Maternal Age and Temporal Effects on Stillbirth Rates

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Stillbirth rates among single and multiple births show markedly decreasing temporal trends. In addition, several studies have demonstrated that the stillbirth rates are dependent on maternal age, in general, showing a U- or J-shaped association with maternal age. In this study, the temporal trends in and the effect of maternal age on the stillbirth rate were considered simultaneously. Our goal was to split the variation into temporal trends and maternal age effects. We applied two-dimensional analysis of variance because no linear association between maternal age and stillbirth rate can be assumed. The temporal trends of stillbirth rates also were not clearly linear. However, the possibility of applying regression analyses based on linear time trends was also considered. Our study is mainly based on official data from England and Wales for the period between 1927 and 2004. These results were compared with registered birth data from Finland between 1937 and 1997. The best fit was obtained when the models were built for the logarithm of the stillbirth rate. Our interpretation of this result is that an association exists between the effects of the factors and the mean stillbirth rate, and consequently, a multiplicative model was applied. Relatively high stillbirth rates were observed among twin births of young mothers and among all births of older mothers.

Keywords: ANOVA, regression models, single births, twin births

Stillbirth rates (SBRs) among single, twin and higher multiple births show markedly decreasing temporal trends. Eriksson and Fellman (2006) and Fellman and Eriksson (2006) found that the relative decreases in SBRs among single, twin and higher multiple births in Sweden are almost the same.

In addition, earlier studies have shown that SBRs depend on maternal age, showing U- or J-shaped associations. James (1968, 1969) introduced hypotheses concerning the variation in SBR. He considered sibship data and analysed how SBR depended on the birth order. James's hypotheses indicated that for some mothers the tendency for stillbirths decreases and for some it increases with increasing birth order. He also assumed that mothers with a U-shaped disposition for stillbirths may also exist. In birth register studies data on all mothers are pooled and the U-shaped pattern is in good agreement with James's hypotheses. Relatively high SBRs have been observed among twin births of young mothers and among all births of older mothers (Eriksson & Fellman, 2006; Golding, 1990). For additional references, see James (1968).

Material

SBRs here are based on published register data from England and Wales for the periods between 1927 and 2004 for all births and between 1940 and 2003 for twin births. The Office for National Statistics in the UK has also presented data from England and Wales on the web site http://www.statistics.gov.uk/. For 1981, the age-specific numbers of twin maternities are missing (Botting et al., 1987; Eriksson & Fellman, 2007). To avoid biased twinning rates, all data for this year are ignored in calculating the rates. The SBRs among twins according to maternal age in England and Wales are presented in Table 1.

Table 2 presents the SBR among all births according to maternal age in Finland in 1937, 1957, 1977 and 1997. The Finnish data are based on official statistics published by Statistics Finland and on our earlier studies (Eriksson & Fellman, 2006; Fellman & Eriksson, 2006). Both tables also include the overall SBR for the time periods examined.

Methods

ANOVA Models

Consider that two factors, T (time) and A (maternal age), influence a variable Y and that they are partitioned in I and J classes, respectively. Assume that the factors are independent and that the dataset is balanced, that is, there is exactly one observation in each cell. A layout of the dataset is given in Table 3. Because the effects of the the factors do not show strict linearity, we prefer to use two-dimensional analysis of variance (ANOVA) instead of linear regression models. The ANOVA models are based on

Received 4 December, 2007; accepted 2 June, 2008.

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Table 1

Observed Stillbirth Rates (SBRs) Among Twins According to Maternal Age and Time in England and Wales for 1940–2003

Period	Total	Maternal age						$\hat{\beta}_i$
		Under 20	20–24	25–29	30–34	35–39	40 +	
1940, 1950	60.28	91.86	66.68	53.41	58.99	59.02	65.46	27.18
1951–1960	51.10	56.44	52.75	47.67	49.19	55.25	63.79	15.46
1961–1970	39.24	48.05	38.95	36.73	37.42	42.10	54.30	4.20
1971–1980	28.98	36.87	30.18	26.64	26.87	34.15	36.96	–6.78
1982–1990	16.95	26.43	16.46	16.46	15.56	18.22	21.02	–19.70
1996–2003	16.29	26.56	20.20	17.00	13.70	15.95	16.80	–20.36
$\hat{\mu}_j$		8.98	–1.19	–5.74	–5.10	–1.28	4.33	

Note: Parameter estimates $\hat{\beta}_i$ and $\hat{\mu}_j$ according to the ANOVA model for SBR are included. The estimate of the general mean is $\hat{\alpha} = 38.72$. For the SBR regression model the regression coefficient is $\hat{\beta} = -0.944$ per year.

