

Section C: Assessing Sentinel Facial Features

Fetal exposure to alcohol during the first trimester affects development of facial features. The areas most affected are the orbital region (eyes) and mid-face. The effect of prenatal alcohol exposure on fetal brain growth is also thought to affect the size and shape of the face. A range of facial anomalies can occur as result of prenatal alcohol exposure.

There are three features which commonly occur across age, gender and ethnic groups:

- **Small palpebral fissures:** short horizontal length of the eye opening, defined as the distance from the *endocanthion* to the *exocanthion* (points A and B on photo below)
- **Smooth philtrum:** diminished or absent ridges between the upper lip and nose
- **Thin upper lip:** with small volume

These features are shown in the photo below.



(Photo reproduced with permission from Susan Astley, University of Washington)

Although these facial features may also occur independently as normal variations in the general population (unrelated to prenatal alcohol exposure), when seen ***in combination***,

these facial features are **pathognomonic of and highly specific to prenatal alcohol exposure**. *They are termed the 'sentinel' facial features of FASD*.

Facial anomalies are one of the three diagnostic criteria for FASD, together with prenatal alcohol exposure and neurodevelopmental impairment. A diagnosis of FASD may be made with or without facial features.

- A diagnosis of **FASD with three sentinel facial features** means that the individual has all 3 of the characteristic (or 'sentinel') facial features that have been associated with prenatal alcohol exposure.
- A diagnosis of **FASD with less than 3 sentinel facial features** means that the individual may have 0,1 or 2 of the characteristic facial features

The University of Washington FAS Prevention and Diagnostic Network has developed criteria for FASD sentinel facial features:

- **Short palpebral fissure length (PFL)** 2 or more standard deviations below the population mean (or <3rd percentile). This equates to a z-score of -2 or more.
- **Smooth philtrum** – Rank 4 or 5 on the University of Washington Lip-Philtrum Guide
- **Thin upper lip** – Rank 4 or 5 on the University of Washington Lip-Philtrum Guide

Assessment can be using direct measurement and clinical examination and/or computerised analysis of a digital facial photograph (as described by Astley and Clarren (1, 2). Facial features may alter with age. Diagnosis should be based on the point in time when the features were most clearly expressed.

Further details regarding how to assess sentinel facial features are found in Appendix C.

Considerations regarding assessment of sentinel facial features

Palpebral fissure length (PFL)

PFL growth charts have been developed for populations overseas. In the absence of Australian reference data, we recommend using:

- **Scandinavian (Stromland) charts if a child is under 6 years of age**
- **Canadian (Clarren) charts if a child, adolescent or adult is over 6 years**

The Canadian charts are based on a multi-racial population considered to be a better representation of Australian children, although this has not been qualified by research. As the charts start at 6 years of age, Scandinavian charts need to be used in children under 6 years of age.

For infants and children under 2 years of age, the *corrected age of an ex-premature* child should be used if they are under 2 years of age (similar to other growth parameters such as head circumference, height and weight).

For older adolescent and adults, since PFL matures by 16 years without further changes, PFL norms and z scores for 16 year olds can be used for individuals over 16 years of age (from the Clarren charts).

Upper Lip Thinness and Philtrum Smoothness

Upper lip thinness and philtrum smoothness should be assessed using the University of Washington (UW) Lip-Philtrum Guides, which comprise photographs according to a **5 rank scale**, which the range of **lip thickness** and **philtrum depth** seen in a population (i.e. the normal distribution).

- **Ranks 1, 2 and 3** are not associated with prenatal alcohol exposure, and are **below diagnostic threshold for FASD**
- **Ranks 4 and 5** are also caused by and characteristic of prenatal alcohol exposure and **FASD**, but are also seen in a small proportion of the general population.

The University of Washington has developed guides for two ethnic populations: Caucasian (Guide 1) and African American (Guide 2) – see Appendix C. They recommend:

- Lip-Philtrum Guide 1 should be used for Caucasians and all races (or combinations of races) with lips like Caucasians.
- Lip-Philtrum Guide 2 should be used for African Americans and all races (or combinations of races) with thicker lips like African Americans.



Guides specific to Australian populations have not yet been developed, although research has commenced. In the absence of Australian lip-philtrum guides, the clinician should use charts which best fit the **lip thickness** of the individual they are assessing, *while also considering the ethnic background/s* of the individual.

