Congenital Disorders

Background information on Orofacial Clefts 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 are Orofacial Clefts?

Orofacial Clefts (OFC) comprise a group of malformations of varying degrees of severity. They are divided into two main categories: cleft lip with or without cleft palate (CL/P) and isolated cleft palate (CP). A cleft lip can range from the merest nick to an unsightly gap running all the way to the nose. A cleft palate is a gap in the hard roof of the mouth; it can interfere with speaking, breathing and eating and can also raise the risk of repeated ear infections and resulting hearing loss. Surgical intervention can be very effective, but if left untreated, a cleft palate may even result in death through malnutrition or infection. OFC may present in isolation or along with other structural anomalies. They may also present as a result of chromosomal abnormalities (not the subject of this document).

What are the main risk factors?

The differences in prevalence between the sexes (increased in males), and increased prevalence of OFC among the offspring of affected individuals all suggest a higher genetic contribution to OFC than to many other types of congenital malformation. The environmental contribution to aetiology remains uncertain, with an apparent trend of increasing birth prevalence with deprivation, and uncertainty about the role of nutritional deficiencies, particularly folic acid and multivitamins. Particular teratogens which have been associated with increased rates of OFC include tobacco and alcohol. Some studies have shown an increased risk of OFCs as a result of maternal medications such as antiepileptic drugs, however, this is dependent on the drug and dosage[1].

Global epidemiology

Birth prevalence

There are considerable prevalence differences between populations, ranging from around 1.61/1,000 in parts of Latin America to less than 0.4/1,000 in East Africa. However, under-

[1] Meador KJ. Effects of in utero antiepileptic drug exposure. Epilepsy Curr. 2008;8(6): 143–147.

ascertainment of cleft palate may contribute to the reported low prevalence in Africa. Table 1 shows the estimated annual affected live births by world region.

Population prevalence

This depends on population age distribution, birth prevalence of OFC and in particular, the proportion of affected pregnancies that result in a stillbirth or mortality early in life due to type and quality of treatment and care. The estimated population prevalence of people living with OFC by world regions appears in Table 2.

Mortality

Mortality is dependent on the level of access and quality of health services. Neonatal mortality is assumed to range from 50% in the absence of health services to 2% in areas with modern care. Infant mortality ranges from 55.9% in the absence of health services to 2.2% in areas with modern care. Under-5 child mortality ranges from 61.8% in the absence of health services to 2.2% in areas with modern care. Although survival of people with OFC repaired in infancy is high, there is modestly increased all-cause mortality at all ages. Mortality can be due to starvation/malnutrition caused by feeding difficulties or aspiration pneumonia.

Estimated excess deaths in different age groups due to OFC by world region appear in Table 3.

Disability and quality of life

Surviving infants with OFC have a range of severities from none to residual physical disability, depending on the severity of the defect and the impact of postnatal management. Table 4a shows estimated prevalence of sequelae according to whether 1) the cleft remains un-operated 2) the success of the repair is less than optimal or 3) the cleft is successfully repaired. Table 4b shows estimated numbers in three outcome groups for OFC.

Reducing prevalence, morbidity and mortality

Figure 1 illustrates the determinants and interventions for OFC as they relate to key stages in life. Care for individuals with OFCs requires a multidisciplinary approach; the European Cleft Organisation[2] has developed draft best practice guidelines for cleft care from the prenatal period. The main specific interventions are discussed below.

Interventions before pregnancy

These include the maintenance of good periconception folate nutrition, folic acid food fortification aimed at the whole population, and supplementation either to all women or those in the preconception period. Although the role of dietary or supplemental intake of folic acid in human OFC is uncertain, there is some evidence that periconceptional multivitamin supplementation (including folic acid) may reduce the birth prevalence by 30-50%. As folic acid fortification and supplementation is very effective in reducing the incidence and severity of neural tube defects (NTD) and has thus been introduced in many countries, it is useful to bear in mind the potential additional benefit in lowering OFC birth prevalence.

For optimum results fortification should include food staples that are widely consumed across the country. For country specific data on food fortification, go to

[2] http://www.ecoonline.org/en/health_professionals/

http://www.sph.emory.edu/wheatflour/index.php. The likely reduction in OFC following folic acid food fortification is estimated as 25% of the observed or estimated fall in birth prevalence of NTD.