Table 2

Observed Stillbirth Rates (SBRs) Among All Births According to Maternal Age and Time in Finland in 1937, 1957, 1977 and 1997

Year	Total	Maternal Age						$\hat{\beta}_i$
		Under 20	20–24	25–27	30–34	35–39	40 +	
1937	23.63	20.03	18.72	20.01	24.29	28.81	42.29	11.27
1957	17.09	14.11	12.10	15.16	15.42	28.06	37.45	5.97
1977	5.08	4.12	4.48	4.65	5.53	8.55	14.96	–7.37
1997	3.71	4.82	2.72	3.57	3.92	3.41	8.87	–9.87
$\hat{\mu}_j$		–3.65	–4.91	–3.57	–2.13	2.79	11.47	

Note Parameter estimates $\hat{\beta}_i$ and $\hat{\mu}_j$ according to the ANOVA model for SBR are included. The estimate of the general mean is $\hat{\alpha} = 14.42$. For the SBR regression model the regression coefficient is $\hat{\beta} = -0.384$ per year.

grouped data of the factors, and in the general model no linearity is assumed. According to the assumptions of balanced data, independent and additive effects of factors and restrictions

$$\sum_i \beta_i = 0 \text{ and } \sum_j \mu_j = 0$$

we obtain the following formulae for the expected values:

(1a) cell data: $Y_{ij} = \alpha + \beta_i + \mu_j$ $(i = 1,\ldots,I)$, $(j = 1,\ldots,J)$

(1b) row sums: $Y_{i.} = J\alpha + J\beta_i$ $(i = 1,\ldots,I)$

(1c) column sums: $Y_{.j} = I\alpha + I\mu_j$ $(j = 1,\ldots,J)$

(1d) total sum: $Y_{..} = IJ\alpha$.

From these equations, we obtain the estimates

(2b) $\hat{\beta}_i = \frac{1}{J} Y_{i.} - \frac{1}{IJ} Y_{..}$ $(i = 1,\ldots,I)$

(2c) $\hat{\mu}_j = \frac{1}{I} Y_{.j} - \frac{1}{IJ} Y_{..}$ $(j = 1,\ldots,J)$

(2d) $\hat{\alpha} = \frac{1}{IJ} Y_{..}$.

It is easily seen that

$$\sum_i \hat{\beta}_i = 0 \text{ and } \sum_j \hat{\mu}_j = 0,$$

which reduce the number of independent parameters.

If one expects that the effects are multiplicative (that is the effects are relative), one starts from the model

(3) $Y'_{ij} = \alpha' \beta'_i \mu'_j \varepsilon'_{ij}$.

After a logarithm transformation, one obtains the additive model

$$Y_{ij} = ln(Y'_{ij}) = ln(\alpha') + ln(\beta'_i) + ln(\mu'_j) + ln(\varepsilon'_{ij}) = \alpha + \beta_i + \mu_j + \varepsilon_{ij},$$

Table 3

Schematic Layout of the Dataset

$i \backslash j$	1	…	j	…	J	Row sums
1	Y_{11}	…	Y_{1j}	…	Y_{1J}	$Y_{1.}$
i	Y_{i1}	…	Y_{ij}	…	Y_{iJ}	$Y_{i.}$
I	Y_{I1}	…	Y_{Ij}	…	Y_{IJ}	$Y_{I.}$
Column sums	$Y_{.1}$	…	$Y_{.j}$	…	$Y_{.J}$	$Y_{..}$

Note: Formulae are given in the text.

https://doi.org/10.1375/twin.11.5.558 Published online by Cambridge University Press

where

$ln(Y'_{ij}) = Y_{ij}, ln(\alpha') = \alpha, ln(\beta'_i) = \beta_i, ln(\mu'_j) = \mu_j$ and $ln(\varepsilon'_{ij}) = \varepsilon_{ij}$.

Consequently, the methods proposed in Table 3 are also applicable to the logarithm $ln(Y'_{ij}) = Y_{ij}$.

Regression Models

Comparisons with regression models with a linear time trend were also performed. If we introduce the mean time

$$\bar{t} = \frac{1}{I}\sum_i t_i ,$$

then the regression formulae for the variable Y_{ij} in Table 3 are defined as

(4a) cell data: $Y_{ij} = \alpha + \beta(t_i - \bar{t}) + \mu_j$ $(i = 1,\ldots,I), (j = 1,\ldots,J)$

(4b) row sums: $Y_{i.} = J\alpha + J\beta(t_i - \bar{t})$ $(i = 1,\ldots,I)$

(4c) column sums: $Y_{.j} = I\alpha + I\mu_j$ $(j = 1,\ldots,J)$

(4d) total sum: $Y_{..} = IJ\alpha$.

When we compare the regression model with the ANOVA model, the chosen form of the regression model has several advantages. We obtain the estimates

$$\hat{\alpha} = \frac{1}{IJ}Y_{..} \text{ and } \hat{\mu}_j = \frac{1}{I}Y_{.j} - \frac{1}{IJ}Y_{..} \quad (j = 1,\ldots,J),$$

which are identical to the corresponding estimates for the ANOVA parameters and

$$\sum_j \mu_j = 0 .$$

In addition,

$$\sum_i \beta(t_i - \bar{t}) = \beta \sum_i (t_i - \bar{t}) = 0 .$$

This property is comparable with the condition

$$\sum_i \beta_i = 0$$

in the ANOVA model. To obtain the estimate of the regression parameter β, we must use the regression model

$$\hat{\beta}_i = \beta(t_i - \bar{t}),$$

where $\hat{\beta}_i$ is obtained from equation (2b).