Nonetheless, Lip-Philtrum Guides specific to every racial group may not to be required due to the lack of a homogenous phenotype for many races, the frequency of multiracial ancestry, and the small magnitude of differences involved.(3) In addition, small palpebral fissure length is the most consistent finding in 2D and 3D studies of facial features of FASD in different ethnic populations and ages, suggesting it is particularly sensitive to prenatal alcohol exposure. Smooth philtrum and thin upper lip are also consistent findings across populations. Recent studies indicate there are racial differences in other PAE related facial features (4, 5).

Other dysmorphic features

Other dysmorphic features have been observed in FASD but are not specific to FASD. These should be documented during assessment and include:

- *Facial features:* Flat nasal bridge, midface hypoplasia (flat midface), epicanthic folds, differences in craniofacial width, ear length and facial depth, widened intercanthal distance, anteverted nares (short upturned nose), micrognathia (6, 7)
- *Other minor congenital anomalies:* clinodactyly (abnormal curving of the fifth finger toward the fourth finger), "Hockey stick" configuration of the upper palmar crease, other palmar crease abnormalities, "railroad track" ears, ptosis, strabismus, decreased elbow pronation/supination, incomplete extension of one or more digits, camptodactyly (permanent flexion of one or both finger interphalangeal joints, most commonly fifth and fourth fingers), shortened fifth digits (7)
- Major birth defects of the cardiac, renal, ocular, auditory and skeletal systems such as optic nerve hypoplasia and septal defects (8-10)

Individual dysmorphic features can occur in multiple syndromes and examination for features that differentiate alternate or co-existing syndromes and other disorders during the diagnostic assessment is essential. Differential diagnosis should include consideration of conditions that have a clinical presentation that is similar to FASD.(9)

If a genetic disorder is suspected, or any uncertainty regarding differential diagnosis exists, review by a clinical geneticist is indicated.

See Appendix D for Syndromes with constellations of features which overlap with FASD. (8)

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2. Astley S. FAS Facial Photographic Analysis Software. 1.0.0 ed. Seattle: FAS Diagnostic & Prevention Network, University of Washington; 2003.
3. Astley SJ. Diagnosing Fetal Alcohol Spectrum Disorders (FASD). *Prenatal Alcohol Use and FASD: A Model Standard of Diagnosis, Assessment and Multimodal Treatment*: Benthan Science Publishers Ltd; 2011.
4. May PA, Gossage JP, Smith M, Tabachnick BG, Robinson L.K., Manning M, et al. Population differences in dysmorphic features among children with fetal alcohol spectrum disorders. *J Developmental and Behavioral Pediatrics*. 2010;31:304-16.
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7. Jones KL, Hoyme HE, Robinson LK, del Campo M, Manning MA, Prewitt LM, et al. Fetal alcohol spectrum disorders: Extending the range of structural defects. *American Journal of Medical Genetics Part A*. 2010;152A(11):2731-5.
8. Chudley A, Conry J, Cook J, Looock C, Rosales T, LeBlanc N. Fetal Alcohol Spectrum Disorder: Canadian Guidelines for Diagnosis. *Can Med Assoc J*. 2005;172:S1 - S21.
9. Leibson T, Neuman G, Chudley A, Koren G. The differential diagnosis of fetal alcohol spectrum disorder. *J Popul Ther Clin Pharmacol*. 2014;21((1)).
10. O'Leary CM, Nassar N, Kurinczuk JJ, de Klerk N, Geelhoed E, Elliott EJ, et al. Prenatal alcohol exposure and risk of birth defects. *Pediatrics*. 2010;126:e:834-50.

Appendix C: Assessment of Sentinel Facial Features

1. Measuring Palpebral Fissure Length

Follow these steps to accurately measure PFL manually:

- Use a small transparent ruler
- Align yourself directly in front of the patient's eye
- Remove glasses, if the patient wears them
- Place the ruler as close to the eye without touching the lashes
- Get the patient to open their eyes wide by looking up at the ceiling without tilting their head upwards
- Repeat this for the other eye

Using the PFL Z-score calculator

The mean PFL measurement (average of the left and right PFL) is typed into the PFL calculator (on the right of the screen). The patient's birth date and the date of measurement is also entered in order to calculate the patient's current age.

The PFL Z scores are then automatically calculated (right column).

To download the PFL Z-score calculator follow this link:

<https://depts.washington.edu/fasdpn/htmls/diagnostic-tools.htm#pfl>

Palpebral Fissure Length (PFL) Z-score Calculator

Instructions: Enter data in yellow cells. All remaining cells will automatically compute.

