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Pubertal Development in The Netherlands 1965–1997

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ABSTRACT

We investigated pubertal development of 4019 boys and 3562 girls >8 y of age participating in a cross-sectional survey in The Netherlands and compared the results with those of two previous surveys. Reference curves for all pubertal stages were constructed. The 50th percentile of Tanner breast stage 2 was 10.7 y, and 50% of the boys had reached a testicular volume of 4 mL at 11.5 y of age. Median age at menarche was 13.15 y. The median age at which the various stages of pubertal development were observed has stabilized since 1980. The increase of the age at stage G2 between 1965 and 1997 is probably owing to different interpretations of its definition. The current age limits for the definition of precocious are close to the third percentile of these references. A high agreement was found between the pubic hair stages and stages of pubertal (genital and breast) development, but slightly more in boys than in girls. Menarcheal age was dependent on height, weight, and body mass index. At a given age tall or heavy girls have a higher probability of having menarche compared with short or thin girls. A body weight exceeding 60 kg (+1 SDS), or a body mass index of >20 (+1 SDS), has no or little effect on the chance of having menarche, whereas for height such a ceiling effect was not observed. In conclusion, in The Netherlands the age at onset of puberty or menarche has stabilized since 1980. Height, weight, and body mass index have a strong influence on the chance of menarche. **(*Pediatr Res* 50: 479–486, 2001)**

Abbreviations

BMI, body mass index
P_{50}, 50th percentile
P_3, 3rd percentile
P_{97}, 97th percentile
SDS, SD score

The development and first appearance of secondary sexual characteristics can be regarded as a reflection of the overall physiologic development in adolescence (1). The continuous process of pubertal development is usually subdivided into discrete numerical stages, as proposed by Marshall and Tanner (2, 3).

The assessment of pubertal stages in the individual child or adolescent in the clinic is only useful if recent and reliable reference data from the same population are available for comparison. As in many European countries a positive secular trend with regard to height, accompanied by a decrease of the age at onset of puberty (1, 4, 5), has been observed, nationwide reference data should be collected at 10- to 20-y intervals. If the age at onset of puberty would indeed decrease, the definition of precocious and delayed puberty should be adjusted. In fact, in the United States it was recently proposed to revise the guidelines for the evaluation of girls with precocious puberty (6, 7).

Besides clinical reasons, there are also scientific reasons to study pubertal development in a large population-based sample of healthy children and adolescents. First, it is unclear whether the secular trend with regard to body stature is invariably associated with a trend toward earlier pubertal development. Second, there are few data on the association between the markers of the maturation process of the hypothalamo-pituitary-gonadal axis (breast development in girls and genital stage in boys) and the occurrence of pubic hair. One would suspect that the agreement between gonadal (G or B stage) and pubic hair development (P stage) should be higher in boys than in girls, as pubic hair is caused by androgen production. Third, there are observations suggesting that pubertal development is influenced by anthropometric variables, particularly body weight (8, 9), but the exact nature of the correlation is unknown.

In The Netherlands four consecutive growth studies have been performed since 1955 (1, 10–12). These studies provide the opportunity to thoroughly study the secular changes in

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Table 1. *Puberty sample: percentage of participating boys or girls per age group as percentage of the total age group included in the Dutch national survey**

Age (y)	PH boys	G boys	TV boys	PH girls	B girls	Men
8–9	49.1%	49.1%	42.7%	60.2%	61.1%	59.3%
9–12	73.2%	72.9%	66.5%	78.1%	80.5%	85.6%
12–15	54.4%	54.3%	51.3%	57.4%	58.5%	76.9%
15–18	49.9%	49.9%	47.6%	51.1%	52.1%	74.8%
18–21	42.5%	42.4%	40.4%	33.6%	33.9%	83.8%

* 4019 boys and 3562 girls.

Abbreviations: PH, pubic hair; G, genital stage; TV, testicular volume; B, breast stage; Men, menarche.

height, weight, and pubertal development. In two earlier papers on the study performed in 1997, we concentrated on the secular trend of body stature, weight, and BMI and only briefly discussed pubertal development (12, 13). In the present paper we report on the reference data in more detail, as well as a comparison with the previous growth studies. Furthermore, we investigated the degree of concurrence of breast or genital stages with pubic hair stages and the relationship between the age at menarche and height, weight, and BMI.

