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COO-3387-2

FINAL REPORT

TO THE

UNITED STATES ATOMIC ENERGY COMMISSION

MASTER

TITLE OF PROJECT: Statistical Analysis of Longitudinal Growth Data on Adolescents Exposed In Utero to the Atomic Bombs, Hiroshima and Nagasaki

PERIOD COVERED BY REPORT: January 1, 1971 to February 29, 1972

CONTRACT NUMBER: AT(11-1)-3387
Formerly AT(30-1)-4188

SUPPORTED BY: United States Atomic Energy Commission
Division of Biology and Medicine

DATE OF REPORT: March 31, 1972

SUBMITTED BY

PRINCIPAL INVESTIGATOR: Bernard S. Pasternack, Ph.D.

STAFF: Takao Shohoji, M.S.

BIOSTATISTICS LABORATORY

INSTITUTE OF ENVIRONMENTAL MEDICINE

NEW YORK UNIVERSITY MEDICAL CENTER

MASTER

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ABSTRACT

Since 1950 approximately 1600 exposed and control subjects who were _in utero_ at the time of the atomic bombings (ATB) of Hiroshima and Nagasaki have been studied at ABCC. The PE-86 sample was drawn from the population of _in utero_ children ATB who were either exposed or non-exposed (entering Hiroshima and Nagasaki between October 1945 and October 1955). Matching of subjects was carried out so that all available children exposed under 2,000 m were entered into the study. For each child exposed proximally an attempt was made to include a child exposed distally and one not-in-city ATB--matched by sex, month of birth and economic status. Children at all stages of gestation were included.

During the past year, a four parameter Gompertz-type model was used to characterize growth during adolescence for Japanese subjects who were _in utero_ at the time of the atomic bombings (ATB) of Japan in 1945. Based on maximum likelihood estimates of the four parameters, statistical analyses were performed to test for differences between sexes, cities, trimesters ATB, and exposure groups. The results obtained indicated that: (i) males significantly differed from females in all comparisons; (ii) differences among male exposure groups (indicating some impairment in adolescent growth) were greater than those for females; (iii) males and females in Nagasaki differed from those in Hiroshima, respectively; (iv) differences among trimester ATB groups were, almost without exception, non-significant; and (v) age at onset of menarche and estimated age at the second point of inflection of the Gompertz growth curve were closely related.

CONTENTS

1. INTRODUCTION

Since 1950 approximately 1,600 exposed and non-exposed children who were *in utero* at the time of the atomic bombings (ATB) of Hiroshima and Nagasaki, Japan, have been studied by the Atomic Bomb Casualty Commission (ABCC). The sample used (known as the PE-86 sample) was drawn from the population of *in utero* children ATB who were either exposed or non-exposed (entering Hiroshima and Nagasaki between October 1945 and October 1955). Matching of subjects was carried out so that all available children exposed within 2,000 m from the hypocenters were entered into the PE-86 sample. These subjects will be called the "Inner Proximal" group (or Group I). For each child exposed proximally an attempt was made to include a child exposed distally (3,000 - 5,000 m, Hiroshima, and 2,500 - 5,000 m, Nagasaki) who was of the same sex, month of birth and economic status. These subjects will be called the "Distal" group (or Group II). The same procedure was used in matching the non-exposed children to the proximally exposed. The non-exposed children will be called the "Not-in-city" group (or Group III). Children at all stages of gestation ATB were included. The children in this study were examined annually at ABCC at a time near their birth date. Details on the selection and composition of the PE-86 sample can be found in Burrow *et al* [4], Finch *et al* [6] and Beebe and Usagawa [3]. Milton and Shohoji [9] have estimated the dose (Tentative 1965 Radiation Dose--T65D) in rads to the exposed mothers.

Growth is one of the most basic expressions of life. That radiation affects growth and growth pattern is well established; however, the form of the effect is not clearly understood. In this report, we will examine the radiation effects of *in utero* exposure to the atomic bombs on adolescent growth patterns by characterizing the individual adolescent growth cycles of subjects included in the PE-86 sample.

Most of the previous investigations on the analysis of growth have been concerned with standing heights (or weight) at a particular age, or with gain in an interval of time. Growth has been analyzed as a function of time under the assumption that every individual in the population can be represented by one model and that the parameters of the model are constant. An additive residual term is used to account for all deviations from the model. This logic ignores the fact that individuals give distinct responses which should be considered in order to correctly interpret growth data.

Deming [5] used a Gompertz-type model to fit observed height during the adolescent growth cycle of 48 individual boys and girls, but it is not clear how she determined the asymptotic values. Laird [7] found that human (individual) weight growth data also could be fitted adequately with a Gompertz-type model by breaking the growth into three phases, but it is not clear how to determine the boundaries for these phases. Allen [2] has constructed a general multivariate non-linear model and analysis which he feels is applicable to growth curves. However, his method requires heights to be measured at regular intervals. Welch [13] introduced the technique of fitting the dependent variable (e.g., height) to orthogonal polynomials in the independent variable (e.g., age) coupled with two auxiliary modifications to be used as necessary. Marubini <u>et al</u> [8] recently published the results of a study comparing the fit of two functions--the Gompertz and logistic--to adolescent growth data in girls.

2. MATERIALS AND METHODS

Table 1 shows the PE-86 sample composition by exposure status and city. Table 2 shows the distributions of the PE-86 sample by Trimester ATB, Exposure status, Sex and City. Three numbers appear in each cell for the two tables. The top number indicates the original sample size of the PE-86 sample, the middle number indicates the effective sample size (i.e., the number of PE-86 sample subjects with at least five measurements) and the bottom number indicates the final sample size used for this study (i.e., the number of PE-86 sample subjects used in the final analysis--convergent estimates of the parameters A, B, L, and U were obtained by the method of scoring).

The underlying mathematical model that we will consider for describing an individual's growth during his adolescent growth cycle, for avariable such as "standing height", is

$$y_t \sim N[h(t), \sigma^2]$$

i.e., y_t--the measurement of standing height at age t years--is considered to be normally distributed with mean

$$h(t) = L + (U-L)e^{-e^{A-Bt}}$$

and variance σ^2. This regression function is depicted graphically in Figure 1. A detailed discussion of the Gompertz-type growth model and associated estimation procedures has been described elsewhere ([1], [10] and Appendix 1).

The four parameters A, B, L, and U for each individual in the effective sample were estimated by a linearized least squares method and the method of scoring. The subsequent statistical analysis was then based on these estimates (except for the onset of menarche) rather than the individual measurements. Multivariate analysis of variance and discriminant analysis were the primary statistical techniques utilized. The fitting of the individual growth curves and the subsequent statistical analysis were performed with the use of a high-speed digital computer (the CDC 6600).

3. SEX COMPARISONS

Estimates of the fundamental parameters A, B, L, and U in the Gompertz growth model, as well as other parameters, were calculated for approximately 900 children. Table 3 lists their mean values by city, sex, exposure status and trimester ATB. Here, we will discuss sex differences for the Not-in-city groups (the control groups). Although considerable variation was found amongst the estimates of each parameter in each cell, there were still strikingly significant sex differences with respect to almost all estimated parameters.

Sample mean estimates of the constant A, representing an inherent factor of aging, show a statistically significant difference (Males-Females) of about 5 units in Hiroshima and about 4 units in Nagasaki. The mean sex difference of the estimated rate-constants, B, also shows statistical significance in favor of more rapid "aging" for the females than for the males. The estimated indices of the induced individual growth power constant, e^{-B}, also show a significant sex difference.

Estimates of the lower asymptote, L, show an average 12 cm difference between males and females ($p < 10^{-4}$). This tendency for the females to be shorter at the start of the adolescent growth cycle seems to be natural, as they also tend to be significantly younger than the males (by about 2 to 3 years) at the time of onset, S_o, of the adolescent growth cycle. Estimates of the upper asymptote, U, which corresponds to the adult height attained by the individual, also show an average 12 cm difference between males and females ($p < 10^{-4}$). The estimated mean sex difference in the constant, $K = U - L$, representing the total gain in height during the adolescent growth cycle, is not statistically significant.

The mean ages of onset of the adolescent growth cycle differ by about 2 to 3 years; the male mean being significantly greater than the female mean. The mean age at the point of inflection of the female growth curves is significantly younger than that of the males by about 1.5 to 2.5 years. On the other hand, the age at which the growth cycle is completed, S_c, shows no significant sex difference.

Both the age at the first point of inflection, I_1, of the estimated velocity curves and the age at the second point of inflection, I_2, show significant sex differences. The estimated time intervals between the age at the point of maximum growth rate (the inflection point of the growth or "distance" curve) and either I_1 or I_2 also shows significant sex differences. This is due to the sex difference noted for estimates of the constant B.

Estimates of the maximum rate of growth (or the peak velocity of height growth, BK/e, in cm per month), as represented by the derivative of the Gompertz curve at the point of inflection, shows a significant mean difference of about 0.2 to 0.3 cm per month in favor of males. This is in agreement with results reported by Tanner [12] and Shuttleworth [11], but not with the findings of Deming [5].

The preceding results can be summarized as follows (c.f., Tables and 4, and Figures 2 and 3): (i) The age of onset of the adolescent growth cycle for females (9 to 9.5 years) is significantly younger than for males (11.8 years) by about 3 years; (ii) Females attain their maxi rate of growth more quickly than males by about 1.5 to 2.5 years; (iii) Males take 5.2 years, and females about 6.3 to 7.3 years, to complete t adolescent growth cycle after their maximum rate of growth has been attained; (iv) The maximum rate of growth for females is less than that the males, but females attain their maximum rate of growth at a younger age than do the males.

When the estimates of A, B, L, and U are assumed to be distribute as a 4-dimensional normal variable, no statistically significant differ is found among trimesters ATB for the Not-in-city groups (males, or fema in either Hiroshima or Nagasaki. The same holds for the estimates of S_C A/B, S_c, BK/e and U when treated as a 5-dimensional variable. A summar of these results appears in Tables 6 and 7.

When the vector of mean estimates of A, B, L, and U for Nagasaki compared to that of Hiroshima, no statistical significance was found fo the Not-in-city groups for males, but statistical significance ($p < 0.05$ was found for females (trimester ATB pooled) of the Not-in-city groups (c.f., Figures 4 and 5). The estimates of A and B for females in the Not-in-city group for Hiroshima were consistently smaller than those for Nagasaki. Also, the ages of onset and completion of the adolescent grow cycle for females in the Hiroshima Not-in-city groups were younger and older, respectively, than those for Nagasaki. The mean estimates of K and BK/e for females in the Hiroshima Not-in-city group were greater and smaller than those for Nagasaki, respectively. This means that the period of adolescent growth of females in Hiroshima may have been longer than that of females in Nagasaki (c.f., Tables 3 and 5).

4. CITY COMPARISONS

Table 12 shows city comparisons for the various contrasting groups. No statistically significant differences between Nagasaki and Hiroshima were found for males in Group I or Group III, but significant differences ($p < 0.01$) were found for males (except for the 2nd trimester ATB group) in Group II. It is to be noted that the mean estimates of A, B, L, and U for Group II males in Hiroshima are greater in every comparison than the corresponding mean estimates in Nagasaki. This trend also holds for Group I (except for A of the 3rd trimester ATB and U of the 2nd trimester), but not for Group III (c.f., Table 3). All city comparisons (except for L of the 2nd trimester ATB, A and B of the 3rd trimester ATB, and A, B and L of the pooled trimester ATB in Group II) were not statistically significant (c.f., Table 12).

City differences for females are not as apparent as for males, although those in Nagasaki Group III significantly differ from those in Hiroshima Group III. A similar tendency is indicated for females in Group I. These findings suggest that Nagasaki and Hiroshima samples should not be combined for analysis since there may be different ionizing radiation effects between Nagasaki and Hiroshima. For almost all female comparison groups, the mean estimates of the parameter B (and the maximum rate of growth) in Nagasaki were greater than in Hiroshima. Also, the mean estimates of the length of the adolescent growth cycle, and the age intervals between the maximum point and the points of inflection of the velocity curve were shorter for Nagasaki than for Hiroshima (c.f., Tables 3 and 12).

5. TRIMESTER ATB COMPARISONS

No statistically significant differences were found in any of the trimester ATB comparisons of the mean estimates of A, B, L, and U, except for the males of Group II in Hiroshima (c.f., Table 7).

Nagasaki: For females in Group I, the mean estimates of A, B, A/B, S_o, I_2 and Onset-M (age at onset of menarche) increase with trimester ATB, whereas the mean estimates of S_i, K and BK/e decrease with trimester ATB (c.f., Tables 3 and 7, and Figure 11). The maximum rate of growth estimates for females in Nagasaki Group I were the largest obtained among the three exposure groups. For males in Group II, the mean estimates of A, B and BK/e decrease and those of S_c and S_i increase with trimester ATB, but the differences are not significant. The mean estimates of U for males of Group III in Nagasaki are greater than for any other group of males. For both males and females in Group I, mean estimates of U for the 3rd trimester ATB subgroup were lower than for any other group (c.f., Table 3 and Figures 10 and 11).

Hiroshima: By multivariate analysis of the vector estimates of (A, B, L, U), significant differences ($p < 0.05$) and suggestive differences ($p < 0.10$) among trimester ATB subgroups were found for males in Group II and for females in Group I, respectively. For females in Group I, the mean estimates of U and A/B increase with trimester ATB. The females of the 1st and 3rd trimester ATB in Group I appear to begin their adolescent growth cycle somewhat later than the females in Group III, but they end at about the same age. On the other hand, the females of the 2nd trimester

ATB in Group II also start their adolescent spurt somewhat later than their counterparts in Group III, but they end their cycle at an earlier age. The mean estimates of A and B for females of both the 1st and 2nd trimester ATB in Group I are greater than those in Group III. The mean estimates of "age at onset" and "length" of the adolescent cycle for 1st trimester ATB females in Group I are significantly later and shorter, respectively, than those of Group III. The mean estimates of A, B, L and S_o for 2nd trimester ATB females in Group III are larger than for any other female groups in Hiroshima, whereas the estimate of S_i is the smallest. Significant differences ($p < 0.05$) were found among the three trimester subgroups of females in Group II for A, B, S_o, B and BK/e.

For males in Group I, the estimates of A, B, L, U and BK/e decrease and the estimates of S_i increase with trimester ATB, but there is no statistical significance among the trimester ATB subgroups. The estimates of L and U for Group II decrease significantly ($p < 0.05$) with trimester ATB. There are also significant differences among the mean estimates of (A, B, L, U) for the trimester ATB subgroups. The estimates of A, B, L and U for 3rd trimester ATB males in Group I are the lowest that were obtained for any group. On the average, the 3rd trimester ATB males in Group I start their adolescent growth cycles a little earlier, and attain a smaller stature, then the 1st and 2nd trimester ATB males in Group I who grow in a similar fashion as the males in Group III.

6. SOME EXPOSURE COMPARISONS

Here we will be concerned with the radiation effects of <u>in utero</u> exposure to the atomic bombs on adolescent growth patterns. The three groups to be compared are the Inner Proximal Group (Group I), the Distal

Group (Group II) and the Not-in-city Group (Group III), defined in Section 1. Tables 8 and 9 show the results of exposure comparisons (univariate and multivariate) based upon the estimates of (A, B, L, U) and (S_o, A/B, S_c, BK/e, U)--assumed to be distributed as 4-dimensional and 5-dimensional normal variables, respectively. Linear discriminant analysis was also performed using the estimates of A, B, L and U (c.f., Table 8 and Figures 14 and 15).

When the estimates of (A, B, L, U) are assumed to be distributed as a 4-dimensional normal variable, no statistically significant difference for females (Nagasaki and Hiroshima) is found among the three exposure comparison groups for any trimester ATB subgroup. For males, however, significant exposure differences ($p < 0.05$) are found among the three groups within Hiroshima 3rd trimester ATB subgroups and within Nagasaki pooled trimester ATB (= 1st + 2nd + 3rd trimester ATB) groups. Suggestive exposure differences ($p < 0.10$) are also found among the three exposure groups (for the 2nd trimester ATB subgroups) in Hiroshima (c.f., Table 8). When we consider partial exposure comparisons (Groups I vs. II, II vs. III, III vs. I), significant differences are found for the following comparisons: (1) (II, III)--2nd trimester ATB males, Nagasaki; (2) (I, III)--1st trimester ATB females, Hiroshima; (3) (I, II)--3rd trimester ATB males, Nagasaki; and (4) (II, III)--2nd trimester ATB males, Nagasaki (c.f., Table 9).

<u>Females in Hiroshima</u>: The only significant finding using multivariate analysis resulted from a partial exposure comparison for the 1st trimester ATB. However, when the estimate of A, B, L and U were considered singly, significant exposure differences ($p < 0.05$) for the mean estimates of A and B were found. For the 1st trimester ATB, the mean estimates of A and B

in Group I differed ($p < 0.01$) from those in Group III. For the 2nd trimester ATB, the mean estimates of A and B in Group I differed ($p < 0.05$) from those in Group II. A suggestive exposure difference ($p < 0.10$) in the mean estimates of U was also found among the three exposure groups of the 1st and pooled trimester ATB (c.f., Figure 9). The mean estimate of U for the 1st trimester ATB in Group I was the smallest for Hiroshima-females; it significantly differed from that for Group III ($p < 0.05$). The mean estimate of U for the 3rd trimester ATB in Group I was the largest for the Hiroshima-females, being close to that obtained for Group III. The mean estimate of U in Group I increased with trimester ATB (c.f., Figure 13). The mean estimates of A, B, S_o, S_i and U for 1st trimester ATB in Group I were all significantly different ($p < 0.05$) from those in Group III. The estimates of U, A/B and S_o for the 2nd trimester ATB in Group I were also significantly different ($p < 0.05$) from those in Group III. Thus, the females of 1st trimester ATB in Group I show a relatively late onset of the adolescent growth cycle, quick maturity, and somewhat shorter adult standing heights. The estimates of U for females (1st trimester ATB) having highly exposed mothers (total T65D > 100 rads) were all less than 151 cm (except for one case), where 151 cm was arbitrarily choosen. The estimates of U for 12 out of 25 females in Group I (the mothers of 6 out of 12 received greater than 100 rads as total T65D) is less than 151 cm, but only 20 out of 111 females in Group III were less than 151 cm. For pooled trimester groups, the mean estimate of U in Group I was significantly smaller ($p < 0.05$) than that in Group III. The mean estimates of A, B, S_o and I_i in Group II were consistently smaller than those in Group III, and those of U and S_i in Group II were consistently smaller and larger, respectively, than those in Group III.

Females in Nagasaki: No statistical significance was found among the exposure comparisons of females in Nagasaki (c.f., Tables 8, 9 and 10, and Figure 7). As discussed previously, there is a relationship between the estimates of A, B, L and U and trimester ATB for Group I females. The 3rd trimester ATB in Group I differs from the other groups in that the mean estimates of A and B for that group were the largest, the mean estimate of U was the smallest, and those of S_o and S_i were the second largest and smallest, respectively (c.f., Figure 11). A linear relationship between age at onset of menarche and age (estimated) at the second point of inflection of the estimated velocity curve for all Nagasaki females was also demonstrated (c.f., Figure 16).

Males in Hiroshima: Multivariate analysis using the estimates of (A, B, L, U) revealed exposure difference as follows: (i) the 3rd trimester ATB groups ($p < 0.05$)--Group I vs. II ($p < 0.05$); and (ii) the 2nd trimester ATB groups ($p < 0.05$)-- Group II vs. III ($p < 0.01$). When the estimates (A, B, L, U) were considered singly, no statistical significance was found among the three groups (Groups I, II and III) and between the three partial comparison groups (Groups I vs. II, II vs. III and III vs. I).

