

The final version of this paper was published in *Birth Defects Res A Clin Mol Teratol* 2013; 97(2):101-108

## **Descriptive epidemiology of cleft lip and cleft palate in Western Australia**

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### **Support:**

Ms Bell is supported by the Bob and Nancy Edwards Scholarship, University of Sydney.

Dr Raynes-Greenow is supported by a National Health and Medical Research Council (NHMRC) Early Career Research Fellowship (no. 511984)

Prof Bower is supported by a NHMRC Principal Research Fellowship (no. 634341)

Dr Turner is supported by a NHMRC program grant (no. 633003) to the Screening & Test Evaluation Program

Prof Roberts is supported by a NHMRC Senior Research Fellowship (no. 1001066)

Dr Nassar is supported by a NHMRC Career Development Fellowship (no. 632955)

**Running title:**

Orofacial clefts in West Australia since 1980

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## **Abstract**

**Background:** The reported birth prevalence of orofacial clefts varies considerably. This study aimed to determine the prevalence and trends of orofacial clefts in an Australian population.

**Methods:** We studied infants diagnosed with cleft lip, with or without cleft palate (CL±P) and cleft palate only (CPO) since 1980, and reported to the population based Western Australian Register of Developmental Anomalies. We calculated prevalence rates by sex, Aboriginal status, geographic location and socioeconomic status. Associations between clefts and pregnancy characteristics, pregnancy outcomes, other congenital anomalies, and age at diagnosis were also investigated.

**Results:** From 1980-2009, 917 infants with CL±P (12.05 per 10,000) and from 1980-2004, 621 infants with CPO (10.12 per 10,000) were registered. Prevalence rates for CL±P and CPO were 1.9 and 1.3 times higher respectively for Aboriginal Australians. Additional anomalies were reported for 31% of infants with CL±P and for 61% with CPO; chromosomal anomalies and other specific diagnoses accounted for 46% and 66% respectively, of those with CL±P and CPO with additional anomalies. Almost all (99.7%) children with CL±P were diagnosed before one year of age, but 12% of CPO diagnoses were made after one year of age; 94% of these diagnoses were of submucous clefts and bifid uvula.

**Conclusions:** These data provide a picture of the prevalence of OFCs in WA since 1980, and provide a useful reference for OFC data in Australia and internationally. The quality and completeness of the WARDA data are high, reflected in high prevalence rates, and proportions of clefts occurring with other anomalies.

### **Key words:**

Cleft lip, Cleft palate, Congenital anomalies, Prevalence, Epidemiology, Western Australia

## INTRODUCTION

Orofacial clefts (OFCs) are among the most common congenital malformations. Children born with OFCs have difficulty feeding, and need multidisciplinary care from birth to adulthood, including surgery, speech therapy, general dentistry and orthodontics (Mossey et al., 2009). Effects on speech, hearing, and appearance can lead to chronic adverse health and developmental outcomes with higher morbidity and mortality compared with unaffected populations (Mossey et al., 2009). Monitoring the prevalence of OFCs is important for providing information about potential aetiology and prevention, and for quantifying the burden of disease and identifying health service needs.

Historically, prevalence studies of OFCs were limited to hospital based series. In the 1980s the establishment of birth defects registries with associated monitoring programs overcame some of the ascertainment limitations of previous studies. However, OFCs occur infrequently, and ascertainment and reporting have varied considerably, making comparisons between registries and countries difficult. Several factors influence reporting and registration of OFCs, including screening policies and procedures, prenatal diagnostic services, sources of notification, clinician and diagnostic skills and the upper age of registration. Large collaborative studies and networks collating prevalence data from multiple registries, have now been established, such as a European network of population-based registries for the epidemiologic surveillance of congenital anomalies (EUROCAT), the International Collaborative Research on Craniofacial Anomalies project (World Health Organization Human Genetics Programme & United States National Institute of Dental and Craniofacial Research) and the International Clearinghouse for Birth Defects Surveillance and Research (International Clearinghouse for Birth Defects Surveillance and Research). These partly overcome limitations of individual registry reporting by standardising case definitions and analysis. However, underlying differences in case ascertainment remain, and undoubtedly contribute to the wide variation in reported prevalence rates.

