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Individual growth curve models for assessing evidence-based referral criteria in growth monitoring

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SUMMARY

The goal of this study is to assess whether a growth curve model approach will lead to a more precise detection of Turner sydnrome (TS) than conventional referral criteria for growth monitoring. The Jenss–Bayley growth curve model was used to describe the process of growth over time. A new screening rule is defined on the parameters of this growth curve model, parental height and gestational age. The rule is applied to longitudinal growth data of a group of children with TS ($n = 777$) and a reference ($n = 487$) group. The outcome measures are sensitivity, specificity and median referral age. Growth curve parameters for TS children were different from reference children and can therefore be used for screening. The Jenss–Bayley growth model, which uses all longitudinal measurements from birth to a maximum age of 5 years with at least one measurement after the age of 2, together with parental height and gestational age can achieve a sensitivity of 85.2 per cent with a specificity of 99.5 per cent and a median referral age of 4.2 (the last measurement between the age of 2 and 5 of each child is considered to be the moment of referral). Sensitivity increases by 2 percentage points when decreasing the specificity to 99 per cent. The Jenss–Bayley growth model from birth to a maximum age of 8 years with at least one measurement after the age of 2, together with parental height results in a sensitivity of 89.0 per cent with a specificity of 99.5 per cent and a median referral age of 6.1. For a specificity of 98 per cent, we obtain a sensitivity of 92.3 per cent. In comparison to conventional rules applied to the same data, sensitivity is about 11–30 percentage points higher at the same level of specificity for the Jenss–Bayley growth rule. We conclude that from the age of 4, growth curve models can improve the screening on TS to conventional screening rules. Copyright © 2005 John Wiley & Sons, Ltd.

KEY WORDS: Turner syndrome; growth; screening; Jenss–Bayley; longitudinal studies

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INTRODUCTION

Measuring height and weight is a routine part of child health care. The goal is to assess whether growth patterns of individual children deviate from the reference population so as to identify diseases and conditions that manifest themselves through abnormal growth. An example is Turner syndrome (TS), a chromosomal disorder that occurs in about 1 of 2500 female live births and that leads to seriously retarded height. There is an increased risk for cardiac, renal, thyroid and auditory abnormalities associated with TS. Until recently, no evidence-based referral rules existed in growth monitoring. However, recently Van Buuren *et al.* [1] investigated the diagnostic performance of three conventional rules to detect TS. The first rule is based on the absolute height standard deviation score (absolute HSDS rule), which transforms height into the number of standard deviations above or below the median. The second rule takes genetic height potential into account by comparing the height SDS (HSDS) of the child to its target height (TH) SDS (parental height corrected rule) and the third rule signals whether an abnormal deflection in height occurs in terms of a change in HSDS/year (deflection rule). In terms of sensitivity and specificity, the absolute HSDS rule and deflection rule appeared to be inferior to the parental height corrected rule. For children with height from birth to the age of 10, the application of the parental height corrected rule will refer 77 per cent of the girls with TS at a specificity of 99.4 per cent. Combining the parental height corrected rule and deflection rule increases sensitivity to almost 80 per cent with a specificity of 99.4 per cent. The median referral age of the parental height corrected rule and the combined parental height and deflection rule is 5.2 and 5.3 years, respectively [1]. The present study extends this work with referral criteria that are based on fitted individual growth curves, parental height and gestational age.

Growth curve models describe growth over time. They are well suited to analyse longitudinal data when the times of measurements are irregularly spaced. The models include parameters that can be estimated from individual longitudinal data. Some parameters correspond to interpretable quantities such as growth at birth, growth velocity, growth acceleration or deceleration. A number of growth curve models have been suggested in the literature and have been shown to be representative at different periods of life [2, 3]. We considered several of such models, and used the well-known Jenss–Bayley (JB) growth curve for our data. The JB model describes growth of children from birth to 8 years of age. It was successfully applied by Deming and Washburn [4], Manwani and Agarwal [5], Berkey [6] and Dwyer [7]. Other studies investigated the use of growth curve fitting to compare groups. Rarick *et al.* [8] compared the growth pattern of normal children and those with Down's syndrome. Nagai *et al.* [9] studied the growth curves for Japanese patients with Prader–Willi syndrome. Fitted growth curve parameters have also been used as data for analysis of hereditary factors in growth and development [10, 11].