Tables 8 and 9 and Figure 15 show some results based on linear discriminant analysis using the estimates of A, B, L and U. Significant differences ($p < 0.05$) were found among the three exposure groups (2nd and 3rd trimester ATB) by using a chi-square test of the significance of each discriminant function. Differences between Groups I and III were smaller than those between Groups II and III. As mentioned previously, the mean estimates of A, B, L and U in Group I, and L and U in Group II, decrease with trimester ATB. The mean estimates of A, B, U, A/B, S_o, I_1, I_2 and BK/e for the 3rd trimester ATB in Group I were the lowest obtained in Hiroshima. The number of subjects who had estimates of U less than 160 cm was 13 out of 143 in Group III, 24 out of 133 in Group I, and 14 out of 100 in Group II.

Males in Nagasaki: Multivariate exposure comparisons using estimates of (A, B, L, U) revealed a statistically significant difference ($p < 0.05$) among the pooled trimester ATB groups, and a suggestive difference ($p < 0.10$) for the 2nd trimester ATB groups. Significant exposure differences ($p < 0.05$) for the estimates of L and U were also found by univariate methods for the 2nd trimester ATB groups and pooled trimester ATB groups. The mean estimate of U for the 3rd trimester ATB in Group I was the lowest obtained in Nagasaki (as in Hiroshima). The smallest maximum rate of growth was achieved by the 2nd trimester ATB of Group I in Nagasaki (in Hiroshima, it was by the 3rd trimester ATB in Group I). Significant differences ($p < 0.05$) among Groups I, II and III for the 2nd trimester ATB groups and for the pooled trimester ATB group, were also found by the use of linear discriminant analysis. The number of subjects with estimates of U less than 160 cm was 1 out of 47 in Group III, 8 out of 44 in Group I, and 22 out of 59 in Group II. The number less than the smallest estimate of U in Group III (154.9 cm) is 6 (all in Group I).

Tables 10 and 11 summarize the results of the exposure comparisons by city, sex and trimester ATB when Group I (Inner Proximal group) is divided into two sub-groups (according to distance from the hypocenters, and T65D dose to the mothers, respectively. No consistent pattern is evident among these exposure comparison groups.

7. SUMMARY

Since 1950 approximately 1,600 exposed and control subjects who were *in utero* at the time of the atomic bombings of Hiroshima and Nagasaki have been studied at ABCC. The sample was drawn from the population of *in utero* children ATB who were either exposed or non-exposed (entering Hiroshima and Nagasaki between October 1945 and October 1955). Matching of subjects was carried out so that all available children exposed under 2,000 m were entered into the study. For each child exposed proximally an attempt was made to include a child exposed distally and one Not-in-city ATB--matched by sex, month of birth and economic status. Children at all stages of gestation were included.

The primary objectives of this research project were:

(a) to obtain meaningful statistical estimates of biological parameters descriptive of adolescent growth, and

(b) to determine, using these statistics, whether or not exposure to A-bomb ionizing radiation while *in utero* has resulted in impairment of growth during adolescence.

Towards this end, a computer programmed two stage estimation procedure was developed and applied to the estimation of a four parameter Gompertz-type growth curve (using the variable *standing height*) for each subject in the study. Twelve tables and 21 figures describing the methodology used and summarizing the results obtained were presented. Satisfactory estimates (i.e., convergent by the method of scoring) were obtained for 903 out of 1,608 subjects in the study sample. The main findings based on the analysis of the estimates obtained for these 903 subjects were as follows:

1) The growth pattern of males significantly differed from females for all comparison groups. In particular: (i) males start the adolescent growth spurt 2 to 3 years later than females; (ii) females attain their maximum rate of growth about 1.5 to 2.5 years earlier than males; (iii) the maximum rate of growth of females is significantly less than males; and (iv) the estimates of L and U for the females are significantly lower than those of the males.

2) No statistically significant differences were found between Nagasaki and Hiroshima for either Inner Proximal or Not-in-city male group comparisons. Males of the Distal groups, however, differed significantly between Nagasaki and Hiroshima. The mean estimates of A, L, U, A/B, S_o, K. K/L, I_1 and I_2 for Hiroshima were consistently higher than those for Nagasaki for all trimester ATB groups. The Nagasaki Distal group males began their adolescent growth cycle a little earlier than the Hiroshima Distal group males, but attained a somewhat shorter adult stature. Statistically significant differences between Nagasaki and Hiroshima were found for females in the Inner Proximal and Not-in-city groups. The females of the Inner Proximal and the Not-in-city groups in Nagasaki completed their adolescent growth cycles more quickly than those in Hiroshima.

3) With the exception of the Hiroshima Distal group males, there were no significant differences among the trimester ATB groups.

4) Significant differences were found for exposure group comparisons as follows: (i) between the Distal groups and the Not-in-city groups of the 2nd trimester ATB males in both Nagasaki and Hiroshima; (ii) between the Inner Proximal group and the Distal group of the 3rd trimester ATB males in Hiroshima; (iii) between the Inner Proximal group and the Not-in-city

group of the 1st trimester ATB females in Hiroshima; and (iv) among the three exposure groups of the pooled trimester ATB males in Nagasaki.

5) The differences among the three male exposure groups were greater than those for the females--no significant differences were found among the three Nagasaki female comparison groups (Inner Proximal, Distal, Not-in-city) when only the estimates of the four fundamental parameters (A, B, L, U) were used.

6) The mean estimates of U for the 3rd trimester ATB Inner Proximal group males (in both cities) were the smallest obtained for any group of males. The mean estimate of U for the 1st trimester ATB Hiroshima Inner Proximal females was the smallest obtained for any group of females, differing significantly from the corresponding Not-in-city group. In Nagasaki, the mean estimates of U for the exposed males (= Inner Proximal + Distal) by trimester ATB were consistently lower than those for the Not-in-city group. In Hiroshima, the mean estimates of U for the exposed males decreased with trimester ATB.

7) For the males, Nagasaki and Hiroshima, differences between the Inner Proximal group and the Not-in-city group were smaller than differences between the Distal group and the Not-in-city group, except for the 3rd trimester males. For the 3rd trimester males, the Inner Proximal group differed from the Distal and the Not-in-city groups. For the females, differences between the Inner Proximal group and the Distal group were smaller than differences between the Inner Proximal group and the Not-in-city group (when trimester ATB were pooled).

8) A linear relationship between age at onset of menarche and age (estimated) at the second point of inflection of the estimated Gompertz growth curve was found.

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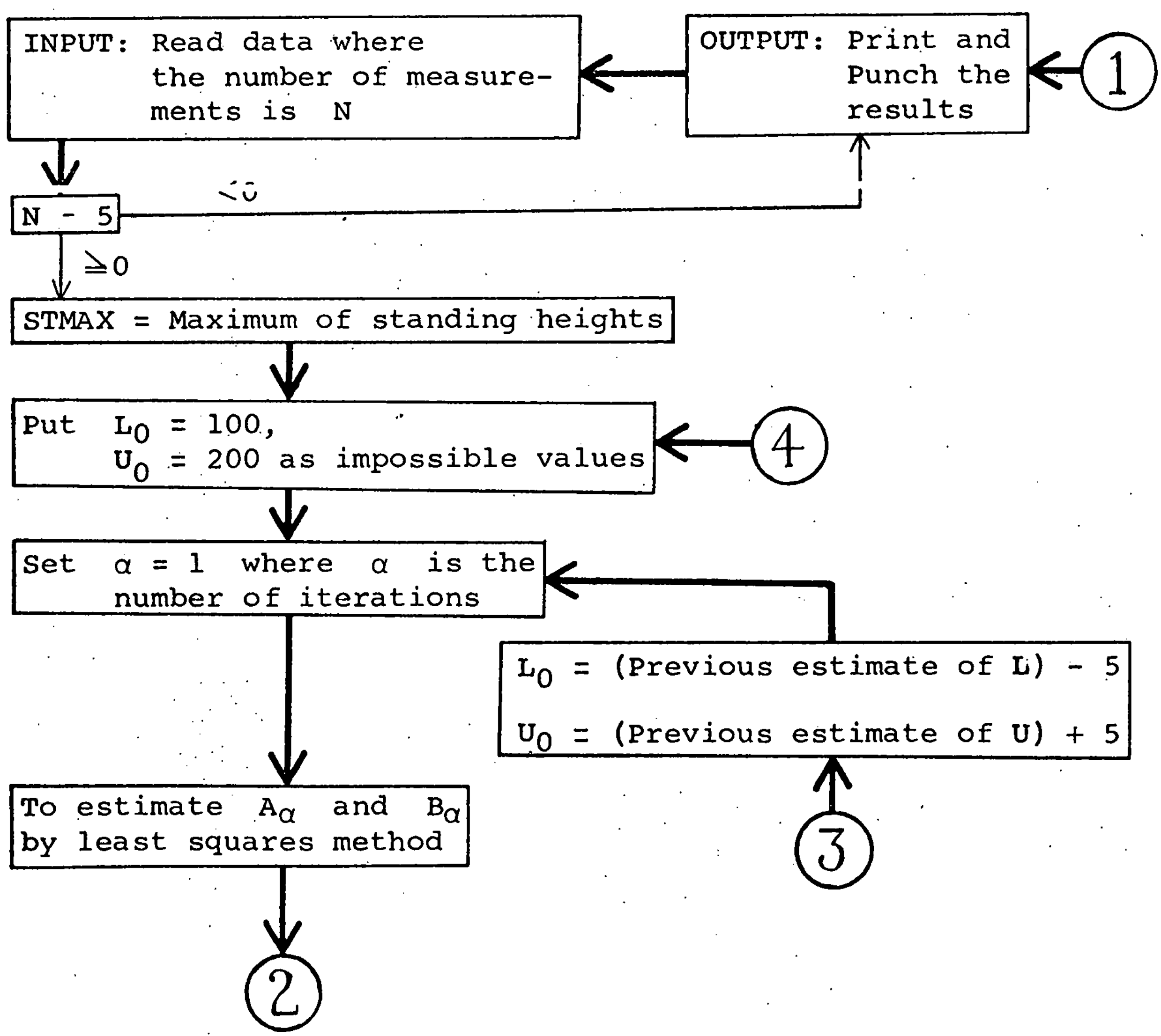
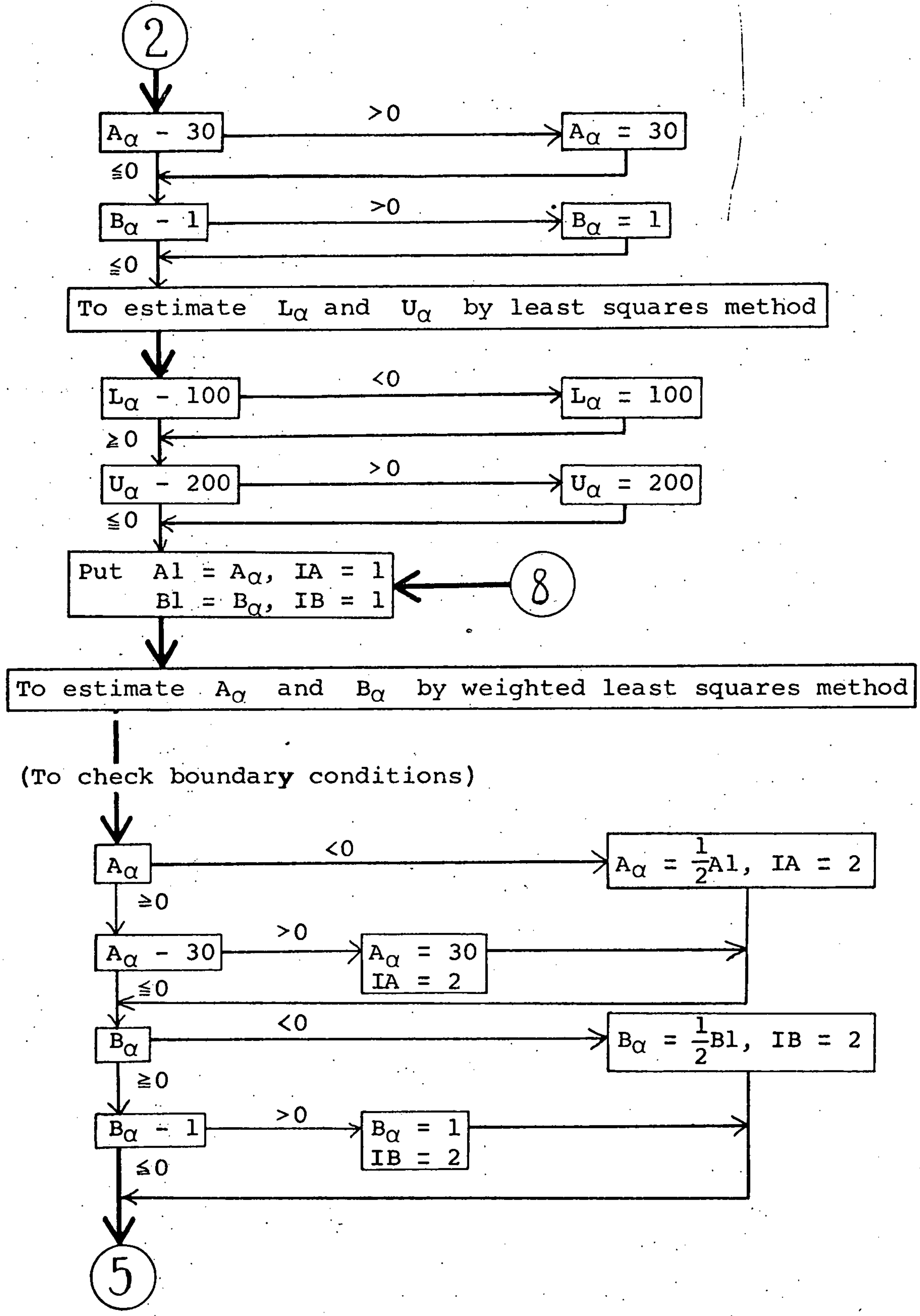
APPENDIX 1

Programming Flow Chart for Fitting Gompertz Growth Curves

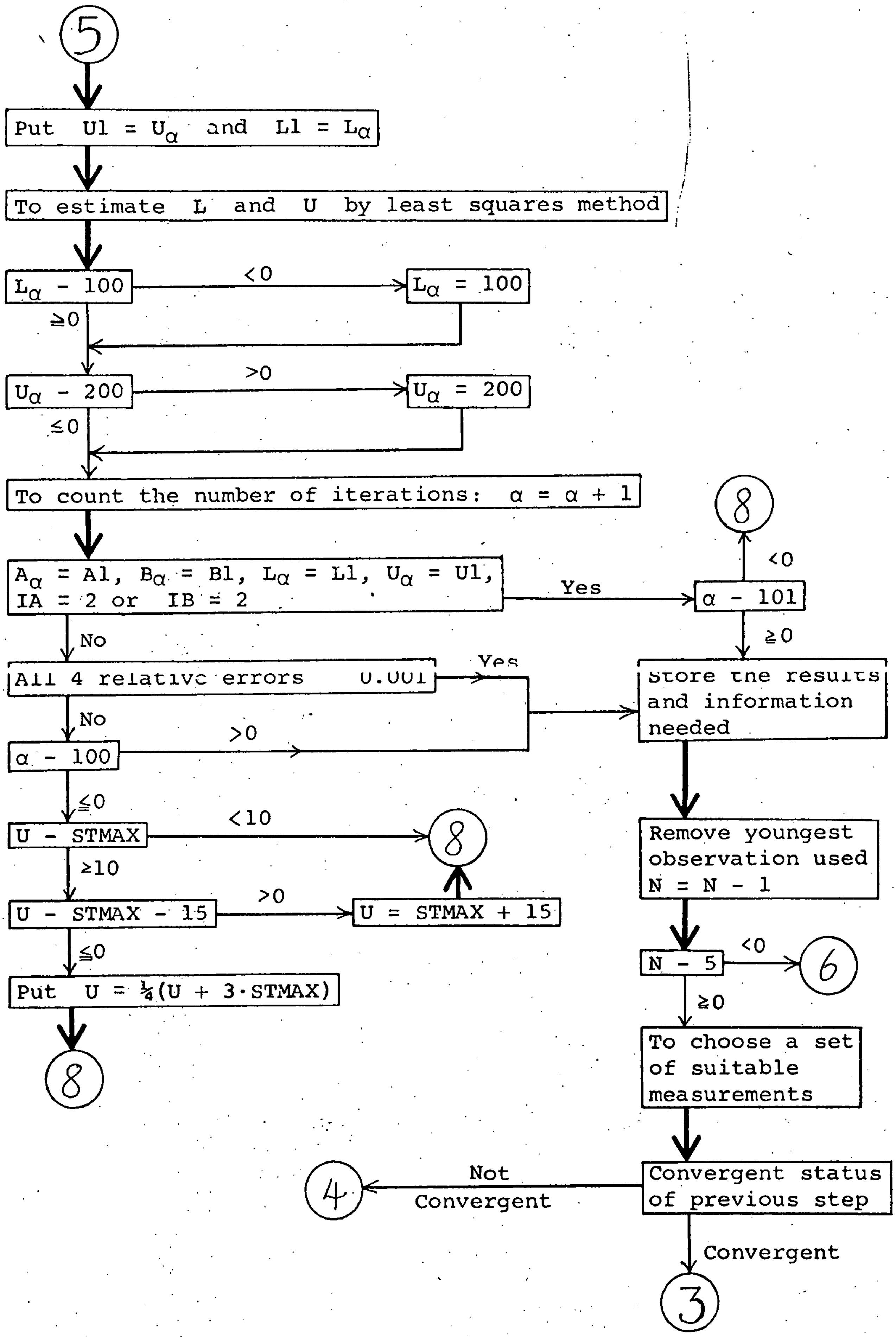
numerical procedure for estimating parameters (A, B, L, U) as discussed in Section 3-2, Part II. The actual Program GROWTH is listed in Appendix 2. A_α, B_α, L_α and U_α denote the estimates of the parameters A, B, L and U, respectively, at the end of the α-th iteration.

