Validation of cleft subphenotyping accuracy as recorded on the CLEFTSiS database.

Dr W.A. McBride BDS, MDSc
Dr K Carroll BDS, MB ChB
Prof P.A. Mossey BDS, PhD
Dr G.T. McIntyre BDS, PhD

University of Dundee, Scotland
Rationale

- Not all CP or CL/P are phenotypically alike, and it is logical to assume that there are genetic differences.

- Genetic differences between CL and CLP have been reported (eg Rahimov et al., 2008).

- Cleft subphenotyping is regarded as a pre-requisite to improving our ability to determine genetic aetiology.
Background
Scotland
Cleft palate 50%
Cleft Lip and Palate 29%
Cleft Lip 21%

East England
Cleft palate 43%
Cleft Lip and Palate 37%
Cleft Lip 20%

Dr K Carroll (2012)
- Unilateral CL was 2x more likely to be incomplete for both registers.

- Clefting of the lip in Unilateral CLP was 9x more likely to be complete for both registers.

- For isolated CP involving the soft palate only completeness was more likely (7.5x in Scotland & 9.25x in England).

Dr K Carroll (2012)
Isolated CP involving the hard palate was more prevalent in Scotland, whilst completeness was approximately 2x more likely for both registers.

Complete clefting of the hard palate was more likely from the English registry than the Scottish for individuals with CLP (97% vs 93%; P<0.05).

Dr K Carroll (2012)
LAHSAL and ICD10

- LAHSAL is compatible with the ICD10 coding yet can describe much more.
- ICD10 coding of Q37.0 (cleft of the hard palate with bilateral cleft lip) has 16 LAHSAL codings when all of the permutations of laterality and completeness are considered.
- The ICD10 codings do not provide scope for the recording of laterality, completeness, microforms or clefts affecting the alveolus.
CLEFTSiS Validation: Method

* Cleft phenotype, as determined by the LAHSAL classification, should be identifiable from the photographs stored on the electronic patient record.

* Cleft phenotype as determined from these clinical records was then compared to the classification as provided in Excel format from the CLEFTSiS team.
Method

- All appropriate electronic records on the CLEFTSIS Database from April 2000 until August 2011 were employed in this study.

- There were 730 patient records identified as appropriate once exclusions were applied.

- Observer 1 (Orthodontic Specialist Registrar) viewed each record and recorded the LAHSAL phenotype where possible.

- Where not possible, additional classifications were required for no views present for patient (x), no views of specified anatomical area (n), and image present but unclear (u).
Thirty cases chosen at random using a web based random number generator (giving 180 variables) were scored by 3 additional observers.

* Observer 2 = Professor in Craniofacial Development and Dentofacial Orthopaedics
* Observer 3 = Consultant in Orthodontics
* Observer 4 = Specialist registrar in Orthodontics

Kappa statistic used to compare inter- and intra-observer reliability.
### Intra- and Inter-Observer Agreement

<table>
<thead>
<tr>
<th>Observer</th>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Observer 3</th>
<th>Observer 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observer 1</td>
<td>.992**</td>
<td>.959</td>
<td>.846</td>
<td>.833</td>
</tr>
<tr>
<td>Observer 2</td>
<td></td>
<td>.822</td>
<td>.809</td>
<td></td>
</tr>
<tr>
<td>Observer 3</td>
<td></td>
<td></td>
<td>.856</td>
<td></td>
</tr>
</tbody>
</table>

Kappa score of 0.81 – 0.99 represents almost perfect agreement.
## Results

<table>
<thead>
<tr>
<th></th>
<th>Kappa Value</th>
<th>No. of records</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lip right</td>
<td>.825</td>
<td>361 (49%)</td>
</tr>
<tr>
<td>Alveolus right</td>
<td>.862</td>
<td>343 (47%)</td>
</tr>
<tr>
<td>Hard palate</td>
<td>.825</td>
<td>142 (19.5%)</td>
</tr>
<tr>
<td>Soft palate</td>
<td>.638</td>
<td>99 (13.6%)</td>
</tr>
<tr>
<td>Alveolus left</td>
<td>.776</td>
<td>343 (47%)</td>
</tr>
<tr>
<td>Lip left</td>
<td>.812</td>
<td>349 (47.8%)</td>
</tr>
</tbody>
</table>
Conclusions

* Subphenotypic variation exists between regions.

* Further evidence that isolated Cleft Lip may be a distinct genetic entity.

* The correlation between Observer 1 and the original CLEFTSiS recording was good.

* Subphenotyping as per the LAHSAL classification is highly reliable, reproducible, relevant and accurate.
Acknowledgements

* Professor Peter Mossey
* Dr Grant McIntyre
* Dr Kris Carroll
* Mrs Mhairi Gallagher

