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A Statistical Analysis of the Seasonality in Sudden Infant Death Syndrome

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Helweg-Larsen K (Retspatologisk Institute, University of Copenhagen, Denmark), Bay H and Mac F. A statistical analysis of the seasonality of sudden infant death syndrome. *International Journal of Epidemiology* 1985, 14: 000–000.
Sudden Infant Death Syndrome (SIDS) has a characteristic peak incidence in the winter months and a peak incidence at the age of two to four months. The present study examines whether the seasonality is related to the time of birth—the time of death or both.
The data for the study relates to 116 cases of SIDS, presenting 95% of all registered cases of SIDS in eastern Denmark in a three-year period 1981 to 1983. They were all autopsied at the Institute of Forensic Medicine in Copenhagen and evaluated by the same people.
The framework of the analysis is a multiplicative Poisson-model with three sets of parameters describing the effects of the age of the infant, the time of death and the time of birth. The analysis proved the seasonality related alone to the time of death.
An identical analysis was performed for 123 infants who in the period 1973–83 in eastern Denmark died from infectious diseases. In these cases no significant effect of the month of birth or the month of death was shown.

Sudden Infant Death Syndrome (SIDS) is defined as the sudden death of infants between one week and one year which is unexpected by history, and in which a thorough post-mortem examination fails to demonstrate an adequate cause of death.[1]

The syndrome has a characteristic age distribution with a clearly defined peak at two to four months. It very rarely affects infants of less than four weeks of age, and about 80% of the cases occur during the first six months of life.[2]

In 1965 the seasonal variation in SIDS was reported[3] with a peak incidence found during winter months. This observation was supported by studies from Ireland,[2] USA,[4] Canada,[5] and England and Wales.[6,7]

Carpenter and Gardner[7] further found that the risk of death also varied with the month of birth. The typical seasonal variation in SIDS was by some authors[8,9] claimed to be a reflection of an event in the early fetal period and the characteristic seasonal distribution related to the time of conception and thus to the time of birth rather than to the time of death.

The aim of the present study is to test the influence of the month of birth and of the month of death upon the seasonal variation of SIDS.

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MATERIAL AND METHODS

Sources of Data

All cases of infant death which occur suddenly, including accidents, homicides, Sudden Infant Death Syndrome and other natural deaths from known causes are covered by regulations in the Danish law concerning certification of death and will result in a medico-legal examination. In the city of Copenhagen police regulations state that a medico-legal autopsy is mandatory to obtain the optimal knowledge of the cause of death in all cases of sudden infant death. This is now common practice in all parts of eastern Denmark resulting in a high autopsy rate in cases of sudden infant death. Thus in the period 1980–82 the classification of 95% of the registered cases of SIDS was based on autopsy.

The Institute of Forensic Medicine in Copenhagen serves the eastern part of Denmark with 230000 inhabitants. A total of 120 cases of SIDS were registered in the area during the period of 1981–83. The birth number during the same period was 65420 infants; the incidence rate of SIDS was 1.8 per 1000 live births.

One hundred and sixteen of the total 120 registered cases of SIDS were autopsied at the Institute of Forensic Medicine in Copenhagen. All cases were evaluated by two forensic pathologists. The autopsies included histological, bacteriological and in some cases virological and toxicological examinations. The cases

were classified in accordance with the definition of SIDS as proposed as the Second International Congress on Causes of Sudden Infant Death Syndrome in Seattle in 1969.[1]

Data concerning age, month of birth and month of death from these 116 cases of SIDS were analysed.

During the period of 1973–1983 a total of 123 infant deaths due to infectious disease (ICD codes, 8th revision: 000–136, 460–474, 480–486, 490–493 and 500–519) were registered at the Central Death Register of the Danish National Health Board. Information about age, month of birth and month of death were obtained from these 123 infants, analysed as to seasonal variation and compared to the data on the 116 cases of SIDS.

Statistical Methods

The 116 SIDS have been grouped by month of birth and by month of death (Table 1). This grouping gives rise to a grouping by age: Age group 1 consists of infants who die inj the same month as they are born, age group 2 consists of infants who die in the month following the month of birth, etc.