Davenport *et al.* [12] noticed that for children with TS growth retardation starts during the first year. We expect that such differences in growth of children with TS and without TS will be captured by the parameters of the JB model. The goal of this study is to assess whether a growth curve model approach will lead to a more precise detection of TS than conventional referral criteria for growth monitoring. Our strategy is to estimate the effect of each JB growth parameter on the probability of having TS given the observed growth data (prognostic score). Several thresholds for the prognostic score (PS) are simulated to determine its sensitivity and specificity.

MATERIALS AND METHOD

Material

Longitudinal heights from 777 girls with TS were collected from three sources. The National Registry of Growth Hormone Treatment in Children of the Dutch Growth Foundation contains data of all children in the Netherlands receiving growth hormone (GH) treatment. From this registry, all girls with TS ($n = 316$) were selected. These patients were born between 1968 and 1996. In addition, data from 87 girls with TS, born between 1973 and 1988 from the Sophia Children's Hospital and the data of 374 Dutch girls described by Rongen *et al.* [13] were used. The first two sources contain data of girls that were treated with GH and other growth promoting treatment. For this analysis we used only height measurements before treatment.

A reference sample of longitudinal height data was obtained retrospectively for a cohort of all girls ($n = 487$) born in 1989 and 1990 in the municipality of Landgraaf, located in the south of the Netherlands. Data were collected from the records of the local child health care. These are routinely collected data, and they thus include all measurement errors that are being made in practice. The median number of observations/girl was 17. Data were collected in 2001, so the oldest girls were about 11 years old. The data are the same as in van Buuren *et al.* [1].

Models and statistical analyses

The advantage of the JB growth model compared with conventional referral rules is that all individual growth data are used in the referral criteria. The approach consists of two steps. Step 1 reduces the number of measurements into four interpretable parameters by the JB mixed-effects model. Step 2 consists of the application of heteroscedastic models fit by discriminant analysis which estimate the effect of the JB growth parameters, parental height and gestational age in order to estimate the PS. We will compare the results of the JB rule to the best conventional referral rules, which are the parental height corrected rule and the combination of the parental height and the deflection rule [1].

Step 1: JB mixed-effects model

Height was modelled by the non-linear JB model. The parameters of this model were estimated by a mixed-effects model. A mixed-effects model assumes that each growth parameter is the sum of a fixed and a random component, where the fixed components are the same for every individual, and the random components may differ between individuals according to a normal distribution. Therefore, this model accommodates individual variations through the random effects, but ties the individuals together through the fixed effects and the covariance matrix of the random effects. A particular advantage of the mixed model is that it borrows strength across individuals in estimating individual parameters. Thus, having few observations in mixed models is less of a problem compared to the simpler method that estimates the parameters for each individual separately. The random effects represent the deviations of the individual coefficients from their subpopulation average.

First, we studied whether the growth pattern of TS children differ from reference children. In this situation, each of the two groups (reference and TS individuals) is viewed as a subpopulation with its own set of parameter values. Second, we studied the possibility of screening according to the JB rule. If we want to determine whether a new child has TS,

we have to choose in which group we estimate the growth parameters for that child. As the prevalence of TS is small, most children are reference children. Therefore, we most likely assume that each child is a reference child.

For each TS girl, we estimated her growth parameters by fitting her height together with the height of all reference children in a mixed-effects model. To obtain good estimates of the parameters of the growth curve for each TS girl, we assume the following minimal data conditions. The girls have to have at least one measurement between birth and 3 months of age, at least one between 3 months of age and 2 years, and at least one between 2 years and, respectively, 5 or 8 years (depending on the age-stopping-point). We have a total of 182 TS girls.

Let n be the number of children, t the age in years and $y_i(t)$ the height (in cm's) of the ith child at age t with $i=1,\ldots,n$. According to Jenss and Bayley [14] the height of the ith child can be modelled as

$$y_i(t) = a_i + b_i t - \exp\{c_i + d_i t\} + \varepsilon_{it}$$

where a_i, b_i, c_i and d_i are unknown parameters at the individual level and ε_{it} is the measurement error at age t. In addition, we require that the parameters follow a multivariate normal distribution across individuals. Then, for $i=1,\ldots,n$, the two types of dependencies of the response variable height on age that were used are given by the following model:

$$y_i(t) = \alpha_1 + \alpha_2 t - \exp\{\alpha_3 + \alpha_4 t\} + \varepsilon_{it}$$

with $\alpha_k = \alpha_{k0} + \alpha_{ki0}, \alpha_{k0}$ fixed effects and α_{ki0} random effects, for $k=1,\ldots,4$.

