, cretinoidism and MDD. The primary data source was the WHO Nutrition and Health for Development Program. The program is in the process of developing and refining a comprehensive database of country-specific estimates of both clinical and sub-clinical IDD from national level and sub-national nutrition surveys (MDIS IDD database, 2002).

Estimates for total goitre rate in school age children (SAC) were provided from the MDIS IDD database. In the GBD 2000, this corresponds to the 5-14 age group. School age children are the standard group assessed in nutritional surveys because, generally, they have the highest prevalence of goitre (Bailey, 1995). All prevalence estimates were reviewed with priority being given to the most recent national level estimates (majority are obtained from studies conducted in last 10 years). When estimates were missing, national-level estimates of neighboring countries were examined. If a neighboring country was deemed similar to another country in terms of overall health status and iodine-nutrition (for example, adult and infant mortality levels, per capita income levels), then the estimate from that country was applied. Last, an alternate data source was the WHO Nutrition and Health for Development Program's document, "Global Prevalence of Iodine Deficiency Disorders" (WHO MDIS, 1993). Although this was a particularly useful data source for the AMRO region where the MDIS IDD Database had no data, preference was given to more recent data sources.

All estimates for SAC were converted to general population (all ages) estimates using the following formula developed in 1987 (G. Clugston):

TGR sac = 1.5 +(TGR gen pop)(1.12)

Using existing data provided by the MDIS IDD database on TGR in both SAC and the general population (n=10) the following regression formula was derived: $TGR_{SAC} = 1.97+TGR_{general\ population}(0.91)$. Given the similarity between both formulas, the original formula was deemed appropriate for use.

From adolescence onward there is a significantly higher prevalence of goitre among females than males (Bailey, 1995). In order to estimate gender-specific rates, it was assumed that the female to male ratio was 1.2:1 (<14 years) and 2:1 (>14 years)(Bailey, 1995). This ratio was confirmed with available data from studies provided from the MDIS IDD database (n=57).

While the MDIS IDD database provided TGR estimates, there was limited data on goitre types (G1, G2), as it is often no longer assessed individually in nutrition surveys. Therefore, after TGR estimates were established for the general population, it was necessary to derive prevalence estimates for G1 (palpable, not visible) and G2 (palpable and visible) goitres. This is important to burden of disease work, as they are associated with different levels of disability. The following formula was used to obtain estimates for G1 and G2. It was originally developed for the GBD 1990 to quantify the proportion of goitre that was visible and palpable and those that were only palpable.

G2 % = EXP (2.08*LN(TGR%)-6.08)

G1 = TGR –G2

Given limited new research on goiter subtypes (palpable only vs. palpable and visible goitres) this partition method was utilized.

The iodisation of salt has been an effective measure in reducing the prevalence of IDD (WHO/UNICEF/ICCIDD, 1999). The impact of salt iodisation on TGR estimates was considered when estimates were available only from pre-iodisation periods. Current global information on the status of salt iodisation was available in two documents, WHO, UNICEF, ICCIDD: *Progress towards the elimination of IDD* (1999) and UNICEF: *Global database on Universal Salt Iodization* (2001). If estimates for TGR were from pre-iodisation periods and the country had iodisation coverage of over 90% (households consuming iodised salt), then it was assumed that TGR would be reduced by 80% (Bleichrodt, 1987; Hetzel, 1987; Shrestha, 1994). A value of 90% or greater coverage was chosen as the WHO/NUNICEF/ICCIDD Report provides coverage only in cut-off points of <10, 10-50, 51-90, >90. Additionally, after expert consult the value of 90% coverage was deemed appropriate in providing sufficient population coverage such that goitre rates would be influenced.