Patient birth date (mm/dd/yyyy)	Date PFL Measured (mm/dd/yyyy)	Patient's age (years)	Patient's PFL (mm)
July 9, 2012	August 25, 2015	3.13	21.00

PFL Normal Growth Chart	Applicable Age Range	Mean PFL for Normal Population (mm)	Patient's PFL Z-score*
Caucasian Male or Female (Hall, 1989)	0-16 yrs	24.97	-3.01
Canadian Female (Clarren et al., 2010)	6-16 yrs	Too Young	Too Young
Canadian Male (Clarren et al., 2010)	6-16 yrs	Too Young	Too Young
Scandinavian Female (Stromland et al., 1999)	0-18 yrs	23.35	-2.07
Scandinavian Male (Stromland et al., 1999)	0-18 yrs	23.80	-2.41

Using software to assess PFL

PFL can be measured on *digital facial photographs using software developed by the University of Washington*. <https://depts.washington.edu/fasdpn/htmls/face-software.htm>

Considerations

- Manual measurement of palpebral fissure length is prone to error and variation between examiners.
- Measurement by photographic facial analysis is more accurate
- If clinicians may not have access to the software then direct manual measurement should be used.
- When software is available, using both manual and photographic facial analysis is recommended. If there is significant discrepancy between measurements, clinical judgement is required regarding which is more accurate.
 - For example, manual measurements may have been inaccurate due to a child moving or not opening their eyes properly.
 - Photographs might be affected by similar issues leading to poor quality photos for analysis.

2. Measuring the Philtrum and Lip

The lip and philtrum can be assessed clinically by direct examination using Lip-Philtrum guides developed by the University of Washington.

To obtain Lip and Philtrum Guides

- Digital version for smart phones or tablets can be downloaded
- Hard copies can be ordered.
- Following this link: <https://depts.washington.edu/fasdpn/htmls/lip-philtrum-guides.htm>

Using the Lip-Philtrum Guides during assessment

To use the guide properly, the clinician should:

- Be just below eye level in front of the patient, at the so-called frankfort level.
 - The *frankfort horizontal plane* is a line (green line) that passes through the patient's external auditory canal and the lowest border of the bony orbital rim (eye socket).
 - The physician's eyes (or camera lens) should be directly in line with this plane (see photo on page 77)
 - This is important, e.g. if the physician stands above the plane looking down on the patient, the patient's upper lip could appear thinner than it truly is.
- Hold the guide next to their face (see photo on page 77).
- The patient must have a relaxed facial expression, because a smile can alter lip thinness and philtrum smoothness.
- A short video tutorial on assessing the lip and philtrum using the guides is available at: <https://depts.washington.edu/fasdpn/htmls/lip-philtrum-guides.htm>

Using software to assess the lip and philtrum

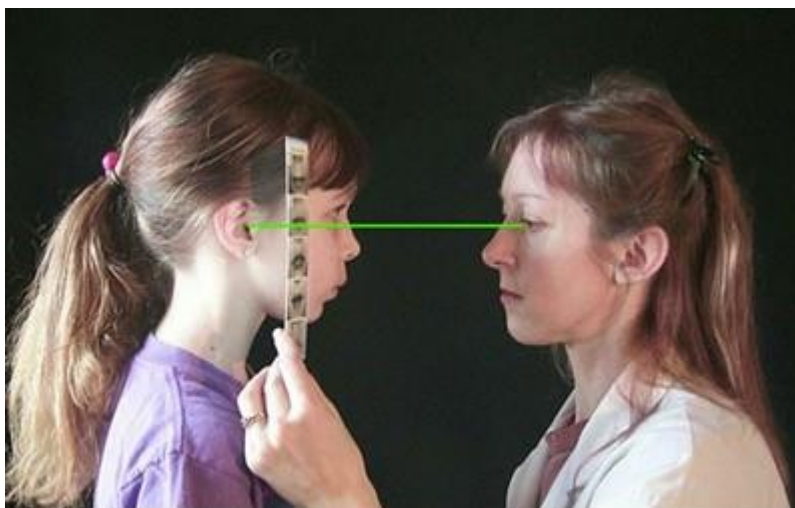
The lip and philtrum can be assessed by *analysis of digital facial photographs using software* developed by the University of Washington.