This model has a linear component $\alpha_1 + \alpha_2 t$ in which the parameter α_2 determines infant growth velocity, and an exponential component $\exp\{\alpha_3+\alpha_4 t\}$, which determines the decreasing growth rate shortly after birth [15]. The height at birth is represented by $\alpha_1 - \exp(\alpha_3)$. The measurement errors ε_{it} are assumed to be independent across individuals and to be normally distributed with mean zero and a common variance. For the non-linear mixed-effects procedure it is assumed that the random effects have a multivariate normal distribution with mean vector zero and are independent of the measurement errors. The calculations were performed with the function nlme() in S-plus version 6.1.

Step 2: Discriminant analysis

Discriminant analysis can be used to create a model that explains the grouping of the reference and TS children. Unlike the JB mixed-effects models, which use a weighting process to control the influence of each individual to the estimates by taking into account the number of measurements, the model fit by discriminant analysis considers each individual to contribute equally. This means that children with a small number of measurements, and therefore a lack of information, will be treated the same way as children with a large number of measurements. This can be solved by only including children with a large number of measurements. A disadvantage is that sample selection may occur. As the main results of the mixed-effects model are the parameters (mean, standard error and covariance matrix) of the multivariate normal distribution for the control group and the TS group, we simulated growth parameters from these two multivariate distributions for 1000 individuals/group to overcome the problem of sample selection. We extended the parameters of the two multivariate normal distributions by adding the mean and standard deviation of parental height and gestational age, and adding the correlation between these variables and the growth parameters. With these extended multivariate distributions, we simulated parental height and gestational age for the 1000 simulated

individuals/group. The growth parameters, parental height and gestational age of the 1000 simulated individuals are the predictor variables in the discriminant analysis. As the TS and reference group have different covariance matrices, we used a heteroscedastic discriminant model, which leads to a quadratic discriminant function of the form:

$$d_i(\bar{x}) = \beta_{i0} + \beta_{i1}\bar{x} + \bar{x}^{\mathrm{T}}\beta_{i2}\bar{x}$$

where $\beta_{i0} = -\frac{1}{2}(p\log|\Sigma_i| + \bar{\mu}_i^{\mathrm{T}}\Sigma_i^{-1}\bar{\mu}_i)$, $\beta_{i1} = \bar{\mu}_i^{\mathrm{T}}\Sigma_i^{-1}$ and $\beta_{i2} = -\frac{1}{2}\Sigma_i^{-1}$ with Σ_i the covariance matrix of group i and p-variate normal random variables $N_p(\bar{\mu}_i, \Sigma_i)$ for $i = 1, 2$ (TS and reference group) and $p = 4$ (four parameters of the JB growth model).

In this way, relationships among predictor variables with respect to the grouping variable can be expressed by their mean values and their variance–covariance matrices. The results are the probabilities of having TS given the observed growth data, also called the PS. The PS may differ by age range, the number of growth parameters, parental height and gestational age.

The calculations were performed with the function discrim( ) and predict.discrim( ) in S-plus version 6.1.

Screening rules based on JB model

The new screening rule uses the PS and several thresholds (h). The PS is obtained under three discriminant models, namely the model with only the JB parameters as predictor variables, the model that adds parental height and the model that adds both parental height and gestational age. Each model was applied to both age groups. This results in 6 outcomes, which are named '0–5 JB screening rule', 0–8 JB screening rule' and '0–5 JB parental screening rule', '0–8 JB parental screening rule', '0–5 JB corrected screening rule', 0–8 JB corrected screening rule'.

We formulated the screening rule as follows:

$$\mathrm{PS} > h, \quad h \in (0, 1)$$

The larger the PS, the more likely the individual will have TS. A child with a large PS will be eligible for referral to a physician for further investigation.

Sensitivity was obtained by the number of TS children who have a $\mathrm{PS} > h$, divided by the total number of TS children. Specificity was calculated by the number of reference children who have a $\mathrm{PS} \leqslant h$, divided by the total number of reference children.

