phg hna toolkit | Congenital Disorders

Background information on Down's Syndrome and the impact of interventions

This document gives a brief overview about the condition, its epidemiology and specific interventions that may reduce its burden.

What is Down's Syndrome?

Chromosomal disorders are caused by changes in either chromosome number or structure usually occurring during the formation of sex cells. They usually result in spontaneous abortion or miscarriage; however, some such as Down's Syndrome (DS) are compatible with life. Down's Syndrome or trisomy 21 occurs when the fetus inherits an extra copy of chromosome 21. DS is associated with variable intellectual impairment, learning difficulties and excess mortality caused by long-term health problems as a result of cardiac, gastrointestinal, immunological, respiratory and orthopaedic anomalies. Approximately 1% of cases are mosaic, i.e. the chromosomes divide incorrectly resulting in a mixed population of aneuploid and normal cells. These individuals have milder symptoms and may be difficult to diagnose.

What are the main risk factors?

Advanced maternal age (AMA) is associated with an increased risk for most but not all chromosomal disorders. The incidence of DS is increased in mothers older than 35 years. This higher risk is associated with as yet unidentified biological factors.

Global epidemiology

Birth prevalence

The Modell Database of Constitutional Congenital Disorders (MGDB) has estimates suggesting that every year at least 220,000 people are born with Down's Syndrome. The birth prevalence estimate for other trisomies, including Patau and Edward's syndromes, is 31,000 and for chromosomal disorders as a whole 520,000. Tables 1a and 1b show the annual affected live births for DS and other chromosomal disorders by world region.

Population prevalence

Approximately 2.6 million people in the world live with Down's Syndrome. The population prevalence of people living with DS by world regions appears in Table 2. Of those born alive with DS and other chromosomal disorders, some 36,000 are expected to die in the first week of life (17,000 will be stillbirths), 120,000 in the first year of life, and 154,000 in the first 5 years of life (calculated based on 133 million births per year worldwide).

Mortality

In a supportive environment, individuals with Down's Syndrome who survive childhood may remain relatively well for long periods, even with limited medical care, until premature ageing sets in. Estimated excess deaths due to Down's Syndrome and other chromosomal disorders by world region appear in Table 3a. Table 3b shows the under 5 deaths by world region.

Disability and quality of life

Surviving infants with DS have a range of severities from mild to severe cognitive and physical disability, depending on the condition and postnatal management. However, they will require follow-up and care throughout life to address complications and associated physical and intellectual disability, which may influence their integration into society.

Reducing prevalence, morbidity and mortality

Figure 1 illustrates the determinants and interventions for Down's Syndrome as they relate to key stages in life. The main specific interventions are discussed below.

Interventions before pregnancy

Family planning and incorporation of information on maternal age-related risks may influence individual choice and decrease the proportion of older mothers. However, there is little information on the effectiveness of these interventions.

Interventions during pregnancy

Prenatal care for Down's Syndrome involves prenatal screening and diagnosis. Such programmes may be able to identify a proportion of other chromosomal disorders. Prenatal diagnosis may allow planning for a future affected baby, or in places where it is legal and acceptable, may lead to a choice of pregnancy termination.

Worldwide, prenatal screening usually has high coverage. However, the quality of the services is variable and often poor. State funded screening for disorders is not common practice in many areas with less developed health services. Prenatal screening may involve different methods, based on maternal blood tests and/or fetal ultrasound scan (USS). Screening is usually carried out towards the end of the first trimester or during the second trimester. For details on types of tests for chromosomal anomalies, please see Chapter on prenatal care.

Diagnostic confirmation involves laboratory tests on fetal cells obtained either by amniocentesis or chorionic villus sampling (CVS). These procedures, which involve sampling amniotic fluid or chorion by inserting a needle through the mother's abdominal wall, typically result in a miscarriage rate of 1-2% respectively (this figure may be reduced if the procedure is performed by a skilled and experienced practitioner). Laboratory tests to detect DS include fluorescent *in situ* hybridisation (FISH), karyotyping and quantitative fluorescent polymerase chain reaction (QF-PCR).