Australia is a good example of differences in the reported prevalence of congenital anomalies. Prevalence rates for OFCs range between 15 to 21 per 10,000 births (Bower et al., 2010a; Gibson et al., 2009; Population Health Research Centre ACT Health, 2007; Roselli, 2006; Vallino-Napoli et al., 2004; Vallino-Napoli et al., 2006), but surveillance methods vary (Abeywardana and Sullivan, 2008).

Cleft lip and cleft palate can occur together (CL+P) or alone (CLO or CPO). As the lip and palate have distinct developmental origins, these orofacial clefts are often classified and investigated as cleft lip with or without cleft palate (CL±CP); or as CPO, in which the lip is not affected (Mossey et al., 2009). The phenotypic variants of cleft lip (CLO and CL+P) are usually considered to be the same defect and are thought to differ aetiologically from CPO. However, there is also some evidence that CLO and CL+P may be aetiologically distinct (Genisca et al., 2009; Harville et al., 2005; Jugessur et al., 2011). OFCs may be further classified as occurring without other congenital anomalies (isolated OFCs), or with other congenital anomalies and may or may not be part of recognised syndromes, or known chromosomal or gene abnormalities (IPDTC Working Group, 2010). Again, variations in ascertainment exist, which influence reported prevalence rates.

Using data from the longest existing Australian registry, this study describes the birth prevalence of OFCs in Western Australia (WA). WA is the largest state in Australia, covering around one-third of Australia's land area, is home to around 10% of Australia's population, and reports approximately 25,000 births per annum (Australian Bureau of Statistics, 2012).

## **METHODS**

Data from the WA Register of Developmental Anomalies (WARDA) were used to identify all infants born in WA with an OFC, between 1 January 1980 and 31 December 2010. The WARDA, established in 1980, is a statutory population based notification system of congenital anomalies, with notifications received from multiple sources. Information is collated on all reported structural and functional anomalies diagnosed in pregnancies terminated because of fetal anomaly, stillbirths and in live born children up to six years of age. Each individual anomaly is coded according to the British Paediatric Association International Classification of Diseases, 9th revision system (BPA-ICD9) with up to 10 diagnostic categories available to allow coding of multiple anomalies per infant.

Infants with OFCs were identified using the BPA-ICD9 codes for CPO (74900-74909), CLO (74910-74919) and CL+P (74920-74929). Infants with a facial cleft (74928) (for example due to amniotic band), and without a cleft lip or palate were excluded. OFCs that were not associated with other anomalies were defined as isolated. If any other congenital anomalies (BPA-ICD9 codes 740–759), were recorded as well as an OFC, these infants were classified into three mutually exclusive groups: having a chromosomal anomaly (if BPA-ICD9 code 758 was recorded);

having another specified diagnosis (such as a syndrome, association or sequence, if BPA-ICD9 codes 7593, 7595-6, 7598 or text description included syndrome was recorded); or having neither of these.

Information on infant's sex, plurality, Aboriginal status, pregnancy outcome and age at OFC diagnosis were obtained from the WARDA. Pregnancy outcomes are categorised as termination of pregnancy, stillborn or live born. Age at diagnosis was categorised as prenatal, up to one year of age (including post mortem diagnoses as these deaths all occurred in terminations, stillbirths or infants), from one to 3 years, or between three and six years of age. If the age of diagnosis is not clear, the WARDA records the earliest mention of the anomaly as the time of diagnosis (Bower et al., 2010b). Postcodes of residence at birth were used to categorise geographic location as major city, inner or outer regional area, or remote or very remote location. This index of remoteness (Accessibility/Remoteness Index of Australia for 2006) classifies locations by their accessibility to service centres, based on the road distance to service towns of different sizes, is unrelated to socio-economic status, and is stable over time (Australian Population and Migration Research Centre). Similarly, postcodes were categorised into socioeconomic quintiles based on their Index of Relative Socio-economic Advantage and Disadvantage from the 2006 Census (Australian Bureau of Statistics, 2008). Increasing scores (categorised into quintiles) reflect increasing advantage. For example, an area with a high score will have a higher prevalence of households with high incomes, or people in skilled occupations as well as fewer households with low incomes, or fewer people in unskilled occupations (Australian Bureau of Statistics, 2008).