Limited data is available on the prevalence of cretinism, cretinoidism and MDD. Therefore, after review of the literature and in consultation with the program experts the following methods were used to estimate these conditions. First, a 1:1 male to female was

assumed for these conditions (Murray, Lopez, GBD 1990). Cretinism is a public health concern only in countries where the TGR is greater than 20% (WHO MDIS, 1993) and new incident cretinism cases would be expected. As cretinism is an irreversible condition, prevalent cases originally reported in GBD 1990 and that were still living were accounted for (regardless of current TGR). This was calculated by adding 10 years in age to the GBD 1990 cretin cases. However, a certain proportion will die annually, therefore region-specific background mortality rates were applied that were multiplied by 6.33, the increased relative risk of death due to mental retardation (Harris, 1998). Next, in countries with over 90% of households consuming iodised salt, it was assumed that the incidence of new cretin cases would be 0 (however prevalent living cases from 1990 will still remain) (Bleichrodt, 1987; Hetzel, 1987; Shrestha, 1994). Where coverage is less than 90% and TGR is greater than 20%, the total number of cretins includes new incident cases and the living cretin cases that were reported in GBD 1990. The following multiple logistic regression formula relates prevalence of TGR to prevalence of cretinism in SAC (5-14 age group) in any community. The formula provides the best fitting relationship between cretinism and total goitre, based on actual data provided from Ecuador, Zaire and Asia (Clugston, 1987).

Functional relationship between cretinism (c) and total goitre rate (g) was established using multivariate analysis & logistic modeling where:

$$\ln[c/1-c] = b_0+b_1g+b_2g_2$$

Beta values (b) were estimated using maximum likelihood method, where

$$c = \exp(b_0+b_1g+b_2g_2)/(1+\exp(b_0+b_1g+b_2g_2))$$

and, $b_0 = -9.3939$

$b_1 = 15.796$

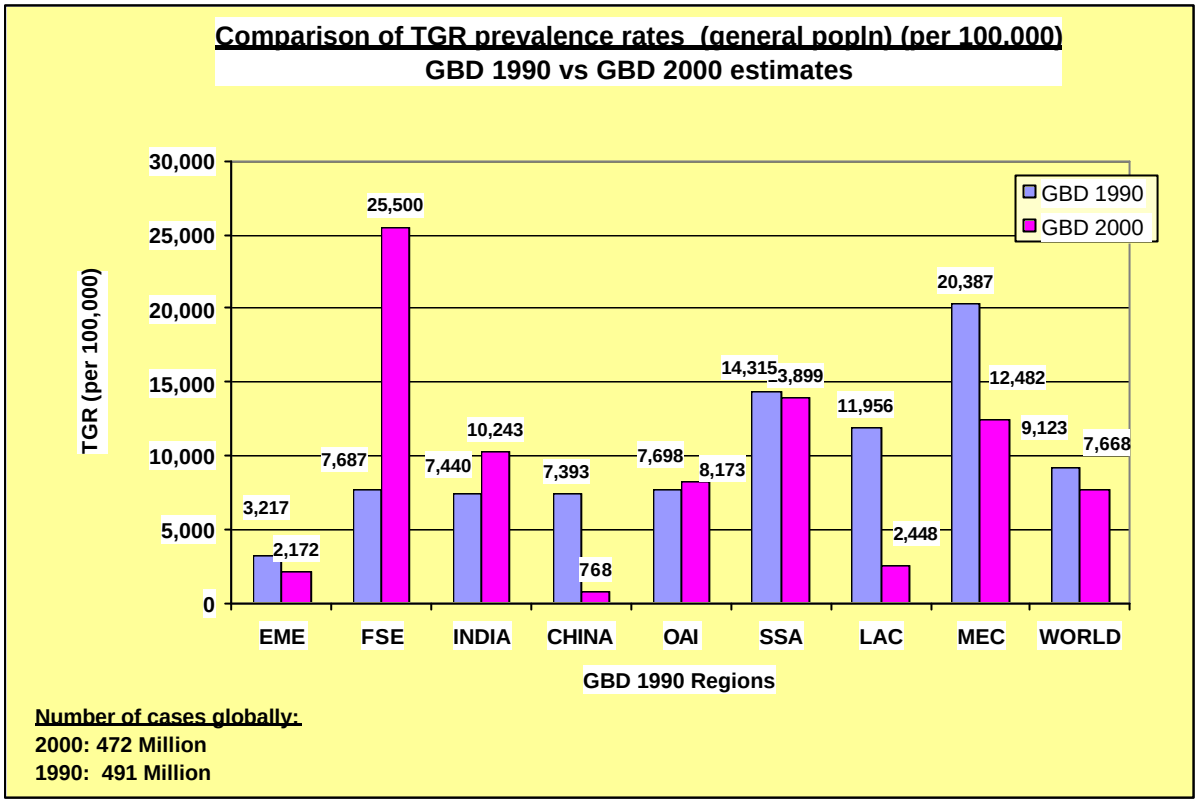
$b_2 = -8.8026$

The formula with the listed beta coefficients was used to estimate the prevalence rate of cretinism in SAC. However, incident cases of cretinism are expected to occur in children < 5 years of age. The disease modelling program, DISMOD, was then used to estimate the expected incidence rate in the < 5 age group given this prevalence rate among SAC (5-14 age group) and a relative risk of mortality of 6.33 and remission being zero.

In countries with greater than 90% of households consuming iodised salt, it was assumed that the incidence of cretinoidism and MDD cases will be negligible. As both of these conditions are considered reversible (Shrestha, 1994), prevalent cases were also considered negligible. Estimates for these conditions are required in areas where salt iodisation is less than 90% and also where the TGR is greater than 20%. Research on the association between population levels of cretinoidism and cretinism indicates that, on average, its prevalence is approximately 50% of the prevalence of cretinism (Clugston, 1987). Similarly, the prevalence of MDD has been estimated to be approximately three times the prevalence of cretinoidism (Murray, Lopez, GBD 1990). These proportions were used in estimating prevalence rates for cretinoidism and MDD in SAC by country and region. Again, DISMOD was used to estimate incidence rates in children less than 5 age group (where incident cases are expected) given the prevalence rates in the 5-14 age group for both cretinoidism and MDD, and a case-fatality of zero and remission of 0.

Figure 1-4 present the total prevalence rates (per 100,000) of TGR, Cretinism, Cretinoidism, MDD, respectively, by regions with a comparison of GBD 1990 and GBD 2000 estimates.

Figure 1. TGR (per 100,000), by regions, 1990 and 2000



Important Note on GBD 1990 & current 2000 estimates for cretinism, cretinoidism & MDD:

Upon review of the GBD 1990 IDD chapter (Bailey, 1995, submitted) and the GBD 1990 reported cretinism prevalence estimates, it was determined that the GBD 1990 prevalence estimates were a factor of 10 lower than what was reported in the IDD chapter. This was evident in the regional prevalence estimates (for example, 0.16% cretins in the IDD chapter should be a prevalence rate of 160 per 100,000 however is reported as 16 per 100,000 for SSA in GBD 1990). This has been reported across all regions, and additionally the IDD chapter reports an overall prevalence of 11 million cretins, however it is reported in GBD 1990 as 1.1 million. This was perhaps done because the disability weight for cretinism was deemed too high given the wide range in clinical condition of cretins, (ie, perhaps only 10% of the actual number reported reflect the disability weight for cretins (0.80)). Given this information, the present estimates for cretinism, cretinoidism and MDD seem reasonable. If the reported estimates for GBD 1990 are increased by a factor of 10, then the current 2000 estimates show a major reduction in the prevalence of cretins, which would be expected given salt iodization. The estimated numbers of cretin cases in SAC in 2000 has been estimated to be 1,477,000. While the number of cases reported in GBD 1990 was 438,000, if it is increased by a factor of 10 to 4,380,000, then we have reported over a 65% reduction in cretins in the year 2000.

