SUPPLEMENTARY DATA.

Algorithms to define abnormal growth in children: external validation and head-to-head comparison

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Supplemental Table 1. Auxological and clinical parameters used in the seven studied algorithms.

	Type of algorithm						
	Clinical practice guidelines				Clinical decision rules		
	Single parameter		Combined parameters		Combined parameters		
	WHO criterion (3)	Coventry consensus (4)	Dutch consensus (5)	GHRS criteria (6)	Grote clinical rule (1)	Saari clinical rule for TS (7)	Saari clinical rule for CD (8)
	1995	1998	1999	1999	2007	2012	2015
Auxological parameters used							
Standardised height	X	X	X	X	X	X	X
Standardised BMI							X
Distance to standardised TH			X	X	X	X	X
Height deflection per time interval			X	X			
Absolute height deflection			X		X		
Standardised height deflection						X	X
Standardised BMI deflection							X
Standardised height velocity				X			
SGA with no catch-up after 2 or 3 years			X		X		
Disproportion and/or dysmorphic features			X		X		

BMI: body mass index; CD: celiac disease; GHRS: Growth Hormone Research Society; TH: target height; TS: Turner syndrome; SGA: small for gestational age; WHO: World Health Organization

14 **Supplemental Table 2.** TRIPOD checklist: prediction model validation.

Section	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5,6
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	6
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6,7
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	7,8
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centers.	6,7
	5b	Describe eligibility criteria for participants.	7
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	-
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	7,8,24
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	9,10
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10c	For validation, describe how the predictions were calculated.	8
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	8,9
	10e	Describe any model updating (e.g., recalibration) arising from the validation, if done.	NA
Risk groups	11	Provide details on how risk groups were created, if done.	NA
Development vs. validation	12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8, Suppl data
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	10, Suppl data
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	10,24
	13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	NA
Model performance	16	Report performance measures (with CIs) for the prediction model.	10,11,25,26
Model-updating	17	If done, report the results from any model updating (i.e., model specification, model performance).	NA

Discussion			
Limitations	18	Discuss any limitations of the study (such as non-representative sample, few events per predictor, missing data).	14
Interpretation	19a	For validation, discuss the results with reference to performance in the development data, and any other validation data.	12,13,14
	19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	12,13,14
Implications	20	Discuss the potential clinical use of the model and implications for future research.	12,13,14
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Suppl data
Funding	22	Give the source of funding and the role of the funders for the present study.	17

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Supplemental Table 3. Adaptations needed for the external validation of the seven algorithms.

Algorithms	Criteria	Discussion	Decision
WHO criterion		No adaptation needed	
Coventry consensus		No adaptation needed	
Dutch consensus	The authors suggest two different ages (from birth or from age 3 years) to start the application of the following criteria: distance to standardized target height, height deflection per time interval, and absolute height deflection.	-	We decided to apply these criteria from age 3 years.
	The authors suggest using pubertal signs from age 9 to 12.3 years in girls and from 10 to 13.4 years in boys, but do not detail how to use them.	These variables were not assessed in case series and referent populations	We did not consider pubertal signs to evaluate algorithm performance.
GHRS criteria	The authors suggest applying the following criteria after 2 years: ▪ Standardized height velocity over 1 year < -2 SD (if standardized height ≥ -2 SD) ▪ Standardized height velocity over 2 years < -1.5 SD (if standardized height ≥ -2 SD) ▪ Standardized height velocity over 1 year < -1 SD (if standardized height < -2 SD).	The variable "standardized height velocity" was not assessed because the WHO does not provide velocity growth charts after 2 years.	We replaced this variable after 2 years of age for height deflection per time interval with a cutoff at -0.5 SD.
Grote decision clinical rule	The authors suggest using emotional deprivation, and disproportion and/or dysmorphic features but do not detail how to use them.	These variables were not assessed in case series and referent populations.	We did not consider these variables to calculate algorithm performance.
Saari decision clinical rule for Turner syndrome	The authors do not provide cut-offs to use for defining abnormal growth. They were contacted to provide a suggested threshold but did not provide a clear cutoff.	-	After discussion within co-authors, we decided to apply the following criteria: ▪ Standardized height < -2.2414 ▪ Distance to standardized target height < -2.2414 ▪ Standardized height deflection < -2.2414

