

Menarche and Fatness: Reexamination of the Critical Body Composition Hypothesis

In a series of articles published during the last few years (1-8), Frisch and her colleagues have developed the hypothesis that menarche requires a critical level of fat stored in the body. They reason that pregnancy and lactation impose a great caloric drain; if fat reserves are inadequate to meet this demand, then fecundity is impaired.

This theory, with its implications for fertility, is attractive because it is both simple and consistent with the observed and well-documented delay of menarche among severely malnourished girls and loss of menstrual cycles during famines. It has long been thought that nutrition may play a role in reproduction, perhaps affecting conception, fetal mortality, the health of the newborn, or the length of postpartum insusceptibility. There is reliable evidence that in some historical populations which do not appear to have practiced birth control age-specific marital fertility rates were only half the observed maximum. If, as Frisch asserts, poor nutrition delays menarche, lengthens the periods of adolescent sterility and postpartum amenorrhea, and lowers fecundability, then the very low fertility observed in these historical populations could perhaps be easily explained (3).

A close examination of the evidence Frisch and her colleagues offer suggests, however, that their reasoning is flawed either by statistical error or by selective interpretation of the data. These findings do not invalidate the hypothesis, but establish clearly that more careful testing is needed.

In support of the hypothesis they offer five pieces of evidence:

1) Sets of weight-for-height standards which have proved to be useful in predicting a minimum weight (for a given height) necessary for the initiation of menses in adolescents or return to menses in anorectic patients are based upon an index of fatness (6).

2) The coefficient of variation of weight at menarche is significantly higher than the coefficient of variation of the ratio of total body water to total weight, a ratio which they estimate from height and weight and which in turn is their index of fatness (8, 9). They emphasize that this finding has biological significance because it identifies fatness as the critical factor governing menarche.

3) Regression equations which predict age at menarche from height and weight yield significantly better estimates when girls are stratified by the index of fatness.

A separate regression equation is provided for girls in each quartile of fatness (4).

4) A higher proportion of girls remain in the same quartile of fatness than in the same quartile of weight or body water from the time of initiation of the adolescent growth spurt to menarche (8, p. 477).

5) Historical data published by Quetelet conform to the hypothesis and establish a historical constancy of average weight at menarche of 46 kg (5).

Before we proceed further, a brief explanation of Frisch's methodology is essential:

Total body weight (WT) is regarded as the sum of lean body weight and fat. Body water (TW) is considered to be a constant 72 percent of lean body weight and is estimated from observations on height (HT) and weight by means of the following regression equation derived by Mellits and Cheek (10):

$$\hat{T}W = -10.313 + 0.252 WT \text{ (kg)} + 0.154 HT \text{ (cm)} \quad (1)$$

where the hat over TW indicates that it is estimated and not observed. Since $WT = TW/0.72 + \text{fat}$, the ratio TW/WT is an inverse index of fatness, which from Eq. 1 can be estimated as a function of height and weight alone:

$$\hat{T}W/WT = -10.313/WT + 0.252 + 0.154 HT/WT \quad (2)$$

At several points during the following discussion reanalysis of the longitudinal data used by Frisch would be desirable. Unfortunately, the only data available in published form are those of the Berkeley Guidance Study (BGS) (11), which is the source of roughly a third of the sample employed by Frisch.

The height and weight standards. Using observations on height and weight at menarche obtained from the BGS and from studies conducted by the Child Research Council and the Harvard School of Public Health, Frisch and McArthur estimated the ratio TW/WT for each of 181 subjects. The distributions of this ratio at menarche and at age 18 were formed and centiles were calculated. For example, 10 percent of the girls at menarche were found to have a $\hat{T}W/WT$ value higher than .598. Hence a line representing the tenth centile can be calculated from Eq. 2 as

$$.598WT = -10.313 + 0.252WT + 0.154HT \quad (3)$$

Using such loci, along which relative fatness is supposedly constant, Frisch and McArthur constructed weight-for-height standards for menarche and for restoration of the menses in amenorrheic women (6). Frisch has suggested that the tenth centile locus represents a critical body composition. Girls below the tenth centile do not have sufficient stored fat and will not menstruate until they gain enough weight to push them above the tenth centile. It was my intention to reproduce the figures presented in (6) by Frisch and McArthur, but as they refused me permission to do so, and as Frisch also refused me the data used to construct them, Figs. 1 and 2 here are derived from Eq. 2. They are not as rich in detail as they would otherwise be but they portray the general notion. The tenth centile in Fig. 1 represents a body composition of 17 percent fat; the tenth centile in Fig. 2 corresponds to a higher level of 22 percent fat necessary for restoration and maintenance of menses. Because of their choice of the tenth centile Frisch and McArthur expect a 10 percent error in classification. It should be noted that the locus is critical in one direction only; being above the locus is necessary but not sufficient for initiation or return of menses.

It should be noted also that the fact that the weight and height standards have been found to be useful in some predictions or diagnoses does not validate the underlying theory. It is possible to formulate alternative theories which result in operationally equivalent standards, in the sense that they would lead to the same clinical recommendations (12).

Since the centiles in Fig. 1 are constructed from Eq. 3, they are in effect centiles of observed weights and heights, not of fatness, which is merely estimated from them according to a formula. Hence a better set of standards could be constructed without reference to any underlying theory whatsoever. A straightforward data analysis of weight and height at menarche would yield more internally consistent loci. For example, a simple regression of weight at menarche on height at menarche would allow construction of centiles whose slopes reflect the structure of the data and not a theoretical construct. For the 65 girls in the BGS that regression is estimated to be

$$WT = .622HT - 49.513 \quad (4)$$

Standards can be constructed by simply varying the constant in Eq. 4. One locus is plotted as a dashed line in Figs. 1 and 2 (13). A similar analysis could be performed on the heights and weights of

previously amenorrheic patients at the time of return to menses to yield more internally consistent standards for Fig. 2.

The coefficient of variation. In her search for the factor which controls menarche, Frisch has examined what women have in common at the point in their lives when menarche occurs. They do not appear to have a common age, weight, or height, but they do have a common (estimated) ratio of total water to total body weight as measured by the coefficient of variation ($CV = \text{standard deviation}/\text{mean}$).