In countries where there are programmes of universal prenatal screening, Down's Syndrome tends to be detected as part of an established programme. Care pathways may document access to supplementary tests or interventions, including access to termination of pregnancy, where legal.

Interventions after birth

Diagnosis of Down's Syndrome is possible at birth through the recognition of associated clinical features. Care will be dependent on available resources and may involve appropriate treatment of associated disorders, e.g. surgery for correction of structural defects, routine health monitoring/follow-up and early identification and treatment of medical conditions for which these individuals may be at increased risk (e.g. leukaemia, heart disease, obesity etc.). There are no cures for Down's Syndrome and affected individuals and their families require varying degrees of long-term support, including lifelong medical care, rehabilitation and counselling. The Down Syndrome Medical Interest Group has developed guidelines for care throughout life (see end of document for link).

Cost-effectiveness of interventions

A number of strategies can be adopted for prenatal screening of DS and comparison of their cost-effectiveness is available in the general literature. Analysis is based on assessing the efficacy of the method and the costs of screening per DS pregnancy averted. Although the main conclusion of such studies is that screening is cost-effective, conclusions vary as to which strategy to adopt. Issues of cost-effectiveness are quite specific to each country as costs can vary tremendously depending on factors such as access to and use of services, cost of services for care and perceived burden of the disease. Cost-effectiveness is highest in countries with the highest prevalence, given that there is access and uptake of prenatal screening and diagnosis.

Care of individuals with DS can vary from simple interventions such as health monitoring and providing social support to more costly treatment of associated complications such as heart disease. The cost of care is likely to vary in countries depending on available resources and the extent to which it is provided.

For cost-effectiveness cut-off points for different regions of the world, go to http://www.who.int/choice/costs/CER_levels/en/index.html, and for costs for specific items by region and county, go to http://www.who.int/choice/costs/en/.

For information on cost-effectiveness analysis of prenatal screening based in the UK, go to http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11947.

What are the main ethical legal and social issues (ELSI) to consider?

Acceptability of prenatal diagnosis and termination of pregnancy

In many low and middle income countries (LIMC), legal termination of pregnancy is unavailable or severely restricted to cases where termination is necessary to protect the woman's life. In some countries access to procedures to terminate a pregnancy may also depend upon parental or spousal consent. In practice, in many countries, procedures are often offered illegally, and these tend to lead to higher maternal morbidity and mortality than legal termination. In countries where termination of pregnancy is legal in cases of fetal abnormality, opinions may vary on the ethical justification of termination for chromosomal abnormalities that are not lethal, such as Down's Syndrome.

Some people regard programmes of prenatal screening as eugenic programmes that devalue the lives of disabled people. Others hold the view that such programmes are

ethically acceptable as long as they are restricted to conditions that cause serious disability and the programmes are not coercive: parents undergoing screening must make an autonomous choice to do so, must give their formal consent, and must be free to continue with an affected pregnancy if they choose to do so. However, issues such as autonomy may be considered more important in individualistic cultures than in those in which a larger entity such as the extended family or community has a wider role in decision-making, and in which duty to community may trump individual wishes.

Equity of access to services

Economic development may be linked with increasing incidence of DS because of a trend towards higher maternal age. Access to effective family planning services and preconception care are important to inform women about these risks.

Parents with limited financial resources may not be able to afford prenatal screening and diagnostic services unless state or charitable funding is available. Timely prenatal screening (before the middle of the second trimester) is vital to avoid late terminations; those in charge of screening programmes should ensure that women from poorer socioeconomic backgrounds receive information about, and access to, services early in pregnancy.

Psychosocial issues

Diagnosis of DS, whether prenatally or after birth, is likely to cause shock and distress in the parents and the wider family. There may be shame or stigma associated with such conditions.