The Western Australian Department of Health provided denominator data (numbers of live births and stillbirths of 20 weeks gestation or more) in Western Australia. We examined birth prevalence rates by cleft type, sex, and for Aboriginal and non-Aboriginal children, and by geographic location and socio-economic status. Infants for whom sex, geographic location and socio-economic status were unknown were excluded from analyses involving those variables. The one infant whose Aboriginal status was unknown was coded as non-Aboriginal. We calculated birth prevalence by dividing the number of registrations of OFC by the total number of births (live births and stillbirths) in the relevant year(s). Using univariate log-linear regression with a negative binomial distribution, we determined prevalence rate ratios (by sex and Aboriginal status) and assessed the average yearly rate change for OFCs by cleft type. As up to 12% of anomalies on the WARDA are diagnosed between one and six

years of age (Bower et al., 2010b), we investigated the age at diagnosis for cleft types, using data from 1980 to 2004, so that infants born in 2004 and earlier had the full six years for reporting of any congenital anomalies.

We also investigated associations with maternal age at child's birth, plurality, pregnancy outcomes, other congenital anomalies, and age at diagnosis of OFC. Difference in maternal age was analysed by t-test, and categorical data were analysed using Chi-squared ( $\chi^2$ ) tests. All data were analysed using SAS, release 9.2 (SAS Institute, Cary, NC, USA). Results are presented for CL±P, CLO, CL+P and for CPO. To avoid potential re-identification of infants, we have not presented results with cell numbers less than 10.

The study protocol was approved by the Western Australian Department of Health Human Research Ethics Committee and the Western Australian Aboriginal Health Ethics Committee. These approvals were recognised by the University of Sydney's Human Research Ethics Committee.

## RESULTS

Between 1980 and 2004, almost all children with CL±P (99.7%) were diagnosed before one year of age (CLO 99.3%; CL+P 100%) but only 87.6% of children with CPO were diagnosed during the first year of life. The majority of diagnoses of CPO after one year of age occurred between three and six years of age (9.0% of all CPO). Therefore, findings for CL±P are presented for 1980 to 2009 and results for CPO are presented for the period 1980 to 2004, to allow for completeness of enumeration. For the same reason, the occurrence of OFCs with other anomalies is also reported for 1980 to 2004.

Birth prevalence rates of OFCs are shown in Table 1. From 1980 to 2009, 917 infants with CL±P were reported to the WARDA, a birth prevalence of 12.05 per 10,000 births (1 in 833 births). For CPO, 621 infants were registered between 1980 and 2004 (10.12 per 10,000 births or 1 in 990 births). For CL±P, rates were significantly higher in males than females (prevalence rate ratio 1.62 [95%CI 1.40, 1.89; P <0.0001]). For CPO, the prevalence rate in females was 1.31 (95%CI 1.10, 1.55; P=0.002) times higher than for males. Compared with non-Aboriginal Australians, birth prevalence rates for Aboriginal Australians were 1.89 (95%CI 1.53, 2.34; (P<0.0001) times higher for CL±P and 1.30 (95%CI

0.95, 1.79; P=0.10) times higher for CPO. Birth prevalence of all forms of OFC did not differ by geographic location, or by socio-economic status. From 1980 to 2009, there was no significant change in annual rates for CL±P [-0.10% (95% CI -0.93%, 0.73%)], but rates for CPO increased by an average of 1.97% per year (95% CI 0.80%, 3.16%).