METHODS

In a cross-sectional design the presence of secondary sexual characteristics was studied. All participants of the 1997 nationwide growth study aged ≥9 y completed a questionnaire on demographic variables (3909 boys and 3454 girls). This sample can be regarded as representative of the general population. In a subgroup (puberty sample) we determined the stage of sexual maturation and age at menarche. The age distribution in the puberty sample showed an overrepresentation of children <15 y of age (approximately 250 in each age group) compared with children >15 y (100–150 per age group; Table 1). Data were available from an additional group of 110 boys and 108 girls between 8 and 9 y of age who had also completed the questionnaire. Pubertal data were available from approximately 50% of these children (Table 1). These observations were randomly distributed across the country.

In the analyses in this article age was used as a covariate, so this skewed age distribution will not affect the results. The composition of the puberty sample was comparable with the sample of a national survey with regard to region and level of education.

The measurements of height and weight were performed by trained staff. The pubertal stages were determined by visual inspection, using Tanner's criteria (14) as described in Table 2. In boys testicular volume was assessed using an orchidometer. To validate the accuracy of the measurement of testicular volume, the testicular volumes in 79 boys were measured by two observers. The Spearman correlation coefficient between the measurements of two observers was 0.82; the 95% confidence interval for the

Table 2. *Definitions of Tanner stages*

Sex	Tanner stage	Description
F	B1	Preadolescent; elevation of papilla only
	B2	Breast bud stage; elevation of breast and papilla as a small mound, enlargement of areolar diameter
	B3	Further enlargement of breast and areola, with no separation of their contours
	B4	Projection of areola and papilla to form a secondary mound above the level of the breast
	B5	Mature stage; projection of papilla only, owing to recession of the areola to the general contour of the breast
F	P1	Preadolescent; no pubic hair
	P2	Sparse growth of long, slightly pigmented downy hair, straight or only slightly curled, appearing chiefly along the labia
	P3	Considerably darker, coarser, and more curled; spreads sparsely over the conjunction of the pubes
	P4	Hair is adult in type, but the area covered by it is still considerably smaller than in most adults. There is no spread to the medial surface of the thighs
	P5	Adult in quantity and type, distributed as an inverse triangle of the classic feminine pattern. Spread to the medial surface of the thighs, but not up the linea alba or elsewhere above the base of the inverse triangle
M	G1	Preadolescent; testes, scrotum, and penis are of about the same size and proportion as in early childhood
	G2	The scrotum and testes have enlarged and there is a change in the texture of the scrotal skin. There is also some reddening of the scrotal skin
	G3	Growth of the penis has occurred, at first mainly in length but with some increase in breadth. There has been further growth of testes and scrotum
	G4	Penis further enlarged in length and breadth with development of glans. Testes and scrotum further enlarged. Further darkening of the scrotal skin
	G5	Genitalia adult in size and shape. No further enlargement takes place after stage 5 is reached
M	P1	Preadolescent; no pubic hair
	P2	Sparse growth of long, slightly pigmented downy hair, straight or only slightly curled, appearing chiefly at the base of the penis
	P3	Considerably darker, coarser, and more curled; spreads sparsely over the junction of the pubes
	P4	Hair is adult in type, but the area covered by it is still considerably smaller than in most adults. There is no spread to the medial surface of the thighs
	P5	Adult in quantity and type, distributed as an inverse triangle of the classical feminine pattern. Spread to the medial surface of the thighs, but no up the linea alba or elsewhere above the base of the inverse triangle

Descriptions are taken from Marshall and Tanner (2, 3). Abbreviations: B, breast stage; P, pubic hair stage; G, genital stage.