Programming Flow Diagram
*********** **** *******

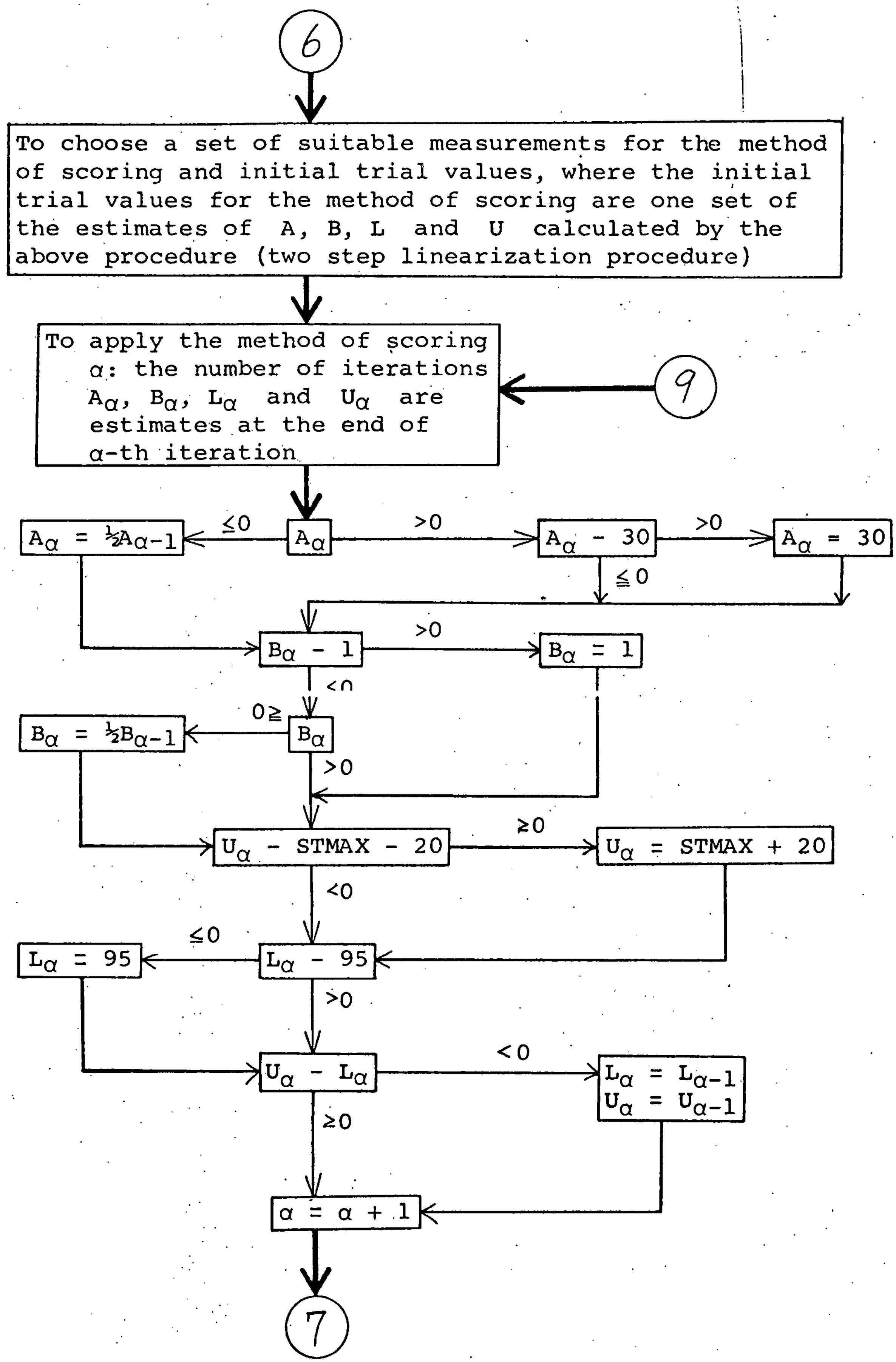


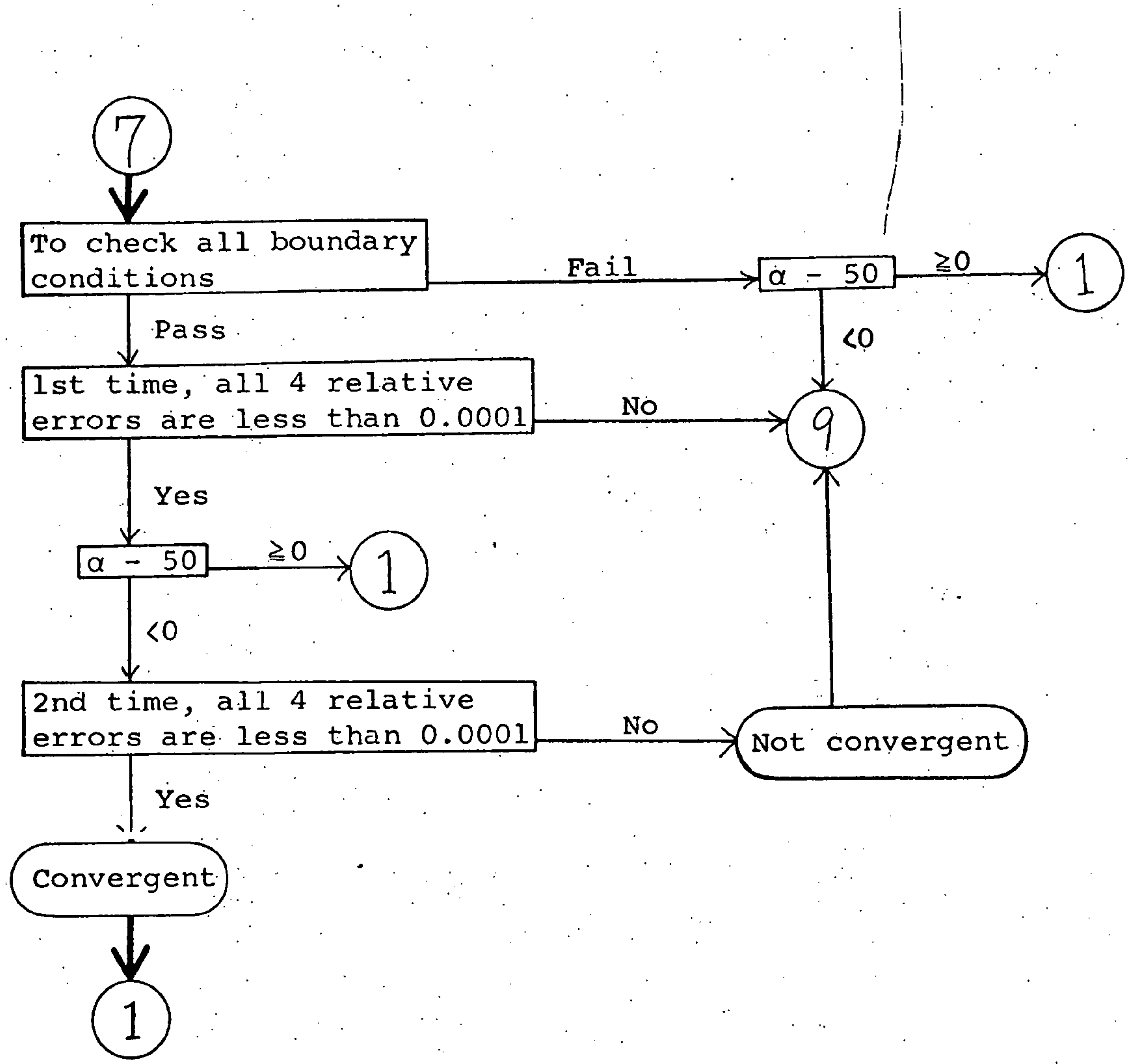


2
Aα - 30
>0
Aα = 30
≦0
Bα - 1
>0
Bα = 1
≦0
To estimate Lα and Uα by least squares method
Lα - 100
<0
Lα = 100
≧0
Uα - 200
>0
Uα = 200
≦0
Put A1 = Aα, IA = 1
B1 = Bα, IB = 1
8
To estimate Aα and Bα by weighted least squares method
(To check boundary conditions)
Aα
<0
Aα = 1/2A1, IA = 2
≧0
Aα - 30
>0
Aα = 30
IA = 2
≦0
Bα
<0
Bα = 1/2B1, IB = 2
≧0
Bα - 1
>0
Bα = 1
IB = 2
≦0
5



5
Put U1 = Uα and L1 = Lα
To estimate L and U by least squares method
Lα - 100
<0
Lα = 100
≧0
Uα - 200
>0
Uα = 200
≦0
To count the number of iterations: α = α + 1
Aα = A1, Bα = B1, Lα = L1, Uα = U1,
IA = 2 or IB = 2
Yes
α - 101
<0
8
≧0
No
All 4 relative errors 0.001
Yes
Store the results and information needed
No
α - 100
>0
≦0
U - STMAX
<10
8
≥10
U - STMAX - 15
>0
U = STMAX + 15
≦0
Put U = ¼(U + 3·STMAX)
8
Remove youngest observation used
N = N - 1
N - 5
<0
6
≧0
To choose a set of suitable measurements
Convergent status of previous step
Not Convergent
4
Convergent
3


6
To choose a set of suitable measurements for the method of scoring and initial trial values, where the initial trial values for the method of scoring are one set of the estimates of A, B, L and U calculated by the above procedure (two step linearization procedure)
To apply the method of scoring
α: the number of iterations
Aα, Bα, Lα and Uα are estimates at the end of α-th iteration
9
Aα = ½Aα-1
≤0
Aα
>0
Aα - 30
>0
Aα = 30
≤0
Bα - 1
>0
Bα = 1
<0
0≧
Bα = ½Bα-1
Bα
>0
Uα - STMAX - 20
≥0
Uα = STMAX + 20
<0
Lα = 95
≤0
Lα - 95
>0
Uα - Lα
<0
Lα = Lα-1
Uα = Uα-1
≥0
α = α + 1
7



Remark: Possible overflow and underflow are checked at each calculation, where necessary.

2
MF NO, 53260 — NAGASAKI — MALE

EXPOSURE GROUP DISTAL — COORINATES (5.50, 62.88) — DISTANCE 3283 (M) — CALCULATED AT SEPT, 28, 1971,
DATE OF BIRTH NOV, 14, 45, — DATE OF DEATH - -0, — BLOOD AB — INJURY 9999
TRIMESTER ATB 2

	AIR	T65D
GAMMA	0	0
NEUTRON	0	0
TOTAL		0

NO,	AGE	ATE	MONTH	STANDING MEASUR	STANDING INCRIM	SITTING MEASUR	SITTING INCRIM	HEAD MEASUR	HEAD INCR	WEIGHT MEAUR	WEIGHT INCR
1	9	54 - 11	108	111.0	0,00000	63.5	0.00000	52.0	0.00000	21,9	3,73333
2	10	55 - 11	120	116.0	5,00000	66.0	2,50000	52.3	.30000	24.0	2,10000
3	11	56 - 11	132	121.0	5,00000	68.5	2,50000	52.2	-.10000	26.0	2,00000
4	12	57 - 11	144	127.0	6,00000	68.5	0.00000	52.8	.60000	26,0	0,00000
5	13	58 - 11	156	129.0	2,00000	71.1	2.60000	53.3	.50000	29.8	3,80000
6	14	59 - 12	169	139.0	9,23077	76.2	4.70769	54.1	.73846	34.5	6,03077
7	15	61 - 1	182	149.0	9,23077	83.8	7.01538	55.2	1.01538	44.6	7,47692
8	16	61 - 11	192	154.0	6,00000	85.3	1.80000	54.8	-.48000	46.2	1.92000
9	17	63 - 2	207	155.0	.80000	86.3	.80000	55.6	.64000	51.6	2,72000
10	18	63 - 10	215	155.0	0.00000	86.9	.90000	55.6	0.00000	49.5	-3.15000
11	19	64 - 10	227	156.0	1,00000	87.3	.40000	55.4	-.20000	51,3	1,80000

USED	REPL,		A-ESTIMATE	B-ESTIMATE	L-ESTIMATE	U-ESTIMATE	MEAM DIFF,	S.S.	MEAN SS	A/B	100B/K	ONSET	ATTN	INT
11	27	CONVERGE	5.532784	.036773	112.351892	160.04066	2,9552	51.3125	7.3304	150.485	.077	106.35	288,24	181,9
10	10	CONVERGE	8.221812	.051954	118.697665	157.85390	2.8535	39,0530	6.5088	158.253	.133	127,78	251,95	124,2
9	17	CONVERGE	13.216073	.080270	124.006680	156.17149	1,8924	20.1182	4.0236	164.646	.250	145.43	222,83	77,4
8	16	CONVERGE	16.014003	.095540	127.246908	155.81656	.7461	1.4683	.3671	167.616	.334	151.74	215.25	63,5
7	49	CONVERGE	17.049400	.101234	128.172239	155.70849	.7870	1.1953	.3984	168.416	.368	153.52	213,01	59,5
6	12	CONVERGE	16.142601	.097096	124.230730	155.74076	1.2083	1.2820	.6410	166.253	.308	150.42	214,14	63,7
5	14	CONVERGE	20.836117	.163713	135.290020	155.40237	1,2886	.5751	.5751	176.138	.814	167,36	201,78	34,4

***** THE DATA USED FOR SCORING METHOD *****

8	16CONVERGE	16.014003	.095540	127.246908	155.816561	.746090	1.468330	.367083

***** RESULT OF METHOD OF SCORING *****

8	6	CONVERGE	15.680127	.093562	127.203809	155.890775	.7073	1.4421	.3605	167.591	,326	151,37	216,28	64,9

DL/DX DL/DA = -5.5245E-07 DL/DB = 8.9222E-05 DL/DL = 1,2342E-12 DL/DU = 4,2215E-12
SHOW LOCAL MAX DETER-1 = -1.67E+02 DETER-2 = 2.09E+06 DETER-3 = -2.42E+06 DETER-4 = 5.35E+06 LOMAX
KOLOMOGOROV ONE SAMPLE TEST --- MAX OF DIFFERENCES = 2,4981E-01 PROBABILITY = GT .20

*** INFORMATION MATRIX ***	1,69559032E+02	-2,90172085E+04	-1.19083359E+01	-1,25264019E+01
		4,97857880E+06	1.98130321E+03	2,27404054E+03
			2.30186753E+00	5,95831762E-01
				4,50646894E+00
*** INVERSE OF INFORMATION ***	4,47851805E+00	2,61409592E-02	8,91033606E-01	-8,60292347E-01
		1,52974513E-04	4.90569096E-03	-5,17954462E-03
			8.50308929E-01	-1,11159333E-01
				4,58975535E-01
*** NORMALIZED INVERS INFO***	1,00000000E+00	9,98722678E-01	4,56602778E-01	-6,00045422E-01
		1,00000000E+00	4,30131956E-01	-6,18139795E-01
			1.00000000E+00	-1,77935879E-01
				1,00000000E+00

MONTH	ESTIMATE	MONTH	ESTIMATE	MONTH	ESTIMATE	MONTH	ESTIMATE	MONTH	ESTIMATE	MONTH	ESTIMATE
100	127,20	105	127,20	110	127,20	115	127,20	120	127,20	125	127,20
130	127,20	135	127,20	140	127,20	145	127,21	150	127,36	155	128,32
160	130,95	165	135,23	170	140,12	175	144,60	180	148,18	185	150,78
190	152,57	195	153,77	200	154,54	205	155,04	210	155,35	215	155,55
220	155,68	225	155,76	230	155,81	235	155,83	240	155,86	245	155.87

(U-L)	28,68696632	(U-L)/U	,18451965	100B/U-L	,32614748
0,9625/B	10,28731627	1ST INFL	157,30377839	2ND INFL	177,87841092
B(U-L)/E	,98739015	EXP(-B)	,91058172		

53260212211080032833 0 0 0 .0 0 8 6 1611156801 9356112720315589011
53260 15759 3201 15137 21628 6490 2869 184 1029 15730 17788 9373 910619

APPENDIX 2

APPENDIX 3

List of Tables

Index of Symbols Used in Tables

Index of Symbols Used in Tables

S_o	the age of onset of the adolescent growth cycle,
S_c	the age of completion of the adolescent growth cycle,
S_i	the interval (in months) of the adolescent growth cycle,
K	= U - L, the total gain in height during the adolescent growth cycle,
I_1	the age at the first point of inflection of the estimated velocity curve,
I_2	the age at the second point of inflection of the estimated velocity curve,
A/B	the age at the point of inflection of the estimated distance curve (Gompertz-type growth curve),
BK/e	the maximum rate of growth,
Onset-M	the age at onset of menarche,
Roy's θ	Roy's largest characteristic root criterion,
L-ratio	Likelihood ratio test,
NS	Not significant,
S	Suggestive ($p < 0.10$),
*	Significant ($p < 0.05$),
**	Highly significant ($p < 0.01$)

TABLE 1: Distribution of PE-86 Sample by Exposure Status and City

	Hiroshima			Nagasaki			Both Cities		
Exposure Status	Male	Female	Total	Male	Female	Total	Male	Female	Total
Inner Proximal	226*	209	435	54	48	102	280	257	537
	150**	147	297	46	37	83	196	184	380
	133***	89	222	44	36	80	177	125	302
Distal	218	211	429	71	61	132	289	272	561
	141	140	281	60	51	111	201	191	392
	100	55	155	59	43	102	159	98	257
Not-in-city	199	197	396	60	54	114	259	251	510
	151	125	276	48	45	93	199	170	369
	143	111	254	47	43	90	190	154	344
Total	643	617	1260	185	163	348	828	780	1608
	442	412	854	154	133	287	596	545	1141
	376	255	631	150	122	272	526	377	903

* The original PE-86 sample size

** The number of PE-86 sample subjects with at least five measurements

*** The number of PE-86 sample subjects used in the final analysis (i.e., convergent estimates of parameters (A, B, L, U) were obtained by the method of scoring)

TABLE 2: Distribution of PE-86 Sample by Trimester ATB, Exposure Status, Sex and City

	Male				Female			
	Trimester ATB				Trimester ATB			
Exposure Status	I	II	III	Total	I	II	III	Total
				Hiroshima				
Inner Proximal	74*	86	66	226	64	88	57	209
	42**	63	45	150	41	60	46	147
	35***	56	42	133	25	36	28	89
Distal	69	86	63	218	68	84	59	211
	44	62	35	141	43	57	40	140
	28	41	31	100	10	21	24	55
Not-in-city	52	83	64	199	53	86	58	197
	36	71	44	151	37	54	34	125
	32	67	44	143	33	46	32	111
Total	195	255	193	643	185	258	174	617
	122	196	124	442	121	171	120	412
	95	164	117	376	68	103	84	255
				Nagasaki				
Inner Proximal	23	17	14	54	14	16	18	48
	21	14	11	46	11	12	14	37
	20	13	11	44	11	12	13	36
Distal	30	24	17	71	19	16	26	61
	26	19	15	60	15	14	22	51
	26	19	14	59	13	14	16	43
Not-in-city	23	25	12	60	16	16	22	54
	20	19	9	48	13	14	18	45
	19	19	9	47	12	13	18	43
Total	76	66	43	185	49	48	66	163
	67	52	35	154	39	40	54	133
	65	51	34	150	36	39	47	122

* The original PE-86 sample size

** The number of PE-86 sample subjects with at least five measurements

*** The number of PE-86 sample subjects used in the final analysis (i.e., convergent estimates of parameters (A, B, L, U) were obtained by the method of scoring)

TABLE 3: Averages of Estimated Growth Parameters --- Nagasaki

	Groups	Sizes	A	B	L	[illegible]	A/B	100B/K	S_o	S_c	S_i
Inner Proximal	(1) M I	20	12.5659	.076633	135.14	1[illegible]5.20	163.42	.2663	142.84	225.50	82.65
	(2) M II	13	11.1338	.068742	135.52	1[illegible]7.19	161.32	.2343	137.68	232.79	95.11
	(3) M III	11	12.2442	.075093	130.11	1[illegible]0.87	163.14	.2575	141.55	228.45	86.90
	(4) M P	44	12.0624	.073916	134.29	1[illegible]4.71	162.73	.2546	140.99	228.39	87.40
	(5) F I	11	8.0117	.061049	123.06	1[illegible]4.98	130.68	.1958	104.98	208.49	103.51
	(6) F II	12	8.7430	.062352	125.81	1[illegible]5.00	139.36	.2258	114.05	215.50	101.44
	(7) F III	13	9.7098	.067655	123.45	1[illegible]1.02	142.16	.2676	118.53	213.06	94.53
	(8) F P	36	8.8687	.063869	124.12	1[illegible]3.56	137.72	.2318	112.90	212.48	99.58
Distal	(9) M I	26	12.6776	.079701	135.87	1[illegible]6.55	158.23	.2742	137.95	219.53	81.58
	(10) M II	19	12.4781	.076242	132.11	1[illegible]2.97	163.46	.2519	142.02	228.20	86.18
	(11) M III	14	10.7788	.068744	132.04	1[illegible]4.33	157.50	.2237	133.43	230.54	97.10
	(12) M P	59	12.1628	.075987	133.75	1[illegible]4.87	159.74	.2550	138.19	224.94	86.75
	(13) F I	13	8.4228	.061304	123.66	1[illegible]2.76	136.57	.2264	110.94	213.67	102.73
	(14) F II	14	9.1184	.065946	127.03	1[illegible]4.85	137.84	.2519	113.83	209.88	96.05
	(15) F III	16	8.4279	.060260	124.60	1[illegible]3.98	140.31	.2092	114.59	217.68	103.08
	(16) F P	43	8.6512	.062427	125.11	1[illegible]3.89	138.38	.2283	113.24	213.93	100.69
Not-in-city	(17) M I	19	12.7909	.078021	137.48	1[illegible]7.48	164.03	.2763	143.98	224.44	80.47
	(18) M II	19	12.7304	.077977	138.43	1[illegible]8.58	162.40	.2667	141.48	225.57	84.10
	(19) M III	9	11.7315	.073057	137.56	1[illegible]8.95	160.90	.2349	139.02	227.03	88.00
	(20) M P	47	12.5636	.077053	137.88	1[illegible]8.20	162.77	.2645	142.02	225.39	83.38
	(21) F I	12	7.9951	.059756	125.54	1[illegible]5.34	133.26	.2607	106.63	213.60	106.97
	(22) F II	13	9.4760	.065396	127.56	1[illegible]2.64	144.98	.2714	121.69	214.25	92.56
	(23) F III	18	8.4480	.059370	123.88	1[illegible]3.02	142.54	.2093	116.59	220.50	103.91
	(24) F P	43	8.6324	.061299	125.45	1[illegible]3.55	140.69	.2425	115.35	216.68	101.33

Notes: M- males, F - females.