Billewicz *et al.* (14) have shown that this reduction in CV is purely the result of a mathematical identity. The standard deviation and mean, and therefore the CV of the fatness index \hat{TW}/WT , are determined solely by the observations on height and weight (15). Whether the CV of the estimated ratio is lower or higher than the CV of WT therefore could have no biological significance (16). Suppose, however, that direct observations on TW were available and that the reduction in CV were found to be real. Is the CV a particularly revealing statistic in this context? It is attractive because it is dimensionless; it would have the same value whether TW/WT were measured as liters per kilogram or gallons per pound. Unfortunately, a large part of its denominator (WT) is accumulated prior to pu-

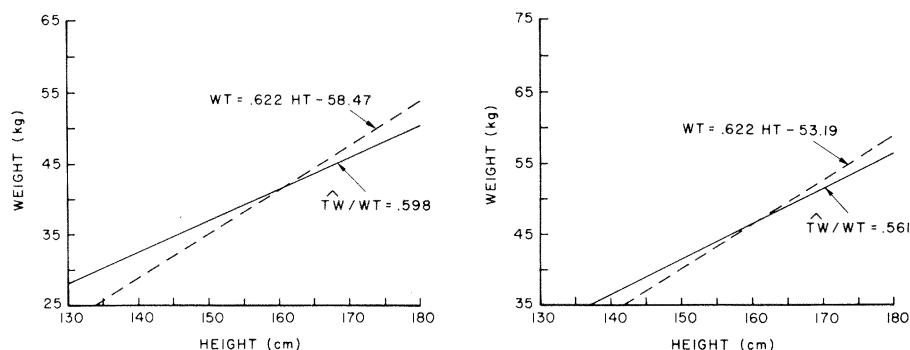


Fig. 1 (left). The minimum weight necessary at a particular height for onset of menses is represented by the solid line for the Frisch and McArthur standards and by a dashed line for the standards obtained by regression of weight at menarche on height at menarche. Fig. 2 (right). The minimum weight necessary at a particular height for the resumption of menses is indicated by the solid line for the Frisch and McArthur standards and by a dashed line for the standards obtained by regressing weight at menarche on height at menarche. The solid lines (Frisch and McArthur standards) were derived by substituting, respectively, .598 and .561 into Eq. 2.

berty; hence the statistic is in effect deflated. For example, if all girls wore platform shoes 30 cm high, then the CV of total height (with shoes) at menarche for girls in the BGS sample would be 15 percent smaller than that of height without shoes. Likewise, body temperature at menarche would have a lower CV if measured in degrees Kelvin than in degrees Celsius. This point is particularly relevant when discussing the estimated ratio TW/WT , since it is bounded away from zero at every age; its smallest value oc-

curs among short, fat girls; a reasonable lower bound of .42 might occur for a girl whose height and weight are 110 cm and 40 kg respectively. If one regarded the natural zero of the ratio as .42, then the coefficient of variation would be 4.2 times as large as that reported by Frisch (17); but since the ratio has no natural zero, comparisons employing its mean and coefficient of variation are totally without meaning.

Predicting age at menarche. Frisch has devised a procedure for predicting

Table 1. Sum of squared residuals (SSR) obtained from the regression of age at menarche on a constant and either height or weight. The F ratio for segmentation is given in the last row for each age. The letter beside each SSR indicates whether the regressor was height (H) or weight (W).

Age	Quar- tile	N	Total (over all subjects)	\hat{TW}/WT	HT	WT	WT/HT	\hat{TW}
9	1	16		13.9885 <i>H</i>	14.6880 <i>W</i>	11.9428 <i>W</i>	17.4529 <i>W</i>	15.0482 <i>W</i>
	2	16		6.5913 <i>W</i>	10.1095 <i>W</i>	18.5082 <i>W</i>	8.4101 <i>H</i>	10.2741 <i>H</i>
	3	16		7.8654 <i>W</i>	10.4110 <i>H</i>	7.7604 <i>W</i>	8.7201 <i>W</i>	9.8381 <i>H</i>
	4	17		20.4596 <i>W</i>	16.7642 <i>W</i>	11.8453 <i>H</i>	11.8453 <i>H</i>	11.4228 <i>H</i>
	Total	65	55.8819 <i>W</i>	48.9048	51.9727	50.0567	46.4284	46.5832
	$F(6,57)$			1.3553	0.7146	1.1055	1.9343	1.8963
10	1	16		9.7558 <i>H</i>	11.8363 <i>W</i>	13.1568 <i>W</i>	14.3379 <i>W</i>	12.6949 <i>W</i>
	2	16		8.6679 <i>H</i>	14.0664 <i>W</i>	14.8433 <i>W</i>	15.0483 <i>W</i>	12.2149 <i>W</i>
	3	16		7.4138 <i>H</i>	6.5297 <i>H</i>	6.7116 <i>W</i>	6.3783 <i>H</i>	12.4351 <i>W</i>
	4	17		18.3366 <i>W</i>	16.0149 <i>W</i>	9.9149 <i>H</i>	9.9149 <i>H</i>	11.3358 <i>H</i>
	Total	65	51.5319 <i>W</i>	44.1741	48.4473	44.6266	45.6794	48.6807
	$F(6,57)$			1.5824	0.6049	1.4700	1.2172	0.5564
11	1	16		9.4564 <i>H</i>	8.9511 <i>W</i>	11.6178 <i>W</i>	12.4922 <i>W</i>	12.0031 <i>W</i>
	2	15		3.6261 <i>W</i>	8.7422 <i>H</i>	8.0377 <i>H</i>	7.9780 <i>H</i>	8.0955 <i>H</i>
	3	15		7.7981 <i>H</i>	3.3624 <i>H</i>	5.9297 <i>H</i>	5.3204 <i>H</i>	6.0750 <i>H</i>
	4	16		12.9300 <i>W</i>	14.0243 <i>W</i>	7.8625 <i>H</i>	7.4025 <i>W</i>	7.0434 <i>W</i>
	Total	62	44.0385 <i>W</i>	33.8106	35.0800	33.4477	33.1931	33.2170
	$F(6,54)$			2.7226	2.2984	2.8497	2.9406	2.9320
12	1, 2	25		8.9137 <i>H</i>	15.2453 <i>W</i>	14.9420 <i>W</i>	15.9764 <i>W</i>	11.5099 <i>W</i>
	3, 4	25		14.1510 <i>W</i>	10.1941 <i>W</i>	6.2397 <i>W</i>	6.0260 <i>W</i>	11.3817 <i>H</i>
	Total	50	27.3829 <i>W</i>	23.0647	25.4394	21.1817	22.0024	22.8916
	$F(2,46)$			4.3061	1.7571	6.7335	5.6245	4.5126
13	1, 2	13		2.2441 <i>H</i>	4.7094 <i>W</i>	6.3850 <i>W</i>	4.9872 <i>W</i>	6.1912 <i>W</i>
	3, 4	14		8.5582 <i>W</i>	3.7797 <i>H</i>	3.7453 <i>H</i>	5.5138 <i>H</i>	3.6977 <i>H</i>
	Total	27	12.6451 <i>W</i>	10.8023	8.4891	10.1303	10.5010	9.8889
	$F(2,23)$			1.9618	5.6300	2.8548	2.3481	3.2052