Note that equation $\hat{\beta}_i = \beta(t_i - \bar{t})$ has no intercept. Consequently, we obtain

$$(5) \quad \hat{\beta} = \frac{\sum_i \hat{\beta}_i (t_i - \bar{t})}{\sum_i (t_i - \bar{t})^2} .$$

If for $ln(Y'_{ij})$ we use the additive regression model (4a), then the multiplicative model is $Y'_{ij} = \alpha' e^{\beta(t_i - \bar{t})} \mu'_j \varepsilon'_{ij}$. While this model is too complicated for analysis, the regression model of the logarithm is easily handled.

Models for Stillbirth Rates

In this study, the variable Y_{ij} in theory is the SBR or alternatively the ln(SBR), and the factors are time and maternal age. Consider the models

$$(6) \quad SBR_{ij} = \alpha + \beta_i + \mu_j + \varepsilon_{ij}$$

and

$$(7) \quad ln(SBR_{ij}) = \alpha + \beta_i + \mu_j + \varepsilon_{ij}.$$

The intercept α is the total mean, the parameters β_i $(i = 1,\ldots,I)$ are the effects associated with the subperiods and μ_j $(j = 1,\ldots,J)$ are the parameters associated with the maternal age groups. These parameters measure deviations from the total mean.

We consider also a regression model assuming that the monotone temporal trend is linear. One can expect that compared with the ANOVA models the goodness of fit is reduced. We obtain the regression models

$$(8) \quad SBR_{ij} = \alpha + \beta(t_i - \bar{t}) + \mu_j + \varepsilon_{ij}$$

for SBR and

$$(9) \quad ln(SBR_{ij}) = \alpha + \beta(t_i - \bar{t}) + \mu_j + \varepsilon_{ij}$$

for ln(SBR).

Results

Temporal Trends in Stillbirth Rates

Figure 1 presents the SBR and the natural logarithm of the SBR, ln(SBR), among all births (1927–2004) and twin births (1940–2003) in England and Wales. Almost monotonically decreasing trends can be observed. Up to 1940, the decreasing trend is slight. After this, the decreasing trend is accentuated and finally, after 1990, it is again slight. Consequently, the trends are not linear, but the linear correlation coefficients are high. The correlation coefficient between time and SBR among all births is –0.960 and between time and ln(SBR) is –0.977. The corresponding values for twin births are –0.960 and –0.967. Consequently, the correlation coefficients for ln(SBR) are slightly stronger and a more marked linearity is discernible. To emphasize the universality of the decreasing trends in the SBR, we include in Figure 1 the SBR values for all births in Finland in 1937–1997. For Finland, the correlation coefficient between time and SBR is –0.968, being similar to the coefficients for the data in England and Wales.

For England and Wales, the curves rise notably in 1992. These increases are caused by the redefinition of stillbirth. From October 1992, the *Still-Birth Act 1992* redefined stillbirths in England and Wales to also include losses between 24 and 27 weeks of gestation (Fellman & Eriksson, 2006). In 1987, stillbirths were also redefined in Finland. The definition of stillbirth

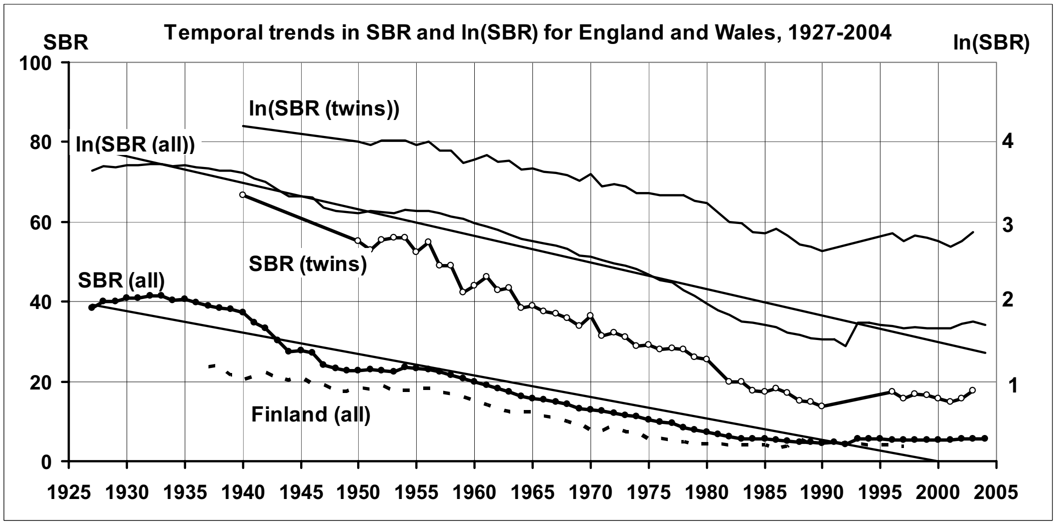

Figure 1

The stillbirth rates (SBRs) and the ln(SBR) for all births in 1927–2004, and twin births in 1940–2003 in England and Wales.