I - 1st trimester ATB, II - 2nd trimester ATB, III - 3rd trimester ATB and P - trimesters pooled

S_o and S_c indicate age at onset and completion of adolescent growth cycle, respectively.

I_1 and I_2 indicate age at 1st and 2nd point of inflection of velocity curve, respectively.

Onset-M indicates age at onset of menarch.

TABLE 3(continued): Averages of Estimated Growth Parameters --- Nagasaki

Groups	K(=U-L)	K/U	.9625/B	I_1	I_2	BK/e	Exp(-B)	Onset-M
(1)	30.05	.181	12.957	150.47	176.38	.8308	.92627	-
(2)	30.67	.183	14.818	146.50	176.13	.7557	.93363	-
(3)	30.76	.191	13.519	149.52	176.66	.8228	.92771	-
(4)	30.41	.184	13.648	149.08	176.38	.8066	.92880	-
(5)	31.92	.205	16.058	114.62	146.74	.7110	.94075	154.82
(6)	29.19	.188	16.005	123.36	155.36	.6545	.93957	158.08
(7)	27.57	.181	15.039	127.[illegible]2	157.19	.6552	.93462	166.23
(8)	29.44	.191	15.673	122.04	153.39	.6720	.93814	160.03
(9)	30.69	.184	12.722	145.51	170.96	.8752	.92350	-
(10)	30.86	.189	13.459	150.00	176.92	.8612	.92670	-
(11)	32.30	.196	14.980	142.52	172.48	.7960	.93364	-
(12)	31.13	.188	13.495	146.25	173.24	.8519	.92694	-
(13)	29.10	.190	16.221	120.34	152.79	.6398	.94055	163.31
(14)	27.82	.179	15.280	122.56	153.12	.6541	.93622	159.36
(15)	29.38	.190	16.251	124.06	156.56	.6456	.94151	164.00
(16)	28.79	.187	15.926	122.45	154.30	.6466	.93950	162.28
(17)	30.00	.178	12.658	151.37	176.69	.8498	.92496	-
(18)	30.15	.179	13.148	149.26	175.55	.8466	.92509	-
(19)	31.39	.185	13.690	147.20	174.59	.8398	.92957	-
(20)	30.33	.180	13.054	149.72	175.83	.8466	.92590	-
(21)	29.79	.191	16.856	116.40	150.11	.6179	.94201	153.92
(22)	25.08	.163	15.065	129.92	160.04	.5937	.93668	163.15
(23)	29.15	.190	16.452	126.09	158.99	.6353	.94233	165.28
(24)	28.10	.182	16.146	124.[illegible]4	156.83	.6179	.94053	161.47

→

TABLE 3(continued): Averages of Estimated Growth Parameters --- Hiroshima

	Groups	Sizes	A	B	L	U	A/B	100B/K	S_o	S_c	S_i
Inner Proximal	(1) M I	35	13.4290	.081412	136.55	167.67	163.18	.3028	143.07	223.96	80.89
	(2) M II	56	13.5756	.081102	135.76	166.01	164.64	.3110	143.68	228.00	84.33
	(3) M III	42	12.2313	.075668	134.30	164.58	160.31	.2669	138.89	224.92	86.03
	(4) M P	133	13.1125	.079468	135.51	165.99	162.89	.2949	142.00	225.97	83.96
	(5) F I	25	8.5199	.060104	123.21	151.75	140.83	.2337	114.43	220.11	105.68
	(6) F II	36	7.4546	.055267	122.02	152.84	133.98	.2034	105.03	221.41	116.39
	(7) F III	28	8.3849	.060882	126.64	155.02	137.33	.2464	111.28	215.43	104.15
	(8) F P	89	8.0465	.058392	123.81	153.22	136.96	.2255	109.64	219.16	109.53
Distal	(9) M I	28	13.2974	.078867	139.28	169.16	167.05	.2932	146.79	228.11	81.32
	(10) M II	41	14.3231	.085546	137.66	165.57	166.27	.3319	147.82	221.60	73.78
	(11) M III	31	14.1574	.084362	132.90	164.90	165.26	.2964	145.50	225.17	79.67
	(12) M P	100	13.9845	.083309	136.64	166.37	166.17	.3101	146.81	224.53	77.72
	(13) F I	10	7.9531	.058429	121.22	153.58	134.62	.2108	105.86	221.99	116.13
	(14) F II	21	9.1934	.064595	127.82	154.47	141.54	.2684	117.56	213.14	95.58
	(15) F III	24	7.9638	.056199	124.50	153.75	140.02	.2359	111.34	226.27	114.93
	(16) F P	55	8.4313	.059810	125.17	153.99	139.62	.2438	112.72	220.48	107.76
Not-in-city	(17) M I	32	14.0708	.084861	137.89	167.43	165.44	.3073	146.23	223.31	77.08
	(18) M II	67	12.4087	.075753	135.02	167.30	162.99	.2471	141.46	228.28	86.83
	(19) M III	44	12.8573	.077620	135.74	166.32	164.23	.2711	142.92	228.59	85.67
	(20) M P	143	12.9187	.078366	135.89	167.02	163.92	.2680	142.97	227.27	84.29
	(21) F I	33	6.9639	.050991	122.71	155.07	135.92	.1878	104.41	231.36	126.95
	(22) F II	46	8.1524	.058054	126.39	155.51	139.46	.2300	112.06	221.89	109.83
	(23) F III	32	7.4448	.055014	122.79	154.34	134.30	.1943	105.16	222.44	117.28
	(24) F P	111	7.5951	.055078	124.26	155.04	136.92	.2072	107.80	224.86	117.07

TABLE 3(continued): Averages of Estimated Growth Parameters --- Hiroshima

Groups	K(=U-L)	K/U	.9625/B	I_1	I_2	BK/e	Exp(-B)	Onset-M
(1)	31.11	.185	12.638	150.54	175.81	.8987	.92199	-
(2)	30.24	.182	13.154	151.48	177.79	.8492	.92238	-
(3)	30.28	.184	13.498	146.81	173.81	.8271	.92725	-
(4)	30.48	.183	13.127	149.76	176.01	.8552	.92382	-
(5)	28.53	.188	16.779	124.05	157.61	.6177	.94169	158.62(24)#
(6)	30.83	.201	18.263	115.72	152.24	.6085	.94625	157.40(35)
(7)	28.38	.182	16.646	120.58	153.97	.6266	.94098	157.64
(8)	29.41	.192	17.337	119.52	154.29	.6168	.94331	157.82(87)
(9)	29.88	.176	12.795	154.25	179.84	.8393	.92424	-
(10)	27.91	.168	11.752	154.52	178.02	.8562	.91811	-
(11)	32.00	.193	12.357	152.91	177.62	.9612	.91931	-
(12)	29.73	.178	12.232	153.94	178.40	.8840	.92020	-
(13)	32.36	.210	17.900	116.72	152.52	.6498	.94335	158.00(9)
(14)	26.65	.173	15.412	126.13	156.95	.6182	.93747	161.90(20)
(15)	29.25	.190	18.287	121.74	158.31	.5797	.94541	158.23(22)
(16)	28.82	.187	17.119	122.50	156.74	.6071	.94200	159.63(51)
(17)	29.54	.176	12.113	153.32	177.55	.8961	.91881	-
(18)	32.27	.192	13.425	149.56	176.41	.8820	.92714	-
(19)	30.57	.183	13.379	150.35	177.60	.8485	.92549	-
(20)	31.14	.186	13.117	150.30	177.03	.8749	.92477	-
(21)	32.36	.207	19.770	116.[illegible]4	155.69	.5864	.95030	157.62(32)
(22)	29.12	.187	17.379	122.08	156.83	.5990	.94363	156.29(42)
(23)	31.56	.204	18.284	116.02	152.58	.6200	.94648	157.59
(24)	30.79	.198	18.351	118.57	155.27	.6013	.94643	157.08(106)

The number of subjects used for calculating average months of age at onset of menarche.

TABLE 4: Sex Comparisons for the Not-in-city Group --- Nagasaki

Items	Means for Males	Means for Females	Differences between Means	Statistical Significance F	P
Size	47	43			
A	12.5636	8.6324	3.9312	65.195	<.0001
B	0.07705	0.0613	0.01575	32.063	<.0001
L	137.88	125.45	12.43	87.376	<.0001
U	168.20	153.55	14.65	214.921	<.0001
A/B	162.77	140.69	22.08	90.932	<.0001
100B/K	0.2645	0.2425	0.0220	0.887	>.1
S_o	142.02	115.35	26.67	98.663	<.0001
S_c	225.39	216.68	8.71	5.114	<.05
S_i $(=S_c-S_o)$	83.38	101.33	17.95	15.694	<.001
K(=U-L)	30.33	28.10	2.23	3.678	>.05
K/L	0.180	0.182	0.002	0.116	>.1
0.9625/B	13.054	16.146	3.092	24.740	<.0001
I_1	149.72	124.54	25.18	105.518	<.0001
I_2	175.83	156.83	19.00	65.667	<.0001
BK/e	0.8466	0.6179	0.2287	65.802	<.0001
Exp(-B)	0.92590	0.94053	0.01463	32.061	<.0001

S_o: Age at onset of adolescent growth cycle,
S_c: Age at completion of adolescent growth cycle,
I_1: Age at 1st point of inflection of velocity curve,
I_2: Age at 2nd point of inflection of velocity curve.

→

TABLE 4 (continued): Sex Comparisons for the Not-in-city Group --- Hiroshima

Items	Means for Males	Means for Females	Differences between Means	Statistical Significance F	P
Size	143	111			
A	12.9187	7.5951	5.3236	187.651	<.0001
B	0.07837	0.05508	0.02329	113.925	<.0001
L	135.89	124.26	11.63	130.730	<.0001
U	167.02	155.04	11.98	313.514	<.0001
A/B	163.92	136.92	27.00	369.714	<.0001
100B/K	0.2680	0.2072	0.0608	18.008	<.0001
S_o	142.97	107.80	35.17	340.020	<.0001
S_c	227.27	224.86	2.41	1.037	>.1
$S_i(\ddagger S_c - S_o)$	84.29	117.07	32.78	90.404	<.0001
K(=U-L)	31.14	30.79	0.35	0.141	>.1
K/L	0.186	0.198	0.012	4.534	<.05
0.9625/B	13.117	18.351	5.243	121.858	<.0001
I_1	150.80	118.57	32.23	386.194	<.0001
I_2	177.03	155.27	21.76	278.244	<.0001
BK/e	0.8749	0.6013	0.2736	137.469	<.0001
Exp(-B)	0.92477	0.94643	0.02166	115.266	<.0001

TABLE 5: City Comparisons for the Not-in-city Groups by Sex

Items	Male F	Male P	Female F	Female P
d. f.	(1, 188)		(1, 152)	
A	0.368	.552	8.896	.004**
B	0.165	.688	8.828	.004**
L	3.438	.062	0.558	.537
U	1.795	.178	2.594	.105
A/B	0.463	.504	2.930	.085
100B/K	0.040	.836	2.521	.110
S_o	0.192	.666	6.750	.010*
S_c	0.419	.526	5.151	.023
$S_i(=S_c-S_o)$	0.054	.811	9.327	.003**
K(=U-L)	0.775	.617	3.137	.075
K/L	1.281	.258	2.712	.098
0.9625/B	0.013	.905	10.251	.002**
I_1	0.314	.583	5.709	.017*
I_2	0.573	.544	0.556	.536
BK/e	0.713	.596	0.478	.502
Exp(-B)	0.144	.706	8.923	.004**

* $p < 0.05$
** $p < 0.01$

TABLE 6: Trimester ATB Comparisons for the Not-in-city Group --- Males, Nagasaki

Items	Trimester			Significance	
	I	II	III	F	P
Size	19	19	9		
A	12.7909	12.7304	11.7315	.474	.63
B	0.07802	0.07798	0.07306	.355	.71
L	137.48	138.43	137.56	.165	.85
U	167.48	168.58	168.95	.435	.66
A/B	163.03	162.40	160.90	.274	.76
100B/K	0.2763	0.2667	0.2349	.678	.52
S_o	143.98	141.48	139.02	.542	.59
S_c	224.44	225.57	227.03	.058	.94
$S_i(=S_c-S_o)$	80.47	84.10	88.00	.412	.67
K(=U-L)	30.00	30.15	31.39	.367	.70
K/L	0.178	0.179	0.185	.284	.76
0.9625/B	12.658	13.148	13.690	.370	.70
I_1	151.37	149.26	147.20	.442	.65
I_2	176.69	175.55	174.59	.118	.89
BK/e	0.8498	0.8466	0.8398	.013	.99
EXP(-B)	0.92496	0.92509	0.92957	.351	.71

Multivariate Test of Equality of Mean Vectors (A, B, L, U):
Roy's largest root criterion; θ = .0407, s=2, m=0.5, n=19.5, $p > 0.05$

Likelihood ratio = 0.9520, Asymptotic chi-square = 2.0905 with 8 d.f., p = 0.9772,

→

TABLE 6 (continued): Trimester ATB Comparisons for the Not-in-city Group --- Females, Nagasaki

Items	Trimester			Significance	
	I	II	III	F	p
Size	12	13	18		
A	7.9951	9.4760	8.4480	3.403	.042*
B	0.05976	0.06540	0.05937	1.653	.203
L	125.54	127.56	123.88	0.988	.617
U	155.34	152.64	153.02	1.072	.353
A/B	133.26	144.98	142.54	4.360	.019*
100B/K	0.2607	0.2714	0.2093	1.004	.377
S_O	106.63	121.69	116.59	4.754	.014*
S_C	213.60	214.25	220.50	0.691	.511
$S_I (=S_C-S_O)$	106.97	92.56	103.91	1.555	.222
K(=U-L)	29.79	25.08	29.15	2.008	.146
K/L	0.191	0.163	0.190	1.900	.161
0.9625/B	16.856	15.065	16.452	1.385	.261
I_1	116.40	129.92	126.09	4.929	.012*
I_2	150.11	160.04	158.99	3.320	.045*
BK/e	0.6179	0.5937	0.6353	0.483	.626
EXP(-B)	0.94201	0.93668	0.94233	1.647	.204
Onset-M	153.92	163.15	165.28	4.744	.014*

Multivariate Test of Equality of Mean Vectors (A, B, L, U):
Roy's largest root criterion; $\theta = .2371$, s=2, m=0.5, n=17.5, $p > 0.05$
Likelihood ratio = 0.7140, Asymptotic chi-square = 12.9705 with 8 d.f., p = 0.1139.

→

TABLE 6 (continued): Trimester ATB Comparisons for the Not-in-city Group --- Males, Hiroshima

Items	Trimester I	Trimester II	Trimester III	Significance F	Significance p
Size	32	67	44		
A	14.0708	12.4087	12.8573	2.273	.10
B	0.08486	0.07575	0.07762	2.266	.11
L	137.89	135.02	135.74	2.036	.13
U	167.43	167.30	166.32	0.536	.59
A/B	165.44	162.99	164.23	0.707	.50
100B/K	0.3073	0.2471	0.2711	3.576	.03*
S_o	146.23	141.46	142.92	1.404	.25
S_c	223.31	228.28	228.59	1.150	.32
$S_i(=S_c-S_o)$	77.08	86.83	85.67	1.888	.15
K(=U-L)	29.54	32.27	30.57	2.722	.07
K/L	0.176	0.192	0.183	2.878	.06
0.9625/B	12.113	13.425	13.379	1.801	.17
I_1	153.32	149.56	150.85	1.142	.32
I_2	177.55	176.41	177.60	0.299	.75
BK/e	0.8961	0.8820	0.8485	0.531	.59
EXP(-B)	0.91881	0.92714	0.92549	2.243	.11

Multivariate Test of Equality of Mean Vectors (A, B, L, U):
Roy's largest root criterion; $\theta = .0465$, s=2, m=0.5, n=67.5, $p > 0.05$
Likelihood ratio = 0.9367, Asymptotic chi-square = 9.0549 with 8 d.f., p = 0.3384.

→

TABLE 6 (continued): Trimester ATB Comparisons for the Not-in-city Group --- Females, Hiroshima

Items	Trimester			Significance	
	I	II	III	F	p
Size	32	42	32		
A	7.0630	8.1206	7.4448	3.212	.043*
B	0.05169	0.05811	0.05501	2.907	.058
L	123.12	126.86	122.79	2.345	.099
U	155.23	155.44	154.34	0.419	.665
A/B	136.03	139.43	134.30	1.796	.169
100B/K	0.1914	0.2318	0.1942	1.368	.258
S_o	105.27	112.31	105.16	2.566	.080
S_c	229.12	220.90	222.44	1.731	.180
$S_i(=S_c-S_o)$	123.85	108.59	117.28	2.748	.067
K(=U-L)	32.11	28.58	31.56	1.780	.172
K/U	0.205	0.184	0.204	1.893	.154
0.9625/B	19.338	17.259	18.284	2.789	.064
I_1	116.69	122.17	116.02	2.380	.096
I_2	155.37	156.69	152.58	1.196	.306
BK/e	0.5914	0.5932	0.620	0.433	.655
EXP(-B)	0.94963	0.94356	0.94681	2.918	.057
Onset-M	157.62	156.29	157.59	0.229	.798

Multivariate Test of Equality of Mean Vectors (A, B, L, U):

Roy's largest root criterion; $\theta = .0695$, s=2, m=0.5, n=51.5, $p > 0.05$

Likelihood ratio = 0.9144, Asymptotic chi-square = 9.5287 with 8 d.f., p = 0.3002.

TABLE 7: Summary Table for Tests of Comparisons among Trimesters ATB

Exposure Group	Inner	Distal	Non	Inner	Distal	Non
Sex		Male			Female	
			Nagasaki			
4 variables (A, B, L, U):						
Roy's θ	NS	NS	NS	NS	NS	NS
L-ratio	NS	NS	NS	NS	NS	NS
5 Variables (S_O, A/B, S_C, BK/e, U):						
Roy's θ	NS	NS	NS	NS	NS	NS
L-ratio	NS	NS	NS	S	NS	S
			Hiroshima			
4 variables (A, B, L, U):						
Roy's θ	NS	NS	NS	NS	NS	NS
L-ratio	NS	*	NS	S	NS	NS
5 variables (S_O, A/B, S_C, BK/e, U):						
Roy's θ	NS	NS	NS	NS	NS	NS
L-ratio	S	S	NS	S	NS	NS

NS Not significant

S Suggestive ($p < 0.10$) for the likelihood ratio test

* $p < 0.05$

TABLE 8: Summary Table of Tests of Comparison among Exposure Groups (Inner Proximal, Distal, Not-in-city)

Males, Nagasaki:	Trimester ATB I	II	III	Pooled
(Multivariate)				
4 variables (A, B, L, U):				
Roy's θ	NS	NS	NS	*
L-ratio	NS	S	NS	*
5 variables (S_O, A/B, S_C, BK/e, U):				
Roy's θ	NS	NS	NS	*
L-ratio	NS	NS	NS	*
(Univariate)				
A	.9720	.6194	.3503	.6957
B	.8087	.3463	.6129	.6675
L	.5664	.0167*	.1000	.0047**
U	.5976	.0078**	.0650	.0065**
Discriminant Analysis:				
Coefficients#				
A (1)	-4.814×10^{-3}	-7.272×10^{-3}	-1.290×10^{-2}	5.282×10^{-3}
(2)	7.880×10^{-3}	-1.618×10^{-3}	7.455×10^{-3}	-4.393×10^{-3}
B (1)	1.000	1.000	1.000	-1.000
(2)	-1.000	1.000	-1.000	1.000
L (1)	-3.351×10^{-4}	1.489×10^{-3}	2.937×10^{-3}	1.345×10^{-3}
(2)	5.005×10^{-3}	-1.018×10^{-3}	-4.476×10^{-5}	-7.149×10^{-4}
U (1)	3.520×10^{-4}	1.971×10^{-3}	-1.621×10^{-4}	8.522×10^{-4}
(2)	8.240×10^{-3}	1.253×10^{-3}	4.596×10^{-4}	9.431×10^{-4}
Root 1				
% Variances	71.35	84.11	61.90	75.75
p	.3936	.0438*	.2560	.0246*
Root 2				
% Variances	28.65	15.89	38.10	24.25
p	.5475	.5008	.2403	.2343

Coefficients (1) and (2) correspond to the largest and the second largest characteristic roots, respectively.