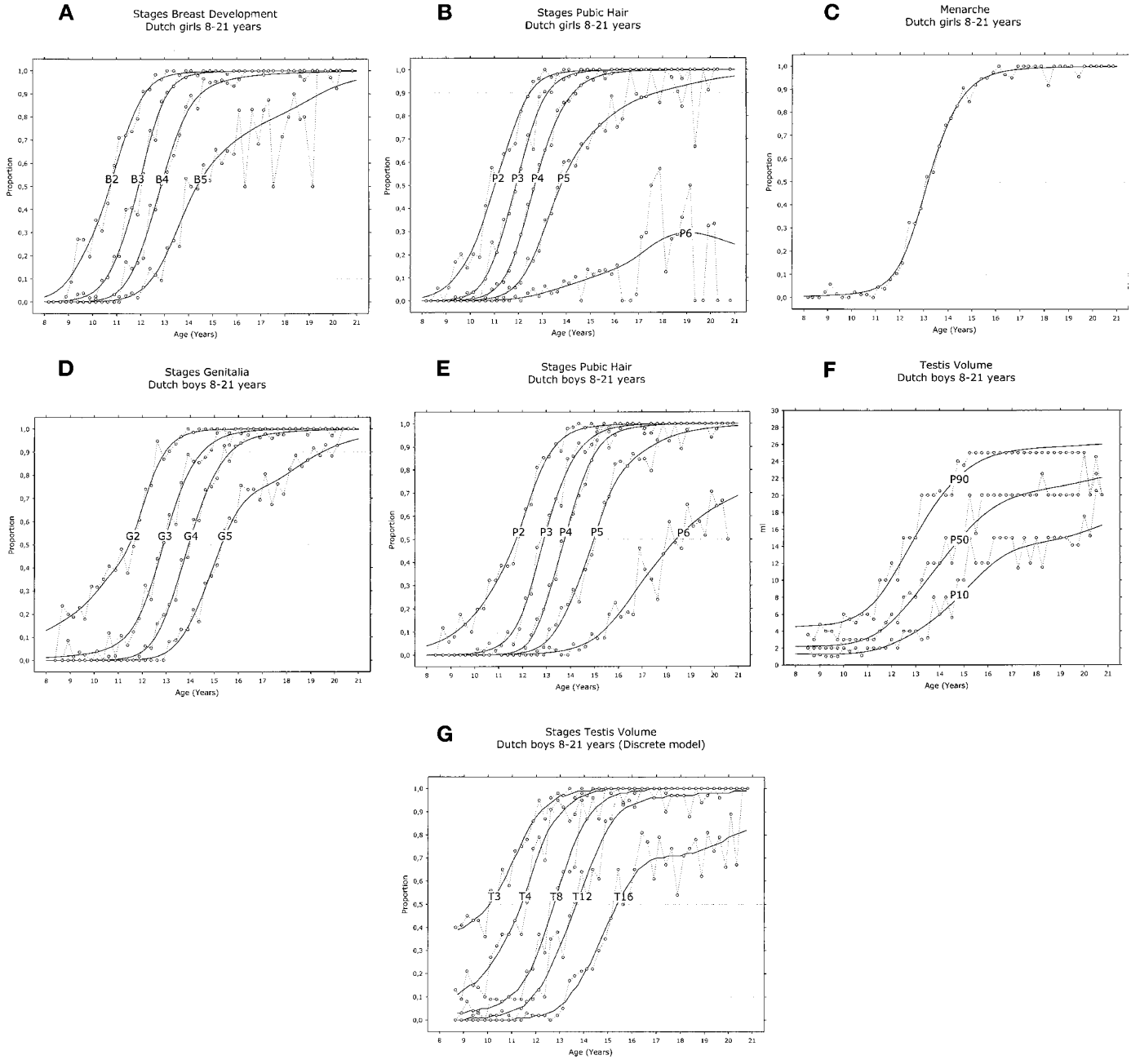

Figure 1. Reference curves for secondary sexual characteristics in The Netherlands, 1997. *A*, breast stage in girls; *B*, pubic hair stage in girls; *C*, menarche; *D*, genital stage in boys; *E*, pubic hair stage in boys; *F*, mean testicular volume; *G*, testicular volumes in early and midpuberty (3, 4, 8, 12, and 16 mL).

difference between observers appeared to be 0.4–2.0 mL (1.2 ± 0.8 mL). In midpuberty the interobserver differences were highest. Zachman *et al.* (15) reported a correlation coefficient of 0.83 and a mean difference in testicular volume between two observers of 2.9 mL. The age at menarche was determined by the status quo method, asking a girl whether she had had her first period at the moment of the survey.

Demographic variables were assessed by a questionnaire. The highest level of completed education of the parents was used as a measure for socio-economic status. The country was divided in five geographical regions, one of them containing the four largest cities (12).