The software allows the clinician to visually re-assess the patient using the digital photographs, and to calculate lip thickness (lip circularity)

<https://depts.washington.edu/fasdprn/htmls/face-software.htm>

Lip Philtrum Guides

Caucasian		African American		
FASD 4-Digit Diagnostic Code © 2014 Susan Astley, University of Washington fasdpu.org		FASD 4-Digit Diagnostic Code © 2014 Susan Astley, University of Washington fasdpu.org		
5	5	5	5	Sentinel Facial Features
4	4	4	4	
3	3	3	3	Not associated with prenatal alcohol exposure, below diagnostic threshold for FASD
2	2	2	2	
1	1	1	1	
Lip-Philtrum Guide 1	Philtrum Guide	Lip-Philtrum Guide 2	Philtrum Guide	
For use as a digital image on a smartphone or tablet. Printing invalidates Guide. Square ensures length by width ratio of image is correct.		For use as a digital image on a smartphone or tablet. Printing invalidates Guide. Square ensures length by width ratio of image is correct.		
□		□		
Frontal view and ¾ view		Frontal view and ¾ view		



Images: Courtesy of Professor Susan Astley

Photo demonstrating how to use lip-philtrum guides including positioning at the *Frankfort* level (green line).

Appendix D: Syndromes with constellations of features which overlap with FASD

Syndrome	Overlapping features	Features of this syndrome that differentiate it from FASD
Aarskog syndrome	Widely spaced eyes, small nose with anteverted nares, broad philtrum, mid-facial recession	Round face, down-slanted palpebral fissures, widow's peak, prominent "lop" ears, specific contracture of digits on extension. Inherited as an x-linked trait. Molecular defect identified
Brachman-deLange or Cornelia deLange syndrome	Long philtrum, thin vermilion border of upper lip, depressed nasal bridge, anteverted nares, microcephaly	Single eyebrow across eyes and forehead (synophrys), long eyelashes, downturned corners of mouth, short upper limbs particularly involving ulnar side, very short stature. Molecular defect identified
Dubowitz syndrome	Short palpebral fissures, widely spaced eyes, epicanthal folds, variable ptosis (droopy eyes) and blepharophimosis, microcephaly	Shallow supraorbital ridges, broad nasal tip, clinodactyly
Fetal anticonvulsant syndrome (includes fetal hydantoin and fetal valproate syndromes)	Widely spaced eyes, depressed nasal bridge, mid-facial recession, epicanthal folds, long philtrum, thin vermilion border of upper lip	Bowed upper lip, high forehead, small mouth
Maternal phenylketonuria (PKU) fetal effects	Epicanthal folds, short palpebral fissures, long poorly formed philtrum, thin vermilion border of upper lip, microcephaly	Prominent glabella, small upturned nose, round face
Noonan syndrome	Low nasal bridge, epicanthal folds, wide spaced eyes, long philtrum	Down-slanted palpebral fissures, wide mouth with well-formed philtrum, protruding upper lip. Molecular defect identified
Toluene embryopathy	Short palpebral fissures, mid face hypoplasia, smooth philtrum, thin vermilion border upper lip, microcephaly	Large anterior fontanelle, hair patterning abnormalities, ear abnormalities
Williams syndrome	Short palpebral fissures, anteverted nares, board long philtrum, maxillary hypoplasia, depressed nasal bridge, epicanthic folds, microcephaly	Wide mouth with full lips and pouting lower lip, stellate pattern of iris, periorbital fullness, connective tissue dysplasia, specific cardiac defect of supravalvular aortic stenosis in many. Chromosome deletion on 7q (by chromosome microarray or specific 7q FISH (fluorescent in situ hybridization) probe analysis
Other chromosome deletion and duplication syndromes	Many have short palpebral fissures, mid-facial hypoplasia, smooth philtrum	Chromosomal analysis by chromosome microarray

Adapted from: Chudley AE, Conry J, Cook JL, Loock C, Rosales T, LeBlanc N. Fetal Alcohol Spectrum Disorder: Canadian guidelines for diagnosis. *Can Med Assoc J.* 2005;**172**:S1-S21, (with permission of the author & journal)

Additional reference: Leibson T, Neuman G, Chudley AE, Koren G. The Differential Diagnosis of Fetal Alcohol Spectrum Disorder. *J Popul Ther Clin Pharmacol.* 2014; **21**: e1-30.

<http://www.jptcp.com/pubmed.php?articleId=448>