age at menarche which is being widely used (4, p. 384). From the same body of data used to construct the height and weight standards, quartiles of $\hat{T}W/WT$ were constructed at each age from 9 to 13 (18). Each girl who had not yet reached menarche was classified into one of four quartiles at each age. Within each quartile, at each age, age at menarche was regressed as a function of height or weight. The equation that yielded the highest significant R^2 was chosen (19). The same procedure was repeated for height, weight, and weight-for-height quartiles. Frisch found that segmentation into $\hat{T}W/WT$ quartiles gave higher significant R^2 than when all subjects were combined at each age and that segmentation into height or weight or weight-for-height quartiles "gave either worse standard errors of the estimates" (lower R^2) than classification by $\hat{T}W/WT$ quartiles, "or insignificant results" (4, p. 386).

These findings are indeed interesting, but Frisch presented no test of whether the segmentation itself was necessary. Such a test can be formulated rather easily, and can be applied to the BGS subjects.

If the same regressors had been used in the regression equation for each quartile, then the test would be a straightforward F test (20). However, in some quartiles Frisch found that weight was more significant and in others that height was more significant; hence the assumptions of the standard F test are violated. Nevertheless, because we are interested in the significance of segmentation and not in the actual functional form (for which the only tests are complicated asymptotic ones), we can form an F test which is biased in favor of rejecting the null hypothesis that pooling is not a significant restriction. For each quartile we pick the lower of the SSR 's (sum of the squared residuals) from the regression on weight or height. We next compare the sum of the SSR 's over all quartiles at each age with the lower of the pooled SSR 's resulting from a regression on either height or weight (21) in a conventional F ratio. That this test is biased in favor of rejecting the null hypothesis and accepting segmentation is obvious: the numerator of the F ratio must be biased upward, and the denominator downward. No conclusion can be drawn if the F ratio is significant; but if it is not, one can conclude that segmentation is not warranted. Results for the BGS data are presented in Table 1. It can be seen that no F ratio is even remotely significant when the data are segmented by $\hat{T}W/WT$

Table 2. Percent of BGS subjects who remained in the same quartile from age 8 through age at menarche.

Height	46.2
Weight	40.0
WT/HT	44.6
$\hat{T}W$	41.5
$\hat{T}W/WT$	43.1

except at ages 11 and 12, and even at these ages segmentation by weight or WT/HT quartiles produces a higher F ratio. We conclude that either no predictive power is lost when the segments are pooled or, if it is, segmentations other than $\hat{T}W/WT$ perform equally well or better.

Consistency of classification into quartiles of $\hat{T}W/WT$. Frisch says that "of the 169 girls who could be followed from [the initiation of the adolescent growth spurt] to menarche, 138 (82%) remained in the same quartiles of total water/body weight from initiation of the spurt to menarche, compared to only 79 (47%) remaining in the same quartiles of weight from initiation to menarche, and 66 (39%) remaining in the same quartiles of total water from initiation to menarche" (8, p. 477). She does not mention the percentage who stay in the same quartile of height or WT/HT . This question has been examined for the 65 girls in the BGS; unfortunately, insufficient detail was provided by Frisch to allow the unambiguous determination of the timing of the adolescent growth spurt. Some notion of the answer can be gained by following girls from age 8 to menarche. The percentages who remain in the same quartile of height, weight, WT/HT , $\hat{T}W$, and $\hat{T}W/WT$ from age 8 to menarche are given in Table 2. A higher percentage do indeed remain in the same $\hat{T}W/WT$ than remain in the same weight quartiles, but a still higher percentage remain in the same height and WT/HT quartiles. It would appear that the superiority of the performance of $\hat{T}W/WT$ is due to a constrained, selected comparison; a full comparison based on all 169 subjects would be in order. It is unclear, however, how this finding, even if correct, implicates fatness as a determinant of menarche.

The historical evidence. For historical evidence Frisch places great emphasis on the Belgian data collected by Quetelet. For example, when talking about the interval from the initiation of the growth spurt to menarche she states that "Belgian girls of over a century ago apparently grew more slowly during the adolescent growth spurt as well as before the

spurt, so that this interval to menarche was about 4.5 years (Quetelet, 1869)" (3, p. 18). One might get the impression from the attribution to Quetelet that he discussed age at menarche, but as Frisch states elsewhere (5, p. 448), he did not. Instead, he talks about age at puberty (apparently the time of appearance of secondary sex characteristics), which he places at about 12 years. Frisch argues that the Quetelet data on weight by age for girls are consistent with an age at menarche between 16 and 17 years, and that this finding in turn provides evidence for historical constancy of an average weight at menarche of 46 kg, an important piece of corroborative evidence for her theory.

