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Accounting for both population and familial genetic factors improves the accuracy of growth screening: Turner syndrome as a model

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Background

Height varies between and within populations, and genetic factors explain about 80% of this variation (1). Accounting for genetic factors in the screening of growth disorders may improve its accuracy.

Objective

The aim of this study was to evaluate the impact of population and familial level genetic factors in the screening of growth disorders. Turner syndrome (TS) was used as a target condition for screening.

Subjects and methods

Height data of 124 TS girls (64 with karyotype 45,XO) with 2,020 measurements were converted to height SDS (HSDS) using either a population-specific (2) or a multi-ethnic WHO growth standard (3) for evaluation of population-level genetic factors. The impact of familial-level genetic factors in screening was evaluated by including target height (TH) SDS (4) calculated using parental heights.

ROC curves were calculated comparing the HSDS deviation from the mean of the population, HSDS deviation from the TH SDS and combination of these two (HSDS or TH SDS) using contemporary national growth reference (2).

Results

Accuracy of height screening was better if a population-specific growth reference was used instead of the multi-ethnic WHO standard: with 99% specificity, 50% of TS girls were identified with population-specific reference in and 20% with WHO standard, respectively (**Figure 1**). The screening accuracy was further improved with inclusion of TH SDS deviation rule in combination to population-specific reference HSDS rule (**Figure 2**).

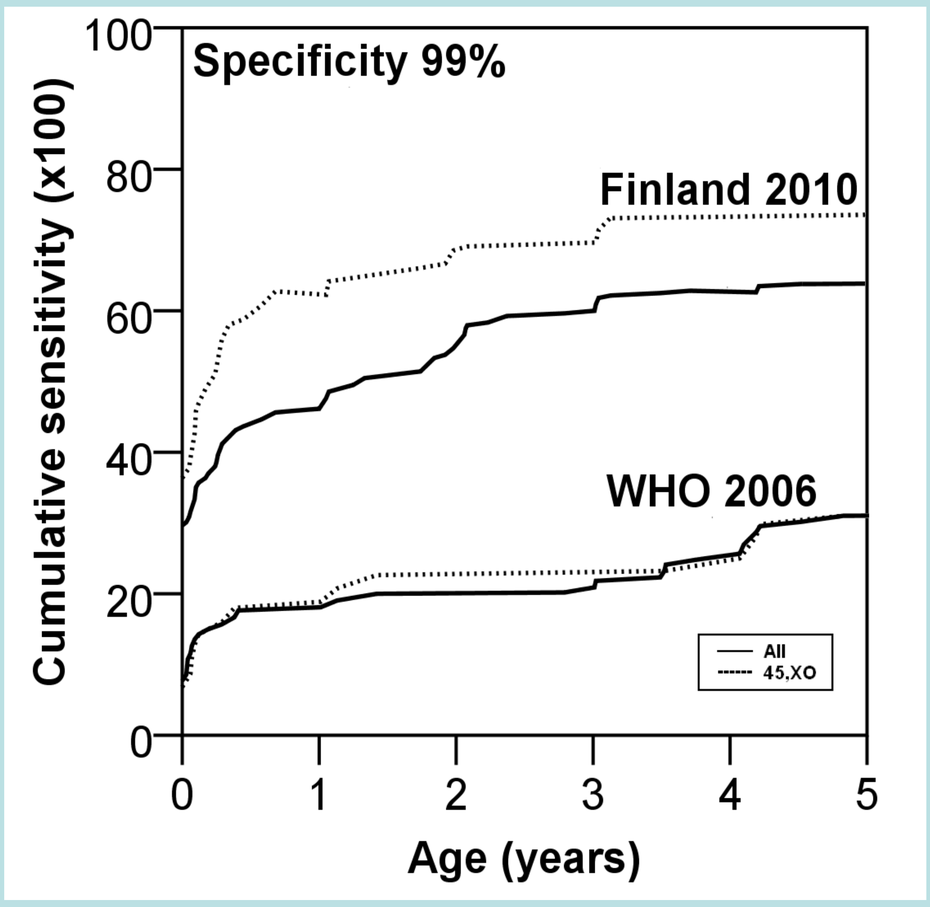

Figure 1. Cumulative sensitivities for growth screening with the specificity of 99% for detecting abnormal height in 124 Turner syndrome (TS) girls (solid lines) and in subsample of TS girls with karyotype 45,XO (dashed lines) when heights were converted to SDSs according to the contemporary Finnish growth reference (upper lines) (2) or the WHO growth standard (lower lines) (3).