Maternal age, plurality and pregnancy outcome by cleft type are shown in Table 2. The mean age of mothers did not differ by cleft type. The vast majority of clefts involving the lip and palate occurred in singletons, similar to the proportion (97.2%) of singletons amongst all births. The majority of infants with an OFC were live born. Ten per cent of pregnancies where a CL±P was detected, and 7.8% of pregnancies in which a CPO was diagnosed, were terminated; all had additional anomalies.

While over two-thirds (69%) of infants with CL±P had isolated clefts, only 39% of clefts of the palate were isolated (Table 3). Chromosomal anomalies occurred in one-quarter of infants with non-isolated CL±P and 16% of those with non-isolated CPO. Over half the infants with non-isolated CPO were classified as having a specific diagnosis, compared with only 20% of infants with CL±P and another anomaly ( $\chi^2_2= 53.97$ , P<0.0001).

While the proportion of diagnoses of chromosomal disorders associated with CL±P rose from 19.5% in the 1980s to 37.7% in the 2000s and the proportion with a non-chromosomal specific diagnosis fell from 26.8% to 13.2%, the overall change in the distribution of these diagnostic categories was not statistically significant ( $\chi^2_4= 8.11$ , P= 0.09). For CPO, diagnoses of chromosomal and other specific diagnoses both decreased slightly, and diagnoses of non-chromosomal non-specified anomalies increased ( $\chi^2_4= 5.00$ , P=0.29).

The distribution of types of additional anomalies between those with chromosomal, other specific diagnoses or those with no specific diagnosis was similar (data not shown). Table 3 shows the additional anomalies reported by system affected and cleft type. The most common types of additional anomalies are those of the musculoskeletal system which affected nearly half of the infants with a non-isolated CL±P, and three-quarters of those with non-isolated CPO. Among infants with an OFC and an additional musculoskeletal anomaly, the distribution of types of musculoskeletal anomalies reported varied by cleft type. Anomalies of jaw size or position were common among infants with CPO and a



musculoskeletal anomaly (61.5%), but uncommon among infants with CL±P (7.1%) ( $\chi^2_1$  95.80 P<.0001). In contrast polydactyly or syndactyly occurred more frequently in infants with CL±P (24.1%) than in infants with CPO (12.2%) ( $\chi^2_1$  8.62 P=0.003); and limb reduction anomalies were also more common in infants with CL±P (13.4%) compared with infants with CPO (6.6%) ( $\chi^2_1$  4.69 P=0.03). The prevalence of talipes with OFCs did not differ by cleft type (P=0.1). There was no difference in the distribution of these same musculoskeletal anomalies between infants with CLO and a musculoskeletal anomaly and CL+P and a musculoskeletal anomaly (data not shown).

The proportion of pregnancies with a prenatal diagnosis of CL±P increased from 1% in the 1980s, to 16% in the 1990s and to 51% in the 2000s. The increase in prenatal diagnosis of CPO was much lower; 0.5% in the 1980s, 1.5% in the 1990s and 5.0% in 2000-04. Diagnoses of CPO after one year of age were primarily of bifid uvulas (51%) and submucous clefts (43%), whereas the vast majority of infants with clefts of the hard and/or soft palate were diagnosed before their first birthday (Table 4). The birth prevalence of submucous cleft palate or bifid uvula was much lower in the ten years 1980-89 (3.47 per 10,000) than in 1990-99 (5.49 per 10,000) and in 2000-04 (6.39 per 10,000).