A closer examination of the Quetelet data (22) reveals, however, that her argument is not unambiguously sound. We have available four pieces of evidence: height and weight profiles for boys and girls by age. Regardless of any quibbles about critical weight or body composition, one is certain that menarche follows rather closely the peak adolescent growth spurt, as Frisch herself has noted (3, p. 18). Single-year velocity curves can be derived from the height-by-age or weight-by-age profiles by differencing. Three of these curves have well-defined peaks: male height, at age 15; female height, at 13; and male weight, at 16. These together indicate that menarche should have occurred no later than age 15, since the interval from the peak spurt to menarche is approximately 1 year (23), and the sex difference between peaks averages about 2 years (24). The velocity curve for female weight does not have a well-defined peak; instead two peaks, one at age 12 and the other at age 17, appear. It should be noted that the height profiles are more likely to be correct, because height was measured with the subjects shoeless, but weight was measured when they were clothed. To avoid the upward bias in weights, Quetelet subtracted, at each age, 1/18 and 1/24 of total weight for males and females respectively. With these considerations in mind, it is difficult to accept Frisch's argument that menarche occurred as late as 16 to 17 years.

Frisch has recently provided a long catalog of historical citations which support her theory of a direct link between nutrition and the biological capacity to reproduce (25). While this summary is impressive for its sheer magnitude, the fact that 18th- and 19th-century writers believed that link existed does not prove that it did; many of the same writers believed in other theories which today can

be rejected conclusively. What is needed is direct human corroboration, not mounds of historical evidence. Her work has inspired at least two direct tests. Bongaarts and Delgado, when analyzing the effects of nutritional status on fertility in rural Guatemala, found no effect on fecundability (monthly probability of conception) and a statistically significant but demographically unimportant lengthening of the period of postpartum amenorrhea by 1.6 months among women of low nutritional status (26). Another study conducted among rural women in Bangladesh found that the length of postpartum infertility was unrelated to maternal nutritional status (27) and that there seems to be no threshold effect of a minimum weight-for-height necessary for the resumption of menses following a birth. Neither of these findings supports the Frisch hypothesis and neither was mentioned by her.

Summary. The theory that fatness is a critical determinant of menarche or fecundity is plausible and merits investigation, but the evidence thus far produced for it is weak indeed. It remains to be seen whether the theory is correct and, if so, whether fatness (or nutrition) is a demographically important determinant of fecundity and thereby fertility. For example, if the period of postpartum amenorrhea were lengthened by 3 months by poor nutrition, the result would be statistically and biologically significant, but demographically unimportant. It is also important to discover whether there is a direct physiological link as Frisch proposes; nutrition might indeed affect fecundity but only indirectly through loss of libido.

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References and Notes

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- In support of the hypothesis of metabolic mass as a trigger, Frisch states, "It is especially significant that the variability of TW [body water] as a percentage of body weight at menarche is 55 percent less than that of weight at menarche" (1, p. 415).
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- It is not even necessary that an alternative theory be plausible in order for it to yield reasonable standards. For example, it could be hypothesized that there is a critical minimum intelligence necessary for the onset and maintenance of menses, on the grounds that women who do not meet this minimum would not be able to cope adequately with pregnancy, hence their fecundity is suppressed so that survival is ensured. I recruited six of my female colleagues and regressed their IQ's on their weights and heights to find

$$\hat{IQ} = 234.63 + 2.00WT - 1.25HT$$
 Better standards than those offered by Frisch could be constructed from the reexpression of the previous equation as

$$WT = \text{constant} + 0.625HT$$
 where the constant equals $0.5(\hat{IQ} - 234.63)$. For example, the locus $WT = -53.625 + .625HT$, along which $\hat{IQ} = 127.38$, if plotted as a dashed line in Frisch and McArthur's figure 2 (6) would discriminate perfectly between subjects who were menstruating and those who were not. These standards, like those of Frisch and McArthur, are weight-for-height standards. A woman of a given height increases her estimated IQ or fatness by gaining weight. Her actual IQ or fatness is irrelevant to the use of the standards.
- One may regard Eq. 4 as a theory, to wit, there is a linear relation between weight and height at the time of menarche. It is certainly more plausible than the IQ theory (12), though they yield equivalent standards, since the slopes (.62) are equal.
- W. Z. Billewicz, H. M. Fellowes, C. A. Hytten, *Ann. Hum. Biol.* **3**, 51 (1976).
- For any equation of the form $y = a + bx_1 + cx_2$, it is always true that $E(y) = a + bE(x_1) + cE(x_2)$ and that $\text{Var}(y) = b^2\text{Var}(x_1) + c^2\text{Var}(x_2) + 2bc\text{Cov}(x_1, x_2)$. Billewicz et al. (14) point out that one finding—that the coefficient of variation of total water is lower than that of weight—merely recaptures these two mathematical identities. Likewise the CV of TW/WT is determined by Eq. 2: $CV(TW/WT) = \sqrt{a/b}$, where $a = (10.313)^2 \text{ var}(1/WT) + (.154)^2 \text{ var}(HT/WT) - 2(.154)(10.313) \text{ cov}(1/WT, HT/WT)$, and $b = -10.313 E(1/WT) + .252 + .154 E(HT/WT)$.
- In the BGS sample the CV of \hat{IQ} at menarche is 39 percent lower than the CV of weight at menarche—a fact which likewise has utterly no biological significance.
- The 181 subjects had a mean ratio TW/WT of .551 (8, p. 472). If the natural zero is .42, then the coefficient of variation would be raised by a multiplicative factor of $.551/(.551 - .42) = 4.2$.
- Frisch defined age from "birthdate anniversary to next birthday anniversary, e.g. age 9 is from the ninth birthday up to the tenth birthday." Therefore, the observations upon which regressions were based should have been centered on the midpoints of each age group. The observations on the BGS subjects are so centered, but the calculations have been made centering on exact age as well; the numbers change slightly, but the qualitative results are the same. Frisch's quartiles of weight, height, and weight-for-height were determined from *national* samples; the quartiles of TW and TW/WT were, however, determined from her own sample. If one wishes to compare the performance of variables, it is more appropriate to use quartiles determined from the same sample. Since there are no national samples from which to compute TW and TW/WT , all quartiles used here were determined from the data in the BGS sample. It is not possible to determine weight-for-height quartiles from such a small sample, however. Hence a ponderal index WT/HT was substituted; such a substitution does not alter the argument that segmentation was not necessary.
- While this criterion may be used, it is more common, when one's aim is merely to predict, to choose the regression with highest R^2 rather than the one with highest significant R^2 . If height and weight had been used as regressors in each quartile regression, then the predictions could not have been worse, as measured by the squared error loss function explicit in least squares regression. F tests of pooling all observations for each age with both weight and height as regressors show that only at age 12 can the null hypothesis (that the observations can be pooled) be rejected at the .05 level, and even for age 12 pooling produces higher F ratios when the data are segmented by WT/HT or by weight than when they are segmented by TW/WT .
- To test whether segmentation by quartiles is significant one runs five regressions for each age, one for each quartile and one for all subjects combined. The F ratio is formed as follows: (i) the SSR 's for each of the quartiles are summed; denote this sum $SSRu$, for unrestricted; (ii) the SSR for the single regression on the pooled observations is denoted $SSRr$, for restricted; and (iii) the quantity