False-positive results in prenatal screening programmes cause anxiety, both because of the possibility that the fetus is affected and because diagnostic testing involves the risk of miscarriage. Those with a false-negative result from prenatal screening may be falsely reassured and are likely to experience even greater shock on the birth of an affected child.

Living with a disability

Those who are born disabled often have a very poor life expectancy, especially in low and middle income countries. This is due to a combination of factors: lack of access to relevant health and social services compounded by social determinants of ill health such as poverty and malnutrition. Whilst in developed countries, the effect of severe physical or psychological disabilities may be ameliorated by substantial support from the state, this may be virtually non-existent in other settings, where the psychological and economic burden of having a handicapped child falls mostly or entirely on the immediate and extended family.

KEY REFERENCES

Cohen WI (ed) for The Down Syndrome Medical Interest Group (DSMIG). Health care guidelines for individuals with Down Syndrome (Down syndrome preventative medical checklist). *Down Syndrome Quarterly* 1996.

Wald NJ *et al.* First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasounds Screening Study (SURUSS). *Health Technol Assess* 2003; **7**.

RELATED TOPICS

Preconception care and screening
Prenatal screening
Newborn screening
Health services

Table 1a: Estimates for the birth prevalence rates of chromosomal disorders by GBD world region, 2005

GBD Region	BIRTH PREVALENCE/ 1000				
	Down's /1,000	Other trisomies/1,000	Turner's/1,000	Klinefelter/1,000	Unbalanced structural rearrangements/1,000
Sub-Saharan Africa, Central	1.76	0.26	0.15	0.32	0.60
Sub-Saharan Africa, East	1.93	0.29	0.15	0.35	0.60
Sub-Saharan Africa, Southern	1.68	0.24	0.14	0.32	0.57
Sub-Saharan Africa, West	1.85	0.28	0.15	0.33	0.60
Middle East	1.82	0.27	0.15	0.33	0.60
North Africa	1.84	0.27	0.15	0.34	0.59
Caribbean	1.66	0.23	0.14	0.31	0.56
Latin America, Andean	1.88	0.28	0.15	0.34	0.60
Latin America, Central	1.57	0.23	0.15	0.28	0.60
Latin America, Southern	1.78	0.27	0.15	0.32	0.60
Latin America, Tropical	1.55	0.23	0.15	0.28	0.60
North America, High Income	1.25	0.14	0.09	0.32	0.46
Asia Pacific, High Income	0.98	0.11	0.08	0.29	0.44
Asia Southeast	1.83	0.27	0.15	0.33	0.60
Asia, Central	1.37	0.21	0.15	0.25	0.60
Asia, East	1.07	0.16	0.14	0.20	0.58
Asia, South	1.41	0.21	0.15	0.26	0.59
Europe, Central	1.19	0.16	0.12	0.25	0.53
Europe, Eastern	1.15	0.14	0.14	0.22	0.53
Europe, Western	1.10	0.12	0.11	0.37	0.41
Australasia	1.26	0.08	0.07	0.37	0.37
Oceania	1.85	0.28	0.15	0.33	0.60
World	1.52	0.22	0.14	0.29	0.58

Table 1b: Estimates for the number of annual births with chromosomal disorders by GBD world region, 2005