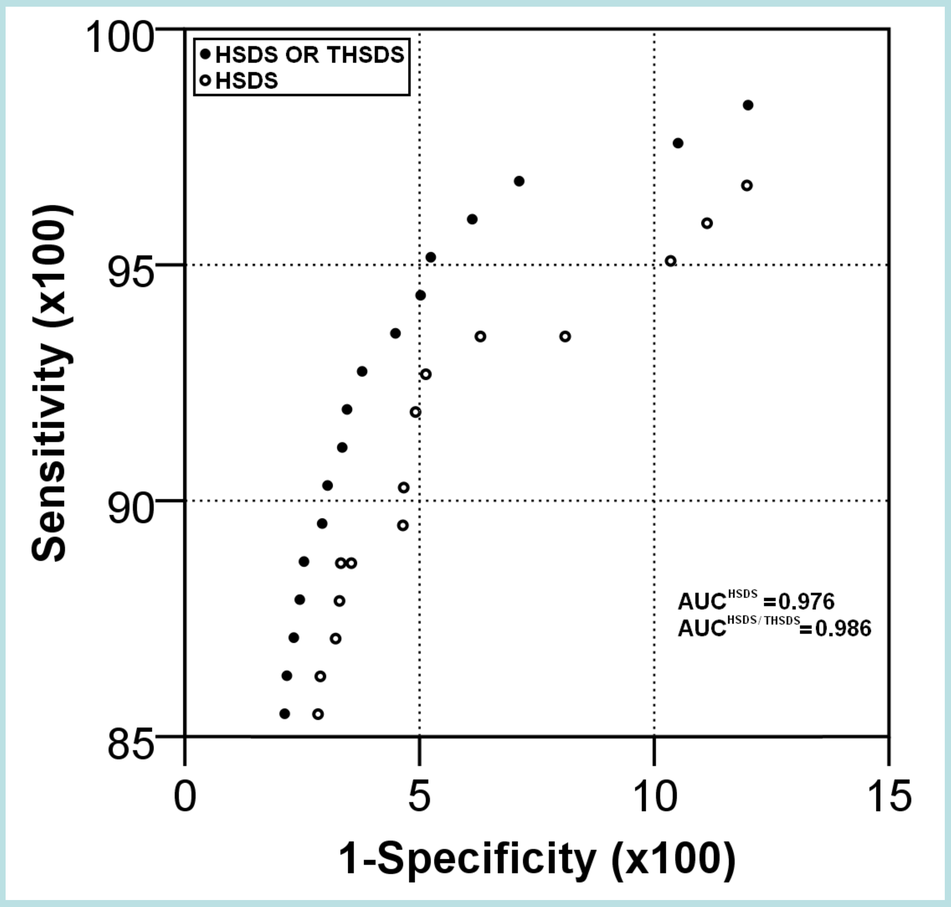

Figure 2. ROC curves for the growth screening using height SDS (HSDS) rule (circles) and combination of HSDS or target height (TH) SDS rule (dots) in the Turner syndrome population (n=124). Areas under curves (AUCs) for both rules are shown.

Conclusions

These findings indicate the superiority of population-specific growth references to a multi-ethnic growth standard in screening for abnormal growth in childhood. The best screening accuracy is obtained by accounting for both population and familial level genetic factors. This is reached by using a population-specific growth reference, and examining HSDS both against population mean and TH based on parental data.

References

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