Statistical methods. For menarche and stages of secondary sexual characteristics, the reference curves were estimated by a generalized additive logistic model for each transition stage separately (16). This model describes the probability of each stage as a smooth function of age. The amount of smoothing was determined by cross-validation. LMS reference curves were derived for testicular volumes, in which the measured volumes were considered as a continuous measure (17).

To compare B or G stages and pubic hair stages in girls and boys, we calculated κ as a measure of agreement (18).

RESULTS

Reference curves for pubertal stages and testicular volume. In Figure 1, *A–F*, we present the reference curves for sexual development. The dotted lines represent the crude data. The P_{50}

ages can be read from the figures. The 10th and 90th percentile ages, which were published earlier as numerical data (12), can also be read from these graphics, being the ages at which the curves cross the 10th and 90th percentiles, respectively.

Figure 1 also shows the intervals between the consecutive pubertal stages, with a general pattern of a shorter interval between the third and fourth stage compared with the interval between stages 2 and 3. In Figure 1*G*, reference curves are presented for various testicular volumes.

The P_3 values for B2 and G2 were 8.2 and 9.8 y respectively, and the P_{97} values were 12.7 and 13.4 y, respectively.

Comparison with the 1965 and 1980 growth studies. In Figure 2, we show comparisons between the timing of pubertal stages in the present study and the previous studies performed in 1965 and 1980. The P_{50} values are shown for both boys and girls. For all stages a decreasing trend is seen between 1965 and 1980 with stabilization afterward. In contrast, G2 in boys increased from 11 y in 1965 to 11.5 y in 1997, whereas the P_{50} of a testicular volume of 4 mL decreased from 12 y in 1965 to 11.5 y in 1997. In all studies the SD of the P_{50} ages is approximately 1 y.

Relationship between pubertal stages. In Table 3 the relationships between the P stage and B or G stages are shown in absolute numbers. In girls in B1, 60 of 531 (11.3%) showed pubic hair development, whereas 23.3% of girls in P1 showed breast development. In boys, G1 was accompanied by the presence of pubic hair in 10.2%; boys in P1 had genital development in 24.9%.

The agreement between P and B or G stage was expressed as κ and Spearman correlation. The κ values were 0.59 and 0.63 for girls and boys, respectively, indicating moderate to substantial agreement. The difference between the two κ values was significant ($p < 0.05$). Spearman rank-order correlation was 0.91 both in boys and girls ($p < 0.001$).

Thus, in line with our hypothesis, in boys the gonadal and pubic hair development shows a closer mutual agreement than in girls, although the difference in κ is only small.

Menarcheal age in relation to auxometric variables. In Figure 3 the probability of having menarche is depicted as function of age (*x* axis) and weight, weight SDS, height, height SDS, BMI, and BMI SDS (plotted on the *y* axis).