Screening rules based on conventional criteria

The best conventional screening rules are the 'parental height corrected rule' and the combination of the parental height corrected rule and the deflection rule [1]. The parental height corrected rule takes genetic height potential into account by comparing the HSDS of the child to its THSDS. The TH is the expected adult height given the heights of the biological parents and corrected for secular trend. For Dutch girls, the relevant formulas are $\mathrm{TH} = (\text{maternal height} + \text{paternal height} - 13)/2 + 4.5$ and $\mathrm{THSDS} = (\mathrm{TH} - 170.6)/6.5$ [16]. The parental height corrected rule is defined as follows.

For ages q to 10 years, refer if $\mathrm{SDS} < c$ and $(\mathrm{SDS} - \mathrm{THSDS}) < d$, with c the SDS cut-off level below which SDS must lie, d the difference between target height SDS and SDS and q

the age (in years) after which the rule is effective. Simulation values are $q = 3$, $c \in \{-2, -2.5\}$ and $d \in \{-2, -2.5\}$.

The deflection rule signals whether an abnormal deflection in height occurs in terms of a change in HSDS/year. In formula:

For any pair SDS_1 and SDS_2 measured at ages X_1 and X_2 (in years), refer if

$$r <= X_1 < X_2 < 10 \text{ and } X_1 - X_2 >= e \text{ and } SDS_2 < f \text{ and } (SDS_2 - SDS_1)/(X_2 - X_1) < g$$

with e the minimal interval (in years) between X_1 and X_2, f the SDS cut-off level below which SDS_2 must lie, g the height velocity change in SDS/year and r the age (in years) after which the rule is effective. For the combination 'parental height corrected and deflection rule', we simulated the values $c = -2$, $d = -2$, $e = 3$, $f = -2$, $g = -0.25$ and q, r are 3. This rule refers children older than age 3 if HSDS is below -2 and if either HSDS is more than 2 SD below the target HSDS, or HSDS shows a deflection of 0.25 SDS/year or more during a period of at least 3 years.

Imputation

Parental height and gestational age were frequently missing (55 per cent of the TS group and 58 per cent in the reference group for parental height and 73 per cent of the TS group and 3 per cent in the reference group for gestational age). We imputed parental height and gestational age under the assumption that the data are missing at random using multivariate imputation by chained equations (mice) [17]. The method created multivariate imputations by applying sequential linear regressions, where each incomplete variable was imputed conditional on all variables in an iterative fashion. The imputation model consisted of age, height SDS, weight SDS, BMI SDS, weight/height SDS, the height of the other parent and gestational age. The number of iterations was set to 15. Predictive mean matching was used to create parental heights imputations. The imputation method includes parameter uncertainty, preserves the multivariate structure in the data and has good coverage properties [18]. The distribution of father's height against mother's height for the real and artificial data is similar in both groups.

Correction

The children in our reference group live in the southern part of the Netherlands, and are on average -0.31 HSDS shorter than the Dutch reference population. This means that in our method the specificity estimate for our Dutch reference sample would become too low. In order to eliminate this bias, we added 0.31 HSDS to the measurements of our reference sample. With the new HSDS, we estimated the new heights for the measurements for the reference children. The outcome measures are based on the new heights.

RESULTS

JB mixed-effect model

We chose to fit the JB mixed-effects model separately for each group. The mixed-effects model assumes each growth parameter to be the sum of a fixed and a random component. Table I

Table I. Results of the JB mixed-effects model. The least squares estimate of the fixed component, the standard error of the random component, residual variances, number of observations, number of children, AIC and BIC are presented for each group.

JB mixed-effects	0–5 years		0–8 years	
model	TS	Reference	TS	Reference
α_1	71.7 (0.38)	72.6 (0.29)	74.3 (0.34)	76.7 (0.29)
α_2	5.78 (0.088)	8.39 (0.072)	5.17 (0.048)	7.16 (0.053)
α_3	3.19 (0.016)	3.08 (0.013)	3.28 (0.012)	3.24 (0.011)
α_4	−1.34 (0.034)	−1.58 (0.028)	−1.12 (0.025)	−1.21 (0.018)
Residuals	1.071	1.073	1.059	1.188
# of measurements	2960	5806	4172	6332
N	525	476	580	484
	AIC = 11 910, BIC = 12 000	AIC = 21 140, BIC = 21 240	AIC = 16 494, BIC = 16 589	AIC = 24 117, BIC = 24 218

shows the least squares estimate of the fixed component along with the standard error of the random component for each group. The fit is represented by the residual variances, Akaike's information criterion (AIC) and Bayesian information criterion (BIC).