		ACTUAL ANNUAL AFFECTED LIVE BIRTHS							
GBD Region	**Annual stillbirths due to trisomies and XO**	**Down's**	**Other trisomies**	**Unbalanced structural rearrangements**	**Turner's**	**Klinefelter**	**Total servere autosomal disorders**	**Total sex chromosome disorders**	**Total chromosomal disorder**
Sub-Saharan Africa, Central	1,259	6,908	1,036	2,341	588	1,243	10,285	1,832	12,117
Sub-Saharan Africa, East	4,226	23,421	3,513	7,242	1,820	4,216	34,175	6,035	40,211
Sub-Saharan Africa, Southern	496	2,783	405	944	227	537	4,132	765	4,897
Sub-Saharan Africa, West	3,922	21,628	3,244	6,997	1,758	3,893	31,869	5,651	37,521
Middle East	2,104	11,588	1,738	3,798	954	2,086	17,124	3,040	20,164
North Africa	1,183	6,569	978	2,106	523	1,205	9,653	1,729	11,382
Caribbean	208	1,204	164	404	105	222	1,771	327	2,098
Latin America, Andean	405	2,238	336	709	178	403	3,283	581	3,864
Latin America, Central	1,410	7,624	1,144	2,906	730	1,372	11,674	2,103	13,776
Latin America, Southern	321	1,762	264	591	149	317	2,617	466	3,083
Latin America, Tropical	1,120	6,045	907	2,330	585	1,088	9,282	1,674	10,955
North America, HI	865	5,594	641	2,047	411	1,430	8,282	1,842	10,123
Asia Pacific, HI	254	1,652	186	737	127	490	2,574	617	3,191
Asia Southeast	3,904	21,510	3,226	7,024	1,764	3,875	31,760	5,639	37,399
Asia, Central	396	2,103	315	914	230	378	3,332	608	3,940
Asia, East	3,624	18,896	2,776	10,216	2,489	3,576	31,888	6,065	37,953
Asia, South	9,616	51,739	7,691	21,555	5,338	9,521	80,985	14,859	95,844
Europe, Central	248	1,398	191	624	144	295	2,213	439	2,652
Europe, Eastern	419	2,423	300	1,109	294	470	3,833	764	4,596
Europe, Western	726	4,654	492	1,730	485	1,569	6,875	2,054	8,929
Australasia	43	382	24	113	22	114	519	136	655
Oceania	99	548	82	177	44	99	807	143	949
World	36,847	202,668	29,652	76,614	18,965	38,401	308,934	57,367	366,301

Table 2: Estimates for people living with Down's Syndrome by age-group and world region, 2005

GBD Region	SS Africa, Central	SS Africa, East	SS Africa, Southern	SS Africa, West	Africa North / Middle East	Caribbean	S America, Andean	S America, Central	S America, Southern	S America, Tropical	N America, H.I.
0-4	9,450	40,714	6,581	35,934	41,955	3,400	7,524	26,660	6,145	20,357	27,766
5-9	5,414	23,037	4,683	21,737	38,699	2,591	6,995	25,486	6,182	18,875	25,593
10-14	2,815	10,503	3,272	9,769	39,651	2,173	6,433	24,488	5,895	17,557	24,058
15-19	527	1,933	1,908	1,696	33,104	1,586	6,076	21,986	5,412	18,774	22,050
20-24	0	0	1,501	0	15,706	1,287	5,674	22,088	5,067	18,569	21,280
25-34	0	0	2,658	0	23,774	3,314	5,380	22,019	5,137	17,967	42,835
35-44	0	0	1,754	0	14,105	3,711	2,985	13,103	3,397	11,808	58,103
45-54	0	0	1,129	0	8,084	2,145	1,380	5,680	1,933	5,316	50,365
55-64	0	0	371	0	2,483	812	350	1,396	552	1,273	18,988
65-74	0	0	0	0	7	1	2	6	3	6	15
75-84	0	0	0	0	0	0	0	0	0	0	0
+85	0	0	0	0	0	0	0	0	0	0	0
Total	18,205	76,187	23,857	69,136	217,568	21,019	42,798	162,911	39,722	130,500	291,051