Figure 2. Cretinism prevalence rate (per 100,000), by regions, 1990 and 2000

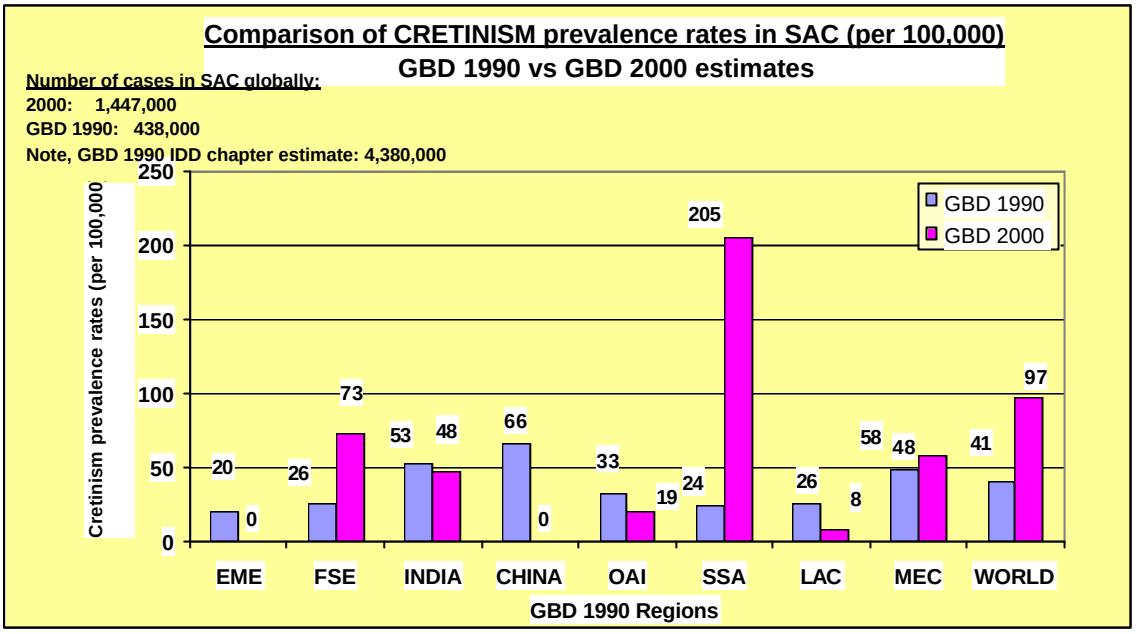


Figure 3. Cretinoidism prevalence rate (per 100,000), by regions, 1990 and 2000

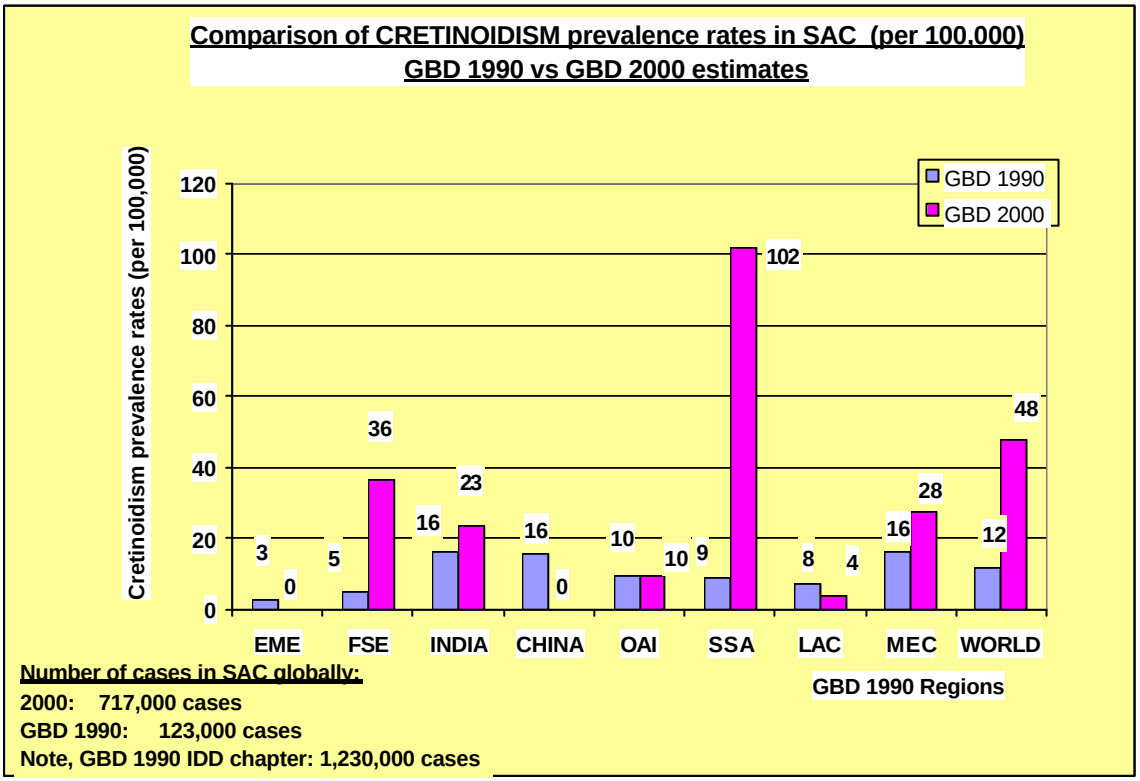
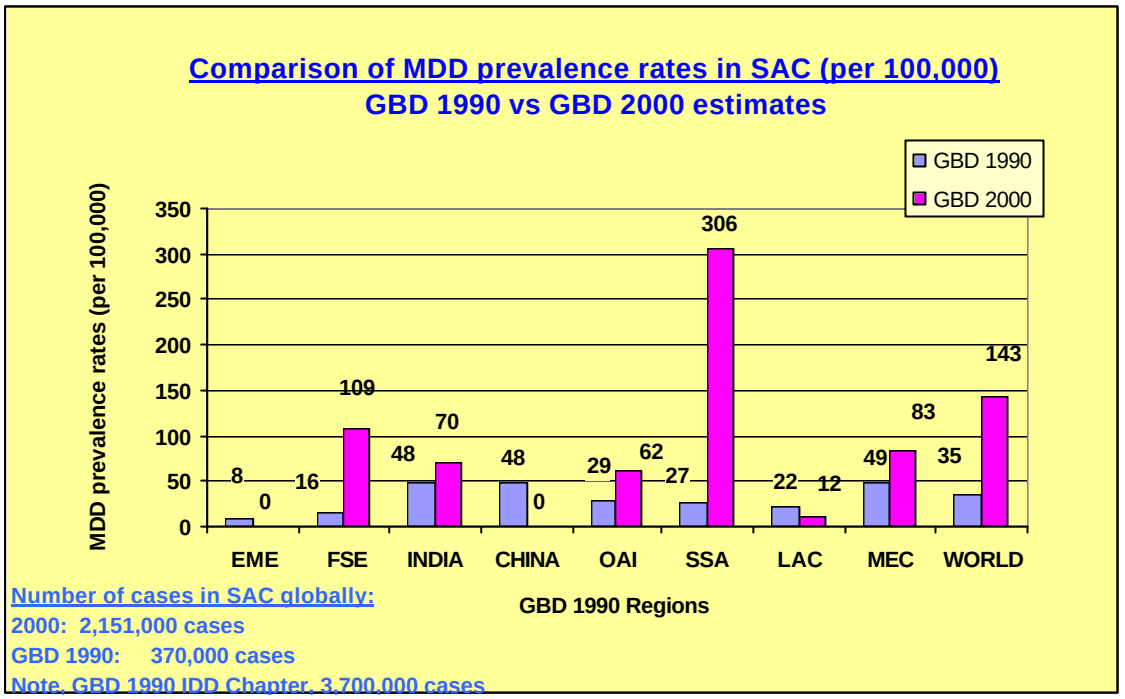


Figure 4. Mild Developmental Disability prevalence rate (per 100,000), by regions, 1990 and 2000



5. Mortality and case fatality

We are modeling IDD as TGR (G1 palpable goiter, G2 visible goiter), cretinism, cretinoidism, and mild developmental disability. Mortality is associated with G2 and Cretinism.