→

TABLE 8 (continued)

Females, Nagasaki:	Trimester ATB			
	I	II	III	Pooled
(Multivariate)				
4 variables (A, B, L, U):				
Roy's θ	NS	NS	NS	NS
L-ratio	NS	NS	NS	NS
5 variables (S_O, A/B, S_C, BK/e, U):				
Roy's θ	NS	NS	*	NS
L-ratio	NS	NS	S	NS
(Univariate)				
A	.8012	.6781	.0718	.8300
B	.9337	.7567	.0667	.6132
L	.7572	.7181	.8869	.6725
U	.6052	.2983	.3401	.9374
Discriminant Analysis:				
Coefficients				
A (1)	-9.670×10^{-3}	-1.569×10^{-3}	-5.096×10^{-2}	3.361×10^{-3}
(2)	-5.895×10^{-4}	-6.850×10^{-3}	-5.321×10^{-3}	-7.577×10^{-3}
B (1)	1.000	1.000	-1.000	1.000
(2)	-1.000	1.000	1.000	1.000
L (1)	7.866×10^{-4}	-2.962×10^{-3}	9.967×10^{-3}	-3.122×10^{-3}
(2)	1.943×10^{-3}	8.623×10^{-4}	1.008×10^{-4}	5.528×10^{-4}
U (1)	2.986×10^{-4}	3.978×10^{-3}	-2.889×10^{-3}	2.577×10^{-3}
(2)	-1.389×10^{-3}	-6.275×10^{-4}	3.846×10^{-4}	-6.979×10^{-5}
Root 1				
% Variances	74.32	82.75	91.63	90.26
p	.3089	.2323	.1641	.2550
Root 2				
% Variances	25.68	17.25	8.37	9.74
p	.5372	.6777	.8553	.8679

→

TABLE 8(continued)

Males, Hiroshima:	Trimester ATB I	II	III	Pooled
(Multivariate)				
4 variables(A, B, L, U):				
Roy's θ	NS	*	*	NS
L-ratio	NS	S	*	NS
5 variables(S_o, A/B, Sc, BK/e, U):				
Roy's θ	NS	NS	NS	NS
L-ratio	NS	NS	NS	NS
(Univariate)				
A	.7121	.0556	.1530	.1192
B	.5436	.0660	.2340	.1974
L	.5356	.2463	.3115	.6045
U	.5418	.3125	.3303	.3535
Discriminant Analysis:				
Coefficients				
A(1)	4.756×10^{-3}	5.779×10^{-3}	6.520×10^{-3}	6.458×10^{-3}
A(2)	1.014×10^{-2}	-5.735×10^{-3}	4.563×10^{-3}	-6.091×10^{-3}
B(1)	-1.000	-1.000	-1.000	-1.000
B(2)	-1.000	1.000	-1.000	1.000
L(1)	1.785×10^{-4}	7.468×10^{-3}	-7.213×10^{-4}	9.554×10^{-4}
L(2)	5.137×10^{-3}	4.583×10^{-4}	5.829×10^{-4}	6.887×10^{-4}
U(1)	1.547×10^{-4}	-9.661×10^{-3}	9.087×10^{-4}	-3.599×10^{-4}
U(2)	6.079×10^{-3}	-9.534×10^{-5}	7.753×10^{-4}	-2.416×10^{-3}
Root 1				
% Variances	88.92	87.54	78.75	74.36
p	.3234	.0212*	.0269*	.2823
Root 2				
% Variances	11.08	12.46	21.25	25.64
p	.8631	.5849	.3129	.5416

→

TABLE 8 (continued)

Females, Hiroshima:	Trimester ATB			
	I	II	III	Pooled
(Multivariate)				
4 variables (A, B, L, U):				
Roy's θ	NS	NS	NS	NS
L-ratio	NS	NS	NS	NS
5 variables (S_o, A/B, S_c, BK/e, U):				
Roy's θ	NS	NS	NS	NS
L-ratio	NS	NS	NS	NS
(Univariate)				
A	.0277*	.0207*	.2855	.0698
B	.0316*	.0310*	.2323	.0627
L	.8487	.0427*	.2479	.7000
U	.0844	.1074	.6521	.0572
Discriminant analysis:				
Coefficients				
A (1)	-1.070×10^{-2}	2.901×10^{-4}	-5.775×10^{-3}	8.004×10^{-3}
A (2)	4.640×10^{-3}	7.643×10^{-4}	8.202×10^{-3}	-8.734×10^{-3}
B (1)	1.000	1.000	1.000	1.000
B (2)	-1.000	-1.000	-1.000	1.000
L (1)	6.300×10^{-4}	3.676×10^{-4}	4.604×10^{-4}	-1.346×10^{-4}
L (2)	2.559×10^{-4}	-9.140×10^{-5}	3.714×10^{-4}	4.685×10^{-4}
U (1)	8.883×10^{-4}	1.513×10^{-3}	1.065×10^{-4}	-9.814×10^{-3}
U (2)	-5.757×10^{-4}	3.274×10^{-3}	5.482×10^{-4}	-8.853×10^{-4}
Root 1				
% Variances	87.68	78.99	72.38	79.46
p	.0389*	.0818	.2762	.1057
Root 2				
% Variances	12.32	21.01	27.62	20.54
p	.6231	.5567	.5165	.5002

TABLE 9: Summary Table of Tests of Partial Exposure Comparisons

Trimester ATB	Male I	Male II	Male III	Female I	Female II	Female III
			Nagasaki			
Comparison 1[1)]	NS	NS	NS	NS	NS	NS
Comparison 2[2)]	NS	NS	NS	NS	NS	NS
Comparison 3[3)]	NS	*	NS	NS	NS	NS
			Hiroshima			
Comparison 1	NS	NS	NS	*	NS	NS
Comparison 2	NS	NS	*	NS	S	NS
Comparison 3	NS	**	NS	NS	NS	NS

1) Comparison between Inner Proximal and Not-in-city
2) Comparison between Inner Proximal and Distal
3) Comparison between Distal and Not-in-city

TABLE 10: Exposure Comparisons#(II) by City, Sex and Trimester ATB

Trim. ATB	Male I	Male II	Male III	Male P	Female I	Female II	Female III	Female P
				Nagasaki				
4 variables(A, B, L, U):								
Roy's θ	NS	NS	NS	NS	NS	NS	NS	NS
L-ratio	NS	S	NS	S	NS	NS	NS	NS
5 variables(S_o, A/B, S_c, BK/e, U):								
Roy's θ	NS	*	NS	NS	NS	NS	NS	NS
L-ratio	NS	**	S	*	S	NS	NS	NS
				Hiroshima				
4 variables(A, B, L, U):								
Roy's θ	NS	NS	NS	NS	NS	**	NS	**
L-ratio	NS	S	NS	NS	S	**	NS	**
5 variables(S_o, A/B, S_c, BK/e, U):								
Roy's θ	NS	NS	NS	NS	NS	*	NS	NS
L-ratio	NS	NS	NS	NS	NS	*	NS	*

In this table, the Inner Proximal group was divided into two sub-groups such that subjects were exposed within 1,500 m or exposed beyond 1,500 m. Exposure comparisons were then made among the four groups.

TABLE 11: Exposure Comparisons[#] (III) by City, Sex and Trimester ATB

Trim. ATB	Male I	Male II	Male III	Male P	Female I	Female II	Female III	Female P
				Nagasaki				
4 variables(A, B, L, U):								
Roy's θ	NS	NS	NS	–	NS	NS	*	–
L-ratio	NS	NS	NS	–	NS	NS	*	–
5 variables(S_O, A/B, S_C, BK/e, U):								
Roy's θ	NS	NS	NS	S	NS	NS	*	NS
L-ratio	NS	NS	NS	*	NS	NS	*	NS
				Hiroshima				
4 variables(A, B, L, U):								
Roy's θ	NS	*	NS	–	NS	NS	NS	–
L-ratio	NS	*	S	–	NS	NS	NS	–
5 variables(S_O, A/B, S_C, BK/e, U):								
Roy's θ	NS	NS	NS	NS	NS	NS	NS	NS
L-ratio	NS	NS	NS	NS	S	NS	NS	NS

\# In this table, the Inner Proximal group was divided into two sub-groups such that the mother of a subject received either greater than or equal to 50 rads (T65D), or less than 50 rads (T65D). Exposure comparisons were then made among the four groups.

TABLE 12: City Comparisons by Sex and Trimester ATB

Trimester ATB	Univariate A	B	L	U	Multivariate# (A, B, L, U)
			Male		
Inner Proximal (Group I):					
I	NS	NS	NS	NS	NS
II	NS	NS	NS	NS	NS
II	NS	NS	NS	NS	NS
Pooled	NS	NS	NS	NS	NS
Distal (Group II):					
I	NS	NS	NS	NS	*
II	S	S	*	NS	NS
III	*	*	NS	NS	*
Pooled	**	*	*	NS	**
Not-in-city (Group III):					
I	NS	NS	NS	NS	NS
II	NS	NS	NS	NS	NS
III	NS	NS	NS	NS	NS
pooled	NS	NS	S	NS	NS
			Female		
Inner Proximal (Group I):					
I	NS	NS	NS	S	**
II	S	S	NS	NS	NS
III	S	NS	NS	S	S
Pooled	S	*	NS	NS	NS
Distal (Group II):					
I	NS	NS	NS	NS	NS
II	NS	NS	NS	NS	NS
III	NS	NS	NS	NS	NS
Pooled	NS	NS	NS	NS	NS
Not-in-city (Group III):					
I	S	*	NS	NS	NS
II	*	S	NS	S	NS
III	*	NS	NS	NS	NS
Pooled	**	**	NS	NS	*

For multivariate analysis, the estimates of (A, B, L, U) are assumed to be distributed as a 4-dimensional multivariate normal variable.

APPENDIX 4

List of Illustrations

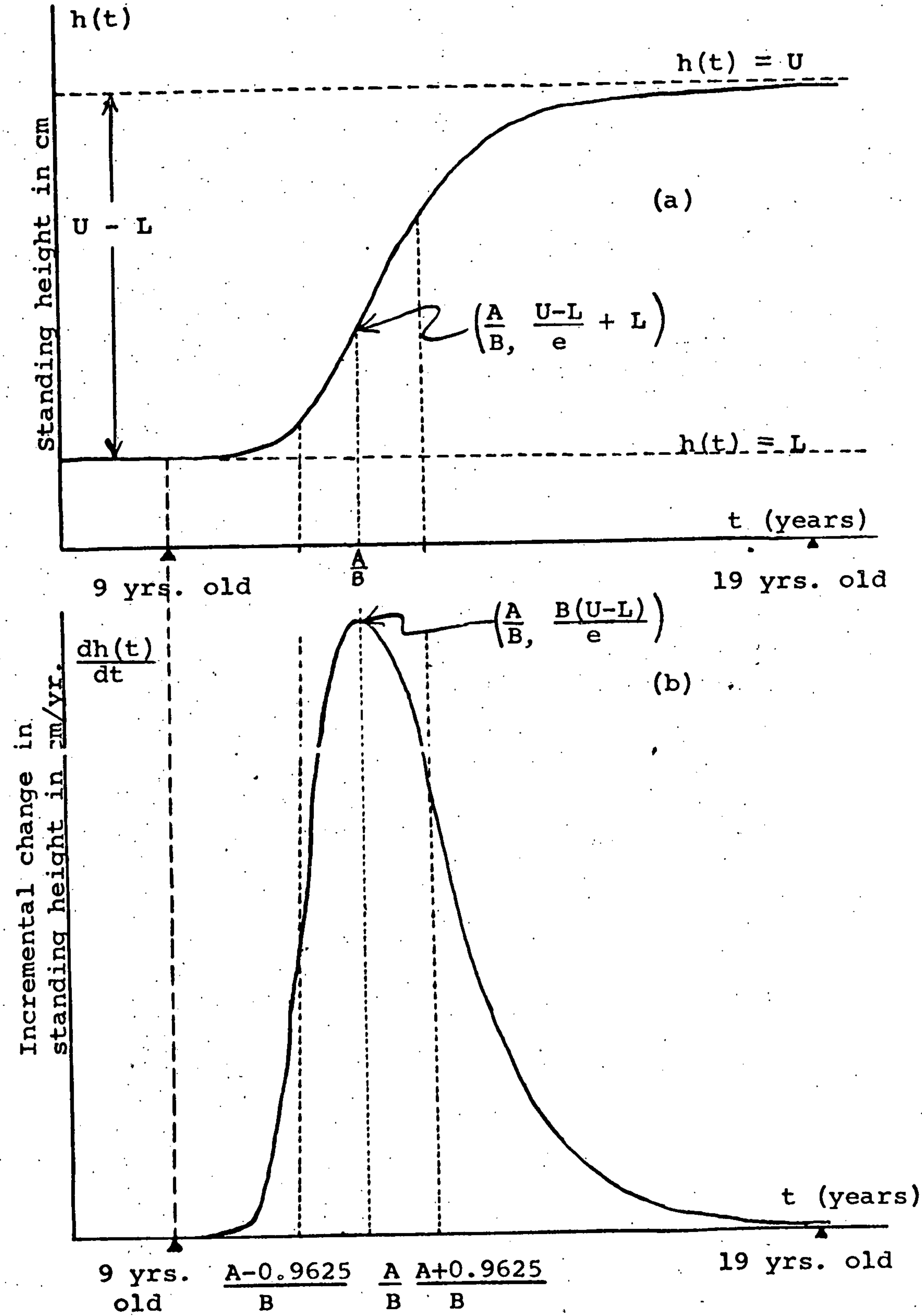


Figure 1: Theoretical Growth Curves -- (a) Gompertz curve $h(t) = U + (U - L)\cdot \exp(-\exp(A - B\cdot t))$, and (b) first derivative curve (velocity curve) $\frac{dh(t)}{dt} = (U - L)\cdot B\cdot e^{A-Bt}\cdot e^{-e^{A-Bt}}$.