Note: For all births, the correlation coefficient between time and SBR is *–0.960* and between time and ln(SBR) *–0.977*. For twin births, the correlation coefficient between time and SBR is *–0.960* and between time and ln(SBR) *–0.967*. Consequently, for ln(SBR), linearity is more discernible. The increase in 1992 is caused by the redefinition of stillbirth. The dotted line indicates the SBR for all births in Finland (see Table 2). For Finland, the correlation coefficient is *–0.968*.

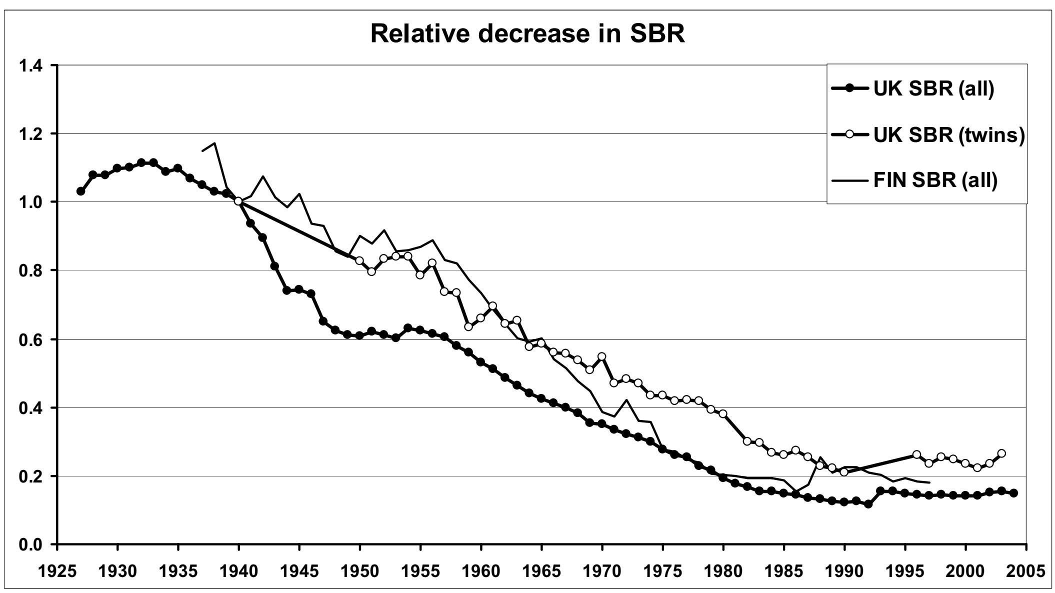

Figure 2

Relative decrease in the stillbirth rates (SBRs) among all births and twin births in England and Wales and among all births in Finland. For all graphs, the index for 1940 is 100. Note the increases for England and Wales in 1992 and for Finland in 1987.

changed from at least 28 weeks of gestation to 22 weeks, thus being slightly different from the new classification in England and Wales. The effect of this change can be observed as a temporary incline of about 1.5 per mille units in the annual level of the SBR in Finland. After this, the decreasing temporal trend in the SBR continued. According to earlier studies (Eriksson & Fellman, 2006; Fellman & Eriksson, 2006), one can expect similar relative decreases for all data sets. This can be seen in Figure 2.

Twins in England and Wales

We group the time period of 1940–2003 into six classes and maternal age is also grouped into six classes (cf. Table 1). In the model, the parameters β_i ($i = 1,...,6$) are the temporal effects associated with the six sub-periods, and μ_j ($j = 1,...,6$) are the parameters associated with the six maternal age groups. We estimate the parameters by using the ANOVA formulae presented in equations (2b), (2c) and (2d). The estimates of the effects are included in Table 1. We obtain

