In Prader-Willi syndrome (PWS), the two common etiologies are paternal deletion of chromosome 15q11-13 (~70% of affected persons) and maternal uniparental disomy 15 (UPD) (~25%). Cassidy et al. [1] evaluated 37 individuals with deletion PWS and 17 with UPD to determine if there were phenotypic differences and reported that those with UPD have a higher likelihood of an atypical face, often rounder displaying a broader forehead and a flatter/broader nasal bridge. Allanson et al. [2] followed up with an objective study of 109 individuals with PWS. Measurements of eyes, ears, nose, mouth, facial widths, lengths and circumferences were taken. The raw data were compared to norms and converted to 2 scores to control for age and sex differences. Results showed agreement with the previous study: persons with UPD have a longer face, more protuberant nose with a narrower base, smaller mouth, and broader or more prominent mandible.

We revisited the 1999 study in order to: (1) Validate the analysis using different statistical machinery; (2) Examine the age-related differences between the two etiologies; and (3) Evaluate image-based differentiation.

For 1+2, The data of 73 patients from [2] were used. Instead of employing population norms to obtain 2 scores, the R Matching package was used to match individuals based on gender and age.

Method:
A series of anthropometric measurements was obtained on each subject using published methods. These dimensions were chosen to represent craniofacial widths, depths, lengths and circumferences plus details of ears, eyes, nose and mouth structure. Measurements were taken by one of the authors (JEA).

Results:
The results reveal that, in the younger age group, nasal base and mouth width are significantly reduced in UPD, while in the older group, inner canthal distance and ear length are larger in UPD. After normalizing measurements by OCR, these results remain significant. Reduced minimum frontal distance is another differentiator of UPD under the age of 8, while reduced mouth width differentiates above age 8. The successful utilization of normalized measurements supports the future use of ratios of distances extracted from images.

CONCLUSIONS AND FUTURE WORK
Since UPD is the less prevalent etiology and has a subtly different phenotype, there is a risk of under-diagnosis. In a future study we plan to test this hypothesis using blinded dysmorphologist assessment and automatic facial analysis tools. We would assess whether this risk could be reduced by training automatic systems to identify the individual etiologies.