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Repeated Multiple Maternities in Triplet Families

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In earlier studies, scientists have attempted to identify genetic and environmental factors affecting the rate of multiple maternities among humans. We contribute to these studies by analysing the frequencies of multiple maternities in sibships containing triplets. Use of the Hellin transformation is included in evaluation of the triplet rate. Our results indicate greater frequencies of repeated multiple maternities in the sibships than expected, based on population frequencies. The excesses obtained are more marked in triplet maternities than in twin maternities. The transformed triplet rate shows results similar to the twinning rate. The findings also indicate that in families, the influence of maternal factors on the frequencies of multiple maternities is stronger than the influence of paternal factors.

■ **Key words:** Hellin's law, maximum likelihood, probability models, parameter transformations

Studies have been performed to identify genetic and environmental factors affecting the rate of multiple maternities among humans (e.g., Bulmer, 1970; Weinberg, 1902). Fellman and Eriksson (1990) developed models previously presented by Hellin (1895), Peller (1946), and Eriksson et al. (1973). They presented the probability model:

$$P_{st} = w^s r^t (1 - w)(1 - r) \quad s, t \geq 0, \tag{1}$$

where P_{st} is the probability that a sibship contains s twin pairs and t triplet sets, w is the probability of a twin set and r is the probability of a triplet set. However, they had no information about sibships without twin pairs and triplet sets. Fellman and Eriksson (1990) stressed that a sibship could be included in their study only if it contained multiple maternities. Consequently, their data sets resulted in the distribution being truncated and they had to cope with the conditional probability

$$P = P(s, t | s \text{ or } t > 0) = \frac{w^s r^t (1 - w)(1 - r)}{r + w - rw} \quad s, t \geq 0, \tag{2}$$

This truncation complicated the parameter estimation. They needed to apply iterative numerical processes in order to obtain maximum likelihood estimates (Fellman & Eriksson, 1990).

In this study, we modify the Fellman-Eriksson model so that it can be applied to sibships that contain triplet sets.

Material and Methods

Material

Our data consist of sibships containing triplets initially presented by Miettinen (1954). We have studied these data in different contexts (Eriksson & Fellman, 1986; Eriksson et al., 1990, 2007; Fellman & Eriksson, 2014). The family data set comprises triplets born in Finland from 1905 to 1959. During this period, 723 triplet sets were registered in the official Finnish birth records. Using genealogical studies, sibships of the triplets and of their parents were collected. The genealogical investigations, initiated by Miettinen (1954) and continued by our group, resulted in birth information for 642 sibships of triplets containing 650 triplet sets and 125 twin pairs. Consequently, almost 90% of all officially registered triplet sets were included in our family series. Our data are presented in Table 1.

For sake of comparison, we include in this study the distributions of multiple maternities in sibships of the triplet mothers and triplet fathers. There are 587 sibships of mothers containing 3 triplet sets and 86 twin pairs (Table 2). For fathers, there are 510 sibships containing one triplet set and 45 twin pairs (Table 3).

Testing the association in Table 1 between the number of twin pairs and the number of triplet sets (sibships with

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TABLE 1
Multiple Maternities in Sibships With Triplets in Finland in 1905–1959

	Number of twin pairs					
Number of triplet sets	0	1	2	3	4	Total
1	537	78	16	2	1	634
2	5	2	0	1	0	8
Total	542	80	16	3	1	642

TABLE 2
Multiple Maternities in Sibships of Triplet Mothers in Finland in 1905–1959

	Number of twin pairs			
Number of triplet sets	0	1	2	Total
0	511	60	13	584
1	3	0	0	3
Total	514	60	13	587

TABLE 3
Multiple Maternities in Sibships of Triplet Fathers in Finland in 1905–1959