In discussing age group in the following, it must be remembered that eg age group 5 covers real life time between the third and the fifth month and age group 1 covers real life time of 1 to 30 days.

(In spite of the overlap between age intervals the grouping of infants does not overlap).

Age was chosen as the double-width variable, because the central parameters of the analyses are the parameters of the month of death and the month of birth; although the age parameters also are estimated.

TABLE 1 *Number of SIDS in age groups and grouped by month of death and month of birth.*

Age group/ month	Number of SIDS in age groups	Number of SIDS in each month of death	Number of SIDS in each month of birth
1	1	19	7
2	9	14	7
3	18	10	4
4	32	7	5
5	25	4	10
6	15	6	8
7	6	3	11
8	5	3	13
9	1	10	23
10	3	10	13
11	1	12	9
12	0	18	6
Total	116	116	116

In the following we thus have three variables by which data can be grouped. The three variables are age group, month of death and month of birth. In Table 1 the data are grouped by each variable, separately.

The following statistical model was used to describe the simultaneous influence of the three factors and to determine which of the three has a significant influence. A more precise description of the statistical method is given in the statistical appendix.

1. The expected number of infants who in a certain month will die from SIDS—among the total number of infants born in a certain month, is—apart from random variations—equal to a product of four factors. The first factor is the total number of infants born in the month in question. The three other factors (parameters) characterize the month of death, the month of birth and the age.

The expected number is $N_k \times A_i \times B_j \times C_k$

Where N_k = the number of infants born in the month
A_i = the parameter of the age
B_j = the parameter of the month of death
C_k = the parameter of the month of birth.

This crucial assumption predicting that there is no interaction between the effect of the month of birth, the month of death and the age will make it possible to separate the three effects by estimating the corresponding parameters.

2. The random variations are described by a Poisson-distribution. Thus the joint distribution of SIDS is described by a multiplicative Poisson-model.

The model contains 36 parameters, 12 paramters for each of the three factors which influence the risk of SID. The influence of a certain factor depends on the difference between the corresponding 12 parameters: the greater the difference between the parameters, the greater is the influence of the factor.

The reason for choosing this model was that it necessitates only a minimum of assumptions. It was thus unnecessary to postulate a specific functional form, for instance a sinusoidal function, describing the variation of the parameters. Although such a function would have made it possible to create tests of greater power for describing the hazard, making it poossible to use the exact time of death.

The expected number of deaths is assumed to be proportional to the number of liveborn infants in the month in question. It would have been more correct to relate the number of deaths to the number of person-months at risk as was done by Osmond and Gardner,[10] but due to the very low infant mortality the difference between the two approaches is negligible, except with regard to the parameter of the youngest age groups. In this group, however, the procedure of multiplying the estimator by the factor 2 (as described in the appendix) must be considered appropriate to compensate for the shorter mean exposure time in this group.

The model is very close to the multiplicative models described by Osmond and Gardner[10] and by Day and Charney[11] where age, period and cohort replace the age, month of death and month of birth in the present model. There is, however, the important difference, that the month of death and the month of birth is repeated after one year in contrast to the period and the cohort. The structure of the present model is therefore equivalent to a latin square with the consequence that the identification problem described by Osmond and Gardner[10] does not occur.

TABLE 2 *Estimates and the standard deviation (data from 116 cases of SIDS).*

	Estimates	Standard deviation*
	Age	
1	0.56×10^{-4}	0.61×10^{-4}
2	2.49×10^{-4}	1.43×10^{-4}
3	4.93×10^{-4}	2.63×10^{-4}
4	8.37×10^{-4}	4.33×10^{-4}
5	5.98×10^{-4}	3.14×10^{-4}
6	3.59×10^{-4}	2.02×10^{-4}
7	1.46×10^{-4}	0.96×10^{-4}
8	1.21×10^{-4}	0.82×10^{-4}
9	0.24×10^{-4}	0.27×10^{-4}
10	0.76×10^{-4}	0.58×10^{-4}
11	0.27×10^{-4}	0.30×10^{-4}
12	0.00	0.00
	Month of death	
1	1.00	0.00
2	0.84	0.30
3	0.67	0.28
4	0.46	0.22
5	0.26	0.15
6	0.37	0.20
7	0.17	0.12
8	0.16	0.11
9	0.53	0.24
10	0.50	0.22
11	0.58	0.23
12	0.85	0.29
	Month of birth	
1	1.00	0.00
2	1.32	0.72
3	0.71	0.46
4	0.91	0.58
5	1.51	0.86
6	0.97	0.57
7	1.10	0.61
8	1.15	0.61
9	1.85	0.90
10	1.08	0.55
11	0.87	0.46
12	0.68	0.38

To estimate the parameters the maximum likelihood method was used. Table 2 contains the estimates which are also seen in Figures 1, 2 and 3. The 95% confidence limits have been denoted by X.