Increased prevalence of OFC among the offspring of affected individuals suggests a genetic contribution; therefore family planning measures may also play a role in decreasing the birth prevalence of OFC in high-risk groups. Increased OFC incidence may also be associated with a short interval between pregnancies: this is thought to be due to nutritional depletion, specifically folate depletion in the mother, particularly in those who are breastfeeding. Increasing the intervals between pregnancies may therefore reduce overall the number of children born with OFC including those born to women with a family history of OFC.

Children born with OFCs have difficulties feeding which leads to increased risk of morbidity and mortality in areas where there is a lack of immediate access to treatment services. This can be reduced by providing mothers with early advice on how to feed an affected child and reassurance that the condition is compatible with life. Targeting of such advice to mothers who are perceived to be at-risk to ensure that they are adequately prepared to care for a child with the condition can also help.

Interventions during pregnancy

Prenatal screening and diagnosis as part of a fetal anomaly scan may identify both isolated OFC and those associated with other malformations. However, this technique does not allow the identification of cleft palates. Early diagnosis allows preparation for the birth of an affected child (e.g. by allowing training of the mother on how to feed her baby) and planning for appropriate care provision at an early point after birth. Worldwide prenatal screening in general has high coverage; however, the quality of the services is variable and the coverage of prenatal screening for structural abnormalities is very low in many places.

Interventions after birth

Newborn screening through physical examination enables early diagnosis of OFC, thereby allowing care to be initiated in a timely fashion. Cleft lips may be obvious at birth, although milder defects may be missed. Cleft palates may be missed at this stage if careful examination of the newborn is not conducted. Worldwide the level of newborn physical examination varies and is dependent on the availability and training of skilled birth attendants.

Improved surgical care reduces early mortality and morbidity associated with OFC. However, as many infants may not have immediate access to surgery, ensuring mothers are given advice on how to feed and care for their baby is important in order to avoid early life mortality. Treatment usually involves one or several surgical interventions, depending on the severity of the defect. This process may extend over several years in cases of severe OFC. Speech therapy and counselling also help improve quality of life and may be long-term requirements.

Cost-effectiveness of interventions

Information relating to the cost-effectiveness of interventions in relation to OFCs could not be identified. Costs of treatment and care from infancy to childhood can be considerable due to the need for special multidisciplinary teams. However, they can allay the social costs as

affected individuals are liable to suffer stigmatisation, social exclusion and barriers to employment.

Issues of cost-effectiveness are quite specific to each country as costs can vary considerably. 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/.

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

The ethical basis for state intervention

When public health interventions (such as folic acid fortification of foods) are targeted at populations rather than individuals the intrusiveness of the intervention, and any risks associated with it, should be balanced against the likely benefits, particularly if a degree of coercion is involved.

Current evidence suggests folic acid fortification and supplementation are very safe interventions, especially with intake levels of up to 1 mg/day of folic acid. Daily intakes under 5mg/day are also likely to be safe. Fortification in high-malaria environments still needs to be examined. Caution has been recommended in these areas. This is because iron, which is often combined with folic acid in food fortification, may increase risk of death in malarial areas; and high doses of folic acid may reduce the efficacy of some antimalarials, such as sulfadoxine and pyrimethamine. At the time of writing, there seems to be no evidence that folic acid in doses used for fortification increases the risk of missing a diagnosis of vitamin B12 deficiency and associated neuropathy. Doses up to 1 mg/day have not been associated with clinically significant drug interactions and can be safely used in controlled epilepsy.

Those that oppose fortification programmes argue that such policies deprive competent adults of the chance to make an autonomous choice. This is particularly the case if all potential sources of a particular product are fortified. As some types of food are less amenable to folic acid fortification than others (for example wheat is more easily fortified than rice), and as some people, usually the most isolated and the less well off in society, may not have access to fortified products (e.g. by relying on subsistence agriculture or local produced products) the exclusive use of food fortification may lead to an unfair distribution and access to the benefits conferred by the fortified foods.

It is possible to preferentially target those who are planning a future pregnancy, or at risk of becoming pregnant, by providing folic acid supplementation in the form of folic acid pills. However, such programmes may be less accessible to vulnerable groups or those of lower socioeconomic class, raising issues of lack of equity in provision of the service.