Goitre 2 (palpable and visible goitre):

There will be some associated mortality with G2 visible goiters in older age groups (15-44, 45-59, and 60+) that stems largely from a carcinogenic evolution in very large goitres. The mortality rates for G2 are region & age group specific and were also used in GBD 1990 (Bailey, 1995) which had comprehensively examined mortality consequences associated with goitre. The region and age-specific mortality rates associated with G2 are listed in Appendix. Given the prevalence of G2 cases in each group, an estimate of mortality from G2 can be derived (Table 2).

Table 2: Mortality due to Goitre 2 (palpable and visible goitre)

REGION	G2 deaths (n)
AFRO D	7
AFRO E	25
SEARO B	1
SEARO D	15
WPRO A	0
WPRO B1	0
WPRO B2	1
WPRO B3	0
EMRO B	5
EMRO D	14
EURO A	1
EURO B1	8
EURO B2	2
EURO C	44

AMRO A	0
AMRO B	2
AMRO D	1
Global	126

Cretinism:

Mortality is also associated with cretinism. We used a relative risk for mortality for mental retardation of 6.33 (Harris, 1998) multiplied by the region-specific background mortality rate (in this 5-14 age group) to estimate the number of deaths. A male to female ratio of 1:1 was assumed.

Table 3: Mortality due to Cretinism

REGION	Cretin deaths (n)
AFRO D	1938
AFRO E	6968
SEARO B	154
SEARO D	1791
WPRO A	0
WPRO B1	0
WPRO B2	817
WPRO B3	37
EMRO B	139
EMRO D	935
EURO A	1
EURO B1	218
EURO B2	34
EURO C	704
AMRO A	0
AMRO B	99
AMRO D	80
Global	13913

6. Health state descriptions and disability weights

Table 4. Disability weights for Iodine deficiency disorders

Stage/sequela	GBD 1990	Netherlands Study	Australian BOD Study
Goitre-Grade 1	0 (treated) 0 (untreated)		
Goitre-Grade 2	0.001 (treated) 0.001 (untreated)		
Mild developmental disability	0.006 (treated) 0.006 (untreated)		
Cretinoidism	0.255 (treated) 0.255 (untreated)		
Cretinism	0.804 (treated) 0.804 (untreated)		

7. Global burden of Iodine deficiency disorders in 2000

General methods used for the estimation of the global burden of disease are given elsewhere. The tables and graphs below summarise the global burden of IDD estimates for the GBD 2000 and compare them with the IDD estimates from the GBD 1990.

Table 5. Global total of YLD, YLL and DALY

	Males	Females	Total
YLL ('000)			
GBD 1990	404.27	391.14	795.41
GBD 2000	154.81	146.31	301.12
YLD ('000)			
GBD 1990	375.20	390.97	766.17
GBD 2000	1616.58	637.44	2254.02
DALY ('000)			
GBD 1990	779.48	782.11	1561.58
GBD 2000	1771.39	783.75	2555.14

Table 6. YLD, YLL and DALY estimates, 2000.

	YLD/100,000		*YLL/100,000*		*Total YLD*	*Total YLL*	*Total DALYs*
	Males	*Females*	*Males*	*Females*	*('000)*	*('000)*	*('000)*
AFRO D	72.7	28.4	13.3	16.7	168	50	219
AFRO E	233.5	92.0	19.6	23.2	548	72	620

AMRO A	0.0	0.2	0.0	0.1	0	0	0
AMRO B	22.6	8.8	0.0	0.0	69	0	69
AMRO D	44.4	17.2	0.2	0.6	22	0	22
EMRO B	89.1	34.5	0.0	0.0	88	0	88
EMRO D	335.5	131.1	0.0	0.0	324	0	324
EURO A	0.6	0.2	0.1	0.0	2	0	2
EURO B1	125.7	48.0	0.1	0.2	144	0	144
EURO B2	46.4	18.1	0.0	0.0	16	0	16
EURO B3	209.3	78.6	0.1	0.1	344	0	344
SEARO B	24.1	9.5	0.4	0.2	66	1	67
SEARO D	33.6	13.4	13.4	11.4	321	168	489
WPRO A	0.0	0.0	0.0	0.0	0	0	0
WPRO B1	0.0	0.0	0.0	0.0	0	0	0
WPRO B2	135.9	52.5	7.7	4.7	133	9	142
WPRO B3	181.6	73.2	0.0	0.0	9	0	9
World	***53.1***	***21.2***	***5.1***	***4.9***	***2,254***	***301***	***2,555***