$$F = \frac{(SSRr - SSRu)/3k}{SSRu/n - 4k}$$
 is distributed as $F(3k, n - 4k)$, where n is the number of women at each age and k is the number of regressors (including the constant) in each regression.
- One might wonder why the smaller of the two SSR 's resulting from the pooled regressions is used. The larger could also be used, but the test then becomes more biased in favor of rejecting H_0 . We seek the better of the two biased tests. Even if the larger of the two SSR 's had been used, only at age 10 would pooling have produced the highest F ratio when the data are segmented by TW/WT .
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6 April 1977; revised 7 October 1977

Trussell's comment (1) contains many incorrect statements, both historical and statistical, including the contention of supposed statistical error, as will be shown in detail. Incorrect also is the presumption that over 24 publications on adolescent events and female reproductive ability are to be construed as offering "five pieces of evidence" for the effect of nutrition on fertility. Beginning with the Frisch-Revelle findings on weight at peak velocity and menarche (2-4) we followed biological clues and asked biological questions of growth data, using the usual statistical procedures (2-7). In Frisch and McArthur (8) data on weight and height of women amenorrheic because of weight loss were studied in relation to a minimum weight for height indicated by a fatness index, total water as percent of body weight.

The data and rationale for this index are described in detail in other papers (7, 9–11). Our clinical data, and that of other workers (12), show that the method is clinically useful in indicating target and threshold weights for the onset and resumption of menstrual cycles, as Trussell admits.

The most important of Trussell's misstatements concern the reasons for estimating total water as percent of body weight (TW/BWt %), a fatness index, and the validity of TW/BWt % as an intermediate variable.

Trussell does not seem to understand the fact that the weight of the body is equal to the weight of water plus the weight of protein plus the weight of bone (minerals) plus the weight of fat (10, 13, 14): Weight of whole body = weight of water + weight of protein + weight of minerals + weight of fat.

The proportion of these different components of weight change with age, water becoming a lower percentage and fat becoming a larger percentage, especially in the female (9, 10, 13). A loss or gain of weight can have different physiological meaning by age, sex, cause, and so on because of the differences in the components lost and gained.

The water in the body can be measured, but it is not a simple process, the usual procedure being by isotope dilution (10, 15).

Contrary to Trussell's statement, the equation used by us to estimate body water of each of the 181 subjects at menarche (10, 15), at initiation of the spurt (15), and at age 18 years (10, 15) are based on *actual* measurements of body water in individual girls and women by the dilution procedure (10, 15). These equations are needed and used clinically for guidance in fluid and electrolyte management of surgical patients, burned patients, and for estimating drug dosages (10).

Contrary to Trussell's statement, new information is contributed by the slope of the estimating equation; total body water is not just a rearrangement of height and weight because of the structure of the estimating equation:

$$\text{Total } \hat{W} = \hat{TW} = a + bH + cWt \quad (1)$$

For any given value of \hat{TW}^* , the form of the equation parametrized on H and Wt becomes:

$$H = \left(\frac{-a + \hat{TW}^*}{b} \right) - \frac{c}{b} Wt \quad (2)$$

Thus the information from the estimating equation survives in the form of the slope of the weight for height equation.

Table 1. Comparison of minimum weight for height for maintenance of menstrual cycles from Frisch and McArthur (8) and "under-weight," weight for height classification by Sargent (23), for over 50,000 women. Weights for height predicted by Trussell are calculated from his equation given on figure 2 (1).

Height (cm)	Frisch-McArthur minimum weight (kg)	Classified "under-weight" by Sargent (kg)	Calculated from Trussell (kg)
146	39.4	39.2	37.6
148	40.4	40.0	38.9
150	41.4	40.9	40.1
152	42.4	41.8	41.3
154	43.4	42.7	42.6
156	44.4	43.7	43.8
158	45.4	44.6	45.0
160	46.4	45.6	46.3
162	47.4	46.6	47.6
164	48.4	47.6	48.8
166	49.4	48.6	50.1
168	50.4	49.7	51.3
170	51.3	50.8	52.5
172	52.3	51.9	53.8
174	53.3	53.0	54.8
176	54.3	54.2	56.3
178	55.3	55.4	57.5
180	56.3	56.6	58.8

This is not equivalent to a direct regression of height on weight (or weight on height), where the resulting slope would be merely a parameter of the joint distribution of the height and weight measurements.

Since the concentration of body water (that is, the ratio of body water to body weight) is biologically and clinically significant, rather than the absolute value (9), the equation is rewritten as:

$$\frac{TW^*}{Wt} = a \cdot \frac{1}{Wt} + b \cdot \frac{H}{Wt} + c \quad (3)$$

For convenience let $R = TW/Wt$. Therefore for any given value of \hat{TW}^*/Wt , such as that bounding the lowest decile at menarche, or at age 18 years in Frisch and McArthur (8):

$$\begin{aligned} R^* &= \left(\frac{\hat{TW}^*}{Wt} \right)^* \\ &= a \cdot \frac{1}{Wt} + b \cdot \frac{H}{Wt} + c \\ -b \frac{H}{Wt} &= -(R^*) + a \cdot \frac{1}{Wt} + c \\ -H &= \frac{Wt}{b} [-R^* + c] + \frac{a}{b} \quad (4) \end{aligned}$$

$$H = WT \left(\frac{R^* - c}{b} \right) - \frac{a}{b} \quad (5)$$

As above, this is not equivalent to a direct regression of height on weight, where the resulting slope would be

merely a parameter of the joint distribution of the height and weight measurements.