Birth spacing and contraceptive use

As noted previously, increasing the intervals between pregnancies may reduce the number of children born to women with a family history of OFC. However, achieving increased birth spacing through access to family planning methods remains challenging in many low and middle income countries (LMIC) and is not religiously or culturally acceptable in some settings.

Living with a disability

Those who are born disabled often have a very poor life expectancy, especially in LMIC. 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 substantive support from the state, in many LMIC health and social services are lacking, and welfare is limited. In such places the psychological and economic burden of having a disabled child falls entirely on the immediate and extended family.

KEY REFERENCES

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Mossey PA, Little J (2002). *Epidemiology of oral clefts: an international perspective*. In Wyszynski DF (Ed) *Cleft lip and palate. From origin to treatment*. Oxford University Press, 2002.

World Health Organisation. *Global strategies to reduce the health-care burden of craniofacial anomalies.* 2002.

LINKS TO OTHER CHAPTERS

Preconception care and screening
Prenatal care and screening
Newborn screening
Neural tube defects (information on folic acid fortification)
Teratogens

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

GBD Region	Total births OFC/1,000 (non-chr)	OFC, stillbirths /1,000 (1.8%)	Total OFC live births /1,000 (non-chr)	Annual affected births		
				Cleft palate (isolated)	Cleft lip w or w'out cleft palate (isolated)	Total isolated
Sub-Saharan Africa, Central	0.54	0.01	0.53	118	1,725	1,843
Sub-Saharan Africa, East	0.38	0.01	0.38	1,177	2,873	4,050
Sub-Saharan Africa, Southern	0.45	0.01	0.45	204	432	636
Sub-Saharan Africa, West	0.54	0.01	0.53	746	4,677	5,424
Middle East	1.02	0.02	1.00	1,515	4,031	5,546
North Africa	0.44	0.01	0.43	450	900	1,350
Caribbean	0.93	0.02	0.92	220	386	606
Latin America, Andean	1.29	0.02	1.27	144	1,228	1,372
Latin America, Central	1.38	0.02	1.36	1,547	4,954	6,501
Latin America, Southern	1.61	0.03	1.58	584	1,436	2,020
Latin America, Tropical	1.61	0.03	1.58	2,303	5,659	7,962
North America, High Income	2.00	0.04	1.96	3,054	4,532	7,585
Asia Pacific, High Income	1.65	0.03	1.62	879	1,473	2,352
Asia Southeast	1.35	0.02	1.33	2,577	11,098	13,675
Asia, Central	1.19	0.02	1.16	755	762	1,517
Asia, East	1.28	0.02	1.26	3,308	15,670	18,977
Asia, South	1.60	0.03	1.57	8,077	41,485	49,561
Europe, Central	1.45	0.03	1.42	651	791	1,442
Europe, Eastern	1.22	0.02	1.20	1,024	1,145	2,169
Europe, Western	1.61	0.03	1.58	1,881	3,935	5,816
Australasia	2.00	0.04	1.97	258	261	519
Oceania	1.85	0.03	1.82	275	184	459
World	1.22	0.02	1.19	31,745	109,636	141,382