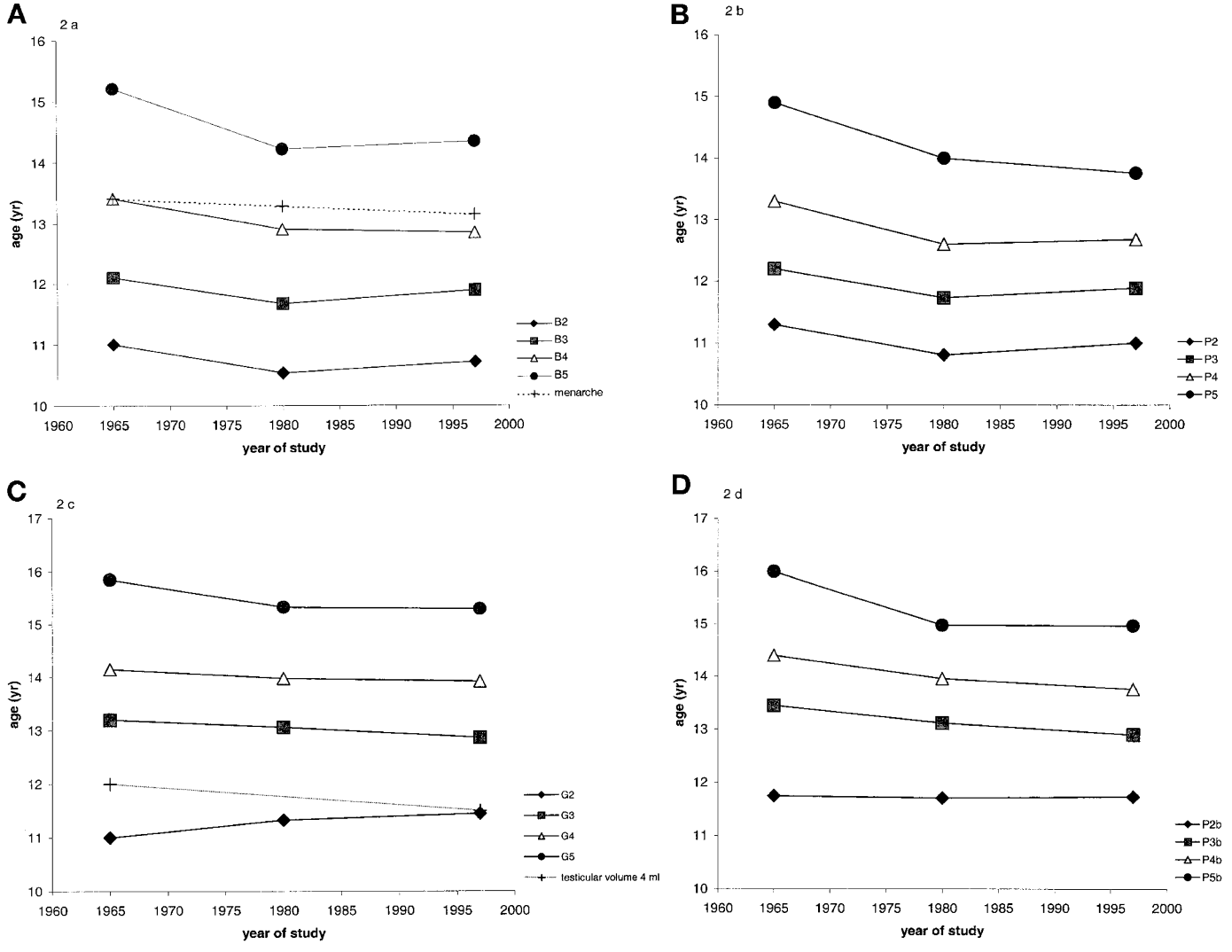

Figure 2. Sexual maturation in The Netherlands 1965–1997 [(1, 11) and this study]; the P_{50} values of the different pubertal stages are given. *A*, breast stage and menarche; *B*, pubic hair stage in girls; *C*, genital stage in boys and testicular volume 4 mL; *D*, pubic hair stage in boys.

Table 3. *Distribution of B and P stages in girls and G and P stages in boys*

Girls (n = 2213)	B1	B2	B3	B4	B5	Total
P1	471	124	19	—	—	614
P2	55	138	50	3	1	247
P3	5	50	118	36	6	215
P4	—	4	58	186	71	319
P5	—	—	17	156	495	668
P6	—	—	5	23	122	150
Total	531	316	267	404	695	2213

$\kappa = 0.59$ ($p < 0.001$).

Boys (n = 2360)	G1	G2	G3	G4	G5	Total
P1	529	151	21	2	1*	704
P2	59	222	53	4	—	338
P3	1	47	124	20	1	193
P4	—	2	56	178	32	268
P5	—	1	10	130	387	528
P6	—	—	1	15	313	329
Total	589	423	265	349	734	2360

$\kappa = 0.63$ ($p < 0.001$); * this boy was 17.1 y old, testicular volume, 20 mL.

All figures show the expected increase in probability of menarche with increasing age and the additional effect of weight, height, and BMI (expressed as nominal values or as SDS).

They demonstrate that at a given age the heavier and taller girls have a higher probability of having menarche. However, the shape of the probability curves is different for the indices of weight (*i.e.* weight and BMI) in comparison to height. When weight or BMI exceeds a certain point, no or little further increase in probability is observed, as the curves have an almost vertical course from there. For weight this point is close to 62 kg (1 SDS), and for BMI it is approximately 20 kg/m^2 or 1 SDS. In the curve for weight expressed in kilograms, the vertical course is more obvious than in the curve for weight SDS.