\hat{TW} is hatted since it is estimated as a function of height and weight, or weight and age, an error of the estimate, of course, being given with each regression. However, *each value* of total body water (TW) was actually measured for each subject by giving an isotope such as tritium or deuterium oxide to each subject (10, 15).

Our estimations of body composition from equations based on isotope dilution were checked for validity with estimates by other methods, such as ^{40}K , and actual carcass dissection (10, 13), as is necessary when an intermediate variable is used, to be sure it is consistent with other methods of measurements, and that it makes sense biologically (7, 11).

The rationale of our research beginning with the Frisch and Revelle findings on critical weights at peak velocity and menarche (2–4) was related to metabolic rate, and therefore body composition. The findings of G. C. Kennedy on body weight, food intake, and puberty, and fat depots, in the rat were particularly important (16–19).

In referring to the fatness index, Trussell chooses statements out of context, omits attribution, or tacks on his own preconceptions to construct his own incorrect version of our work. For example, the statement on body composition in Frisch and McArthur (8) is:

The *average* critical weight (at menarche) represents a critical body composition of fat as a percentage of body weight which is attained at varying weights and heights within a population. For example, the shortest, lightest girls and the tallest, heaviest girls at menarche have the same percentage of their body weights as fat, although they differ in height by about 20 cm and in weight by about 11 kg.

We did not use the phrase, added by Trussell, "as measured by the coefficient of variation."

Frisch and McArthur clearly state that "other factors such as emotional stress affect the maintenance or onset of menstrual cycles. Therefore menstrual cycles may cease without weight loss, and may not resume in some subjects even though the minimum required weight is attained" (8, pp. 950–951); that is, the minimum weight is necessary but not sufficient. Trussell has heard the writer use this phrase to emphasize this point at conferences. I have further stated (20): "We cannot explain as yet the variability of total water/body weight percentage above the minimum weight for a particular height." Trussell gives both these statements as if they were original to

Trussell, citing them without attribution. The second statement (20) is from my published reply to Billewicz *et al.* (20). Trussell cites the latter, but not my reply, of which he is aware (21).

Data from carcass studies of animals and metabolic data suggested that body composition changes, particularly fat/lean ratios, may be important for sexual maturation [reviewed in (17, 18)]. Since the girls whose data we studied had long since grown up, we perforce had to estimate their body composition, using equations based on *actual* measurements of body water (10, 15). The estimated changes in body composition from initiation of the spurt to menarche showed that the biggest change in girls was in fatness, the lean body weight to fat ratio changing from 5:1 to 3:1 (7). Since it was well known that loss of weight in women led to cessation of menstrual cycles [see references in (8)], the interesting question was: How did this known cessation of cycles correlate with changes in fatness?

As described in Frisch and McArthur (8), percentiles of estimated TW/BWt % were drawn on a height-weight grid (8). The equation used was:

$$\text{Body weight (kg)} = \frac{15.4Ht_{cm} - 1031.3}{\frac{TW}{BWt} \% - 25.2}$$

For example, the 10th percentile value of estimated TW/BWt % at menarche, 59.6 percent, and at 18 years, 56.1 percent, were substituted in the equation. Comparing the weights for heights indicated by our TW/BWt percentile, 56.1 percent, at the completion of growth (age 18 years) (11), and the weights and heights observed in cases of women with nutritional, secondary amenorrhea, we found that this tenth percentile (equivalent to about 22 percent fat/body weight) indicated a *minimal* weight for height for the maintenance of menstrual cycles (8); prediction was often within 1 or 2 kg (8, 17). We also found that this was a heavier minimum weight for height than at menarche, where the tenth percentile TW/BWt % for the same subjects was 59.6 percent, equivalent to about 17 percent fat/body weight (8).

These minimal weights are now being used as target weights or threshold weights for the restoration and onset of cycles, for both U.S. and European women with nutritional amenorrhea (12). Subsequent endocrinological and physiological publications of many workers (22) have also confirmed our underlying concept that normal ovulatory cycles are closely correlated with changes in body weight in the range of 10 to 15 percent

below the normal weight for height (Table 1) (23). The minimum weights indicated by the tenth percentile of TW/BWt % at age 18 years, 56.1 percent, are extremely close to those indicated as "underweight" for a large sample of American young women (Table 1) (23). Loss of weight in the range of 10 to 15 percent of body weight is mainly loss of fat (24). It is known that too much fat, in addition to too little fat, is associated with the cessation of reproductive ability in the human female (and male), as well as in other animals (17, 18, 25). Our experimental findings at the first estrus of the rat (26) based on actual carcass components (27), also support the importance of a fat/lean ratio and Kennedy's hypothesis (16, 19).

In the writer's view, it is fruitful, both clinically and for research, to pursue the economical hypothesis that the significant relation in animals of carcass fatness and puberty and reproductive ability (18, 26, 27) is also present in the human female. However, we have never claimed that a fat/lean ratio is the only operant variable or that the usefulness of the method proves it is the operant variable. I have in fact urged that other models be offered (20).

Trussell's emphasis on the coefficient of variation (CV) is Trussell's, not ours. Of course a reduction in variability can be a statistical artifact; it can also be telling you something, particularly if the biological basis is interesting, as I have pointed out in my published reply to Billewicz *et al.* (20), which is not mentioned by Trussell. Trussell states that the CV is attractive because it is dimensionless. We never thought the CV was attractive or unattractive; we used it in the usual routine manner.

By definition of existence, "the body is bounded away from zero:" for height, weight, weight for height, water, and water as percent of body weight. The example given by Trussell "of a reasonable lower bound" of a 40 kg weight (88 pounds) for a 110 cm girl (43 inches) is in fact entirely unreasonable since the average weight of a girl at 110 cm is about 18 to 19 kg (41 pounds).