Figure 5:

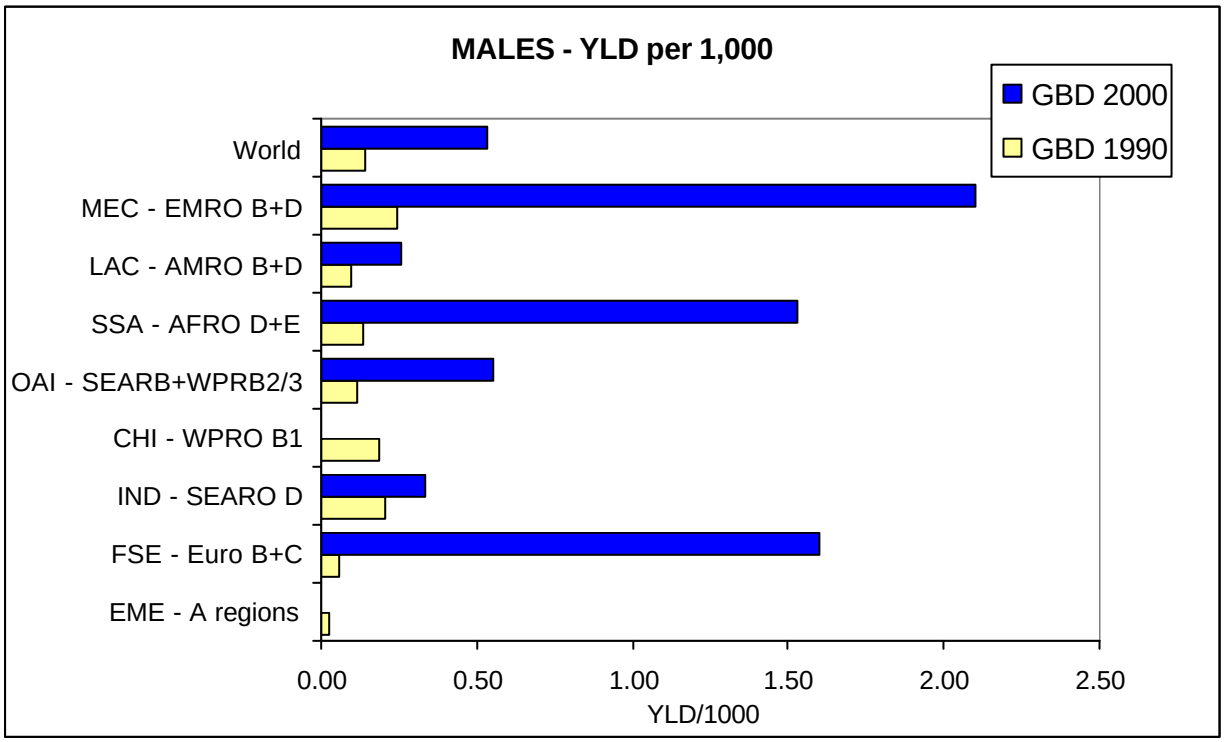
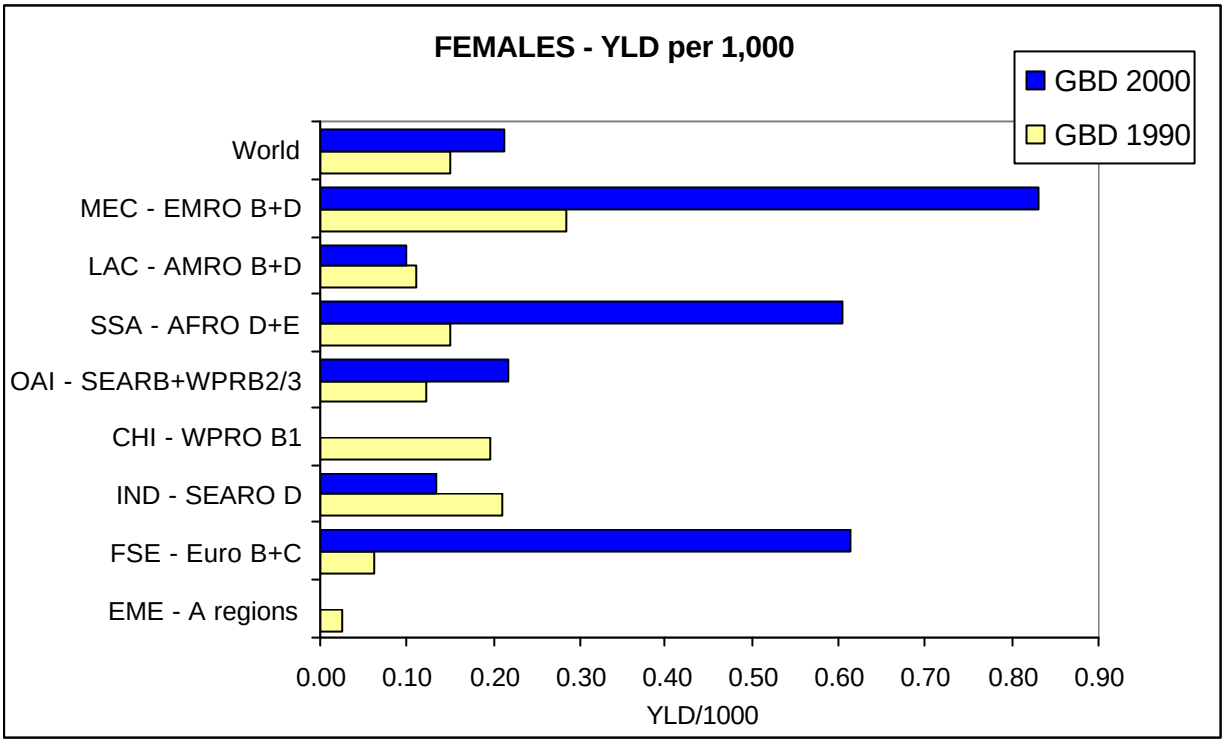