In contrast, the figures on height show a continuing effect of height at a certain age. Some examples of the different ages at which there is 50% probability of having menarche with various SDS for weight, height, or BMI are shown in Table 4.

DISCUSSION

This study provides up-to-date references for pubertal stages in the Dutch population, which can be used for clinical purposes. In the interpretation of the reference curves for the consecutive pubertal stages, one should be aware, however, that our data are derived from a cross-sectional study. The reliability of the data is high, because of the relatively large numbers of subjects. On the other hand, no information is available about the tempo at which a child passes through the consecutive stages. Such information can only be obtained from a longitudinal study, such as the longitudinal assessment of puberty in boys and girls performed by Marshall and Tanner (2, 3). In general, reference centiles based on cross-sectional data have a larger variance than those based on longitudinal data. For pubertal development curves, this implies that the progression of stages for individuals is generally faster than the intervals between P_{50} stages obtained from cross-sectional references.

The second finding is that the positive secular change toward an earlier development of puberty between 1965 and 1980 has almost stabilized thereafter. During the whole period between 1965 and 1997, the P_{50} age of onset of puberty (stage B2) in girls decreased from 11.0 y in 1965 to 10.7 y in this study. The median age at menarche decreased by 0.25 y in the same period, and by 0.5 y from 1955. In the last 17 y only a small decrease of about 1.5 mo, from 13.28 to 13.15 y, was observed. A similar pattern of an apparent stabilization of a previously decreasing trend was observed in Oslo schoolgirls, in whom menarcheal age has reached a stable level for several decades (19). However, in Norway also the secular trend in body stature appears to have stopped (19). Maybe the stabilization reflects a situation in which the environmental conditions have allowed the child to reach the optimal genetic potential given the actual environmental conditions (4).

The only exception to this trend of a slow positive secular trend between 1965 and 1980 followed by near stabilization is the apparent increase of the median age at which boys reach G2 from 11.0 y in 1965 to around 11.5 y in 1997. This finding contrasts with a decrease of the median age at attaining a testicular volume of 4 mL from 12.0 y in 1965 to 11.5 y in 1997. The most likely explanation of this discrepancy is that the interpretation of the definition of stage G2 must have been different in 1965 in comparison to 1980 (1, 20) and 1997.

In fact, the original definition of G2 as proposed by Marshall and Tanner (3) leaves much room for confusion, as it states that "[t]he scrotum and testes have enlarged and there is a change in the texture of the scrotal skin. There is also some reddening of the scrotal skin. . ." (see also Table 2). This description is not pertinent to the question of which of the three criteria mentioned is most relevant, and to whether all criteria have to be met or at least one or two of them. In addition, it does not strictly describe the minimum volume that the testis should