## DISCUSSION

This study reveals high prevalence rates of OFCs in WA (CL±P 12.05 per 10,000; CPO 10.12 per 10,000) compared with most other parts of the world. Over a slightly shorter time period, the average prevalence of CL±P in European centres was 9.1 per 10,000 and the only centres with higher prevalence than WA were Odense in Denmark, Northern Netherlands, Saxony-Anhalt in Germany and Styria in Austria (Calzolari et al., 2007). For CPO, Finland (15.2 per 10,000) was the only European centre to report a higher prevalence; and both WA and Finland have substantially higher prevalence than the average for Europe (6.2 per 10,000 births) (Calzolari et al., 2004). In other parts of the world, prevalence rates in the early 2000s for CL±P were higher in Japan (20.04 per 10,000) and Mexico and South America (13.13 per 10,000) but lower in the United States of America (10.20 per 10,000) (IPDTC Working Group, 2010). The only other Australian states to record congenital anomalies diagnosed after one year of age are Victoria and South Australia. Prevalence rates in South Australia were similar to those in WA (1986-2007: CL±P 11.1 per 10,000, CPO 9.9 per 10,000) (Gibson et al., 2010) while rates in Victoria were slightly lower (1983-2000: CL±P 10.4 per 10,000; CPO 7.3 per 10,000) (Vallino-Napoli et al., 2006).

These data on OFCs from the WARDA, where complete ascertainment of structural and functional congenital anomalies are reported from multiple sources, with follow up until six years of age, highlight the difficulties in comparing prevalence studies of congenital anomalies. Underlying population differences, as well as differences in ascertainment, types of pregnancy outcomes included, antenatal services, cultural and policy differences all contribute to differences in data collection and reported prevalence (Boyd et al., 2011; Christensen, 2002; Mossey and Little, 2002). High rates of CPO prevalence in WA may reflect the longer registration period allowing submucous clefts and bifid uvulas, which are often diagnosed in the pre-school age period of 3-6 years, to be recorded. In WA 12% of CPO are diagnosed after 1 year of age (and 9% between 3 and 6 years of age). These types of clefts comprise nearly 50% of CPO in WA. While submucous clefts and bifid uvulas are part of the cleft palate spectrum diagnosis, restrictions on the maximum age at diagnosis of anomalies will under-estimate their prevalence, and analytical studies identifying cases from these data collections will under-represent these cleft types, potentially biasing results. Only three infants with CL±P were reported as diagnosed after one year of age; in these infants the age at diagnosis was unclear and they were categorised according to the earliest mention of the cleft.

Where trends in prevalence of OFCs have been reported, generally no significant changes have been found (Calzolari et al., 2002; Gibson et al., 2010; Mossey and Little, 2002; Riley and Halliday, 2000). The apparent increase in prevalence of CPO among infants born in WA since 1980 may be due to low numbers of registrations of children with a submucous cleft or bifid uvula in the 1980s, perhaps as a result of diagnoses in earlier years occurring after the six year age registration limit. Reporting of congenital anomalies from multiple sources and the high enumeration of congenital anomalies on the WARDA since 1980 suggest that under-reporting of existing diagnoses is unlikely.

Differences in OFC prevalence between population groups (Canfield et al., 2006; Croen et al., 1998; Tan et al., 2008) may reflect racial and ethnic differences in genetic factors, or may relate to differences in both known (such as maternal smoking) and unknown environmental risk factors, or a combination of these. We found no difference in prevalence by maternal age, plurality, socio-economic status and geographic residence at birth. This study, however, confirms earlier findings from WA for the period 1980-87, where the prevalence of CL±P in Aboriginal populations was almost twice that of non-Aboriginal people (22.7 compared with 12.4 per 10,000), while the prevalence of CPO was no different between Aboriginal and non-Aboriginal populations (7.2 compared with 6.7 per 10,000 respectively) (Bower et al., 1989). Our current