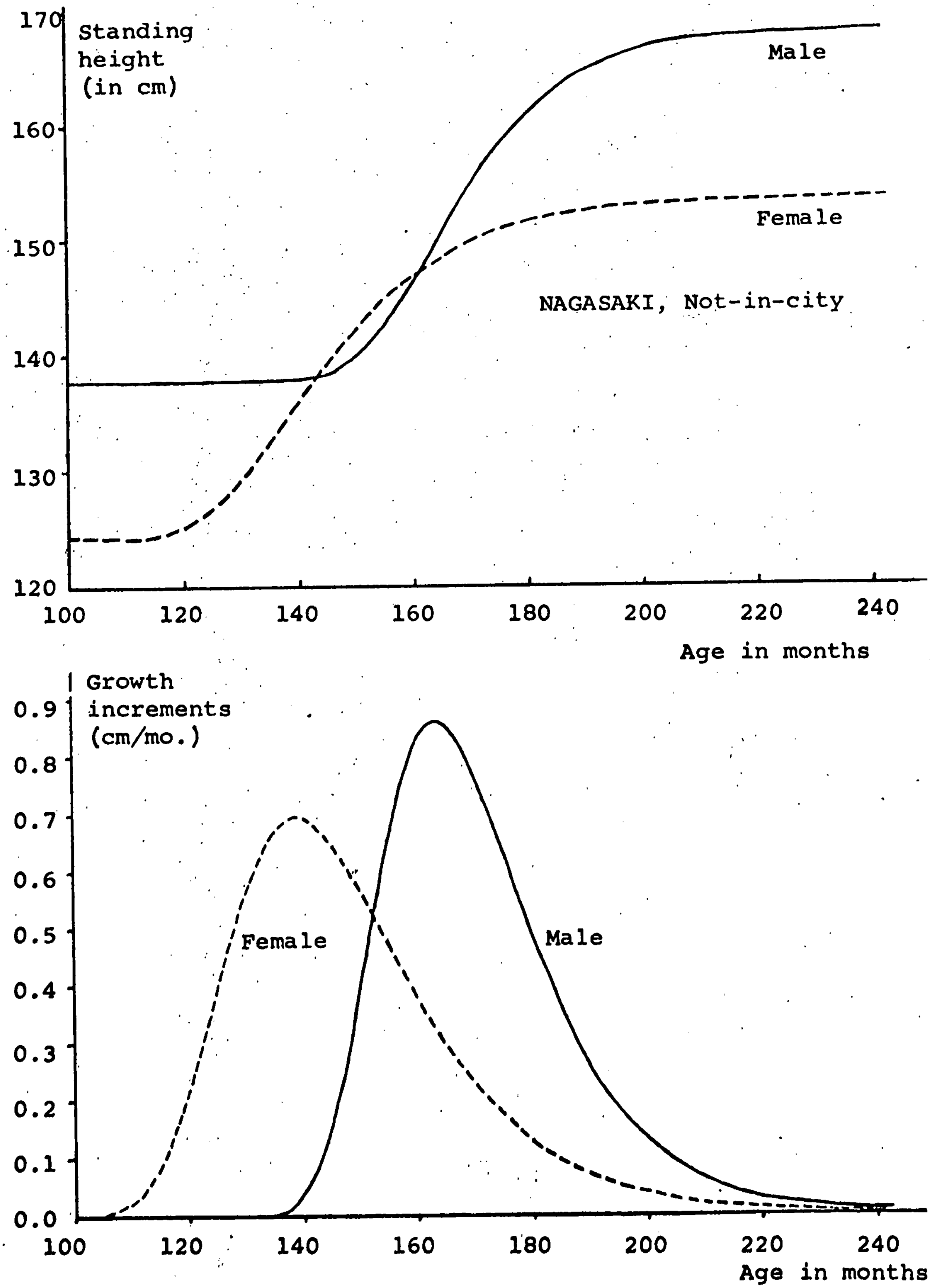


Figure 2: Sex Comparisons for the Not-in-city Group
--- Nagasaki

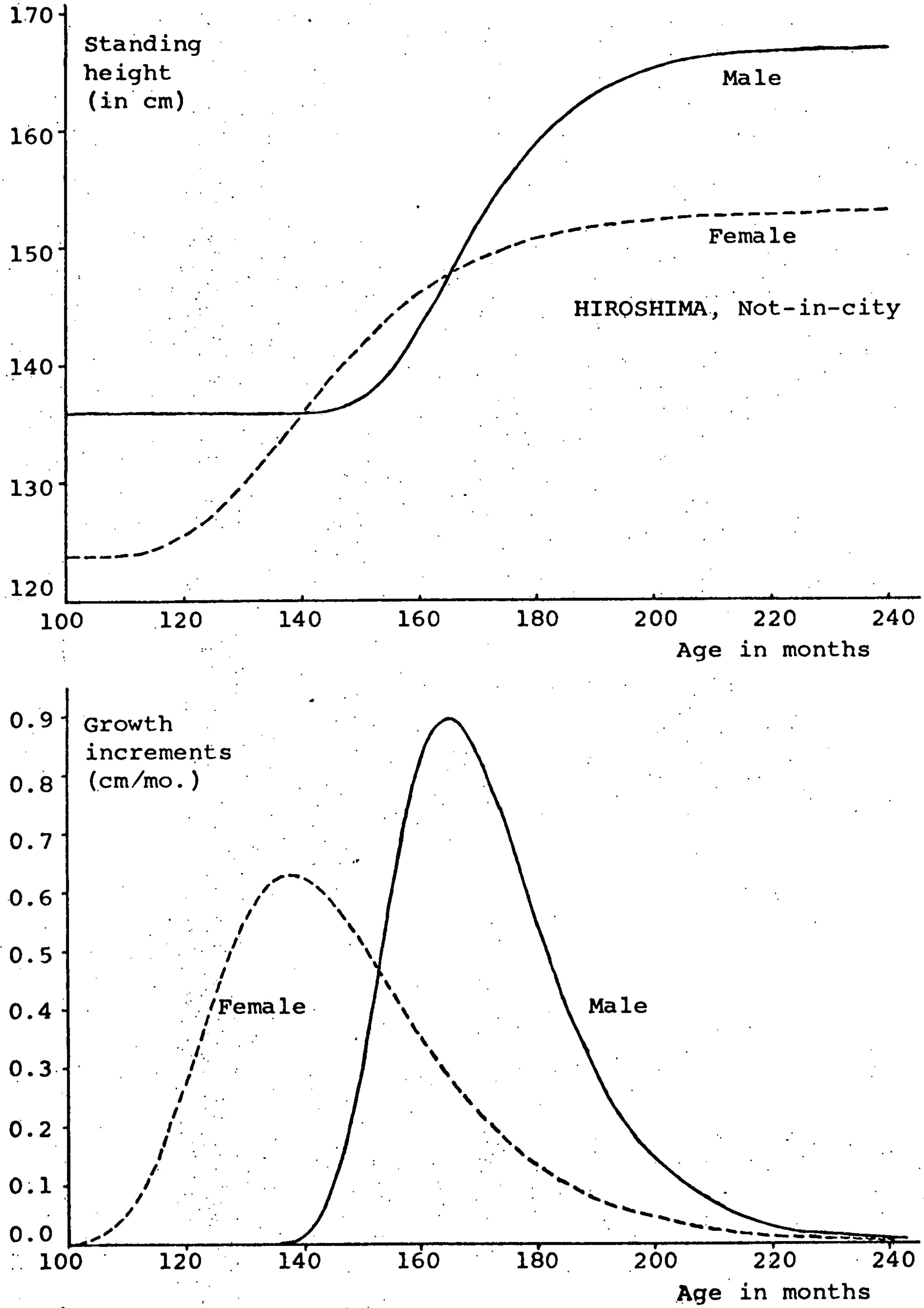


Figure 3: Sex Comparisons for the Not-in-city Group
--- Hiroshima

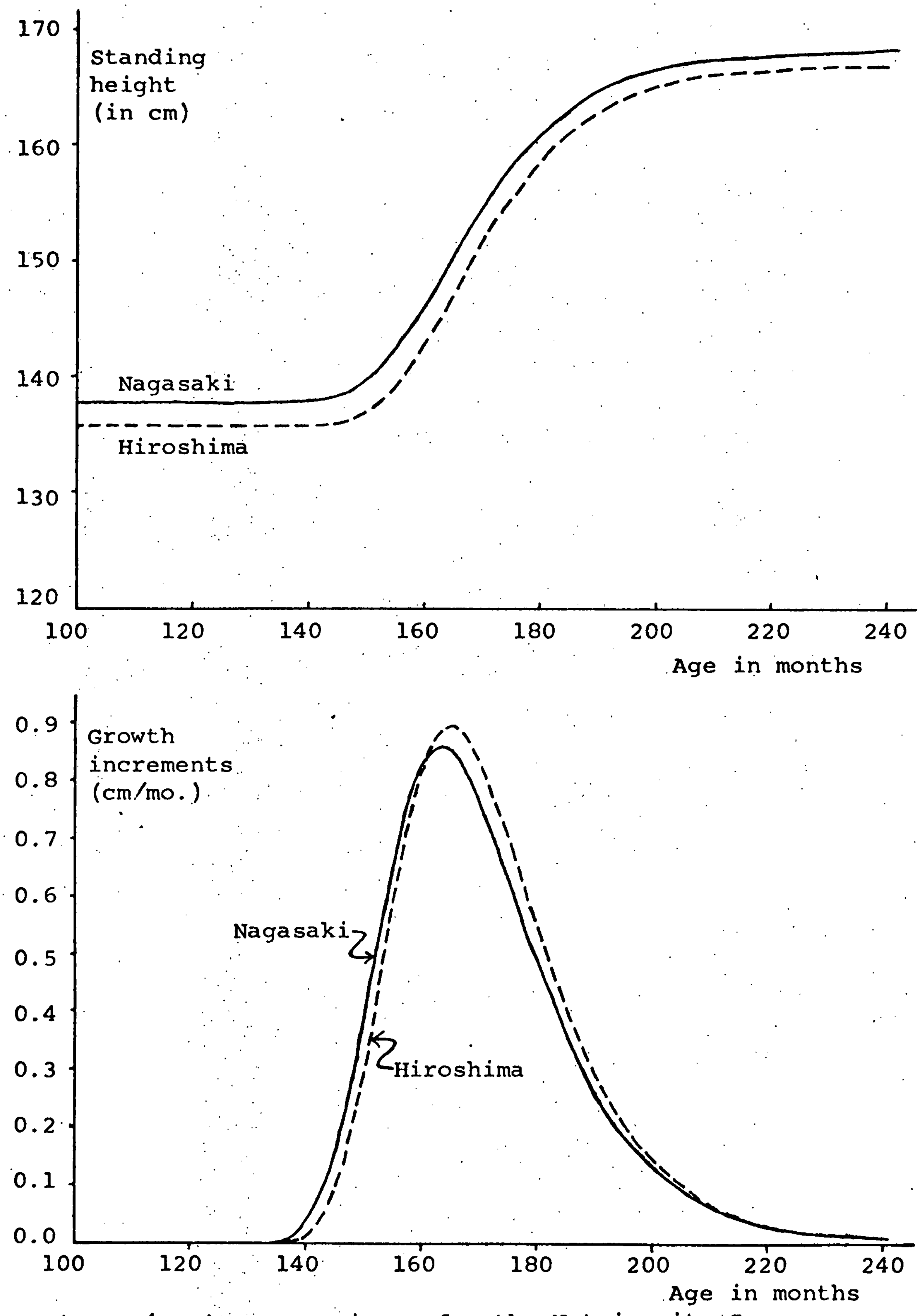
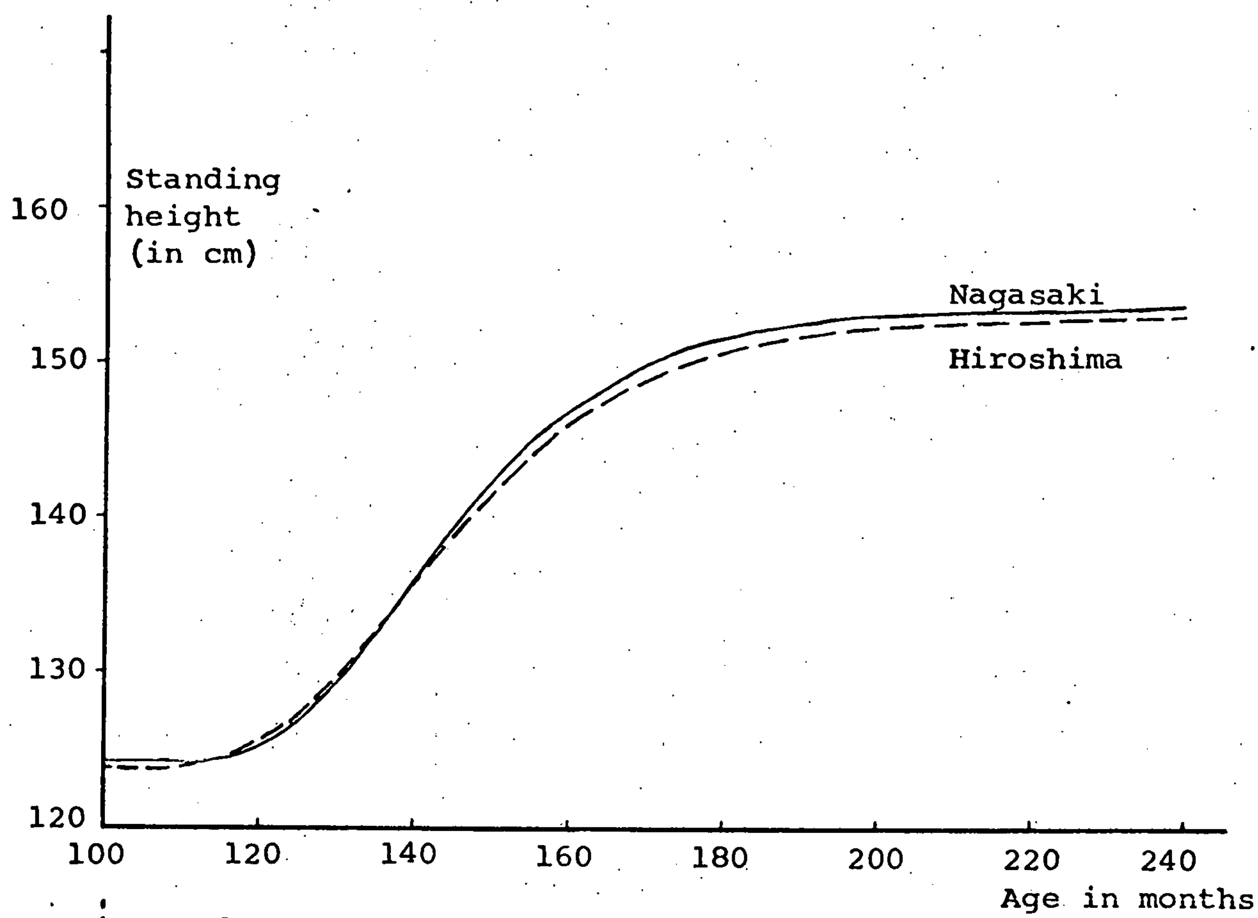


Figure 4: City Comparisons for the Not-in-city Group
--- Males



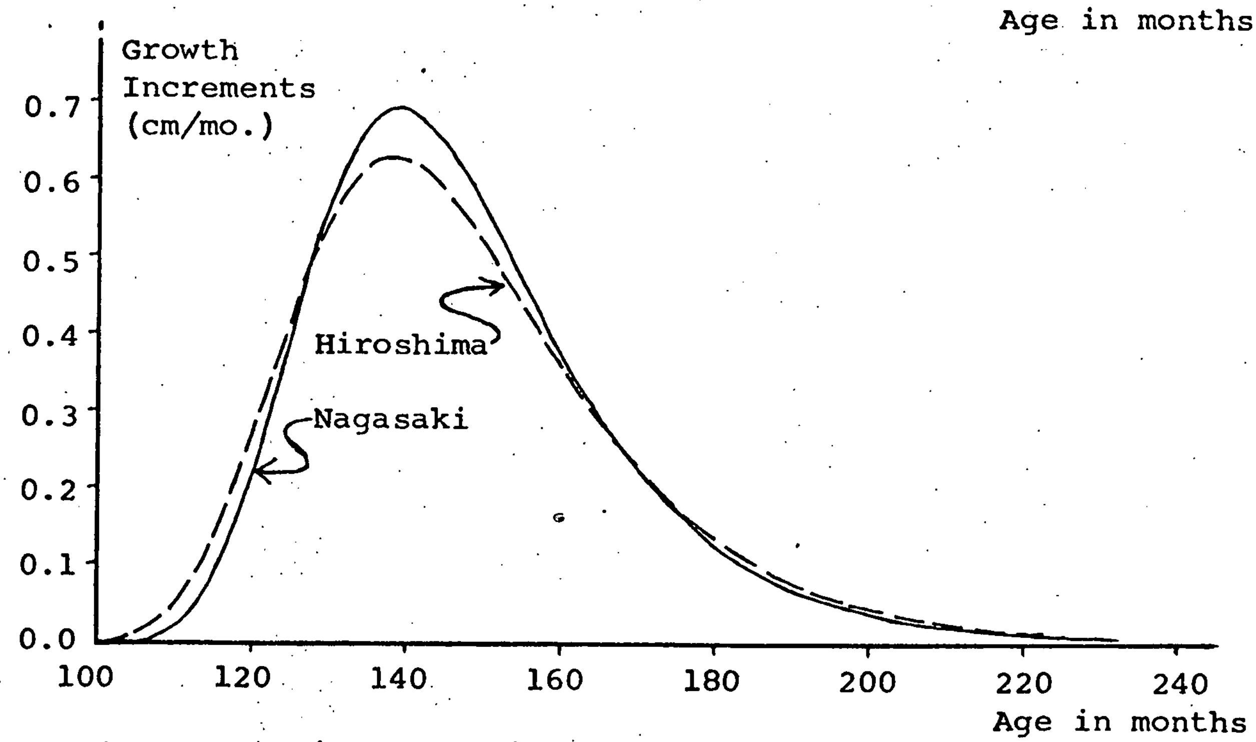


Figure 5: City Comparisons for the Not-in-city Group
--- Females

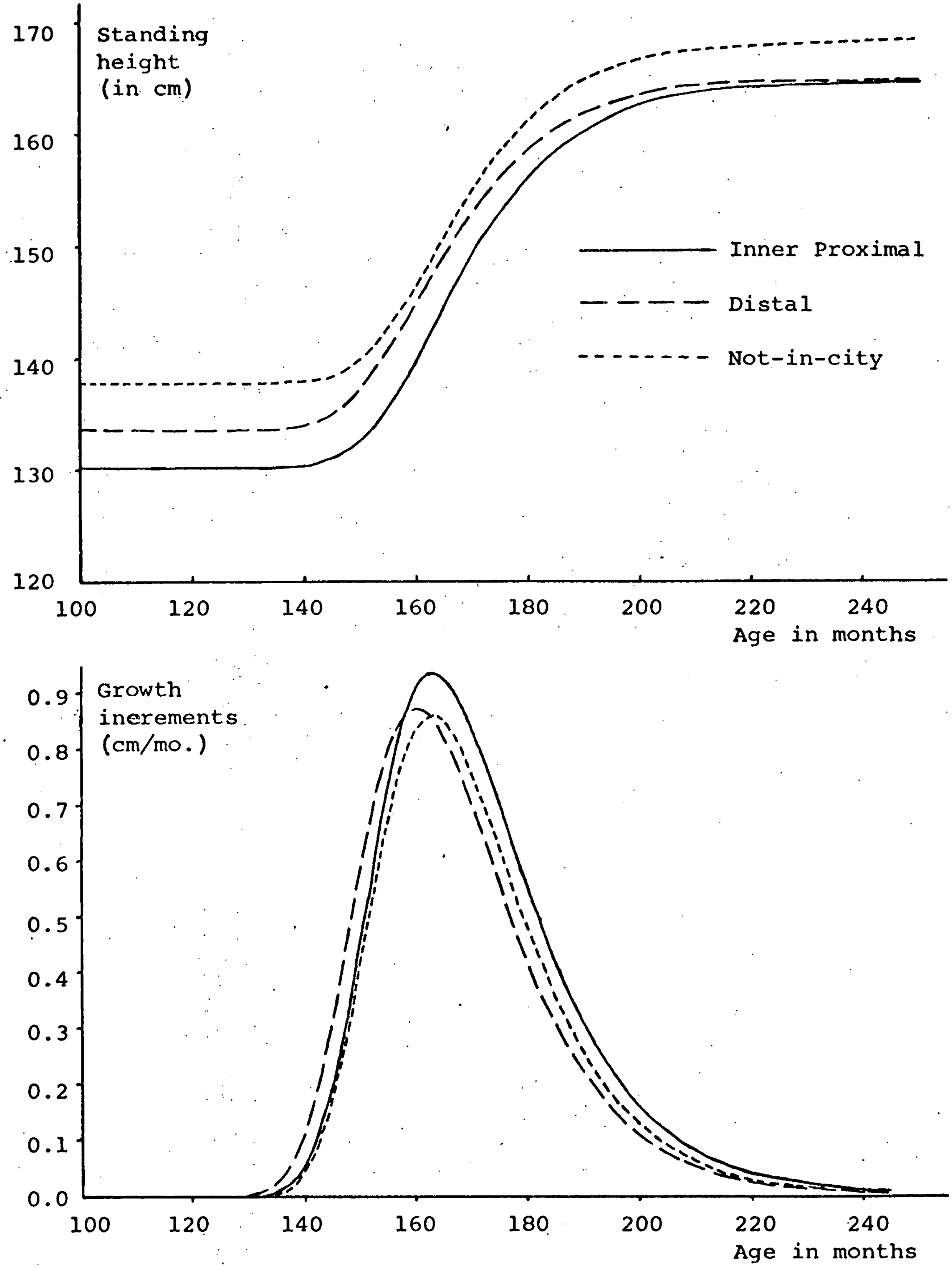


Figure 6: Exposure Comparisons (I) --- Nagasaki, Males
(trimester ATB -- pooled)

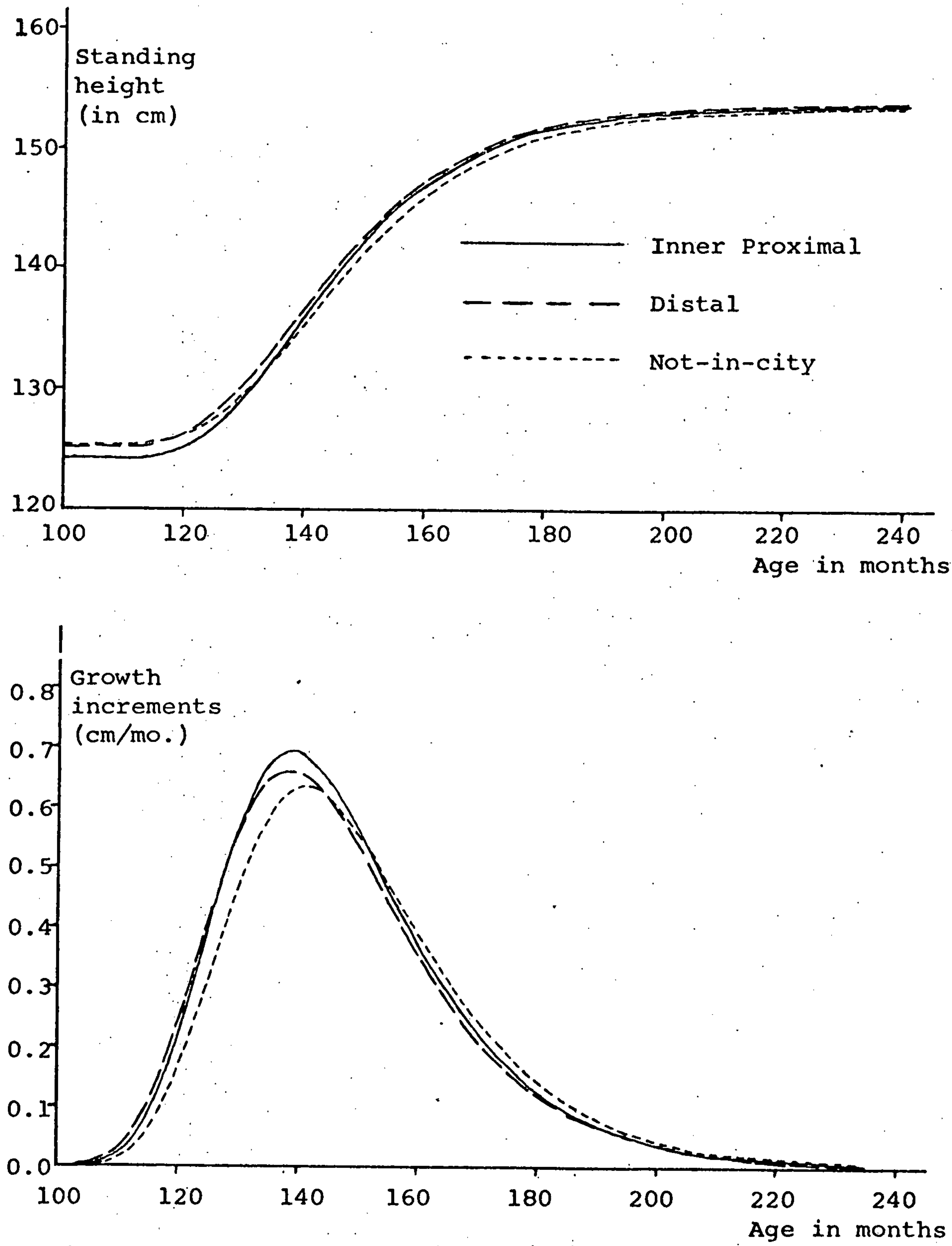


Figure 7: Exposure Comparisons (II) -- Nagasaki, Females
(trimester ATB -- pooled)