Figure 1 shows that the estimated parameters of age are very different, indicating that the influence of age is large.

The effect of age has not been tested since its existence can hardly be questioned, as proved by Carpenter and Gardner.[7]

Table 2 shows that there is a large difference between the estimated parameters of the month of death, and that the variation is somewhat systematic: low values in the summer, high values in the winter. This indicates that the influence of the month of death is large, (though smaller than the influence of age).

On the contrary, it was found that the parameters of the month of birth do not differ much and that this variation is not systematic (Figure 3). This indicates that the time of birth is a factor without an independent influence on the risk of SIDS.

Three statistical tests were performed to determine whether the observed difference between the parameters of the month of death and the parameters of the month of birth respectively could be explained as random.

The tests are all pesrformed at the 5% level.

1. The test for a vanishing effect of the month of birth was not significant (P = 66%).
2. The test for a vanishing effect of the month of death was nearly significant (P = 9%).
3. When simultaneously testing the vanishing effect of the month of birth and the month of death it is found to be significant (P = 1%). Consequently age alone cannot explain the variations in seasonal incidence of SIDS.

Considering the degrees of systematic variation in the estimated parameters of the month of birth and the month of death, the most reasonable conclusion on the basis of the estimates and of the tests is, that the age and the month of death independently influence the risk of SIDS, whereas the large relative frequency of SIDS for infants born in the autumn, as seen in Figure 4, can be explained as the result of the simultaneous influence of age and month of death.

Although there is no significant difference between the parameter of the month of birth, the estimated value of the parameter of September is seen to be somewhat larger than the rest. It might be tempting to explain this as the result of an interaction between the effect of age and month of death, since such an interaction, if it existed, could be expected to have the

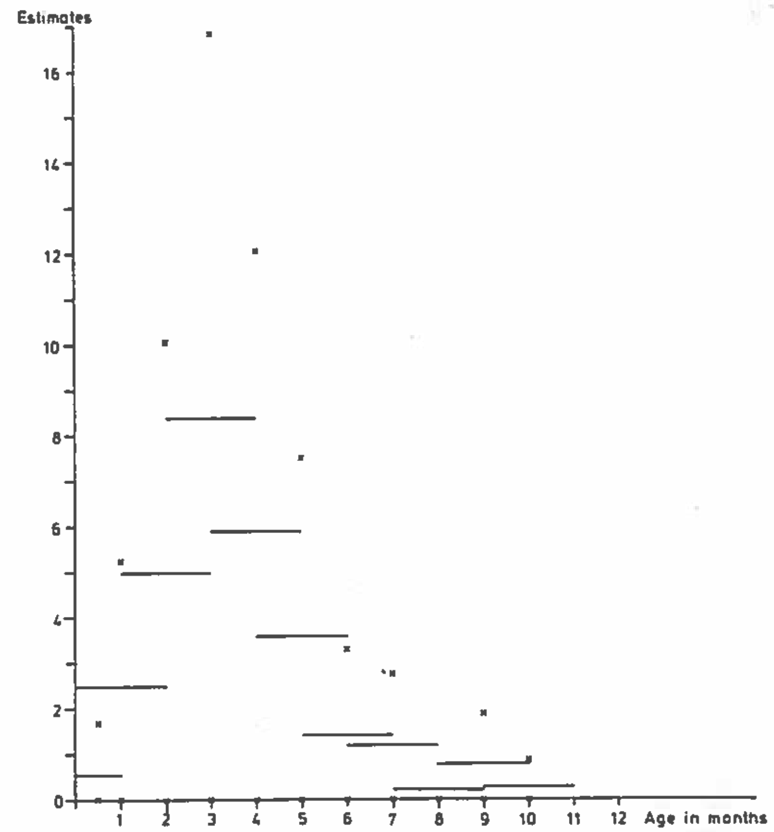

FIGURE 1 *SIDS: Estimated values of age parameters. The 95% confidence limits are shown by x.*