Saari decision clinical rule for celiac disease	The authors do not provide cut-offs to use for defining abnormal growth.	-	After discussion within co-authors, we decided to apply the following criteria: ▪ Standardized height < -2.2414 ▪ Standardized BMI < -2.2414 ▪ Distance to standardized target height < -2.2414 ▪ Standardized height deflection < -2.2414 ▪ Standardized BMI deflection < -2.2414

GHRS: Growth Hormone Research Society; TH: target height; WHO: World Health Organization.

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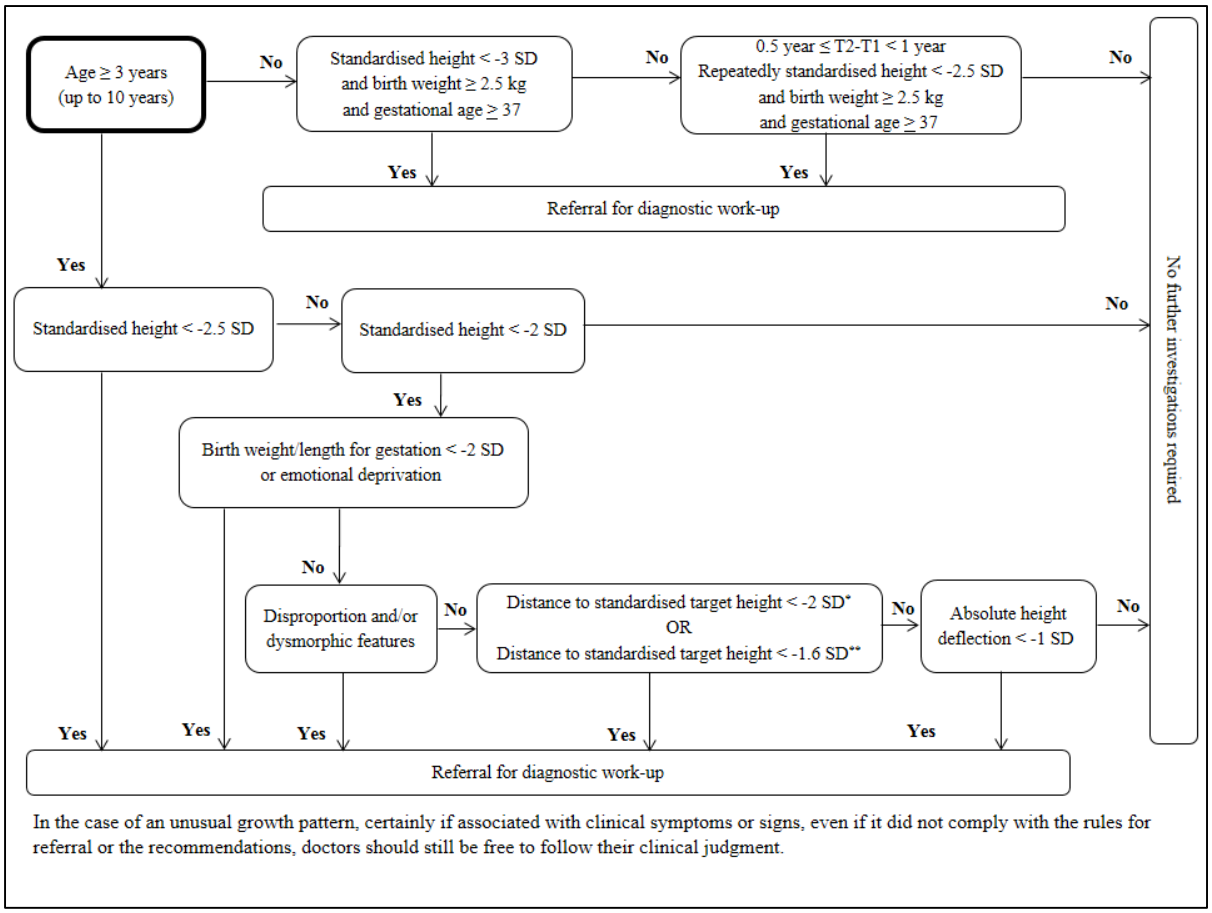
Supplemental Fig. 1. Grote clinical decision rule used to define abnormal growth (1) -from Scherdel and al (2) with permission-.