All parameters have significant differences in means between the TS group and the reference group ($p < 0.01$). Hardly any differences occur between the residual variances of the TS and the reference group, so the JB mixed-effects model fits the TS and reference groups equally well.

Discriminant analysis

The discriminant analysis yields the number of true-positives and false-negatives. The 0–5 JB growth model, which uses all longitudinal measurements from birth to 5 years of age, can separate the TS girls from the reference girls with a sensitivity of 84.5 per cent and a specificity of 100 per cent. After the age of 8, the sensitivity is equal to 91.3 per cent with a specificity of 100 per cent. Including parental height and gestational age and waiting for 5 years result in a sensitivity of 94.7 per cent with a specificity of 100 per cent. Note that these values are fitted from a screening perspective.

The parameters of the growth curves are fitted separately for the TS group and the reference group and the group allocation in the discriminant analysis was known. In an actual screening context, the information as to which group each case belongs is not present. The following step corrects for this.

JB growth parameters for screening

For 182 TS girls we fitted each TS girl with the 1000 simulated reference children in a mixed-effects model and calculated the sensitivity by using the same discriminant function (based on the simulated values) as before. The results are shown in Table II. For the JB corrected rule with 0.5–2 per cent false-positives, we obtained a sensitivity of between 85.2 and 87.4 per cent for growth from birth till 5 years of age and 89–92.3 per cent from birth till 8 years. Doubling the amount of false-positives from 1 to 2 per cent hardly improves sensitivity for growth from birth till 5 years of age.

Table II. Sensitivity, specificity and median referral age for the JB screening rule, the JB parental screening rule and the JB corrected screening rule from birth till 5 and 8 years, respectively.

	0–5 years			0–8 years		
	JB screening	JB parental	JB corrected	JB screening	JB parental	JB corrected
Specificity (per cent)	Sensitivity	Sensitivity	Sensitivity	Sensitivity	Sensitivity	Sensitivity
99.5	83.0	85.2	85.2	86.3	89.0	89.0
99	84.1	86.7	87.2	89.0	90.1	90.1
98	84.6	86.8	87.4	90.7	92.3	92.3
Median referral age	4.2			6.1		

The median referral age for the 0–5 JB rule is 4.2 and for the 0–8 JB rule is 6.1. Note that the last measurement between the age of 2 and 5 or 8 of each child is considered to be the moment of referral. Figure 1 shows the receiver operation characteristic (ROC) curves for the JB rules.

Comparison with conventional screening rules

We applied the parental height corrected rule to the same 182 TS girls. A total of 85 per cent (to 5 years of age) to 87 per cent (to 8 years of age) have at least one measurement after the age of 3 and are presented in the following sensitivity and specificity. The parental height corrected rule has a maximum sensitivity of 57.1 per cent with a specificity of 99.8 per cent from birth till 5 years of age and a sensitivity of 69.6 per cent with a specificity of 99.4 per cent from birth till 8 years of age. The best JB rule from birth till 5 years of age has a sensitivity of 88.3 per cent with a specificity of 99.8 per cent and from birth till 8 years of age has a sensitivity of 90.5 per cent with a specificity of 99.4 per cent. The best conventional rule (for a high specificity) is the combined parental height and deflection rule. As this rule starts at the age of 3 and must have a minimum period of 3 years, we can only apply this rule to children older than 6 years of age. For the TS children from birth till 8 years of age, the sensitivity is equal to 74.7 per cent with a specificity of 99.9 per cent. The best JB rule has an 11 percentage point higher sensitivity with equal specificity.