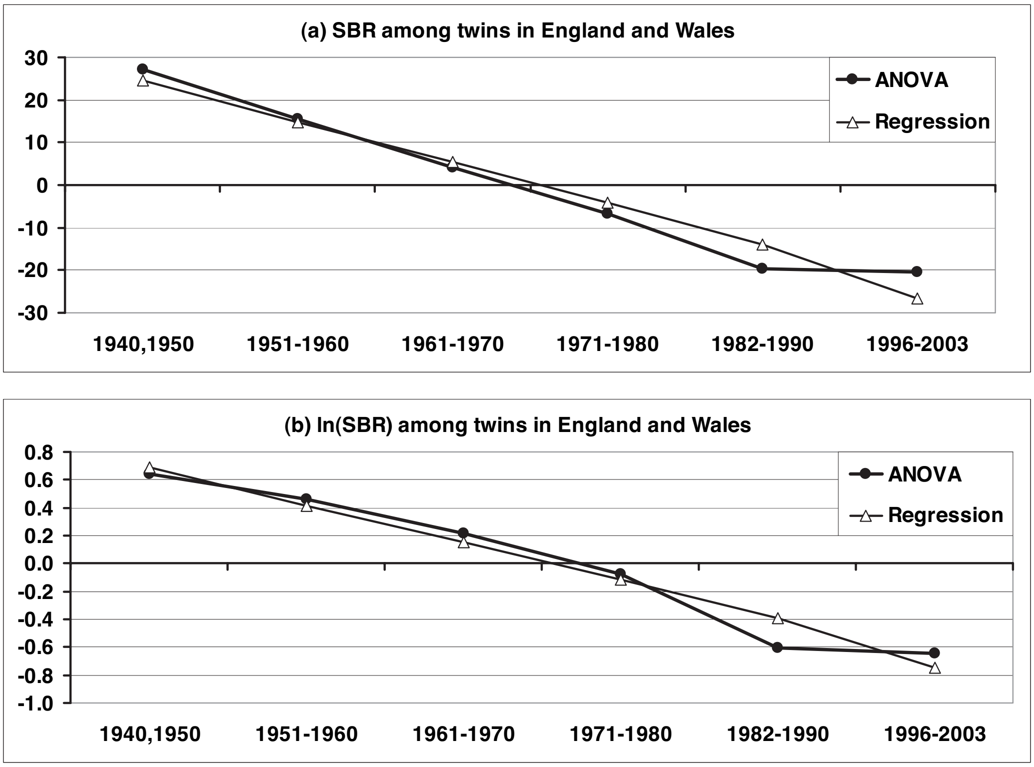

Figure 3

The temporal trends in the stillbirth rates (SBRs) (a) and ln(SBR) (b) for England and Wales in 1940–2003. Trends estimated according to both ANOVA and the regression models are included. The discrepancy in the linearity in ANOVA estimates for 1996–2003 is caused by a redefinition of the SBR in 1992 for England and Wales.

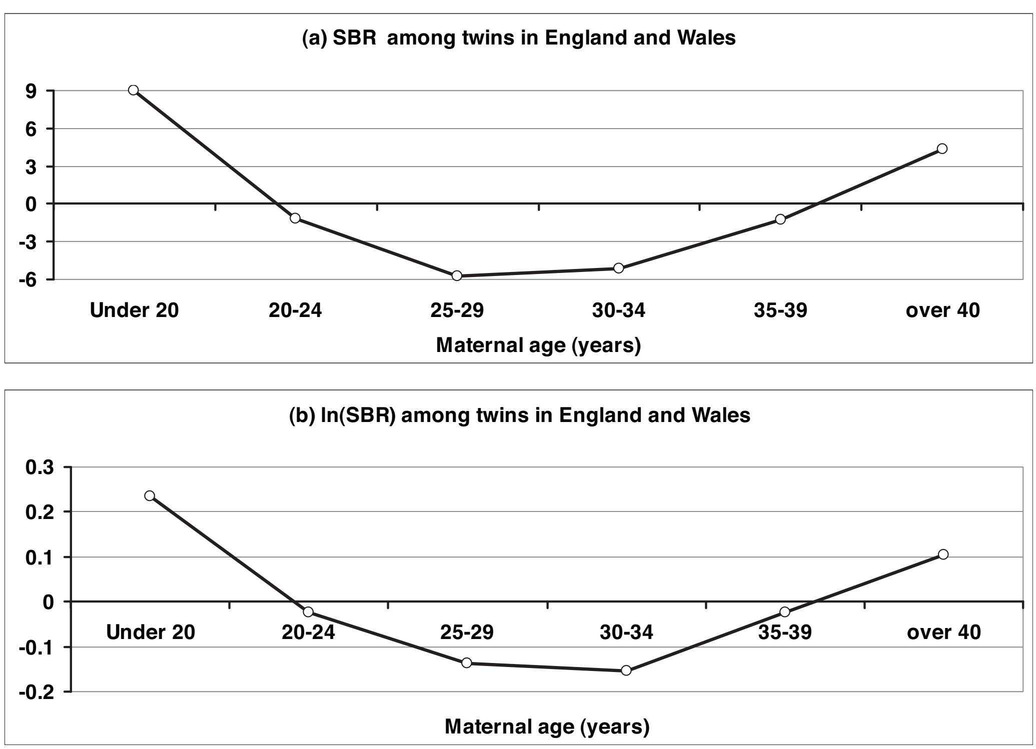

Figure 4

Maternal age effects on the stillbirth rates (SBRs) (a) and ln(SBR) (b) for England and Wales in 1940–2003. ANOVA and regression models give the same estimates for μ_r.