Table 2: Continued

GBD Region	Asia Pacific, H.I.	Asia Southeast	Asia, Central	Asia, East	Asia, South	Europe, Central	Europe, Eastern	Europe, Western	Australasia	Oceania	World
0-4	8,053	59,856	4,803	37,069	102,061	5,841	5,561	27,623	1,928	933	480,210
5-9	8,270	52,049	3,683	34,614	79,508	6,330	4,571	24,642	1,878	638	395,475
10-14	7,622	44,233	2,554	36,887	58,455	7,330	5,095	27,901	1,741	414	338,846
15-19	8,609	34,945	1,229	19,979	31,589	7,049	5,369	27,642	1,773	238	253,476
20-24	10,202	31,454	922	19,119	9,057	6,804	4,618	28,342	1,625	166	203,479
25-34	21,934	61,099	1,829	60,311	16,145	13,669	8,399	50,546	3,420	282	360,716
35-44	15,587	49,542	1,649	49,199	13,385	13,460	7,937	67,274	4,433	216	331,647
45-54	18,683	28,099	944	33,621	8,523	14,217	5,507	51,691	3,834	121	241,270
55-64	13,932	9,349	252	10,226	2,926	6,248	1,613	25,266	1,662	37	97,736
65-74	13	33	0	10	2	16	45	87	1	0	246
75-84	0	0	0	0	0	0	0	0	0	0	0
+85	0	0	0	0	0	0	0	0	0	0	0
Total	112,904	370,659	17,864	301,035	321,650	80,964	48,716	331,015	22,295	3,044	2,703,100

Table 3a: Estimates for excess deaths due to chromosomal disorders by GBD world region. 2005

GBD region	Down's Syndrome	Edwards & Patau syndromes	Unbalanced chromosomal rearrangements	Turner's syndrome	Klinefelter's syndrome	Total severe autosomal	Total sex chromosomes	Total chromosomal disorders
SS Africa, Central	5,601	1,036	1,887	499	29	8,525	528	9,053
SS Africa, East	19,460	3,513	5,945	1,806	86	28,918	1,892	30,810
SS Africa, South	2,890	405	963	581	26	4,259	607	4,866
SS Africa, West	20,469	3,244	5,895	1,710	89	29,608	1,799	31,407
N Africa Middle East	18,232	2,716	5,765	3,196	185	26,713	3,381	30,094
Caribbean	1,380	164	482	290	16	2,026	306	2,332
S Amer, Andean	1,673	336	527	435	22	2,536	457	2,993
Latin America Central	5,923	1,144	2,184	1,892	88	9,250	1,980	11,230
Latin America Southern	1,229	264	415	548	35	1,908	583	2,491
Latin America Tropical	4,520	907	1,707	1,785	83	7,134	1,868	9,002
N America, HI	9,576	641	3,793	3,101	206	14,010	3,307	17,317
Asia Pacific, HI	4,122	186	1,618	1,731	174	5,926	1,905	7,831
Asia SE	23,140	3,226	7,392	4,727	290	33,757	5,017	38,774
Asia, Central	2,235	315	960	610	37	3,510	647	4,157
Asia, East	22,745	2,776	11,956	13,040	846	37,477	13,886	51,363
Asia, South	55,678	7,691	23,011	10,913	649	86,380	11,562	97,942
Europe, Central	3,064	191	1,185	1,299	102	4,439	1,401	5,840
Europe, Eastern	2,874	300	1,247	2,547	187	4,422	2,734	7,156
Europe, Western	10,776	492	3,659	3,961	393	14,927	4,354	19,281
Australasia	745	24	271	230	17	1,039	247	1,286
Oceania	457	82	149	56	3	688	59	747
World	215,438	29,652	81,185	54,956	3,563	326,276	58,519	384,795