Menarche is not delayed "just" for "severely malnourished girls" but in girls with relatively mild undernutrition, or with any factor which slows growth, prenatally or postnatally, for example high altitude, twinning, disease (6, 28, 29). Mildly undernourished Alabama girls had menarche 2 years later than similar well-nourished girls (30, 31). Similarly, menstrual cycles cease not only through famines, but with chronic restriction (8) and/or hard exercise (such as

long distance running) sufficient to produce weight loss in the range of 10 to 15 percent of normal weight or height (see Table 1). Many ballet dancers, professional female runners, and photography models are amenorrheic or have irregular cycles (32).

We have given permission with pleasure to reprint figures 1 and 2 from the 1974 *Science* paper (8) in various textbooks and journals, including in Swedish (12). Our refusal in the case of Trussell has a history which must be referred to here in response to Trussell's complaint of our refusal. Pertinent to this history is a discussion of the Trussell dashed lines shown (1) in his figures 1 and 2, *now* described in the legends as "standards obtained by regressing weight at menarche on height at menarche." On figure 1, "the standard obtained by regressing weight at menarche on height at menarche" is described by the equation: $Wt = .622 Ht - 58.47$. If any particular height is put in the equation, the weight indicated on the plot is in fact given. However, if the mean height at menarche of the BGS girls whose data were used for the equation are inserted in the equation: $49.4 \neq .622 (159.0) - 58.47$; the equation does not balance: $49.40 \neq 40.4$.

On figure 2, we find again a standard obtained "by regressing weight at menarche on height at menarche." The slope is the same as in figure 1, but the constant is different, -53.19 instead of -58.47 . We are given no information why this is so; the description is the same for figure 1 as in figure 2. This is especially inexplicable since the solid line from Frisch and McArthur's (8) figure 2 redrawn on Trussell's diagram represents total water/body weight percent derived from 181 girls *at age 18 years, not at menarche*. At menarche the tenth percentile of estimated TW/BWt % was 59.8 percent, equivalent to about 17 percent fat/body weight percent. But at age 18 years, the value of the tenth percentile of TW/BWt % is 56.1 percent, equivalent to about 22 percent fat of body weight. As we reported (8), we found that women with secondary nutritional amenorrhea, who had completed their growth and were well past the age of menarche, had to have a *heavier* minimal weight for height for the resumption of cycles than had been found at menarche. Study of the change in each girl from menarche to age 18 years showed that this was because they became heavier and fatter from menarche to age 18 years (11).

Now, going back to Trussell's figure 2. If we put any particular height on the graph into Trussell's equation:

$Wt = .622 Ht - 53.19$, one will indeed get the particular weight he plots. However, if one inserts the mean height at menarche of the BGS girls into the equation: $Wt = .622 (159.0) - 53.19$, we obtain $49.1 \neq 45.7$. Nor does height of the BGS girls at age 18 years (166.5 ± 0.78 cm) in relation to weight at age 18 years (59.1 ± 0.9 kg) improve the situation: $Wt = .622 (166.5) - 53.19$; $59.1 \neq 50.4$ kg. We need more information than Trussell gives us on these regressions "at menarche" to clear up these discrepancies.

Trussell in his diagrams has reduced the weight scale relative to height, so it is difficult to read the precise weights for heights compared to ours (8) on our figures 1 and 2, and the wide divergence at both ends of his line, compared to ours, seems reduced. It is clear, however, that his (1) dashed line based on weight regressed on height at menarche on figure 1 and on figure 2 underestimates the weight for the short girls and overestimates it for the tall girls. This is exactly opposite to what is expected at both menarche and at age 18 years. Tanner (33) and many other workers, including Frisch and Revelle (6), have shown that early maturers are shorter than later maturers at menarche and have more weight for height than the average, while late maturers, who are tall, have less weight for height than the average. This is true for girls at age 18 years also.

Now, why we refused Trussell's request for permission to reprint our figures:

Before we received this request on 6 December 1977, Trussell had sent to the writer for comment, on his own volition, papers containing copies of the Frisch and McArthur figures on which a Trussell line had been superimposed. The legends for this Trussell line were then described in two separate papers (the first dated 20 July 1977, the second 11 October 1977) as based on IQ data regressed on height and weight:

$$\hat{IQ} = 135.44 + 0.7 Wt - 0.44 Ht \quad (1)$$

and

$$\hat{IQ} = 234.63 + 2.00 Wt - 1.25 Ht \quad (2)$$

These IQ equations are for lines which are exactly the same lines as are now described as "standards obtained by regressing weight at menarche on height at menarche." A reference was given for IQ data in Eq. 1 but there were no IQ data in the reference. Responses by Trussell to inquiries about the IQ data made it very doubtful that the IQ equa-

tions were being correctly represented. For example, to the question, "Since you had no IQ data, how did you derive equation (1)?" the reply was: "I made up an equation *not* based on data" (8/18/78) (34). The statements by Trussell were supposed by Trussell to be analogous to our use of the total water equation given by Mellits and Check (15) in which actual body water measurements of subjects were regressed on the height and weight of subjects who actually had their body waters measured ("water girls"). Trussell's analogy therefore was a false analogy, as he himself realized, since in his later version he had IQ data from six of his colleagues regressed on their weights and heights; this is Trussell's Eq. 2 above.

The dashed line given for Eq. 2 superimposed on our figures did not differ from that given for Eq. 1, although the equations differed.

When the height and weight of the BGS girls at age 18 years, 166.5 cm and 59 kg respectively, are substituted into Eq. 1, $\hat{IQ} = 103$, an improbable result for middle-class girls (35).

If we substitute these same height and weight values into Eq. 2 above, $\hat{IQ} = 144.5$, also an improbable result for a population of middle-class 18-year-olds (35). Equation 2 above is now in Trussell's (1) note (12), while his dashed lines are now described as standards "obtained by regressing weight at menarche on height at menarche."

Since it was very improbable that the Trussell IQ standards were what Trussell said they were, and since there were discrepancies between Eqs. 1 and 2, both given for the same line, it did not seem appropriate to give permission to reprint our figures.