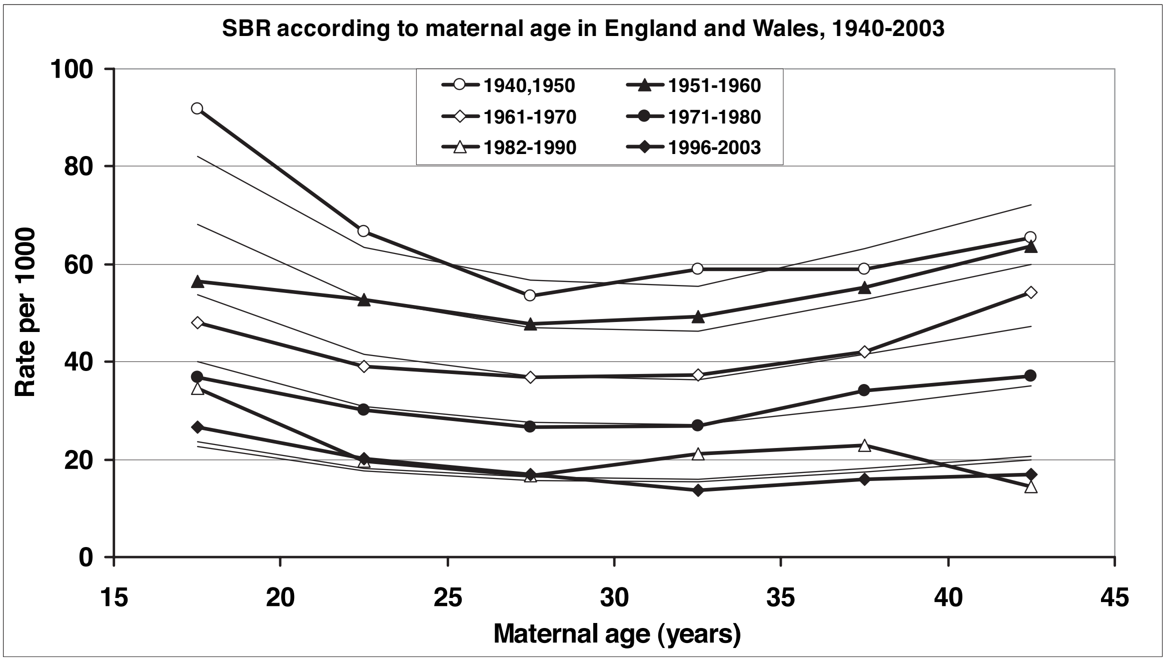

Figure 5

Stillbirth rates (SBRs) according to maternal age among twins in England and Wales for 1940-2003.

Note: The U-shaped pattern is the same for all periods and the temporal decrease in SBR can be noted as downward shifts in the curves. Note the relatively high SBRs for twins in young mothers. Estimated SBRs (antilogarithms) obtained by ANOVA for ln(SBR) are included.

the coefficient of determination $R^2 = 0.948$. To eliminate associations between the effects and the mean level of the SBR, we also consider the ANOVA model for $ln(SBR)_{ij} = \alpha + \beta_i + \mu_j + \varepsilon_{ij}$. Now $R^2 = 0.972$, indicating a slightly better goodness of fit.

For the regression model with a linear time trend, one obtains $R^2 = 0.906$ for SBR, and *0.931* for ln(SBR). Both regression models give a slightly reduced fit, but again the model for ln(SBR) is the better one. For the regression model for SBR, the regression coefficient is $\hat{\beta} = -0.944$ per year. This means that on average the SBR decreases 0.94 per mille units per year. If one applies a simple regression model to the yearly data for SBR among twin births (cf. Figure 1) one obtains the regression coefficient $\bar{\beta} = -0.868$. The discernible deviations from the linearity noted in Figure 1 explain the weaker temporal trend obtained.

The effect of time is presented in Figure 3 and that of the maternal age in Figure 4. Figure 3 also includes the estimation of the temporal trend obtained by both ANOVA and the regression model. Because the estimates of μ_js are the same for both ANOVA and the regression model, only one set of estimates is presented in Figure 4. The statistical analyses indicate that the best fit is obtained for the ANOVA model for ln(SBR). Consequently, this ANOVA model is chosen, but description of the results needs variable transformations. In Figure 5, we compare the observed and the estimated SBRs. In this figure, the estimated SBRs are the antilogarithms of the estimated ln(SBR)s because the ANOVA model for ln(SBR) gave the best fit.

Births in Finland

We consider four time classes (1937, 1957, 1977 and 1997) and maternal age is grouped into six classes (cf. Table 2). When we apply the ANOVA model to the Finnish SBR data, we obtain the coefficient of determination $R^2 = 0.915$. The parameter estimates are presented in Table 2. However, at least the maternal age effect is associated with the level of SBR (cf. Figure 8). Therefore, we also considered the ANOVA model for ln(SBR). This model shows a markedly better fit, with $R^2 = 0.970$. For the Finnish data, the regression models also give a slightly reduced fit. For SBR, the coefficient of determination is $R^2 = 0.875$ and for ln(SBR) $R^2 = 0.928$. For the regression model for SBR, the regression coefficient $\hat{\beta} = -0.384$ per year. Consequently, on average the SBR decreases by 0.38 per mille units per year. However, according to Table 2, the strength in the decrease shows variations. From 1937 to 1957, the decrease is 6.54 per mille units (0.33 per year), from 1957 to 1977 the decrease achieves a maximum of 12.01 per mille units (0.60 per year) and from 1977 to 1997 the decrease is only 1.37 per mille units (0.07 per year). The very low decrease during the last sub-period is caused by the 1987 redefinition of stillbirth. This is also seen in Figures 1 and 5. If one applies a simple regression model to the yearly data for SBR (cf. Figure 1) the regression coefficient is $\bar{\beta} = -0.375$. Good agreement exists between the regression coefficients obtained by the two methods.