study, over a longer period, emphasises the differences in the prevalence of OFCs between these two populations. Australia wide, from 1998 to 2003, while reported rates were lower than those in WA, the birth prevalence of all OFCs was 50% higher among Aboriginal infants than non-Aboriginal infants (25.3 and 17.1 per 10,000 births) (Australian Institute of Health and Welfare, 2009). These lower rates in Australian data compared with WA registrations are likely due to ascertainment (many states report only hospital discharge data, or data to one year of age), and the reporting of Aboriginal status may not be as complete in other Australian states (Australian Institute of Health and Welfare, 2010). Tobacco smoking during pregnancy has been shown to increase the risk of CL±P by 34%, and CPO by 22% (Little et al., 2004). High rates of smoking during pregnancy (42-51%) in Aboriginal women (Australian Bureau of Statistics, 2010; Laws et al., 2010) may be contributing to their high prevalence of OFCs. In contrast, around 14% of non-Aboriginal women report smoking during pregnancy (Laws et al., 2010).

Given the quality and completeness of the WARDA data, it is also not surprising that prevalence rates of OFCs with additional anomalies are high (31% for CL±P and 61% for CPO). Comparisons with other studies are difficult and the reported prevalence of additional anomalies varies widely. While the distinction between isolated and non-isolated cases has improved with newer technology, and wider access to diagnostic services (Wyszynski et al., 2006), these diagnoses may still vary in different areas depending on the availability of clinical services, and their uptake (IPDTC Working Group, 2010).

In pooled data from 14 European registries between the 1980s and 2000, where surveillance methodology is similar to that in WA, 29.2% of individuals with CL±P had associated anomalies (11.4% comprised recognised conditions [including chromosomal, monogenic, sequences and anomalies of known aetiology] and the remaining 17.8% had multiple anomalies of unknown aetiology) (Calzolari et al., 2007). While these results are similar to those from WA, the proportion of clefts occurring with associated anomalies varied considerably by registry.

Including all minor and major anomalies may also contribute to the higher prevalence rates of OFCs with additional anomalies. However, even where minor anomalies are included, some, such as micrognathia, show variability in type and severity and diagnosis may be a subjective opinion (Wyszynski et al., 2006). Compared with WA (where 31% of CL±P and 61% of CPO occurred with additional anomalies) an international collaboration of 54 registries reported that 23% of individuals with CL±P were categorised as having additional anomalies

(IPDTC Working Group, 2010) and data from 30 European registries found that 45.2% of CPO occurred with another anomaly (18.0% unknown aetiology and 27.2% recognised conditions) (Calzolari et al., 2004). In both these studies minor anomalies were not regarded as additional anomalies, and the proportions reported are lower than those for WA. Again, wide variation was reported between individual registries.

The length of follow-up also influences classification between isolated and additional anomalies. In a hospital based study from South America, 7% of OFCs classified as isolated at birth were reclassified as having additional anomalies after one year of follow up (Rittler et al., 2011) and in WA, 12% of all anomalies are diagnosed after one year of age (Bower et al., 2010b). Furthermore, the association of additional anomalies with OFCs will be underestimated if only live born infants are included; European data for infants with CL±P show that only 20% of live born infants have additional anomalies compared with 80% of stillborn infants and 94% of pregnancies terminated (Calzolari et al., 2007).

While ascertainment may alter the prevalence of the additional conditions reported, the pattern of associated diagnoses is similar. Anomalies of the musculoskeletal system, limbs, cardiovascular system and central nervous system are most commonly reported, with the proportion generally higher in CPO than in CL±P (Calzolari et al., 2007; Genisca et al., 2009; Sarkozi et al., 2005). The prevalence of musculoskeletal anomalies occurring with CL±P and CPO was high in WA compared with other studies (Genisca et al., 2009; Sarkozi et al., 2005), but similar for CL±P in Europe (Calzolari et al., 2007). In WA the types of musculoskeletal anomalies varied by cleft type. Polydactyly and syndactyly, and limb reduction anomalies were much more prevalent among CL±P than among individuals with CPO, while anomalies of jaw size and position were associated with CPO. Polydactyly and limb reduction anomalies are also commonly associated with CL±P in Europe (Calzolari et al., 2007). These associations by cleft type may indicate different aetiological influences.