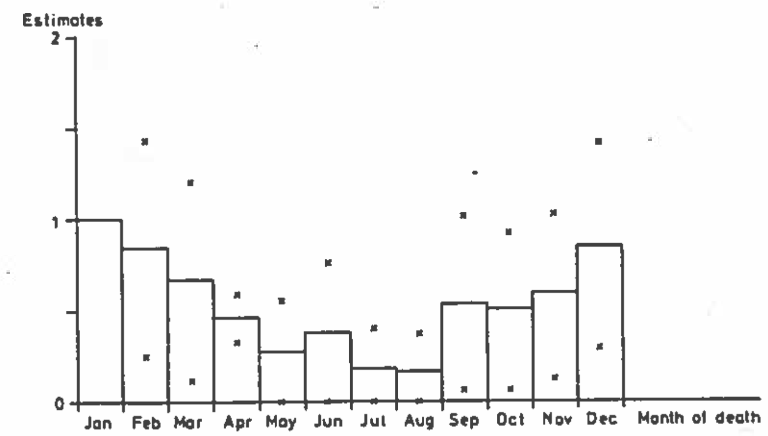

FIGURE 2 *SIDS: Estimated values of the parameters of month of death. The 95% confidence limits are shown by x.*

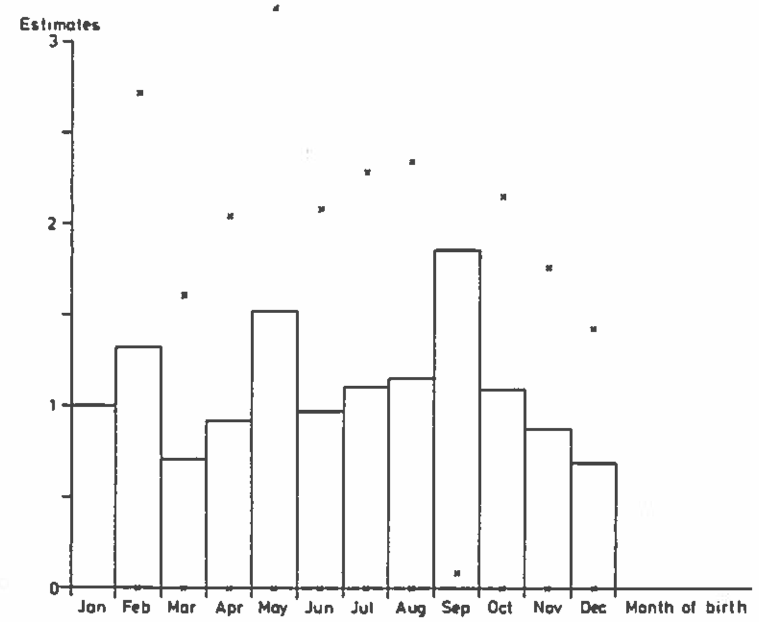

FIGURE 3 *SIDS: Estimated values of the parameters of month of birth. The 95% confidence limits are shown by x.*

largest impact on infants who reach the most risky age at the most dangerous time of the year, that is infants born in the autumn.

The number of observations is not sufficiently large to allow a numerical test of such an interaction.

However, the residuals (the observed values minus the values that could be expected on the basis of the multiplicative model with the parameter of the month of birth equal to one) have been analysed. If such an interaction existed it would result in large, positive residuals for infants born in the autumn and dying in the winter.

In fact, the residuals show no systematic variation and therefore there is no support for a hypothesis of interaction of this material.

Analysis of Infant Deaths from Infectious Diseases

The same analysis as described above was carried out for the 123 infants registered as dying from infectious disease.