	Number of twin pairs			
Number of triplet sets	0	1	2	Total
0	466	41	2	509
1	1	0	0	1
Total	467	41	2	510

one set and with two sets), one obtains $\chi^2 = 26.80$ with four degrees of freedom; the association is statistically significant. The highest contribution, virtually all in the χ^2 value, $\chi^2 = 24.79$, corresponds to cell (2, 3). The observed number (in fact, only one) in this cell is too high. However, the expected numbers on the second line — that is, sibships with two triplet sets — are so small that the χ^2 value and the significance level are not convincing. The corresponding χ^2 value (with two degrees of freedom) for Table 2 is $\chi^2 = 0.428$ and for Table 3 $\chi^2 = 0.092$. These test values are insignificant. The observed rates within the sibships are compared with data given by Fellman and Eriksson (1993) for Finland (1901–1960). Their data yield the twinning rate, TWR = 14.785 per 1,000, the triplet rate, TRR = 15.337 per 100,000 and the transformed TRR, $H = 12.384$ per 1,000.

Methods

In this study, we apply the probability model (1) presented by Fellman and Eriksson (1990). However, the number of single maternities in the sibships is not satisfactorily obtained. We therefore define the rates of the repeated multiple maternities with respect to the sibships, not with respect to the maternities. According to model (1), numbers of twin pairs and triplet sets are independent.

The marginal distribution of a subset of random variables is the probability distribution of the variables contained in the subset. It gives the probabilities of the variables in this subset without reference to the values of the ignored variables. Using the model (1), the marginal distribution of the number of twin pairs in a sibship is

$$P_{s\cdot} = w^s (1 - w) \quad s \geq 0, \tag{3}$$

and the marginal distribution of the number of triplet sets in a sibship is

$$P_{\cdot t} = r^t (1 - r) \quad t \geq 0. \tag{4}$$

From this, it follows that

$$P_{st} = w^s r^t (1 - w)(1 - r) = P_{s\cdot} P_{\cdot t}. \tag{5}$$

A conditional distribution gives the probabilities contingent upon the values of the other variables. Using model (1), the conditional distributions coincide with the marginal distributions (3) and (4). This is a consequence of the model assuming that twin pairs and triplet sets occur independently in the sibships. The χ^2 value connected with Table 1 presented above indicates an association, but the limitation in the data set observed reduces the confidence of this association. The restrictive properties of the model reduce the generalizability, but more advanced models require larger and more structured data and are difficult to apply to the available data. However, the model allows numerical estimates of the rates of twin pairs and triplet sets in sibships to be obtained. Consequently, our study gives indications of the factors influencing the rates of multiple maternities.

Triplet Sibships

First, we consider in this study triplet sibships, that is siblings with at least one index triplet set. No sibship without triplet sets can be identified and included. Hence, the truncation, $t > 0$ of the model presented in equation (6), is caused by this fact. However, it is not neccessary to assume any restrictions on the occurrence of twin sets, and consequently, for the twin pairs the number is still $s \geq 0$. This truncation differs from the truncation used in Fellman and Eriksson (1990), and the statistical analyses are quite different. The truncated probability distribution is

$$P_{st} = w^s r^t (1 - w)(1 - r) \quad s \geq 0, t > 0. \tag{6}$$

Detailed statistical analyses of this model are given in the Appendix. The Appendix gives the following estimates:

The estimate of a twin set (w) is

$$\hat{w} = \frac{S}{S + N},$$

and the estimate of a triplet set (r) is

$$\hat{r} = \frac{T - N}{T}.$$

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Furthermore, we obtain

$$Var(\hat{w}) = \frac{w(1-w)}{N+S}$$

and

$$Var(\hat{r}) = \frac{r(1-r)}{T}.$$

Consequently, the standard deviations are

$$SD_{\hat{w}} = \sqrt{\frac{w(1-w)}{N+S}},$$

$$SD_{\hat{r}} = \sqrt{\frac{r(1-r)}{T}}$$

and

$$Cov(\hat{w}, \hat{r}) = 0.$$

Fellman and Eriksson (2004) stressed that in population studies the Hellin-transformed triplet rate can be compared with the twinning rate. We now evaluate how this holds in sibship studies. The maximum likelihood estimator of a transformed parameter is the corresponding transformation of the estimator of the initial parameter. For the Hellin-transformed rate $h = \sqrt{r}$, the estimate is $\hat{h} = \sqrt{\frac{T-N}{T}}$. According to (A16) and (A17), the variance of the estimate $\hat{h}$ is $Var(\hat{h}) = \frac{1-r}{4T}$ and the standard deviation is $SD_{\hat{h}} = \sqrt{\frac{1-r}{4T}}$.

Parental Sibships

Consider sibships of the mothers and fathers. Now one can accept sibships without multiple maternities and no truncation is necessary. Consequently, the estimates are $\hat{w} = \frac{S}{S+N}$ and $\hat{r} = \frac{T}{T+N}$. The variance estimates are $Var(\hat{w}) = \frac{w(1-w)}{N+S}$ and $Var(\hat{r}) = \frac{r(1-r)}{N+T}$. Finally, the formulae for the standard deviations are $SD_{\hat{w}} = \sqrt{\frac{w(1-w)}{N+S}}$ and $SD_{\hat{r}} = \sqrt{\frac{r(1-r)}{N+T}}$. If the triplet rate r is replaced by the Hellin-transformed rate $h = \sqrt{r}$, then $\hat{h} = \sqrt{\frac{T}{T+N}}$, $Var(\hat{h}) = \frac{1-r}{4(N+T)}$ and the standard deviation is $SD_{\hat{h}} = \sqrt{\frac{1-r}{4(N+T)}}$.

Results

Following Fellman and Eriksson (1990), the approximate associations between the average sibship size (c) and the multiple maternity rates (w, r or h) in the sibship and in the population (TWR, TRR and $H = \sqrt{TRR}$) are:

$$w \approx TWRc \text{ for twin pairs,} \quad (7a)$$

$$r \approx TRRc \text{ for triplet sets,} \quad (7b)$$

$$h \approx Hc \text{ for transformed triplet sets} \quad (7c)$$

TABLE 4
Estimated Parameters in Sibships for Triplets, Triplet Mothers and Triplet Fathers

Data set	Parameters	Triplets Table 1	Sibship of Mothers Table 2	Fathers Table 3
Twin pairs	$\hat{w}$	0.16297	0.12779	0.08108
	$SD_{\hat{w}}$	0.01458	0.01287	0.01158
	$c_{\hat{w}}$	11.023	8.643	5.484
Triplet sets	$\hat{r}$	0.01231	0.00508	0.00196
	$SD_{\hat{r}}$	0.00432	0.00292	0.00195
	$c_{\hat{r}}$	80.248	33.153	12.760
Transformed triplet sets	$\hat{h}$	0.11094	0.07131	0.04424
	$SD_{\hat{h}}$	0.01949	0.02053	0.02210
	$c_{\hat{h}}$	8.958	5.758	3.572

Using data in Fellman and Eriksson (1993), we obtained for Finland for the period 1901–1960, the twinning rate TWR = 14.785 per 1,000, the triplet rate TRR = 15.337 per 100,000m and the transformed TRR $H = 12.384$ per 1000. We apply the formulae (7a), (7b) and (7c) on the parameter estimates based on the data in Tables 1–3 and the observed rates of multiple maternities in Finland (1901–1960) and obtain Table 4.

Note that the transformed triplet rates (h) and the twinning rates (w) yield rather similar results. However, all estimates of h are lower than the estimates of w, but they have larger standard deviations. The c values obtained for triplets in triplet sibships and in maternal sibships are much too large to be considered estimates of the average number of maternities in a sibship. This is especially notable for the estimates obtained from the sibships of mothers (Table 2). Hence, there is a concentration of multiple maternities within some families. This is also, to some extent, the case for paternal sibships. Consequently, our data indicate a large excess of multiple maternities in sibships with triplets, a smaller excess in sibships of the mothers and only a slight excess in sibships of the fathers. These findings show effects of genetic factors, and these effects are mainly maternal.

