The evaluation of dysmorphism remains challenging. The presence of three or more minor anomalies is often used as clinical criterion. However, this requires expertise in the evaluation of facial features. The fields of dysmorphology and syndromology are rapidly advancing, triggered by developments in testing technologies such as next generation sequencing, as well as automated sorting of syndromes. There is a need for tools that offer a more objective and faster recognition of dysmorphism and syndromes. Face2Gene (F2G) is a widely adopted tool for recognition of syndromes from 2D facial photographs.

In the present study, we explored how this tool could aid in the recognition of facial dysmorphism and how it could react to factors such as age, sex and ethnic background. Different cohorts were studied including unselected Congolese newborns, Congolese children with intellectual disability, children with Down syndrome (DS) from DR Congo and Rwanda (African ethnicity), from Belgium (Caucasian) and Guadeloupe (mixed ethnicity), and a cohort of healthy adult Congolese volunteers.

We used F2G to extract facial features from facial photographs, calculate dysmorphism scores and study the effect of ethnic origin, age and gender in different cohorts. We observed that F2G overestimated the incidence of individual minor facial features in the cohort of Congolese newborns. F2G detected facial dysmorphism, defined as the simultaneous presence of three or more minor facial anomalies, with a sensitivity of 37.5% and a specificity between 94-98%. This suggest that F2G performs better in a holistic approach rather than feature based approach in African individuals.

In addition, F2G was able to clearly distinguish Congolese children aged above 15 years from those between 10-14 years based on their facial photographs (AUC=0.874). F2G also distinguished Congolese boys versus girls only from the age of 25 years (AUC=0.998). We concluded that age and gender play a significant role in baseline morphology and in dysmorphism after puberty.

It was not possible to separate unselected Congolese newborns based on the geographical province of parents within DRC. Interestingly, a clear distinction was made between children with DS from different countries. The African (DR Congo and Ruanda) DS patients were very distinct from Caucasian DS patients from Belgium (AUC=1.000 and AUC=1.000) within the same range of age. Moreover, mixed ethnicity DS patients from Guadeloupe were clearly distinct from Belgian patients (AUC=1.000) but closer to Congolese DS patients (AUC=0.741). This suggests that ancestral genetic background influences the phenotypic expression of DS.