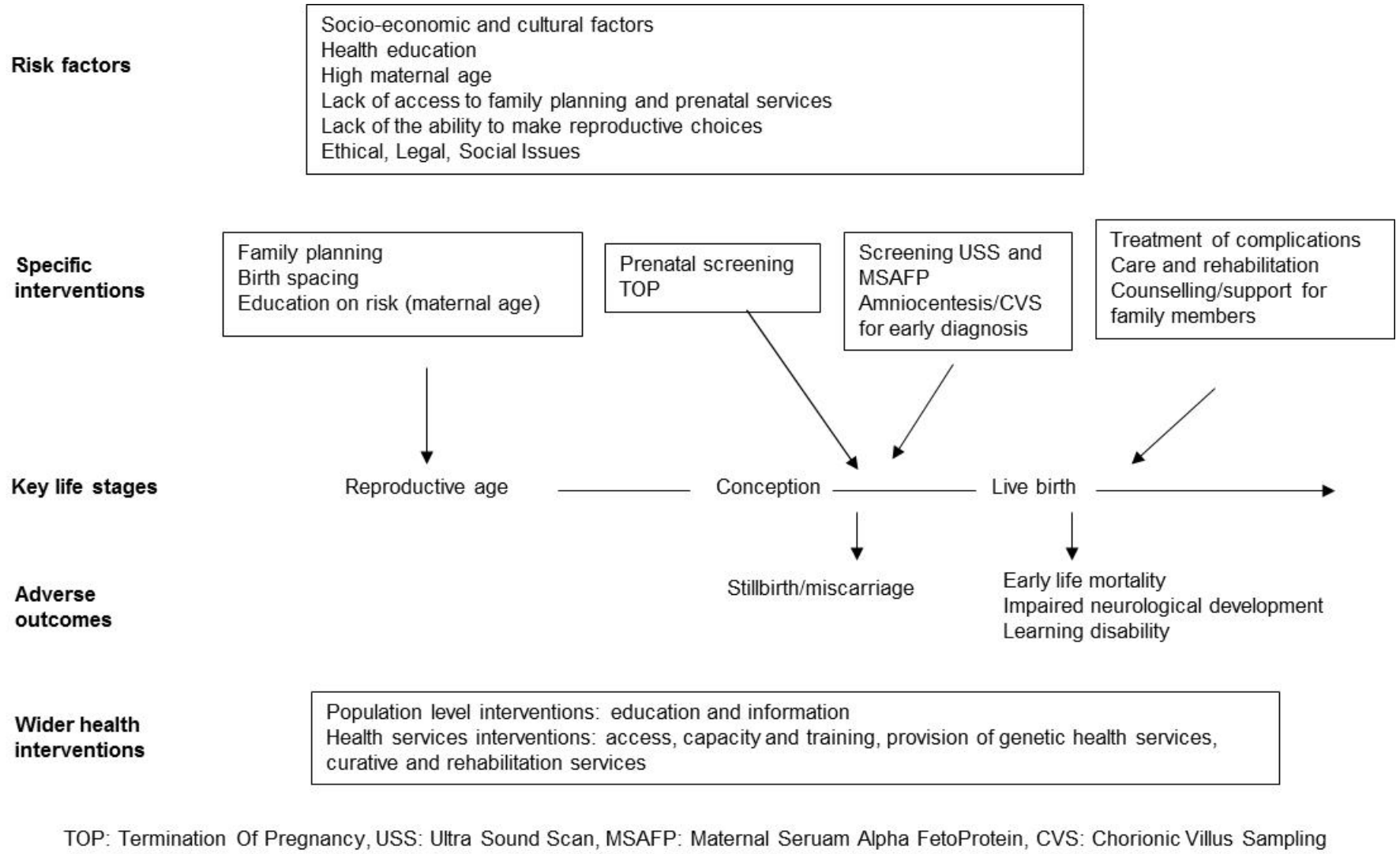
Table 3b: Estimates for early (under-5) deaths by world region: Total deaths of those with chromosomal disorders, 2005