Discussion

Eriksson and Fellman have intensively investigated the recurrence of multiple maternities in families, especially in triplet families. Furthermore, they have recently evaluated the association between birth weight and lifespan of triplets (Fellman & Eriksson, 2014). In the preliminary study of a subset of our data (Eriksson et al., 2007), the recurrence of multiple maternities in the sibships of triplets, triplet mothers and triplet fathers was presented, and the results were similar to those seen here. Among 627 sibships of triplets, 94 (15%) had at least one recurrent multiple maternity. This finding corresponds well to our extended data presented in Table 1, based on 642 sibships and yielding a proportion of 16.4%. The findings in Tables 2 and 3 indicate that the maternal influence is stronger than the paternal.

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Appendix

Triplet sibships. First, we consider triplet sibships and the truncated probability distribution is

$$P_{st} = w^s r^t (1-w)(1-r) \quad s \geq 0, t > 0. \tag{A1}$$

The likelihood function is

$$L(w,r) = w^S r^{T-N} (1-w)^N (1-r)^N, \tag{A2}$$

where $S = \sum\sum sn_{st}$, $T = \sum\sum tn_{st}$ and $N = \sum\sum n_{st}$.

Now we consider the log likelihood function:

$$l(w,r) = \ln(L(w,r)) = S\ln(w) + N\ln(1-w) + (T-N)\ln(r) + N\ln(1-r). \tag{A3}$$

When it is differentiated with respect to the parameter w, one obtains

$$\frac{\partial l}{\partial w} = \frac{S}{w} - \frac{N}{1-w}, \tag{A4}$$

and $\frac{\partial l}{\partial w} = 0$ yields $\frac{S}{w} - \frac{N}{1-w} = 0$.

The estimate of twin set (w) is:

$$\hat{w} = \frac{S}{S+N}. \tag{A5}$$

When the log likelihood function is differentiated with respect to the parameter r, one obtains

$$\frac{\partial l}{\partial r} = \frac{T-N}{r} - \frac{N}{1-r}, \tag{A6}$$

and $\frac{\partial l}{\partial r} = 0$ yields $\frac{T-N}{r} - \frac{N}{1-r} = 0$.

The estimate of a triplet set (r) is

$$\hat{r} = \frac{T-N}{T}. \tag{A7}$$

To obtain the variances of the estimates, we differentiate once more and obtain

$$\frac{\partial^2 l}{\partial w^2} = -\frac{S}{w^2} - \frac{N}{(1-w)^2}, \tag{A8}$$

$$\frac{\partial^2 l}{\partial r^2} = -\frac{T-N}{r^2} - \frac{N}{(1-r)^2} \tag{A9}$$

and

$$\frac{\partial^2 l}{\partial w \partial r} = 0. \tag{A10}$$

Consequently, equation (A10) indicates that the parameter estimates are uncorrelated. One obtains

$$-E\left(\frac{\partial^2 l}{\partial w^2}\right) = \frac{S}{w^2} + \frac{N}{(1-w)^2} = \frac{S - 2Sw + wS}{w^2(1-w)^2} = \frac{S(1-w)}{w^2(1-w)^2} = \frac{S(N+S)}{w(1-w)S} = \frac{(N+S)}{w(1-w)}$$

and

$$Var(\hat{w}) = \frac{w(1-w)}{N+S}. \tag{A11}$$

Furthermore,

$$-E\left(\frac{\partial^2 l}{\partial r^2}\right) = \frac{T-N}{r^2}\frac{N}{(1-r)^2} = \frac{N+(T-N)}{r(1-r)N} = \frac{T}{r(1-r)}$$