It is to be noted that the present (1) Trussell equation (2) in his note (12) has the very improbable characteristic of giving a drop of 20 points in IQ coincident with a change in weight of 10 kg. It is always important to check out an intermediate variable for reasonable results.

Trussell's discussion of the 1974 *Pediatrics* paper (36), which predicts menarche from heights and weights at age 9 to 12 years (36), also has many incorrect statements. Contrary to Trussell, the same regressors were used in each quartile. We reported only those which gave significant results.

The height and weight quartiles used were not based on national samples, but on the comparable middle-class sample of Stuart and Meredith. The weight/height quartile comparison was for age

11 years. It is well established that girls do not remain in the same height percentiles during the adolescent spurt (33). We defined the age in years as defined in the original growth studies.

Trussell's analysis is not comparable to ours in either numbers or method.

We found that prediction was better in quartiles of fatness than in weight for height, which is consistent with our earlier finding (7) that a high percentage of girls remain in the same percentile of $TW/BW\%$ from initiation of the spurt to menarche (not age 8 to menarche, as Trussell tested.)

Trussell's statement "Frisch presented no test of whether the segmentation itself was necessary" presents a new criterion for scientific research: "Is it necessary?" We may ask: Was it *necessary* for Mendel to count green and yellow peas? or for Newton to estimate the mass of the moon? No one said the procedure was *necessary*. The procedure was suggested by the interesting finding that 82 percent of 169 girls remain in the same quartiles of total body water/body percent (which can be thought of as quartiles of fatness) from spurt initiation to menarche, compared to 47 percent (79) remaining in the same weight quartiles (7). It is important to note that these quartiles were followed from the age of initiation of the adolescent spurt to menarche. We had previously determined this age (3) for each girl for whom we also had menarcheal data. Trussell's table 2 is not analogous, and is misleading to the reader, since it is based on quartiles from age 8 to menarche, which is a crude classification without any biological rationale.

Historical data. The original writings of Quetelet, apparently not read by Trussell (who cites excerpts cited in a secondary source), certainly did distinguish between "la puberté" and "l'écoulement périodique," or menstruation, as I quote in my 1972 paper in *Pediatrics* (30). As I state in that paper:

Before "la puberté" girls weigh 50% of what they will attain at "leur développement complet," (55 kg). "La puberté," which takes place in city girls at age 12, seems to be the time of appearance of secondary sex characters (as Tanner noted of Buffon's use of the word) and the initiation of the spurt. It is distinguished from menarche, "l'écoulement périodique," or "menstruation." The most rapid period of weight growth in girls (which is known to precede menarche) is at 15 years. [My emphasis]

The original Quetelet sources are listed in (30).

Consistent with these statements, Quetelet also noted as I cited, the time of

fecundity (*fecundité*) of women is between "18 and 40 years." This shortened reproductive span historically was found for English and Scottish women, as I discussed in detail in my 1978 article (28).

Trussell's statement that my hypothesis "rests on historical data published by Quetelet" is not only incorrect, it is absurd. There are 82 references and notes in my *Science* 1978 article, of which two are from Quetelet (28). This 1978 article presented historical data from primary sources on mid-19th-century growth, food intake, and reproductive data, in support of the hypothesis that the observed submaximum fertility of a historical population was due wholly or in part to undernutrition, rather than contraception. That nutrition can affect reproductive ability of the female and male directly is already known for both human beings and animals (8, 17, 18, 25, 28). For example, loss of libido in men follows a decrease in caloric intake and weight loss (24, 28). Keys *et al.* (24) showed by direct observation that continued caloric reduction to low levels results in a decrease in semen volume, and a decrease of sperm motility and sperm longevity (24, 28). Of course, as we have pointed out for the female (8), the body weight in relation to reproductive ability is necessary but not sufficient; there can be many other causes of loss of libido in the male.

Contrary to Trussell's interpretation of how we do our research, the concept of a direct pathway of food intake to fecundity, published in 1974 (abstract) and 1975 (29), was arrived at after the analysis of the data published in Frisch and McArthur (8) and discussion with colleagues in anthropology and demography.

The fundamental biological finding that slow growth to maturation for a population seems to be subsequently followed by a shortened and less efficient reproductive life span was suggested by our experimental results on the rat (26, 27), in relation to the human data (8, 28). We have suggested possible mechanisms for this finding (17, 25, 27, 28).

Trussell's remark that I have not discussed two unpublished papers (which were presented after my 1978 article was completed) is curious since Trussell does not refer to my published reply (20), (of which he is aware) to a paper he repeats at length; does not refer to our experimental papers on the rat (26, 27), of which he is aware; and does not refer to the many current papers corroborating

our findings (22), many of which have been called to his attention. A recent paper by Cowdhury, Huffman, and Curlin (37) is of particular interest since they show that menarche in Bangladesh women is related to body weight, and that menarche became later when the food supply was curtailed, as would be expected (28, 30).

Trussell estimates an age of peak height velocity on rather poor, cross-sectional historical height data. Trussell then predicates an age of menarche of 15 years based on the peak velocity data (38). Sex difference between age of peak velocity in height averages about 2 years today, but there is little evidence that this was so historically. Similarly, little is known about the interval from peak velocity to menarche historically, but the data from poorly nourished societies suggest this interval would be extended with slower rates of growth (39). Therefore, this estimated age can only be considered accurate to within a year, as I have already pointed out to Trussell (21).

The concept of a critical fat/lean ratio is still in process of formulation. It is obvious that both the absolute and relative amounts of lean body weight and fat are important since the lean body mass and the fat must be in a particular absolute range, that is, the individual must be big enough to reproduce. There is a great deal of research to be done to elucidate this interesting interrelationship, which we have never claimed is the only interrelationship, determining the onset and maintenance of reproductive ability.

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40. I thank W. Alonso for assistance with the statistical analysis of the Trussell comments, and particularly for assistance with the mathematical demonstration of the retention of the new information contributed by the regression of actual total body water measurements on the height and weight of the measured subjects. I also thank R. B. Reed and R. Revelle for reading the manuscript and for helpful suggestions.

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