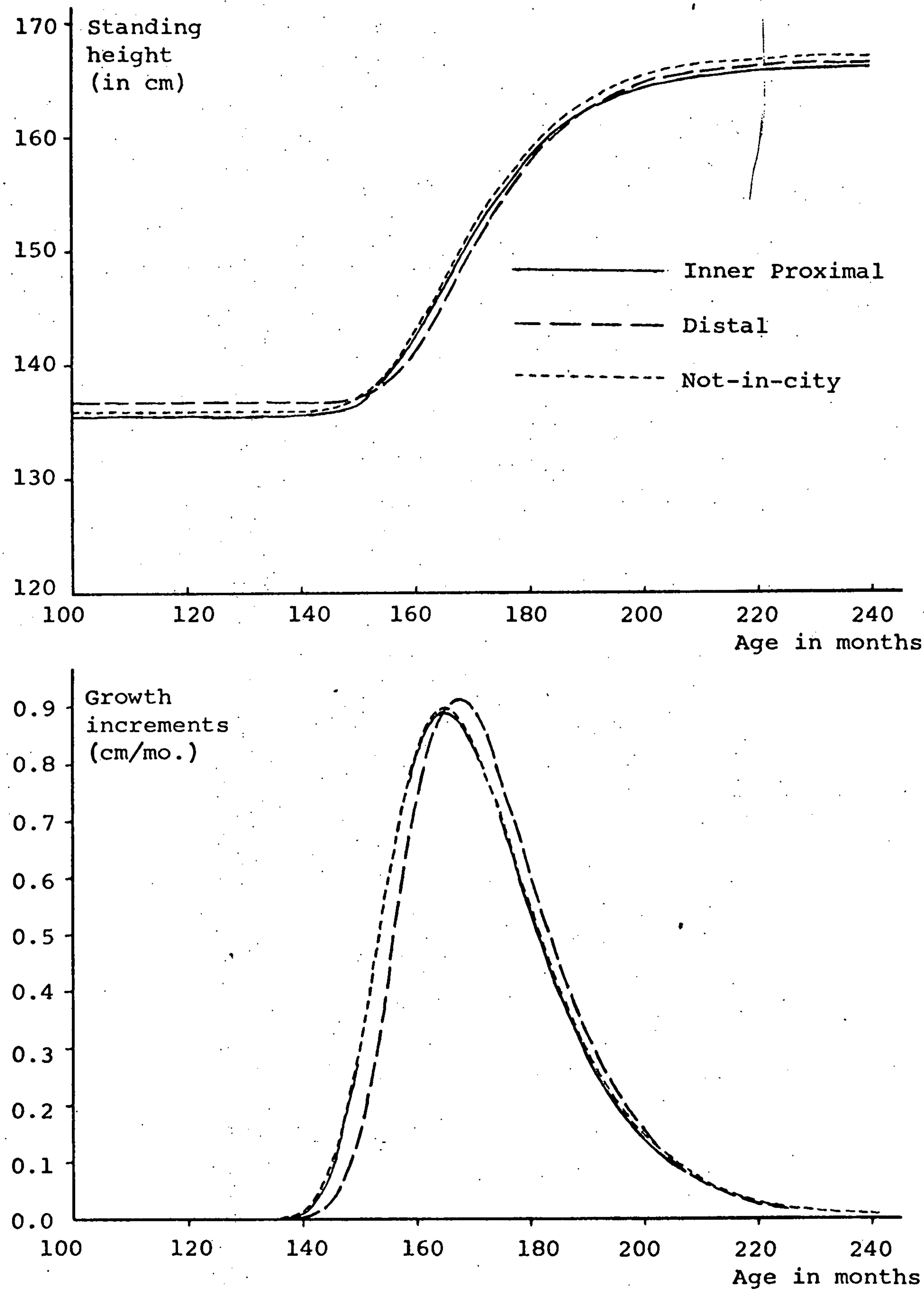


Figure 8: Exposure Comparisons (III) --- Hiroshima, Males
(trimester ATB -- pooled)

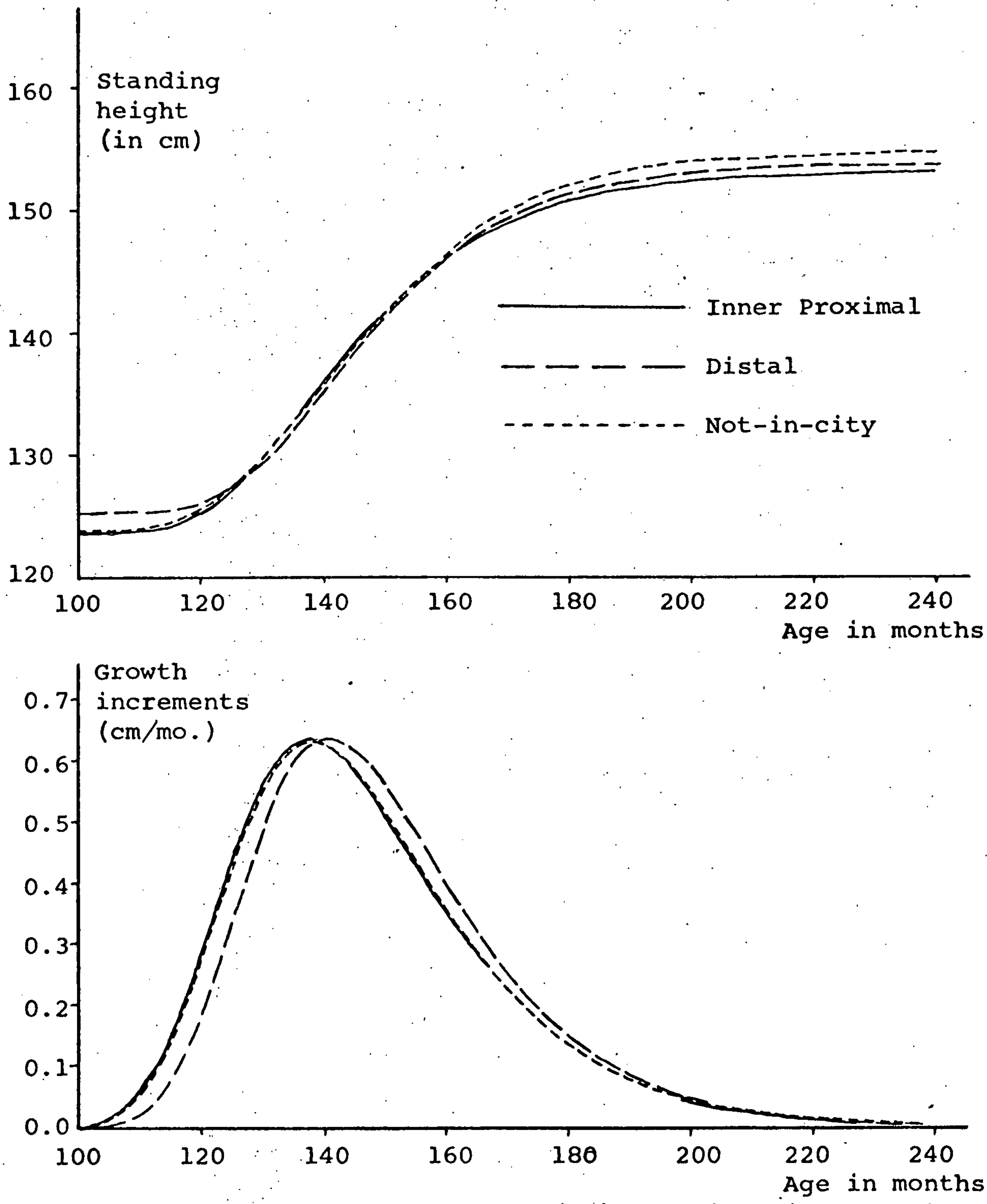


Figure 9: Exposure Comparisons (IV) --- Hiroshima, Females (trimester ATB -- pooled)

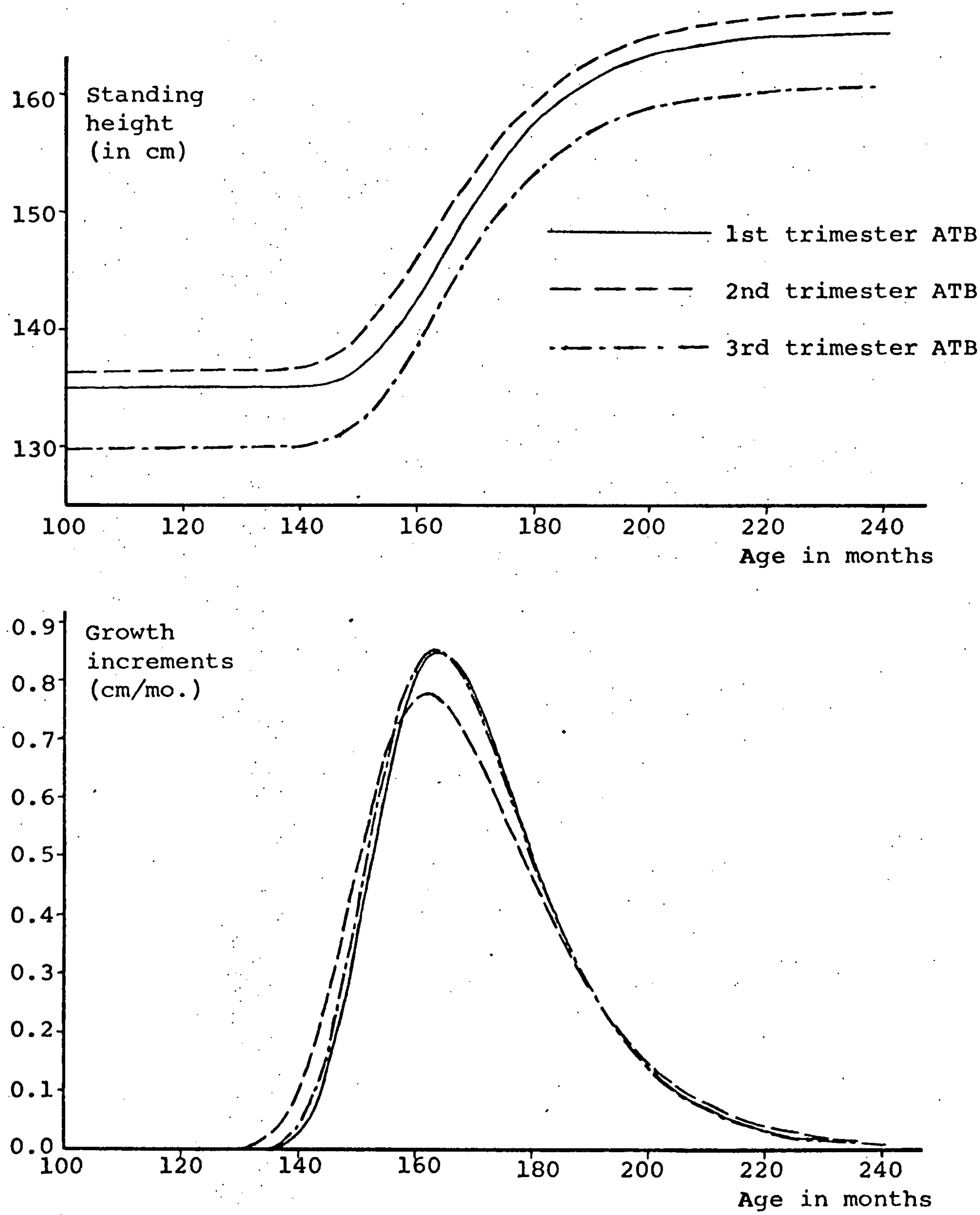


Figure 10: Trimester ATB Comparisons for Inner Proximal Group
--- Nagasaki, Males

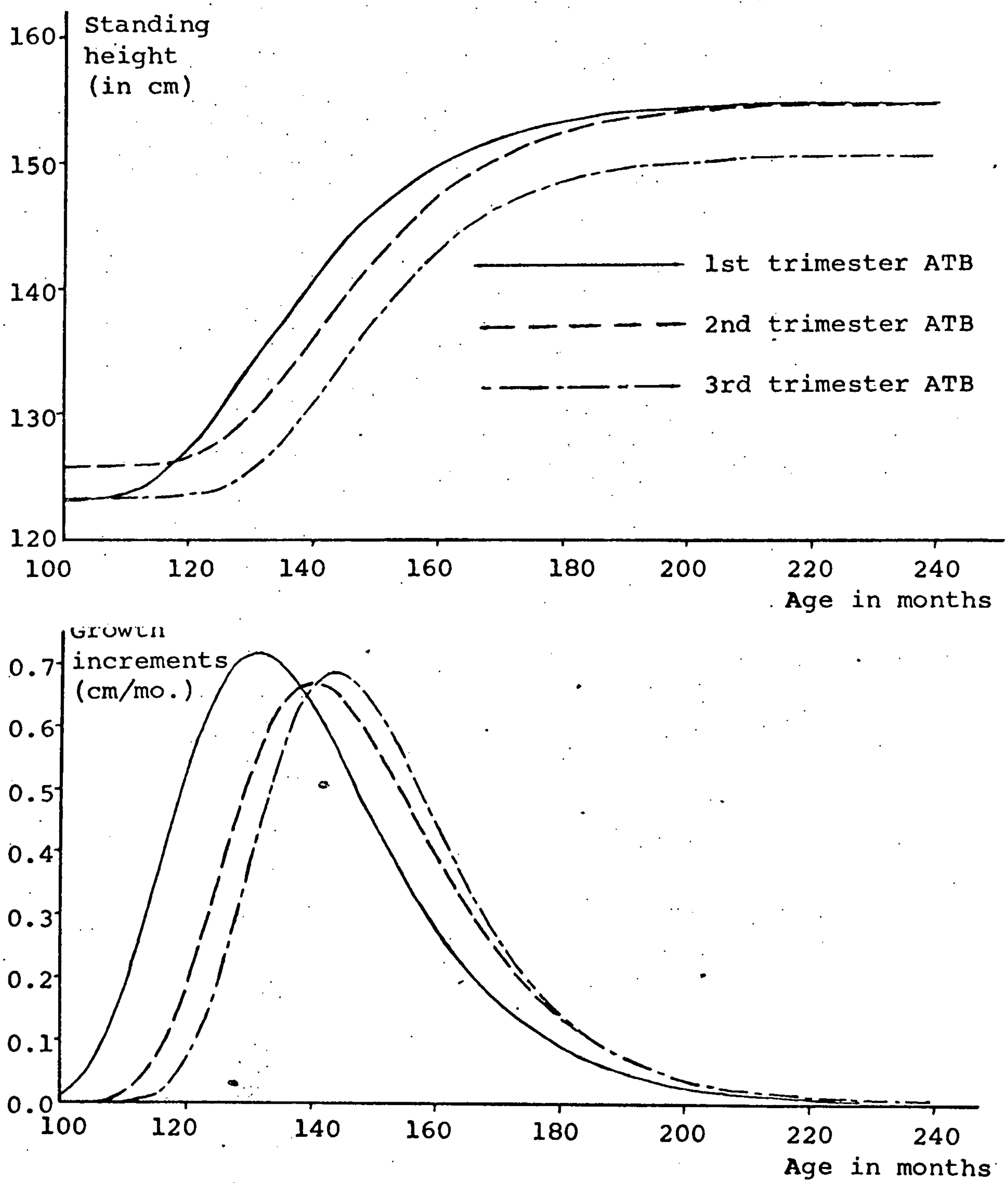
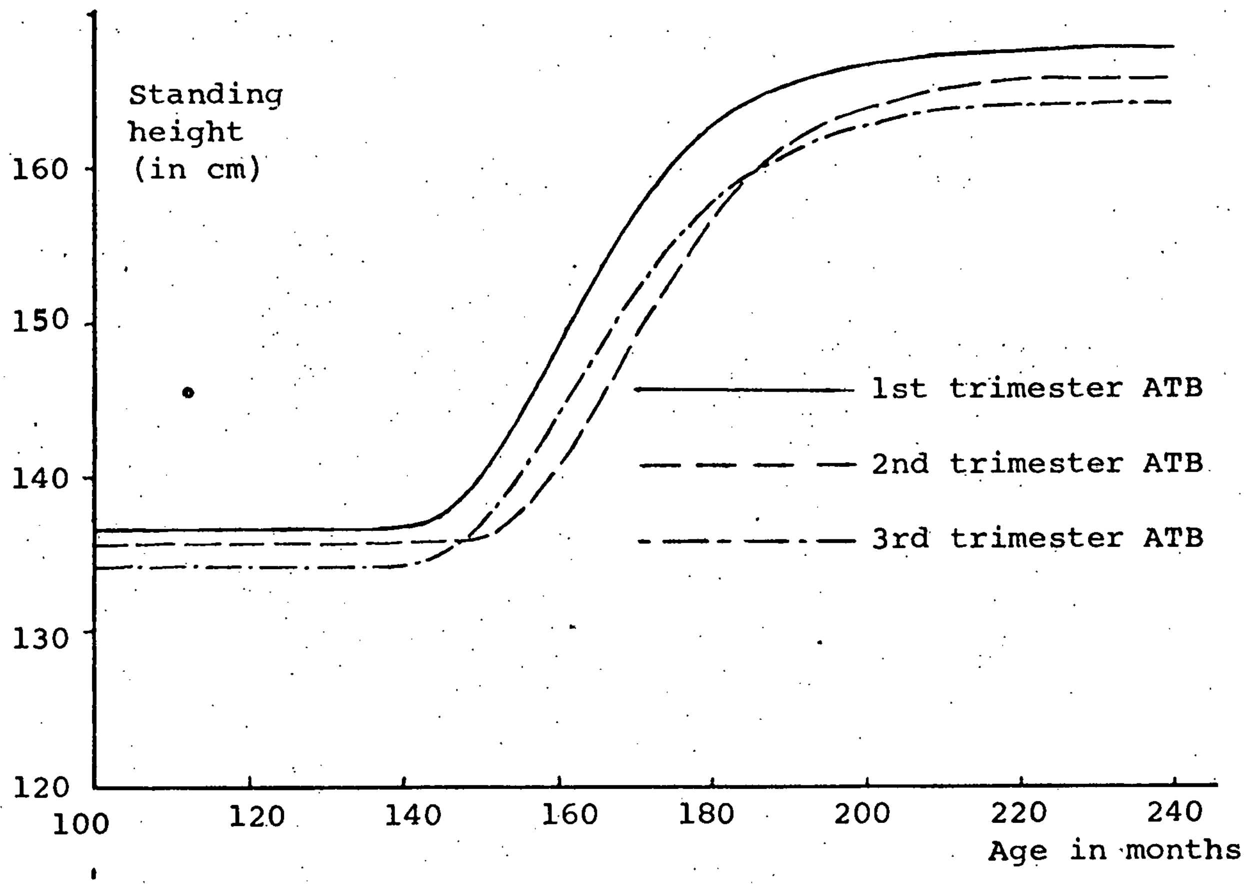