This study provides contemporary population based prenatal diagnosis rates for OFCs. The routine use of ultrasound screening in pregnancy has resulted in half the pregnancies in WA since 2000 with CL±P being diagnosed before birth; similar to recent data from Europe (54% from 23 congenital anomaly registers in 2006-2010) (Eurocat, 2012), and England and Wales (64% from seven registers in 2005-06) (Boyd et al., 2011).

Prenatal detection of CPO remains low (Gillham et al., 2009; Offerdal et al., 2008), but may increase with the availability of three-dimensional ultrasound (Martinez-Ten et al., 2012).

Over thirty years of data from this population based register, where ascertainment and data accuracy are high, where all OFCs and additional major and minor congenital anomalies are recorded, and with follow up to six years of age, make this a remarkable data source. This study confirms differences in OFC prevalence between Aboriginal and non-Aboriginal populations, reports the prevalence and type of additional anomalies occurring with OFCs, and describes the types of CPO reported and the age at which they are diagnosed. These data describe the prevalence of OFCs in WA since 1980, provide a baseline for measuring changes in prevalence due to programs targeting risk factors (such as smoking during pregnancy), and are a useful reference for OFC data in Australia and internationally.

## **ACKNOWLEDGEMENTS**

We are very grateful for the support and input from the families with children with orofacial clefts, WA CleftPALS members, as well as the Consumer Reference Group of the WARDA for their valuable input and advice, and editorial skills. Thank you also to Edwina Rudy and Jennifer Quick from the WARDA who also provided advice and suggestions. Thank you to Alan Joyce in the WA Department of Health and Peter Cosgrove for their support with data provision.

There is no conflict of interest to declare.

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Table 1. Birth prevalence (per10,000 births) of infants with OFCs in Western Australia since 1980

	CL±P (1980-2009)			CLO (1980-2009)			CL+P (1980-2009)			CL±P (1980-2004)		
	N	Prev	(95% CI)	N	Prev	(95% CI)	N	Prev	(95% CI)	N	Prev	(95% CI)
All	917	12.05	(11.28, 12.85)	385	5.06	(4.56, 5.59)	532	6.99	(6.41, 7.61)	621	10.12	(9.34, 10.95)
Sex												
Male	578	14.80	(13.62, 16.05)	248	6.35	(5.58, 7.19)	330	8.45	(7.56, 9.41)	277	8.79	(7.78, 9.89)
Female	338	9.12	(8.17, 10.15)	136	3.67	(3.08, 4.34)	202	5.45	(4.73, 6.26)	343	11.50	(10.31, 12.78)
Aboriginality												
Aboriginal	96	21.65	(17.54, 26.43)	37	8.34	(5.88, 11.50)	59	13.31	(10.13, 17.16)	46	12.96	(9.49, 17.29)
Non-Aboriginal	821	11.45	(10.68, 12.26)	348	4.85	(4.36, 5.39)	473	6.60	(6.02, 7.22)	575	9.95	(9.15, 10.79)
Geographic location												
Major city	547	11.52	(10.57, 12.52)	225	4.74	(4.14, 5.40)	322	6.78	(6.06, 7.56)	406	10.66	(9.65, 11.75)
Inner regional	139	12.62	(10.61, 14.90)	60	5.45	(4.16, 7.01)	79	7.17	(5.68, 8.94)	84	10.04	(8.01, 12.42)
Outer regional	94	12.36	(9.99, 15.13)	44	5.79	(4.21, 7.77)	50	6.58	(4.88, 8.67)	51	7.96	(5.93, 10.47)
Remote	130	14.11	(11.79, 16.75)	51	5.53	(4.12, 7.27)	79	8.57	(6.79, 10.68)	75	9.64	(7.58, 12.08)
Socioeconomic quintile												
1 highest	291	12.10	(10.75, 13.57)	129	5.36	(4.48, 6.37)	162	6.74	(5.74, 7.86)	193	10.24	(8.84, 11.79)
2	180	11.11	(9.55, 12.86)	79	4.88	(3.86, 6.08)	101	6.23	(5.08, 7.57)	137	10.60	(8.90, 12.53)
3	201	13.29	(11.52, 15.27)	85	5.62	(4.49, 6.95)	116	7.67	(6.34, 9.20)	133	10.98	(9.19, 13.01)
4	142	11.61	(9.78, 13.69)	50	4.09	(3.04, 5.39)	92	7.52	(6.07, 9.23)	94	9.23	(7.46, 11.30)
5 lowest	96	12.56	(10.17, 15.33)	37	4.84	(3.41, 6.67)	59	7.72	(5.88, 9.96)	58	8.93	(6.78, 11.54)
Average annual % change in rates		-0.10%	(-0.93, 0.73)		0.97%	(-0.29, 2.24)		-0.86%	(-2.00, 0.29)		1.97% <sup>c</sup>	(0.80, 3.16)