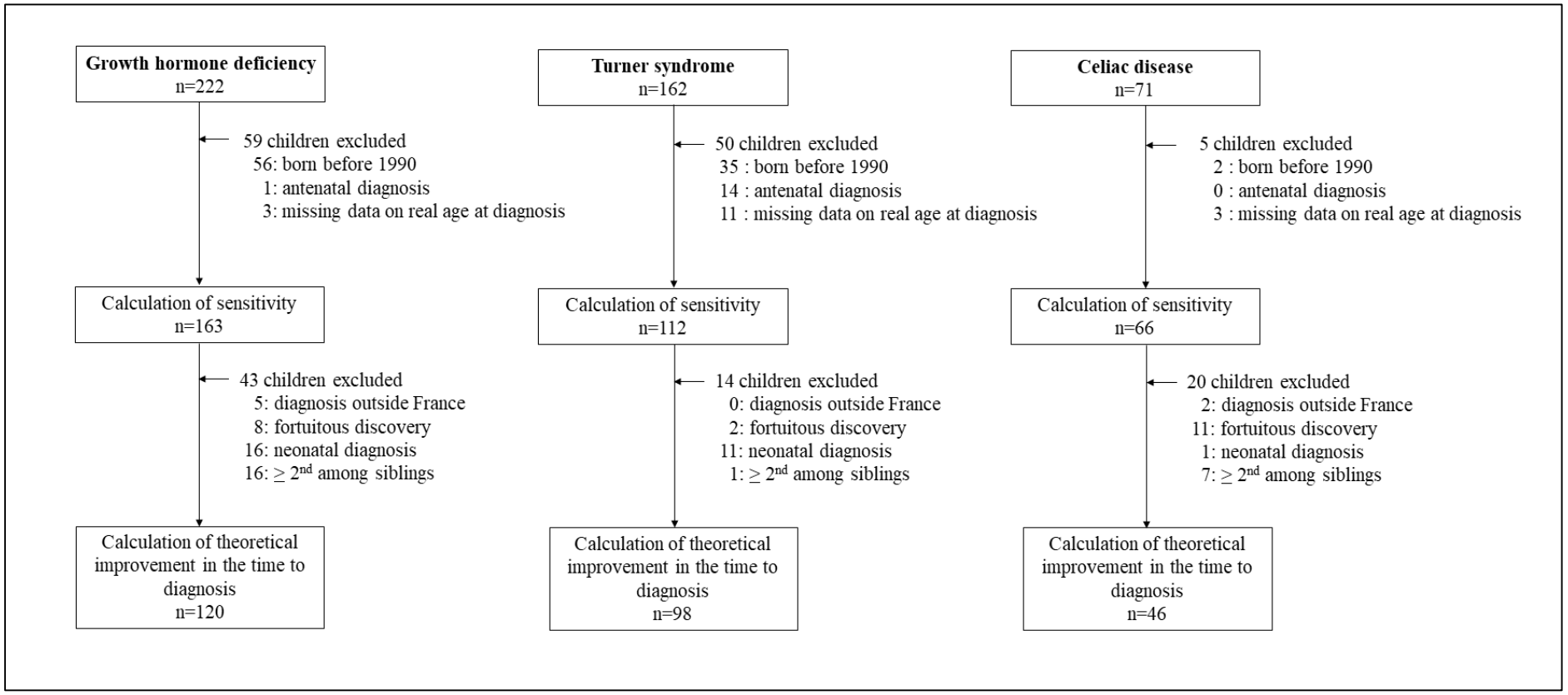


T1: age at first measurement; T2: age at second measurement;

*the target height was calculated by Tanner's second method with additional correction for secular trend.

**the calculation of target height was updated and it was calculated by the Hermanussen and Cole method (9).

Supplemental Fig. 2. Flowchart for the selection of case series.



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