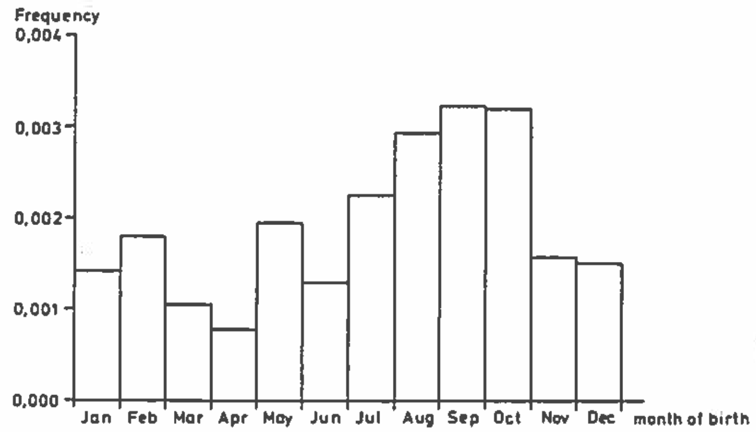

FIGURE 4 *Frequency of SIDS among liveborn infants related to month of birth, calculated for infants born in 1981–1982.*

The datea and the estimated parameters are shown in Table 3 and in Figures 5, 6 and 7. No significant difference was found between the parameters describing the month of death ($p=25\%$) or between the parameters describing the month of birth ($p=94\%$).

CONCLUSION

The lack of positive diagnostic criteria for SIDS necessitates a standardized registration system. This analysis, therefore, was based on cases of SIDS which were identically evaluated by autopsy.

The analysis has shown that the age of the infant and the time of the year (the month of death) have a genuine influence on the risk of SIDS, whereas the effect of time of birth can be explained as the result of the simultaneous influence of the age and the time of death. It is thus unlikely that the risk of SIDS is influenced by a predisposition resulting from a seasonal factor acting at a particular time during the pregnancy or shortly after the birth.

TABLE 3 *Estimates and the standard deviation (data from 123 deaths from infectious disease).*

	Estimates	Standard deviation*
	Age	
1	25.72×10^{-5}	11.27×10^{-5}
2	7.04×10^{-5}	3.29×10^{-5}
3	6.20×10^{-5}	2.93×10^{-5}
4	2.56×10^{-5}	1.42×10^{-5}
5	3.28×10^{-5}	1.72×10^{-5}
6	3.85×10^{-5}	1.99×10^{-5}
7	3.53×10^{-5}	1.84×10^{-5}
8	0.34×10^{-5}	0.41×10^{-5}
9	1.04×10^{-5}	0.74×10^{-5}
10	1.38×10^{-5}	0.89×10^{-5}
11	0.73×10^{-5}	0.59×10^{-5}
12	1.09×10^{-5}	0.77×10^{-5}
	Month of death	
1	1.00	0.00
2	0.81	0.35
3	0.95	0.40
4	0.60	0.28
5	0.77	0.34
6	0.23	0.14
7	0.51	0.25
8	0.42	0.21
9	0.49	0.24
10	0.68	0.30
11	0.98	0.40
12	0.79	0.34
	Month of birth	
1	1.00	0.00
2	1.59	0.77
3	1.87	0.87
4	1.84	0.91
5	1.27	0.66
6	1.93	0.97
7	1.20	0.63
8	1.53	0.77
9	1.52	0.75
10	1.61	0.78
11	1.06	0.55
12	1.20	0.62

There is no evidence of an interaction between age and month of death.

In the cases where the cause of death was registered as infectiou disease neither the month of death nor the month of birth have a significant effect. Considering the degree of systematic variation in the estimated parameters one would hesitate to conclude that the month of death is without importance, in spite of the lack of significance.

STATISTICAL APPENDIX

Let X_{ijk} be the number of SIDS from age group i, who die in the month of j and who are born in the month of k.

It is then assumed that (X_{ijk}) are independent Poisson-variates. The expectation of X_{ijk} is $N_{kj}A_iB_jC_k$ where N_{kj} is equal to the number of infants born in month of k and still alive at the beginning of the month of j. (Due to the fact that death from all causes is less than 1% N_k has been used instead of N_{kj}. N_k is the number of infants born in the month of k).

A_i, B_j and C_k are explained in (1) (see *Statistical Methods*).

The indices i, j, k each take values from 1 to 12, but they are subject to constraints.