Figure 6:



8. Uncertainty analysis

General methods for uncertainty analysis of estimates for the Global Burden of Disease 2000 are outlined elsewhere. Uncertainty analysis for Iodine deficiency disorders has not yet been completed.

9. Conclusions

Given very minimal country or regional data on the prevalence of cretinism, future efforts should examine ways to validate the association between TGR and cretinism prevalence that was used in the present analysis. Moreover, the utility of assessing cretinoidism in future burden work may need to be assessed as it is often not measured or defined in the nutrition literature. Additionally, we relied on GBD 1990 methods to predict the proportion of goiter cases that are G1 (palpable and not visible) and G2 (palpable and visible), which requires further study.

We welcome comments and criticisms of these draft estimates, and information on additional sources of data and evidence. Please contact Colin Mathers or Claudia Stein (EBD/GPE), emails: mathersc@who.int, steinc@who.int.

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Appendix:

Adult mortality rate (per 100,000) associated with G2 (palpable and visible goitre)
(Source: K. Bailey, GBD 1990 IDD Chapter, unpublished, 1995)

AFRO:
ages - adult mortality rate(per 100,000)
15-44: 0.65
45-59: 1.29
60+: 2.32

SEARO D:
15-44: 0.30
45-59: 0.60
60+: 1.20

WPRO B1, B2,B3, SEARO B:
15-44: 0.35
45-59: 0.69
60+: 1.24

AMRO B, D:
15-44: 0.55
45-59: 1.10
60+: 1.99

EMRO B, D, EURO B2:
15-44: 0.95
45-59: 1.91
60+: 3.11

WPRO A, EURO A, AMRO A:
15-44: 0.14
45-59: 0.29
60+: 0.52

EURO B1, C:
15-44: 0.36
45-59: 0.72

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