GBD Region	Down's deaths <1 month	Down's deaths 1-11 months	Down's deaths 1-4 years	Total Down's under 5 deaths	Other trisomies deaths <1 month	Other trisomies deaths 1-11 months	Other trisomies deaths 1-4 years	Total other trisomies under 5 deaths
Sub-Saharan Africa, Central	344	3,093	1,367	4,803	891	145	0	1,036
Sub-Saharan Africa, East	1,122	10,097	4,272	15,490	3,021	492	0	3,513
Sub-Saharan Africa, Southern	128	1,156	466	1,750	349	57	0	405
Sub-Saharan Africa, West	1,068	9,610	4,213	14,890	2,790	454	0	3,244
Middle East	486	4,370	1,788	6,643	1,495	243	0	1,738
North Africa	287	2,581	997	3,865	841	137	0	978
Caribbean	47	419	183	648	141	23	0	164
Latin America, Andean	78	698	265	1,040	289	47	0	336
Latin America, Central	259	2,327	880	3,465	983	160	0	1,144
Latin America, Southern	42	378	166	586	227	37	0	264
Latin America, Tropical	191	1,722	647	2,560	780	127	0	907
North America, High Income	13	116	324	453	551	90	0	641
Asia Pacific, High Income	4	34	96	134	160	26	0	186
Asia Southeast	814	7,330	2,937	11,081	2,774	452	0	3,226
Asia, Central	98	885	363	1,346	271	44	0	315
Asia, East	845	7,606	2,943	11,394	2,387	389	0	2,776
Asia, South	2,545	22,903	9,995	35,443	6,615	1,077	0	7,691
Europe, Central	20	184	110	315	164	27	0	191
Europe, Eastern	73	658	253	984	258	42	0	300
Europe, Western	11	96	270	377	423	69	0	492
Australasia	1	8	22	31	20	3	0	24
Oceania	24	212	88	324	71	11	0	82
World	8,498	76,483	32,644	117,624	25,501	4,151	0	29,652

Table 3b: Continued

GBD Region	Down's deaths <1 month	Down's deaths 1-11 months	Down's deaths 1-4 years	Total Down's under 5 deaths	Other trisomies deaths <1 month	Other trisomies deaths 1-11 months	Other trisomies deaths 1-4 years	Total other trisomies under 5 deaths
Sub-Saharan Africa, Central	116	1,048	463	1,628	1,351	4,286	1,830	7,468
Sub-Saharan Africa, East	347	3,119	1,318	4,783	4,490	13,707	5,590	23,787
Sub-Saharan Africa, Southern	44	392	158	594	521	1,604	625	2,750
Sub-Saharan Africa, West	345	3,108	1,362	4,816	4,203	13,172	5,575	22,951
Middle East	161	1,452	589	2,203	2,142	6,065	2,377	10,584
North Africa	92	830	321	1,243	1,220	3,548	1,318	6,086
Caribbean	16	141	60	217	203	583	243	1,028
Latin America, Andean	25	221	84	329	391	966	348	1,705
Latin America, Central	98	883	334	1,316	1,340	3,370	1,214	5,925
Latin America, Southern	14	129	56	199	284	544	222	1,049
Latin America, Tropical	74	664	249	987	1,045	2,513	896	4,454
North America, High Income	5	42	119	166	568	248	443	1,259
Asia Pacific, High Income	2	15	43	60	165	75	139	379
Asia Southeast	265	2,389	953	3,607	3,854	10,170	3,890	17,914
Asia, Central	43	383	156	582	412	1,312	520	2,244
Asia, East	457	4,112	1,591	6,161	3,689	12,107	4,534	20,330
Asia, South	1,059	9,528	4,151	14,738	10,218	33,509	14,146	57,872
Europe, Central	10	87	50	147	194	298	160	652
Europe, Eastern	33	299	116	448	365	999	369	1,732
Europe, Western	4	36	100	140	437	201	370	1,009
Australasia	0	2	7	9	21	14	29	64
Oceania	8	68	28	105	102	292	117	511
World	3,217	28,950	12,309	44,476	37,216	109,584	44,953	191,752

Figure 1: Needs assessment flowchart for Down's Syndrome



TOP: Termination Of Pregnancy, USS: Ultra Sound Scan, MSAFP: Maternal Seruam Alpha FetoProtein, CVS: Chorionic Villus Sampling