The decreasing temporal trend of the SBR is presented in Figure 6. The trend estimated by the

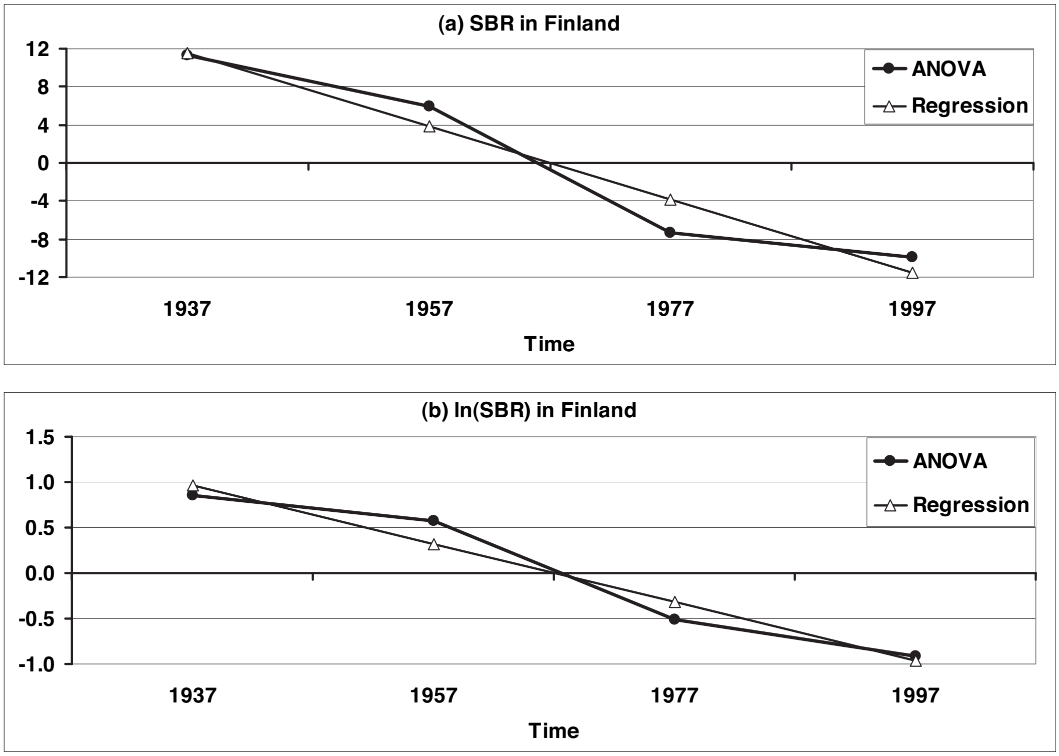

Figure 6

Temporal trends in the SBRs (a) and ln(SBR) (b) for Finland in 1937, 1957, 1977 and 1997. Trends estimated according to both ANOVA and regression models are included.

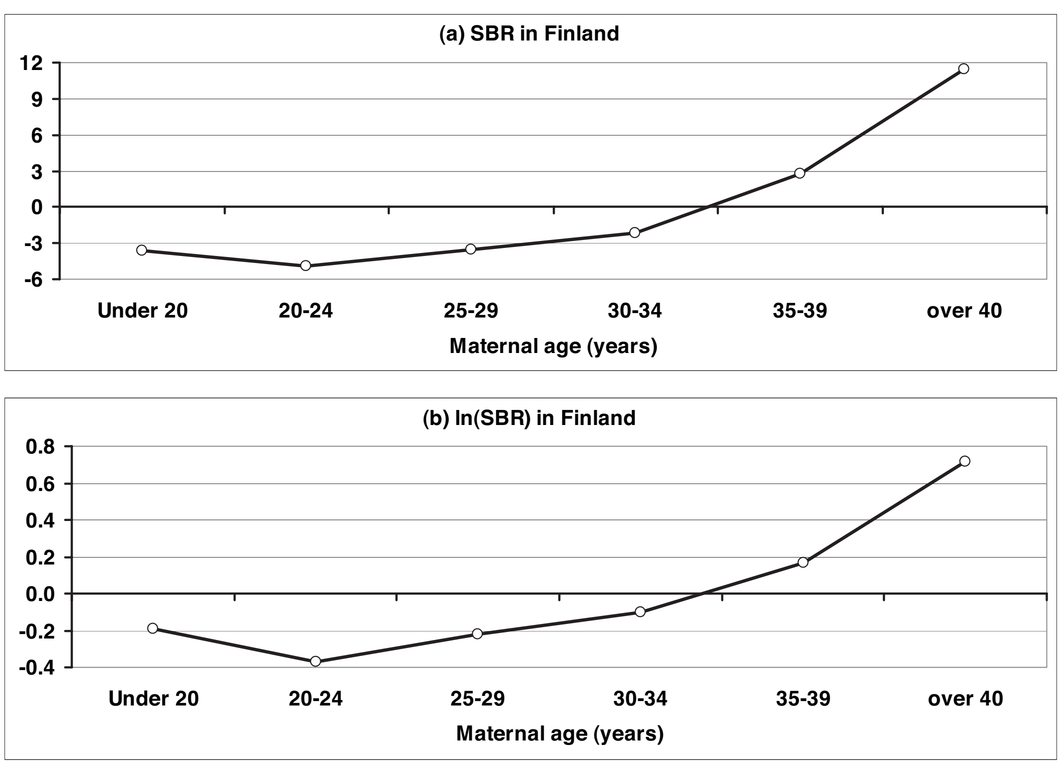

Figure 7

Maternal age effects on the SBRs (a) and ln(SBR) (b) for Finland in 1937–1997. Both ANOVA and regression models give the same estimates for the maternal age effects (μ_j). Note the high levels of SBR for offspring of older mothers.