$j=k+i-1$ if $k+i-1 \leq 12$

$j=k+i-1-12$ if $k+i-1>12$

The structure is equivalent to a latin square

The log-likelihood function is proportional to the expression in (2).

$$(2) \sum_{ijk} X_{ijk}(\ln(A_i)+\ln(B_j)+\ln(C_k)) - \sum_{ijk} A_iB_jC_kN_k$$

Note that the indices are linked together.

From (2) you get the sufficient statistics $(X_{i..})$, $(X_{.j.})$ and $(X_{..k})$.

$X_{i..}$ = the total number of SIDS in age group i

$X_{.j.}$ = the total number of SIDS died in the month of j

$X_{..k}$ = the total number of SIDS born in the month of k

To get the maximum likelihood estimates you have to solve the following equations

$$(3) \quad X_{i..}/A_i = \sum_{jk} N_kB_jC_k$$

$$X_{.j.}/B_j = \sum_{jk} N_kA_iC_k$$

$$X_{..k}/C_k = \sum_{ij} N_kA_iB_j$$

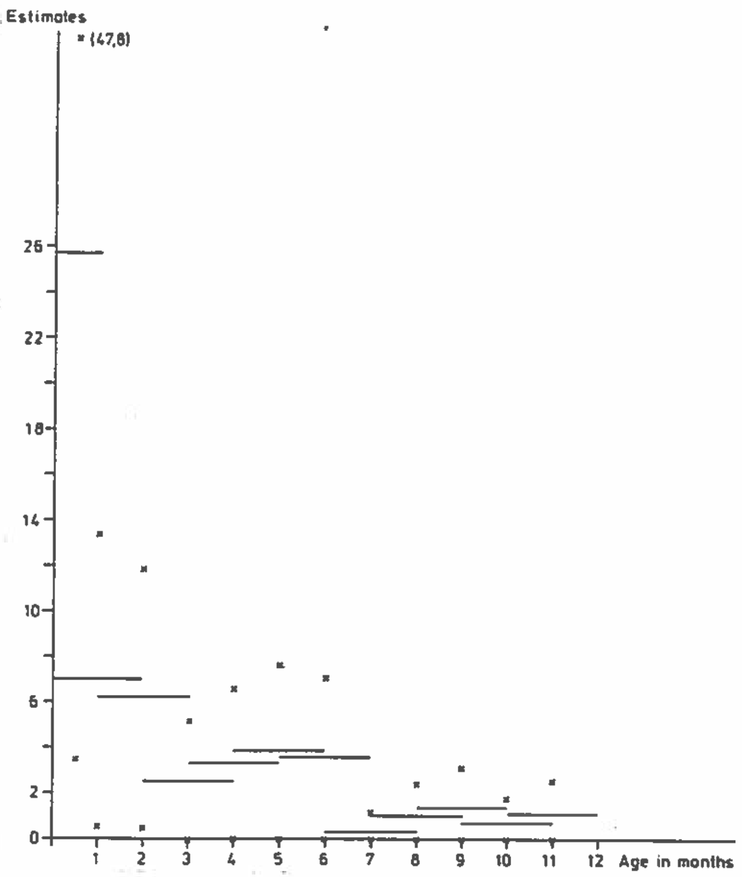

FIGURE 5 *Estimated values of age-parameters for infectious disease. The 95% confidence limits are shown by x.*

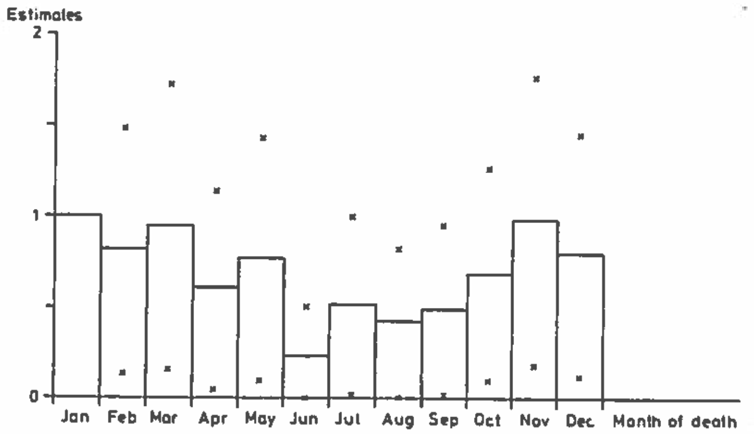

FIGURE 6 *Estimated values of the parameters of the month of death. Infectious disease. The 95% confidence limits are shown by x.*

