Estimation of the Stillbirth Rate in Twin Pairs According to Zygosity

Johan Fellman and Aldur W. Eriksson

Folkhälsan Institute of Genetics, Population Genetics Unit, Helsinki, Finland

It is common opinion that the stillbirth rate is higher among monozygotic (MZ) than among dizygotic (DZ) twins. This is supported by the fact that stillbirth rates are higher among same-sexed than among opposite-sexed twins, and the relatively high stillbirth rates among twins of young mothers. In this study we present a method to estimate the stillbirth rates for MZ and DZ twins and identify the difference. We performed analyses based on the assumptions of (a) Weinberg's differential rule, including the assumption that the secondary sex ratio is 100, (b) the stillbirth rates among opposite-sexed twins hold for all DZ twins, and (c) the stillbirth rates estimated for MZ and DZ male and female twins yield for both sexes the observed total number of stillborn twins. Our methods are applied to data from Sweden, 1869–1967, the Åland Islands, 1750–1949, Saxony, 1881–1900, and England and Wales, 1996–2003. We observed that the ratio between the estimated stillbirth rates among MZ and DZ twins were on average 1.75, and the ratio among same-sexed and DZ (opposite-sexed) twins were on average 1.31. For Sweden and Saxony similar values were obtained, but for England and Wales the values were higher and for Åland lower. With exception of Åland, the estimated stillbirth rates were in all populations the lowest for DZ, medium for same-sexed and highest for MZ twins.

It is commonly accepted that the stillbirth rate (SBR) is higher among monozygotic (MZ) than among dizygotic (DZ) twins (Derom & Derom, 2005; Fellman & Eriksson, 2006b; Lommatzsch, 1902; Machin, 2001; Wedervang, 1924, and for review see Campbell & MacGillivray, 1988). This is supported by the fact that SBRs are higher among same-sexed (SS) than among opposite-sexed (OS) twins or higher multiple births. The relatively high SBRs among twins born to young mothers also support this assumption. In this study we present a method to estimate SBRs for MZ and DZ twins and identify the differences. In a recent paper, Fellman and Eriksson (2006b) analyze the effect of the dependence between outcomes in multiple maternities. As a preliminary result we can state that zygosity as such cannot wholly explain that dependence.

In general, twinning maternities are divided into DZs and MZs. Furthermore, MZs can be divided into subclasses based on the chorionicity of the twins (Machin, 2001). However, our studies are based on national birth registers and, therefore, a more detailed classification than DZ and MZ obtained by Weinberg's differential rule (WDR) cannot be considered.

Boklage (1985, 1987) analyzed the SBR among MZ and DZ twins. Inter alia he used WDR and considered the fact that the sex ratio may differ from 100. He also applied other methods and noted discrepancies between his results.

The literature on the validity of the WDR is controversial (Boklage, 1985, 1987, 2005; James, 1979, 1992). In the largest prospective population-based study to date, Vlietinck et al. (1988) investigated a consecutive series of 2589 twin pairs, of whom 99.5 per cent were of known zygosity and placentation. The estimates according to WDR agreed well with the results of direct zygosity determination. Consequently, WDR has been cause for debate, and results in favor of and against the rule have been documented. The rule cannot be considered as an exact one, but it must be accepted as a rule of thumb. Furthermore, until a convincing solution to this problem has been documented, analyses should continue.

Material

Our methods are applied to data summarized in Table 1.

Our Swedish series starts with birth data published by Berg (1880), who gave exact observed numbers of multiple maternities including information on the sex combination of the multiples, and the combination of live- and stillbirths (condition at birth). Statistics Sweden published similar information for the period 1901–1967. Swedish data were also considered by Fellman and Eriksson (2006a, 2006b, 2006c) and Eriksson and Fellman (2006).

Received 27 February, 2006; accepted 22 November, 2006.

Address for correspondence: Johan Fellman, Folkhälsan Institute of Genetics, Population Genetics Unit, POB 211, FIN-00251 Helsinki, Finland. E-mail: johan.fellman@shh.fi

Table 1

Summary of Data Sets

Population	Period	n^1	Compiled by
Sweden	1869–1878	19295	Berg (1880)
Sweden	1901–1967	102692	Eriksson & Fellman this study
Saxony	1880–1900	35243	Lommatzsch (1902)
England and Wales	1996–2003	69638	Eriksson & Fellman this study
Åland	1750–1949	1752	Eriksson (1973)

Note: The Swedish data sets, both that published by Berg (1880) and that compiled by us, are considered as one series. The Åland data are compiled from original church records. All other data sets are compiled from published official data.

[1] Number of twin pairs

Fellman and Eriksson (2006a) considered temporal variations in the SBR among singletons, twins and triplets. In that study we were only interested in the time trends and not in the effect of influential factors. Therefore, we could consider the whole period 1869–2001. Eriksson and Fellman (2006) also included influential factors, such as marital status, rural and urban regions and sex combination of the multiple births. The analyses were based on Swedish data for the period 1869–1967. Fellman and Eriksson (2006b) studied how reliable WDR is.

Lommatzsch (1902) analyzed in detail data from Saxony, 1881–1900. In particular, he presented multiple birth data containing information about the sex combination and the condition at birth.

Eriksson (1973) presented twin data from Åland, 1653–1949. In this study we include his data from the period 1750–1949. The sex combination of the twin pairs is crucial and consequently, in our opinion, the data before 1750 contain too many cases with unknown sex and information about the condition at birth. The registered number of twin pairs also indicates that the series before 1750 may contain missing data. In fact, Eriksson (1973) stressed that there were no precise regulations for registering stillbirths until 1749, which means that the stillbirth rate for 1653–1749 cannot be considered sufficiently reliable.