Prevalence= prevalence per 10,000 births

Table 2. Characteristics of births with OFCs in Western Australia since 1980

	1980-2009		1980-2004	
	CL±P N=917	CLO N=385	CL+P N=532	CPO N=621
Mean maternal age yrs (95%CI)	28.5 (28.1, 28.9)	28.9 (28.3, 29.5)	28.3 (27.8, 28.7)	29.2 (28.8, 29.6)
	%	%	%	%
Singleton	96.9	95.8	97.7	95.6
Pregnancy outcome				
Live birth	86.3	93.3	81.2	89.5
Stillbirth	3.7	1.3	5.5	3.7
Termination	10.0	5.5	13.4	6.8

Missing data: maternal age n=7, plurality n=3

Table 3. Associations of OFCs with other congenital anomalies Western Australia 1980-2004

	CL±P		CPO	
	N=747		N=621	
	n	(%)	n	(%)
Associated with other anomaly	230	(30.8)	379	(61.0)
Chromosomal <sup>a</sup>	58	(25.2)	59	(15.6)
Other specified diagnosis <sup>b</sup>	47	(20.4)	191	(50.4)
Non chromosomal, non-specified	125	(54.4)	129	(34.0)
System affected <sup>c</sup> (BPA code)				
Nervous (740, 741, 742)	83	(36.1)	80	(21.1)
Eye (743)	35	(15.2)	33	(8.7)
Other facial anomaly (744)	62	(27.0)	134	(35.4)
Cardiovascular (745, 746, 747)	64	(27.8)	91	(24.0)
Respiratory (748)	31	(13.5)	28	(7.4)
Gastrointestinal (750, 751)	34	(14.8)	48	(12.7)
Urogenital (752, 753)	60	(26.1)	72	(19.0)
Musculoskeletal (754, 755, 756)	112	(48.7)	286	(75.5)
Integument (757)	11	(4.8)	30	(7.9)
Other (7590-2,7594, 7597, 7599)	11	(4.8)	18	(4.8)

<sup>a</sup>Chromosomal anomaly BPA code 758

<sup>b</sup>Syndrome, Sequence or Association, BPA codes (7593, 7595-6, 7598)

<sup>c</sup>More than 1 system may be affected

Table 4. Age at which CPO diagnosed, by type of cleft, WA 1980-2004

Age at diagnosis	Hard ± soft palate		Soft palate		Submucous cleft		Bifid uvula	
	N=243		N=77		N=213		N=88	
	n	(%)	n	(%)	n	(%)	n	(%)
<1 year	238	(97.9)	77	(100.0)	180	(84.5)	49	(55.7)
1-<3 years	2	(0.8)	0		9	(4.3)	10	(11.4)
3-6 years	3	(1.2)	0		24	(11.3)	29	(33.0)