and

$$Var(\hat{r}) = \frac{r(1-r)}{T}. \quad \text{(A12)}$$

The standard deviations are

$$SD_{\hat{w}} = \sqrt{\frac{w(1-w)}{N+S}}, \quad \text{(A13a)}$$

$$SD_{\hat{r}} = \sqrt{\frac{r(1-r)}{T}} \quad \text{(A13b)}$$

and

$$Cov(w, \hat{r}) = 0. \quad \text{(A13c)}$$

If the triplet rate r is replaced by the Hellin-transformed rate $h = \sqrt{r}$, the log likelihood function is $l(w, r(h))$. Now,

$$\frac{\partial l}{\partial h} = \frac{\partial l}{\partial r}\frac{dr}{dh}. \quad \text{(A14)}$$

The equation $\frac{\partial l}{\partial h} = 0$ yields the estimate $\hat{r}$ and $\hat{h} = \sqrt{\hat{r}}$. Furthermore,

$$\frac{\partial^2 l}{\partial h^2} = \frac{\partial^2 l}{\partial r^2}\left(\frac{dr}{dh}\right)^2 + \frac{\partial l}{\partial r}\frac{d^2 r}{dh^2}. \quad \text{(A15)}$$

For $\hat{r}$ and $\hat{h}$, one obtains $\left(\frac{\partial l}{\partial h}\right)_{r=\hat{r}} = 0$ and $\frac{\partial^2 l}{\partial h^2} = \frac{\partial^2 l}{\partial r^2}\left(\frac{dr}{dh}\right)^2$. In our case,

$$-E\left(\frac{\partial^2 l}{\partial h^2}\right)\left(\frac{dr}{dh}\right)^2 = -E\left(\frac{\partial^2 l}{\partial r^2}\right)\left(\frac{dr}{dh}\right)^2$$
$$= \left(\frac{T-N}{r^2}\frac{N}{(1-r)^2}\right)(2h)^2 = \frac{T}{r(1-r)}4h^2.$$

Consequently, for the estimate $\hat{h}$ of the transformed triplet rate $h = \sqrt{r}$, the variance is

$$Var(\hat{h}) = \left(\frac{1}{2\sqrt{\hat{r}}}\right)^2 Var(\hat{r}) = \frac{1}{4r}\frac{r(1-r)}{T} = \frac{1-r}{4T}, \quad \text{(A16)}$$

and the standard deviation is

$$SD_{\hat{h}} = \sqrt{\frac{1-r}{4T}}. \quad \text{(A17)}$$

Parental sibships. For parental sibships, no truncation is necessary, and one can, for w, r and h, use the estimation formulae for the parameter w in (A5).

$$\text{The estimates are } \hat{w} = \frac{S}{S+N} \quad \text{(A18)}$$

and

$$\hat{r} = \frac{T}{T+N}. \quad \text{(A19)}$$

The variance estimates are

$$Var(\hat{w}) = \frac{w(1-w)}{N+S} \quad \text{(A20)}$$

and

$$Var(\hat{r}) = \frac{r(1-r)}{N+T}. \quad \text{(A21)}$$

Finally, the formulae for the standard deviations are

$$SD_{\hat{w}} = \sqrt{\frac{w(1-w)}{N+S}} \quad \text{(A22)}$$

and

$$SD_{\hat{r}} = \sqrt{\frac{r(1-r)}{N+T}}. \quad \text{(A23)}$$

If the triplet rate r is replaced by the Hellin-transformed rate $h = \sqrt{r}$, then

$$\hat{h} = \sqrt{\frac{T}{T+N}} \quad \text{(A24)}$$

and

$$Var(\hat{h}) = \frac{1-r}{4(N+T)}, \quad \text{(A25)}$$

and the standard deviation is

$$SD_{\hat{h}} = \sqrt{\frac{1-r}{4(N+T)}}. \quad \text{(A26)}$$