Figure 11: Trimester ATB Comparisons for Inner Proximal Group
--- Nagasaki, Females



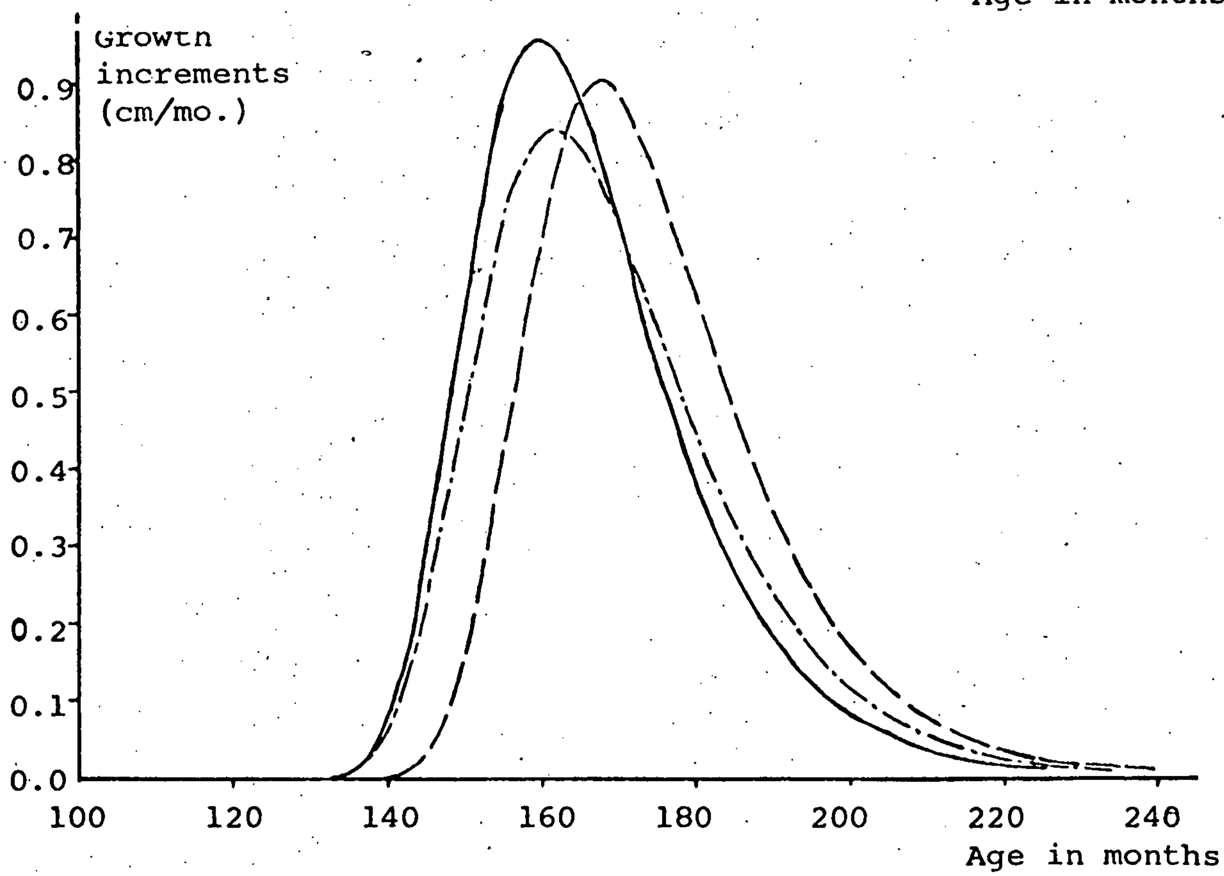


Figure 12: Trimester ATB Comparisons for Inner Proximal Group --- Hiroshima, Males

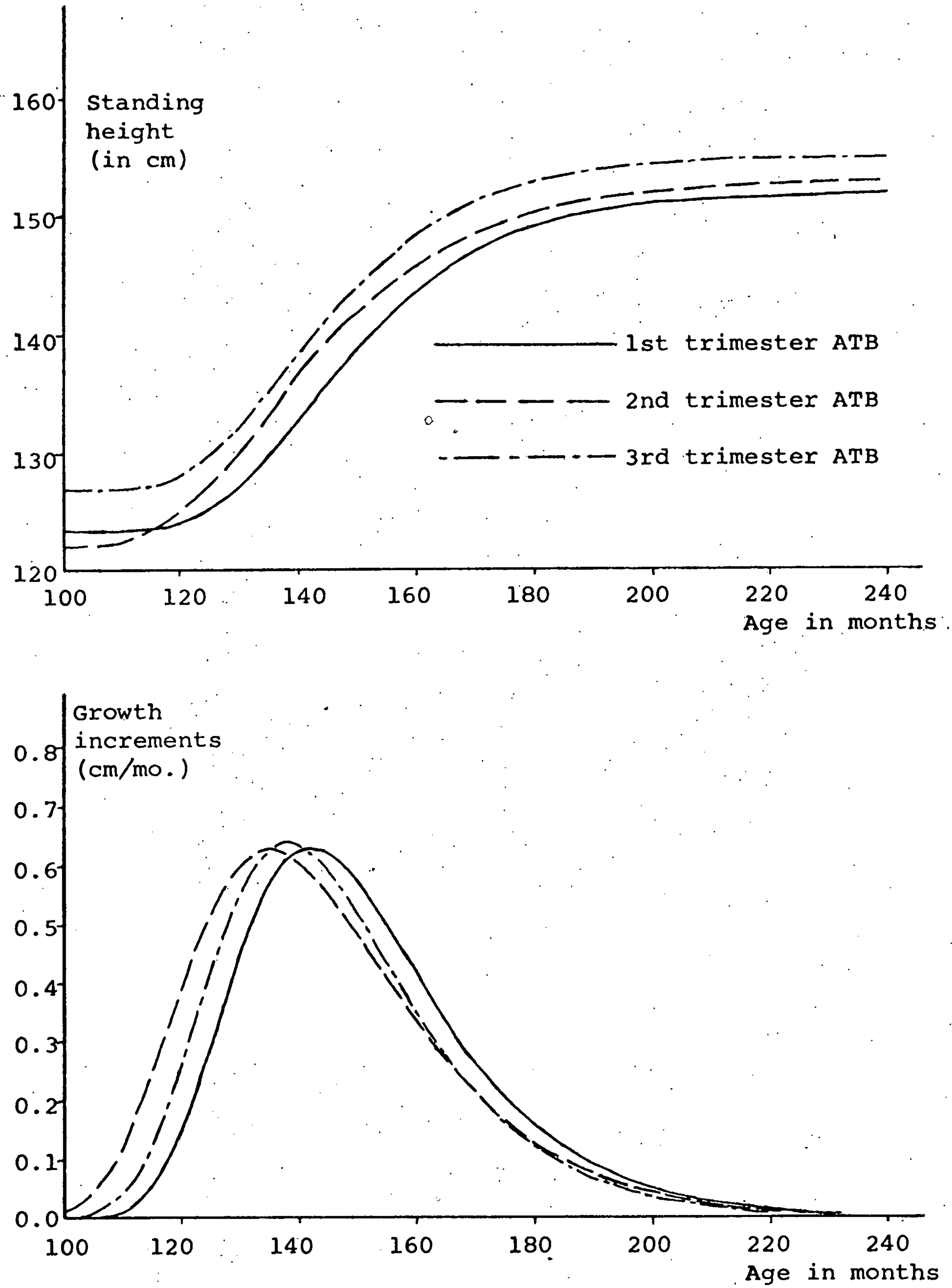


Figure 13: Trimester ATB Comparisons for Inner Proximal Group
--- Hiroshima, Females

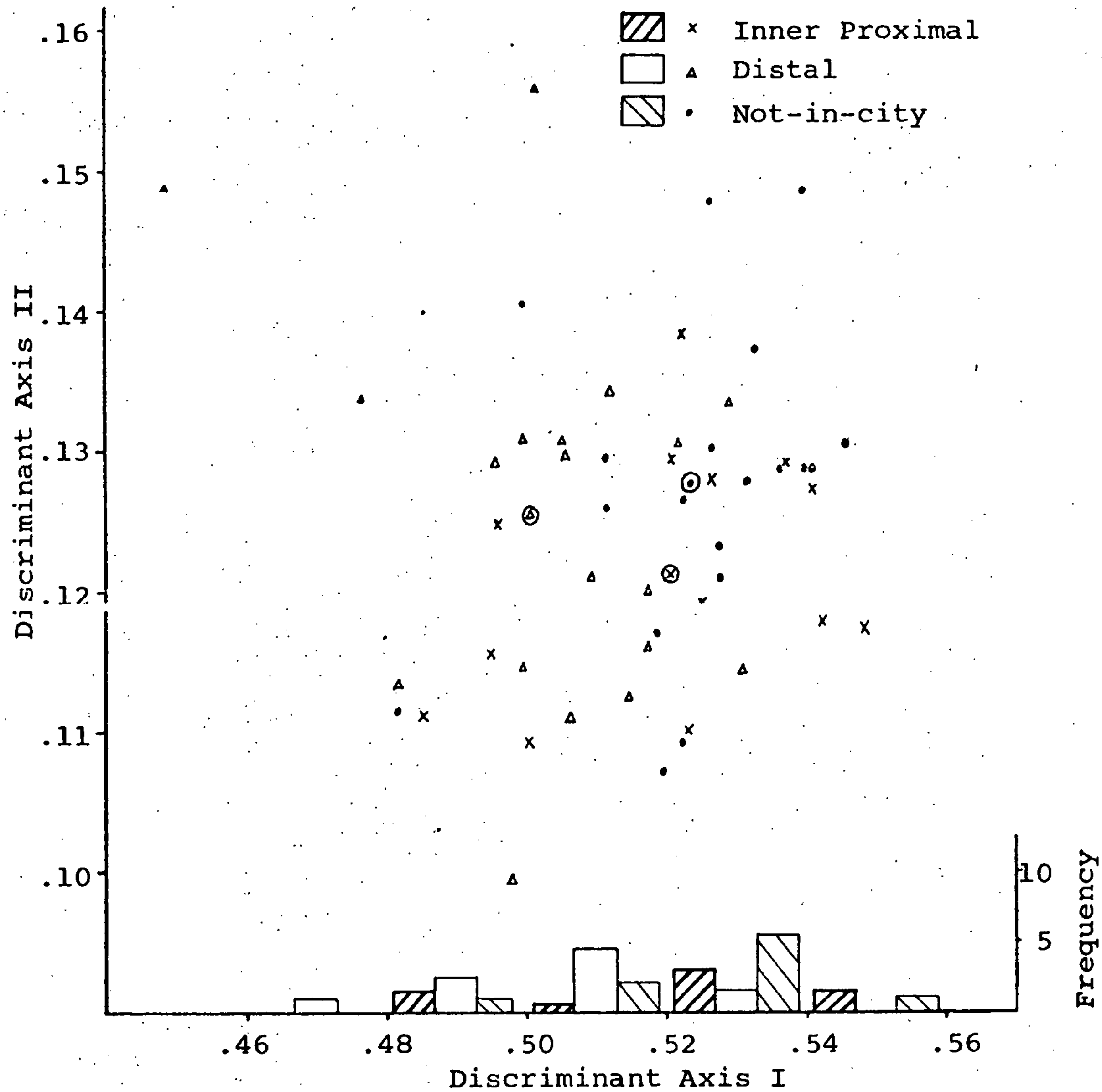


Figure 14: Group Centroids(○) and Subject Points for Males (2nd trimester ATB), Nagasaki. Discriminant axes I and II are for the scores corresponding to the largest and the second largest characteristic roots, respectively. The frequency distributions are for the scores corresponding to the largest characteristic root.

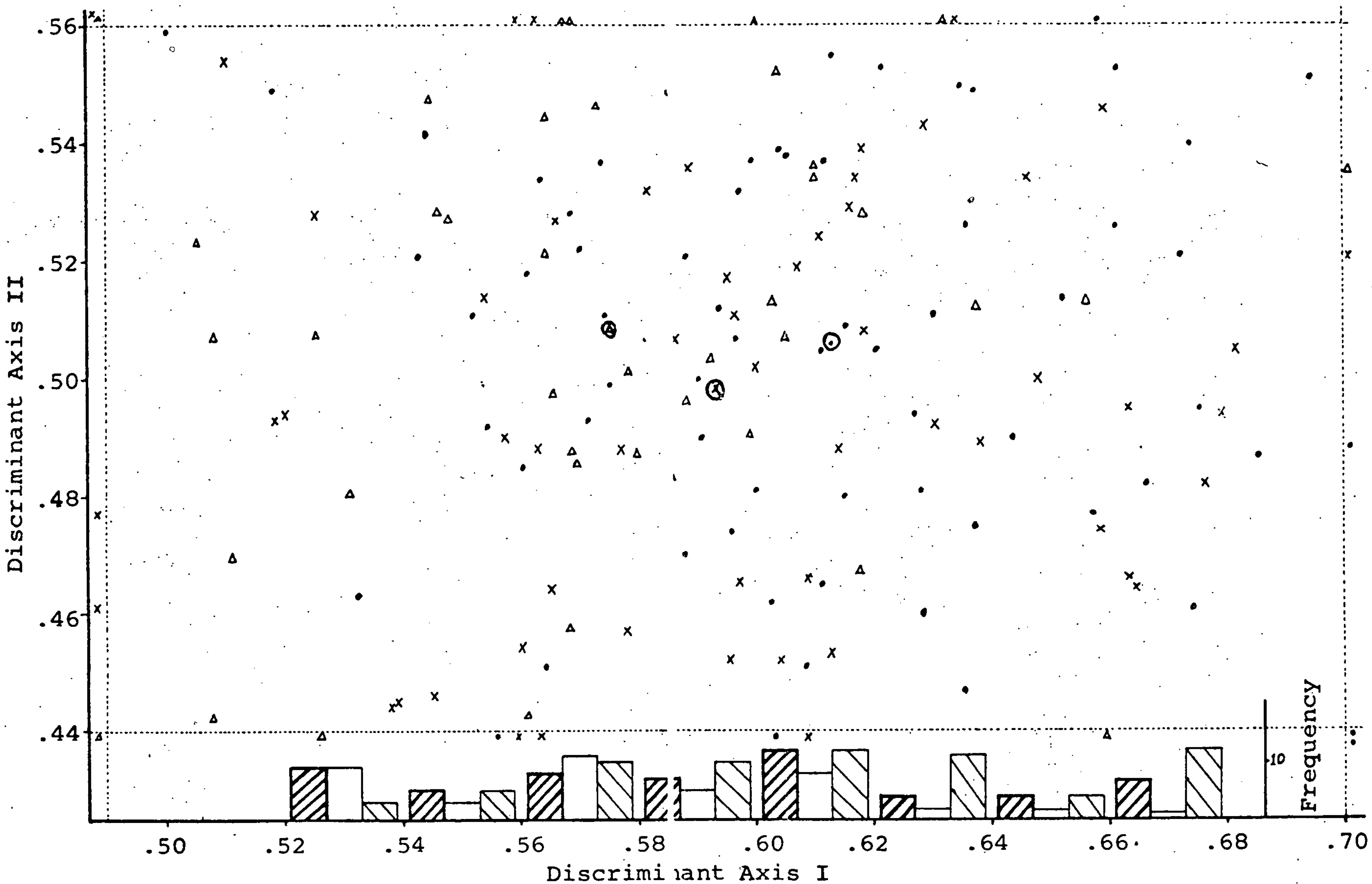


Figure 15: Group Centroids (○) and Subject Points for Males (2nd trimester ATB), Hiroshima.
See the footnote for Figure 14.

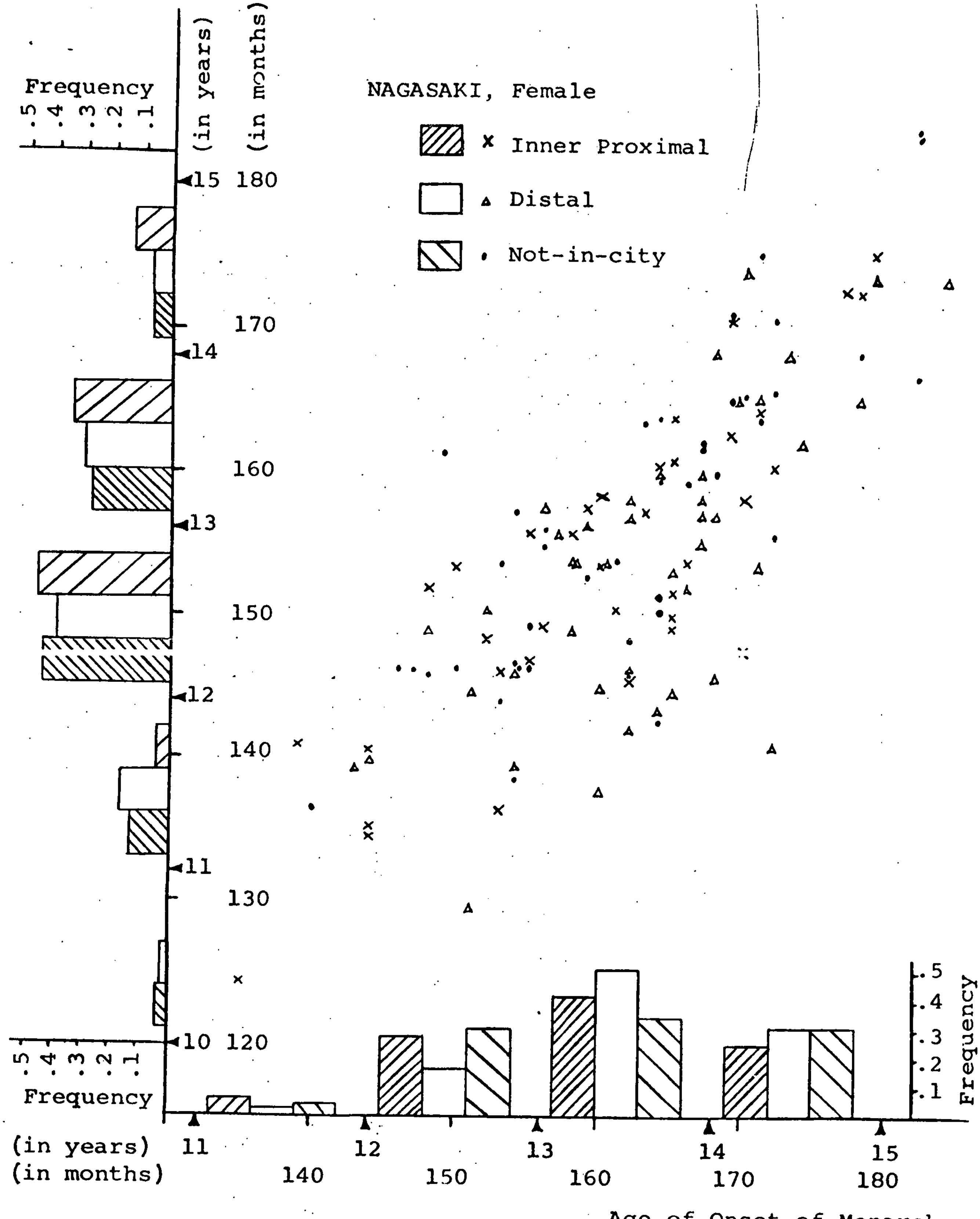


Figure 16: Relationships between Age at Onset of Menarche and Age (Estimated) at the 2nd Point of Inflection of the Velocity Curve.