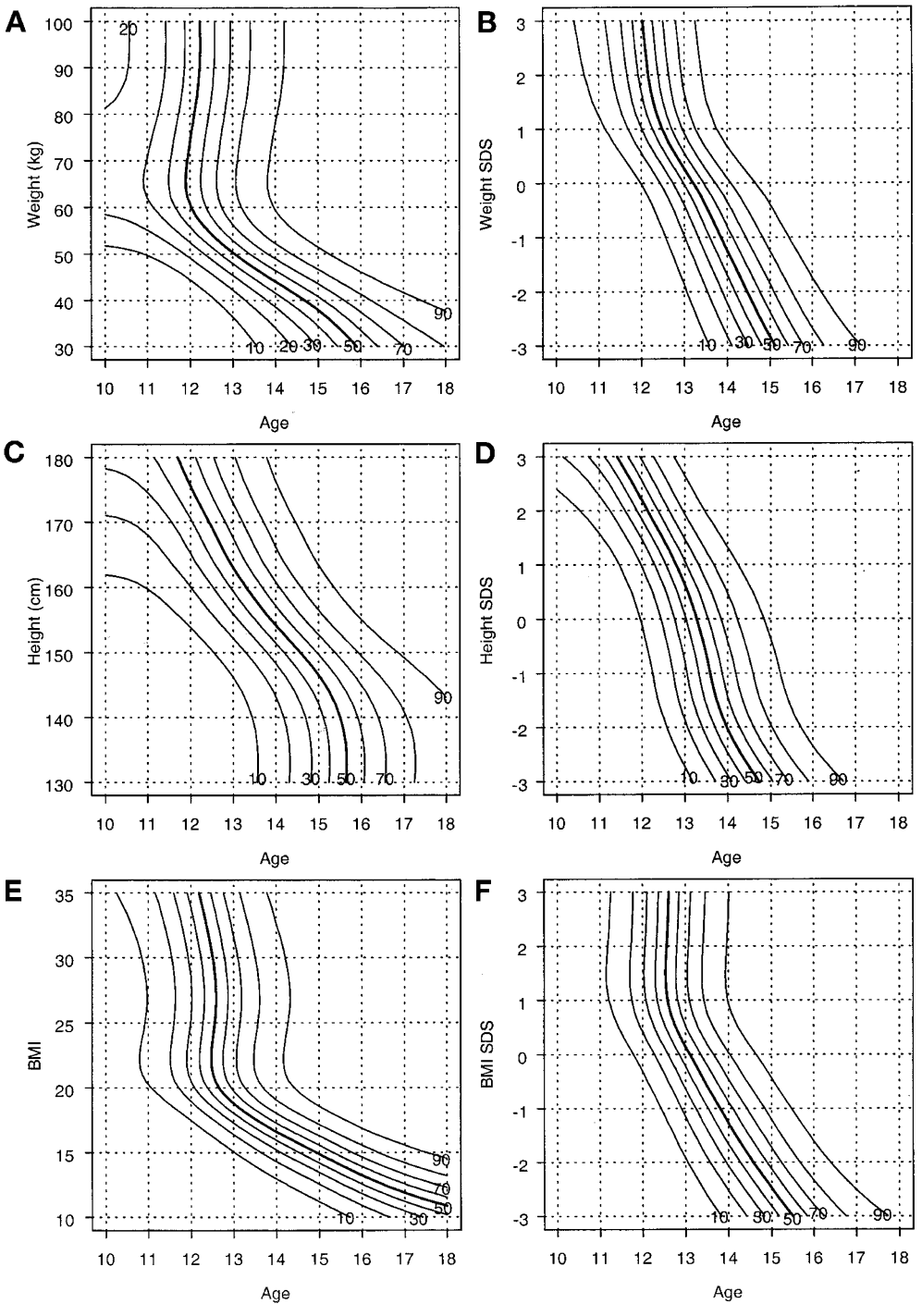

Figure 3. Probability of having menarche as a function of age and weight (*A*), weight SDS (*B*), height (*C*), height SDS (*D*), BMI (*E*), and BMI SDS (*F*). The probability is expressed as a percentage. A vertical course of the lines means that at a certain age the variable on the *y* axis does not further contribute to increase the probability of having menarche. A transverse course implies additional effect of the variable on the *y* axis on the probability of having menarche.

have before the genital stage may be labeled as G2. For example, there are good arguments that a testicular volume of 3 mL can already be considered as a sign of puberty (15, 21). In the present study the observers were taught to describe the genital stage as G2 if both enlargement of testicular volume and scrotum was observed and reddening of the scrotal skin was present. It appears likely that in 1965 the observers might have labeled the genital stage as G2 if at least one of the three criteria was present.

Based on these findings, but also on our experience in clinical trials (22), we believe that it is opportune to come to a redefinition of stage G2, to prevent more confusion in the future. We would prefer that the testicular volume, the criterion that is most easily measured, should be used as the only criterion. Furthermore, a volume of 3 mL appears a better indication of the onset of puberty than 4 mL (21, 23).

Relatively few data are available on the accordance between P and G or M stages during puberty. Based on the theoretical

Table 4. *Influence of different SDS for weight, height, and BMI on the P_{50} age of chance of menarche*

	SDS	Age P_{50} (y)*
Weight	+2	12.1
	+1	12.7
	0	13.2
	−1	13.8
	−2	14.5
Height	+2	12.2
	+1	12.8
	0	13.3
	−1	13.7
	−2	14.0
BMI	+2	12.7
	+1	12.7
	0	13.1
	−1	13.8
	−2	14.7