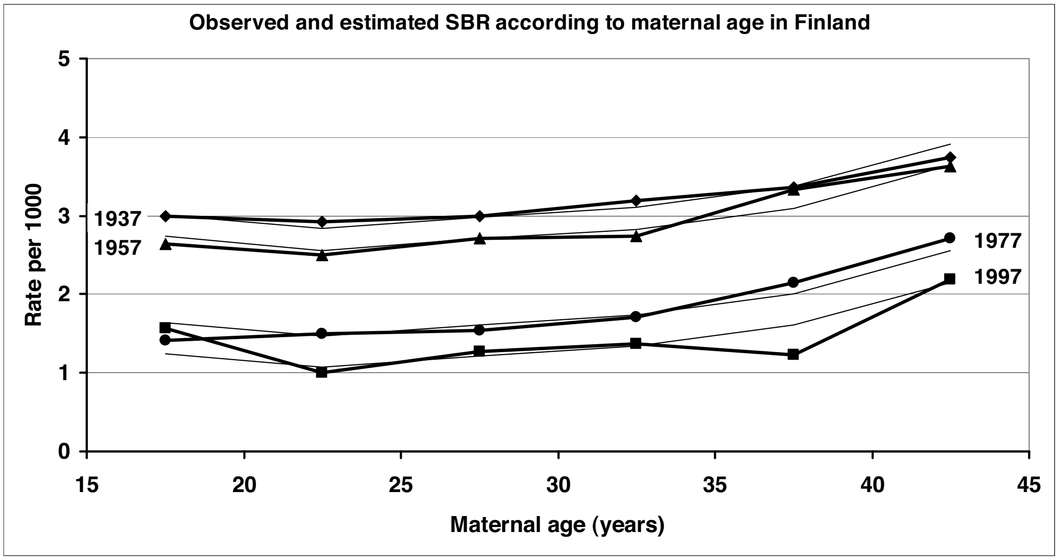

Figure 8

SBR according to maternal age among all births in Finland in 1937, 1957, 1977 and 1997.

Note: The high SBR for births of older mothers yields a J-shaped pattern for all times. The strong temporal decrease in the overall SBR can be identified as a downward shift in the curves. Note that during 1957–1977 the strongest improvement occurs in SBR. This is also seen in Figures 1 and 5. Estimated SBRs (antilogarithms) of the values estimated for ln(SBR) are included.

regression models is also shown in this figure. The maternal age effects on the SBR are displayed in Figure 7. As before, the estimated μ_js are the same for both the ANOVA and the regression models.

In Figure 8, we present the observed and estimated SBRs with respect to maternal age. The estimated levels are the antilogarithms of the ln(SBR) values obtained by the ANOVA model for ln(SBR). Note that the temporally decreasing SBR levels are observable as a downward shift in the curves and that the shift from 1957 to 1977 is the most marked.

Discussion

In conformity with earlier studies, we found that SBRs depend on maternal age, showing U- or J-shaped associations. James (1968, 1969) analysed sibship data and noted strong evidence that stillbirths more often occur at either end of sibships than in the middle. This result could be explained by following hypotheses: (a) within individual sibships, the risks are higher in earlier and in later birth ranks than in middle ones and (b) the probability of stillbirth in some sibships is a function that curves upward with birth rank (type 1) and other sibships is a function that curves downward with birth rank (type 2). James's approach indicated that birth order is a more convenient factor than maternal age. Because the correlation between maternal age and birth order is very strong, James's findings can easily be applied in our study. In birth register studies data on all mothers are pooled and the U-shaped pattern can be obtained when both hypotheses hold. Consequently, James's hypotheses are in good agreement with our findings. However, so far we have not noted any satisfactory explanation why both young and old mothers are prone to an increased number of stillbirths. Neither any suggestion has been given if there are specific factors for young mothers and specific factors for old mothers or if it is the same factors for both maternal age groups. Therefore, the question remains of why mothers of twins more commonly belong to type 2 and mothers of single births to type 1. This must, however, be the case for James's hypotheses to hold, because relatively high SBRs have been observed among twin births of young mothers and among all births of older mothers.

Acknowledgements

This work was supported by grants from the Finnish Society of Sciences and Letters and the 'Liv och Hälsa' Foundation. We are very grateful to Dr Kari Degerstedt, Statistics Finland, for providing information, definitions and data concerning stillbirths in Finland, and to an anonymous referee for calling our attention to additional relevant references.

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