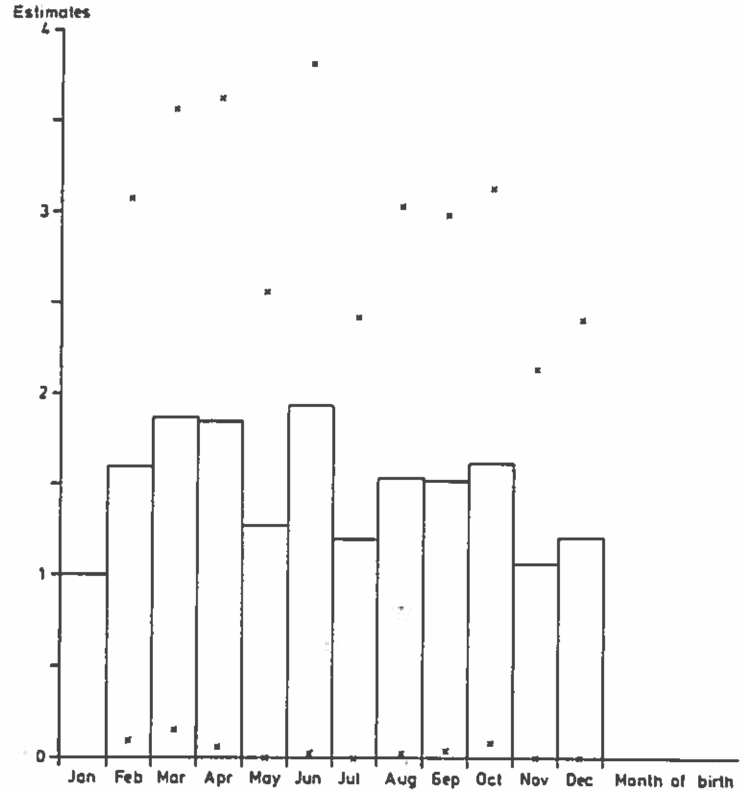

FIGURE 7 *Estimates values of the parameters of the month of birth. Infectious disease. The 95% confidence limits are shown by x.*

You get (3) either by derivation of (2) or by taking the expectation of the sufficient statistics and setting it equal to the sufficient statistics. The last result is due to the fact that the statistical model is an exponential family.[12]

There are too many parameters in the model, eg

$$A_iB_jC_k = A_i\,(100B_j)\ \frac{1}{100}C_k.$$

Therefore B_1 and C_1 have been set equal to 1. The uniqueness of the solution follows from the theory of exponential families.

(3) has to be solved by iteration.* The parameter A_1 resulting from this iteration has been multiplied by 2 to compensate for the shorter mean exposure time for infants who die in the month in which they are born.

Three tests have been performed—H_1, H_2 and H_3.

$H_1 : B_1 = \ldots\ldots = B_{12} = 1$
$H_2 : C_1 = \ldots\ldots = C_{12} = 1$
$H_3 = (H_1 \text{ and } H_2) : B_1 = \ldots\ldots\ldots = B_{12} = C_1 = \ldots\ldots\ldots = C_{12} = 1$

* A program in ALGOL was written to do the iteration.

In all three cases the likelihood-ratio test (Q) has been used. $-2\ln(Q)$ is asymptotically chi-square distributed with df equal to the decrease in the number of free parameters.

For all three tests the $-2\ln(Q)$ can be written as

$$(4)\quad 2\Big(\sum_i X_{i..}\ln(\hat{A}_i/\hat{\hat{A}}_i) + \sum_j X_{.j.}\ln(\hat{B}_j/\hat{\hat{B}}_j) + \sum_k X_{..k}\ln(\hat{C}_k/\hat{\hat{C}}_k)$$

where $\hat{}$ denotes the maximum-likelihood estimates (under the model) and $\hat{\hat{}}$ denotes the maximum-likelihood estimates under the hypothesis.

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