non-chr: non-chromosomal

Table 2: People living with OFCs by age-group and GBD world region, 2005

GBD Region	OFC live births 2005	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	Total living with OFC
Sub-Saharan Africa, Central	2,094	2,905	1,725	872	467	248	179	55	24	19	15	1	0	0	0	0	0	6,509
Sub-Saharan Africa, East	4,559	10,882	7,386	5,063	3,781	2,869	2,374	1,065	777	617	465	2	0	0	0	0	0	35,281
Sub-Saharan Africa, South	707	2,235	1,734	1,390	1,223	1,061	936	310	224	189	153	1	0	0	0	0	0	9,456
Sub-Saharan Africa, West	6,242	11,244	7,692	4,088	2,450	1,471	1,247	718	513	409	314	3	0	0	0	0	0	30,149
Africa North / Middle East	7,862	24,403	23,703	23,783	21,917	18,248	16,708	7,498	5,960	2,826	2,119	226	119	61	32	13	4	147,620
Caribbean	628	2,237	2,036	1,997	1,801	1,523	1,501	1,393	1,363	1,140	816	641	517	396	291	145	54	17,852
Latin America, Andean	1,413	6,231	6,164	5,812	5,330	2,872	2,570	1,795	564	470	385	2	0	0	0	0	0	32,196
Latin America, Central	6,404	29,954	31,929	31,590	29,767	19,328	17,639	12,354	6,729	4,115	3,291	1,161	840	550	338	185	70	189,839
Latin America, Southern	1,370	7,423	7,953	8,147	7,863	7,412	7,135	6,282	5,749	5,452	4,835	4,121	3,279	2,465	1,687	1,025	413	81,243
Latin America, Tropical	5,592	29,291	27,982	27,919	29,470	14,592	12,548	11,296	3,229	2,819	2,226	9	0	0	0	0	0	161,381
North America, High Income	8,232	39,481	41,890	45,029	44,104	44,415	41,278	42,705	43,677	46,867	43,903	37,299	29,474	20,071	13,091	8,060	3,686	545,030
Asia Pacific, High Income	2,723	13,440	14,036	14,337	15,674	17,777	19,887	22,137	19,435	17,612	16,969	18,842	17,984	14,346	10,039	6,295	2,613	241,422
Asia Southeast	15,543	65,110	64,392	61,815	57,255	46,601	42,468	25,413	20,223	11,724	9,668	4,993	3,339	2,201	1,432	711	441	417,788
Asia, Central	1,741	4,833	4,240	3,938	3,468	2,814	2,436	1,116	969	938	746	3	0	0	0	0	0	25,501
Asia, East	22,281	63,908	75,127	94,856	73,518	64,925	79,655	26,907	21,449	15,512	15,891	59	0	0	0	0	0	531,808
Asia, South	57,544	115,263	91,888	68,175	47,094	32,611	28,218	23,068	18,534	15,407	12,490	58	0	0	0	0	0	452,806
Europe, Central	1,669	8,266	9,112	11,169	12,776	13,270	13,177	11,448	10,068	10,317	11,491	10,614	7,822	5,398	4,174	2,708	1,080	142,891
Europe, Eastern	2,515	11,544	11,952	15,924	21,388	20,752	18,590	17,247	16,176	19,248	18,559	15,925	10,348	8,208	8,173	4,023	1,846	219,904
Europe, Western	6,681	34,016	34,838	37,303	38,262	39,729	40,759	45,189	49,050	46,818	41,182	37,223	32,038	25,686	19,604	11,791	5,141	538,630
Australasia	599	2,988	3,125	3,271	3,233	3,234	3,053	3,405	3,269	3,389	3,060	2,702	2,290	1,548	1,046	632	291	40,537
Oceania	538	1,134	909	711	591	415	360	278	220	169	135	50	36	22	13	5	2	5,050
World	156,935	486,788	469,815	467,190	421,434	356,171	352,717	261,681	228,203	206,055	188,713	133,934	108,086	80,951	59,920	35,595	15,641	3,872,892