DISCUSSION

The use of individually fitted growth curves for detecting TS leads to better results in sensitivity and specificity than the conventional screening rules. Sensitivity increases by up to 30 per cent by specificities near 100 per cent. This improvement may be caused by the fact that conventional screening rules only use part of the information of a growth curve. The JB rule incorporates all available information of the growth process. When it is possible to wait for 4 years, as is typically the case for TS, our results suggests that growth monitoring according to the JB rule generally improves upon the conventional screening rules. The JB rule and the conventional screening rule were developed and tested using the same sample. However, this

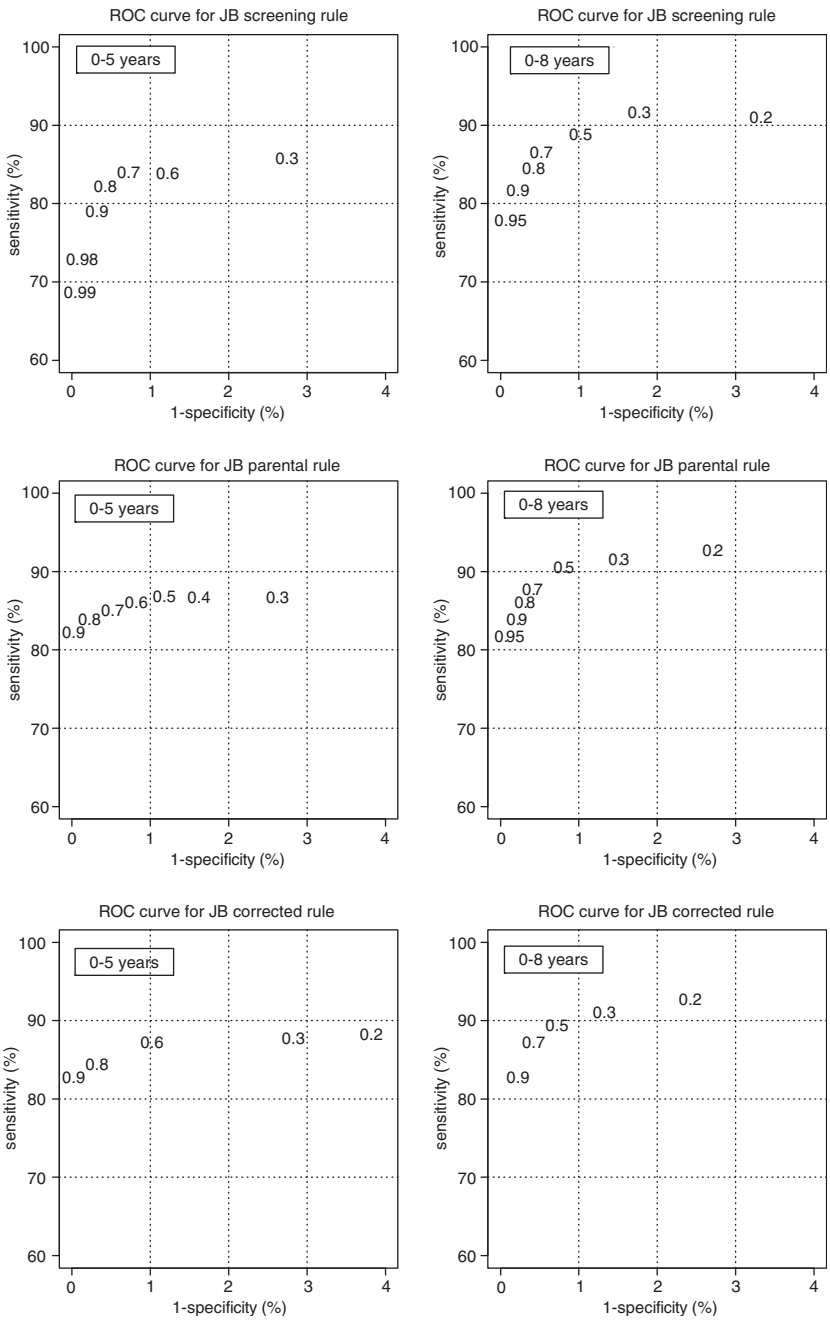

Figure 1. The ROC curves for the JB screening rule (based on growth parameters), the JB parental screening rule (based on growth parameters and parental height) and the JB corrected screening rule (based on growth parameters, parental height and gestational age) from birth till 5 and 8 years, respectively. Several thresholds for the prognostic score (h) are given.

sample is not representative of the larger population of Dutch girls. Therefore, the absolute value of sensitivity and specificity may be different for our population. However, we consider it to be very unlikely that our conclusion that the JB rule is superior to the conventional rules will be different in another sample.