* estimated from curves in Fig 3, *B, D,* and *F.*

view that, for girls, breast development is the initial event in pubertal development and testicular development for boys, these measures should be used as markers in clinical practice. In girls P stage is primarily a reflection of adrenal maturation, although the role of ovarian androgens is acknowledged in pubertal girls (24). In boys, P stage is the reflection of a combined adrenal and testicular maturation, so that a higher agreement would be expected in boys than in girls. In fact, we found a higher agreement between P and G or B stage (expressed as κ) in boys than in girls, but both were significant. This suggests that pubertal development and pubic hair development frequently synchronize. With regard to the timing of both phenomena, we found that in general breast development starts somewhat earlier than pubic hair, in line with the findings of Marshall (2). However, pubic hair was seen before breast development in approximately one third of all girls in the English study (2), and in approximately 10% in our study. In stages B3 and G3 the distribution of P stages is equally divided and in the higher B or G stages the P scores tend to shift to the right, especially in boys, with higher P than G or M stage.

The definition of precocious puberty and delayed puberty should be based on the normal occurrence of secondary sexual characteristics in the population, but there is no consensus whether −2 SDS or −2.5 SDS should be used as a cutoff. We chose to use the usual cutoff measure of −2 SD, which is close to the P_3 and can be read from the reference curves in Figure 1.

The P_3 age for B2 (8.2 y) is close to the age of 8.0 y, which is generally and internationally used as the age limit for the definition of precocious puberty, and we would therefore propose to continue using this figure. For boys the P_3 of G2 stage is 9.8 y, whereas no reliable P_3 data for testicular volume of 4 mL can be presented. Thus, the current cutoff ages for precocious puberty, *i.e.* 8 y for girls and 9 y for boys, can be maintained in our country.

For delayed puberty, the P_{97} for B2 and G2 presented in "Results," as well as the P_{97} age for testicular volume of 4 mL (13.8 y), point to a cutoff age for delayed puberty of 13 y in girls and 14 y in boys.

As mentioned before, in the United States a decrease in the age at onset of puberty in girls was observed (6). However, in that study the sample was not representative of the general population, as the girls were examined when they visited a general practitioner. The girls were heavier and taller than in the national American growth survey, and in 15% of the girls rated B2 by visual inspection no breast tissue was found at palpation (7).

We have shown that in addition to age, weight, height, and BMI influence the chance of having menarche in the age range 11–15 y as well. Interestingly, the probability lines for weight and BMI show an almost vertical pattern in the range at which the SDS exceeds approximately 1. Beyond such degree of (over)weight, weight or BMI hardly affects the probability of having menarche anymore. The cutoff level for BMI data are consistent with the results published in our earlier report, showing that premenarcheal girls in all age ranges had mean BMI $<$ 20 kg/m^2 (13). Our data are in contrast to those of Marshall (25), who stated that the occurrence of menarche was not related to the attainment of a particular height, weight, or body composition, but mostly occurred after the peak of the adolescent growth spurt. However, the limited number of subjects in that study may have precluded the appearance of statistical significance in this respect. An interesting phenomenon is that height, in contrast to weight and BMI, exerts its influence on the probability of menarche over the full range.

It is generally assumed that the increase in socio-economic conditions and general health is the main contributing factor for the trend toward earlier maturation (4, 26, 27). In most industrialized countries the increase in public health and socio-economic conditions was accompanied by an increase in adult height and a decreasing age at attainment of pubertal events (28). The mechanisms through which these changes occur are unknown. On the physiologic substrate for earlier pubertal development, several hypotheses were discussed, for example, the so-called critical weight hypothesis (8, 29). Recent studies on leptin have suggested that this protein could act as a link between fat tissue and the central activation of the hypothalamus (30–32). Another line of research concerns the possible influences of estrogenlike substances in the environment on the timing of puberty, for example, phytoestrogens present in soy-based feeding (33). However, no human data are available that show an influence of infant feeding, containing phytoestrogens, on sexual maturation (34). The stabilization of the age at onset of puberty in a period when an increasing exposure to estrogenlike substances can be assumed argues against a causal link.

We conclude that the secular change toward earlier puberty has been stabilized in the last two decades in The Netherlands. No change in the definition of precocious puberty is warranted. The occurrence of menarche is not only dependent on age, but also on height, weight, and BMI. Beyond a weight or BMI of +1.0 SDS, this dependency is less apparent. The agreement between the expression of gonadal maturation and pubic hair is slightly higher in boys than in girls.

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