Table 3: Estimated excess deaths due to OFCs by GBD world region, 2005

GBD Region	OFC live births 2005	< 1 mo	1-11 mo	1-4 yr	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	Total excess deaths 2005
Sub-Saharan Africa, Central	2,094	975	36	40	221	89	25	7	1	1	0	0	0	0	0	0	0	0	0	1,394
Sub-Saharan Africa, East	4,559	1,658	103	108	693	378	153	67	10	15	7	2	1	0	0	0	0	0	0	3,194
Sub-Saharan Africa, South	707	240	19	23	146	92	43	22	4	4	2	1	0	0	0	0	0	0	0	595
Sub-Saharan Africa, West	6,242	2,722	167	92	898	381	120	41	6	11	5	1	1	0	0	0	0	0	0	4,444
Africa North / Middle East	7,862	1,386	128	140	851	651	346	183	48	37	27	12	10	2	2	2	2	1	1	3,829
Caribbean	628	321	32	33	90	58	25	14	4	6	6	5	5	7	10	12	15	12	7	661
Latin America, Andean	1,413	159	15	15	96	66	33	18	7	6	3	2	2	0	0	0	0	0	0	422
Latin America, Central	6,404	141	10	12	94	64	50	45	39	35	24	20	21	12	16	17	17	15	9	642
Latin America, Southern	1,370	278	8	10	4	3	7	13	15	17	20	27	31	42	63	75	84	83	56	837
Latin America, Tropical	5,592	37	0	0	16	11	26	26	27	31	11	14	14	0	0	0	0	0	0	214
North America, High Income	8,232	166	-3	0	23	18	39	78	89	116	154	232	283	381	563	614	654	653	496	4,556
Asia Pacific, High Income	2,723	54	5	0	8	6	14	31	43	60	68	87	109	192	344	439	502	510	352	2,825
Asia Southeast	15,543	2,060	182	186	889	548	266	180	101	82	76	57	60	51	64	67	72	58	59	5,057
Asia, Central	1,741	612	52	64	379	281	133	62	10	15	8	3	2	0	0	0	0	0	0	1,621
Asia, East	22,281	5,798	609	627	5,128	5,326	2,267	1,187	310	285	154	55	56	0	0	0	0	0	0	21,801
Asia, South	57,544	24,260	2,313	2,335	10,828	6,568	2,458	977	144	371	181	39	19	0	0	0	0	0	0	50,494
Europe, Central	1,669	37	2	0	5	4	11	23	28	31	35	51	74	108	149	165	209	220	145	1,300
Europe, Eastern	2,515	74	0	0	7	6	19	37	40	47	57	95	120	163	198	251	408	326	249	2,095
Europe, Western	6,681	133	13	0	20	15	34	70	88	123	173	232	265	380	612	785	979	956	692	5,570
Australasia	599	12	1	0	2	1	3	6	7	9	12	17	20	28	44	47	52	51	39	350
Oceania	538	150	13	15	70	39	16	7	1	3	1	1	1	1	1	1	1	0	0	320
World	156,935	41,743	3,778	3,765	20,468	14,606	6,087	3,092	1,024	1,305	1,024	953	1,095	1,366	2,065	2,475	2,994	2,885	2,107	112,832

Table 4a: Estimated prevalence of sequelae according to whether: 1) the cleft remains unoperated; 2) the success of the repair is less than optimal; or 3) the cleft is successfully repaired

Problem	Sequelae group 1	Sequelae group 2	Sequelae group 3
	Unrepaired OFC	Repaired OFC, residual problems	Repaired OFC, effective cure
Unable to be understood	60%	25%	0%
Some problems in speech	100%	66%	50%
Multiple (primary) operation	N/A	50%	50%
Repeat operations	N/A	60%	30%
Severe facial deformity	50%	40%	0%
Moderate facial deformity	50%	50%	20%
Hearing problems	20%	20%	10%
Psychological problems	60%	50%	25%

Table 4b: Estimated numbers in the three outcome groups for OFCs

GBD Region	Total living patients	Living with unoperated OFC	Operated, effectively cured	Operated, residual disability
Sub-Saharan Africa, Central	6,509	5,628	705	176
Sub-Saharan Africa, East	35,281	11,391	19,112	4,778
Sub-Saharan Africa, Southern	9,456	2,199	5,806	1,451
Sub-Saharan Africa, West	30,149	18,360	9,431	2,358
Africa North / Middle East	147,620	12,927	108,080	26,613
Caribbean	17,852	1,305	13,668	2,879
Latin America, Andean	32,196	1,124	24,857	6,214
Latin America, Central	189,839	1,662	150,542	37,635
Latin America, Southern	81,243	0	66,132	15,111
Latin America, Tropical	161,381	1,250	128,105	32,026
North America, High Income	545,030	0	463,276	81,755
Asia Pacific, High Income	241,422	0	205,209	36,213
Asia Southeast	417,788	17,067	324,005	76,716
Asia, Central	25,501	5,972	15,623	3,906
Asia, East	531,808	40,652	392,925	98,231
Asia, South	452,806	192,649	208,125	52,031
Europe, Central	142,891	33	120,279	22,579
Europe, Eastern	219,904	4	176,476	43,424
Europe, Western	538,630	0	457,835	80,794
Australasia	40,537	0	34,457	6,081
Oceania	5,050	1,163	3,109	777
World	3,872,892	313,385	2,927,757	631,750

Figure 1: Needs assessment flowchart for Orofacial Clefts