The results show that the four JB parameters taken together are very effective at separating the two populations, but it would be interesting to know which of the four are most important. Table I compares the two sets of parameters, and expressing the differences between them in terms of their standard errors. This shows that α_2 is more than 4 times as important as α_1, α_3 and α_4 (t=48 *versus* t=3, -10 and -10). Therefore, the main growth defect appears to be in the linear part of the JB growth curve model. This means biologically that TS growth appears as constant centile crossing downwards or negative deflection, which suggests that a simpler approach than the JB growth curve model may be equally effective. Therefore, we repeated the analysis using HSDS instead of height, and summarized each child's growth as a linear trend with two parameters; HSDS at birth and a slope. Sensitivity increases from 79 to 89 per cent for the linear HSDS rule from birth to both 5 and 8 years of age with 0.5–2 per cent false-positives. This means that sensitivity is large for the linear HSDS model. However, sensitivity is less optimal than the JB growth curve model. The results of the linear HSDS rule with the combined parental height deflection rule are almost similar, which is not surprising as both rules investigate the deflection of HSDS in combination with maternal and paternal height. The differences lie in the starting point of the linear regression and the number of measurements used to obtain the slope (i.e. the combined rule compares two HSDS measurements successively while the linear HSDS rule takes all measurements into account).

The estimation of specificity and sensitivity for the JB rule is obtained from the same sample of children for which we developed the model. This estimation would be more convincing if they were obtained from a validation sample of children. However, at present we do not have access to a suitable validation data set. A split-sample technique, in which one half of the sample is used to develop the model and the other half is used to measure its performance, was contemplated but the number of children in each group would become too low. Obviously, independent validation and replication would further enhance the credibility of our results.

Requirements of the JB rule as applied here are to have a least two measurements before age 2 and having at least one measurement after the age of 2 to obtain good estimates of the growth parameters. We do not recommend using the JB rule when the minimal data conditions are not met, as the growth curve of a TS child will be smoothed too much toward the average curve for the reference population, which makes it more difficult to distinguish TS from reference children (low sensitivity). When our requirements are met, we see that the predicted curves for TS children will not be smoothed so much toward the reference population. The size of residuals is a good predictor of the smoothness toward a reference population. When the residuals are small, we obtain a good estimation of the growth parameters and not so much pulling toward the reference population. The standard deviation of the residuals of the 182 predicted curves for all TS cases is equal to 0.79. This is less than 1 cm which is small considering the fact that the height range varies between 40 and 130 cm. When the data conditions are not met, conventional screening rules are recommended. More work is needed to determine fruitful combinations of both types of rules.

The median referral age for the JB rule from birth to 5 years of age is 4.2 years. A decrease in median referral age might be obtained by applying the JB rule from birth to the first measurement after the age of 2. Choose a threshold with a large specificity. Some TS

girl will be referred soon after the age of 2 and all other TS girls have to wait until the age of at most 5 years. In this case, the median referral age can be minimized while sensitivity and specificity will stay the same.

In this paper, we used the JB model, but we also considered the first two components of the infancy–childhood–puberty (ICP) growth curve model. The ICP growth curve decomposes linear growth mathematically into three additive and partly superimposed components—infancy, childhood and puberty [3]. The starting point of the childhood component represents the age of onset. Most healthy infants show an abrupt increase in growth rate [3]. Finding the exact age at onset of the childhood phase can only be determined when the interval between measurements is small. As a great number of children do not satisfy this condition, we decided to fix the age of onset at 9 months. Due to computational problems (i.e. convergence problems) of the first two components of the ICP growth curve in the mixed-effects model, we decided to choose the JB growth curve. We also fitted the count model, but this model had convergence problems as well. We applied a polynomial of degree four. To make a comparison between the fit of the JB and a polynomial of degree four (P4), we compared the residuals, AIC and BIC. JB has a better fit than P4.

Application of the JB rule requires a computer system to perform the calculations. Child health care is slowly adopting the use of computers to record the biometrical data. Where this is done, we think that the JB rule can be implemented without too much effort.

CONTRIBUTORS

P.vD. performed statistical analysis and wrote the manuscript. S.vB. and P.V. designed the study, acquired the grant and provided suggestions for improvement. G.Z. contributed the Turner data.

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