We include in this study also data from England and Wales (1996–2003) compiled by us from the website http://www.statistics.gov.uk/

Methods

The basic assumptions in our method are

(a) WDR, including the assumption that the sex ratio is 100

(b) SBRs estimated for OS twins hold for all DZ twins and

(c) SBRs estimated for MZ and DZ male and female twins should yield for both sexes the observed total number of stillborn twins.

If condition (b) is dropped, the information in the data is not sufficient to estimate the unknown parameters. In addition, our method presupposes that among both SS and OS twin pairs, our data allow us to estimate the SBRs for both males and females.

Our model is based on the following information and notations:

Table 2

Estimated Stillbirth Probabilities for Sweden

Period	p_{mm}	q_{ff}	$p_{DZ} = p_{mf}$	$q_{DZ} = q_{mf}$	p_{MZ}	q_{MZ}	Singletons
1869–78	.1132	.0912	.0853	.0739	.1511	.1192	.0295
1901–10	.1021	.0821	.0642	.0585	.1541	.1220	.0231
1911–20	.0985	.0770	.0670	.0592	.1420	.1080	.0222
1921–30	.0886	.0794	.0681	.0589	.1171	.1138	.0237
1931–40	.0919	.0815	.0679	.0633	.1246	.1088	.0261
1941–50	.0686	.0600	.0542	.0446	.0860	.0814	.0208
1951–60	.0521	.0419	.0319	.0317	.0752	.0571	.0160
1961–67	.0380	.0390	.0276	.0240	.0485	.0558	.0106
All	.0868	.0726	.0624	.0552	.1186	.0995	.0220
Relative decrease (%)	66	57	68	68	68	53	64

Note: The notations of the stillbirth rates are defined in the section Methods and the total number of twin pairs are given in Table 3. When the probabilities are multiplied by 1000 one gets the SBRs per 1000 total births. In the last column we include as a comparison the SBRs among singletons given as probabilities (Fellman & Eriksson, 2006a). The relative decreases in the SBRs from 1869–1878 to 1961–1967 vary between 53 and 68%, being almost similar and comparable with the relative decrease among singletons (64%).

Let n_{mm} be the number of male–male twin pairs, n_{ff} the number of female–female twin pairs and n_{mf} the number of male-female twin pairs. Consequently, $n_{ss} = n_{mm} + n_{ff}$ is the number of SS and $n_{os} = n_{mf}$ is the number of OS twin pairs. In order to include in our general model the assumption that the SBR is different for males and females we assume that both n_{mm} and n_{ff} are known. If not, sex differences cannot be identified and one has to simplify the calculations and assume that there are no sex differences in the SBR.

We introduce the following parameters:

p_{mm} is the SBR for males in male–male twin pairs,

q_{ff} is the SBR for females in female–female twin pairs,

p_{mf} is the SBR for males in male–female twin pairs, and

q_{mf} is the SBR for females in male–female twin pairs.

These parameters can be calculated as the relative frequencies in the data set. Our unknown parameters are

p_{MZ}, being the SBR for males in MZ twin pairs,

q_{MZ}, being the SBR for females in MZ twin pairs,

p_{DZ}, being the SBR for males in DZ twin pairs, and

q_{DZ}, being the SBR for females in DZ twin pairs.

All parameters, although interpreted as SBRs, are considered as probabilities. If the probabilities are multiplied by 1000 one obtains the SBRs per 1000.

Based on the initial notations above, the total number of stillborn males is $2n_{mm}p_{mm} + n_{mm}p_{mf}$ and the total number of stillborn females is $2n_{ff}q_{ff} + n_{mf}q_{mf}$. Following WDR, we obtain $n_{MZ} = n_{mm} + n_{ff} - n_{mf}$ and $n_{DZ} = 2n_{mf}$. Assuming that the sex ratio is 100, the number of males in the MZ pairs is $n_{mm} - 1/2n_{mf}$ and the number of females is $n_{ff} - 1/2n_{mf}$. Consequently, if we use the unknown parameters p_{MZ}, q_{MZ}, p_{DZ} and q_{DZ}, the total number of stillborn males is $(2n_{mm} - n_{mf})p_{MZ} + 2n_{mf}p_{DZ}$ and the total number of stillborn females is $(2n_{ff} - n_{mf})q_{MZ} + 2n_{mf}q_{DZ}$. Combining all these formulae we obtain

$2n_{mm}p_{mm} + n_{mf}p_{mf} = (2n_{mm} - n_{mf})p_{MZ} + 2n_{mf}p_{DZ}$ for stillborn males and

$2n_{ff}q_{ff} + n_{mf}q_{mf} = (2n_{ff} - n_{mf})q_{MZ} + 2n_{mf}q_{DZ}$ for stillborn females.

If we use the assumptions that $\hat{p}_{DZ} = p_{mf}$ and $\hat{q}_{DZ} = q_{mf}$, we obtain

$$\hat{p}_{MZ} = \frac{2n_{mm}p_{mm} - n_{mf}p_{mf}}{2n_{mm} - n_{mf}} \quad \text{and} \qquad [1]$$

$$\hat{q}_{MZ} = \frac{2n_{ff}q_{ff} - n_{mf}q_{mf}}{2n_{ff} - n_{mf}} \qquad [2]$$

In general, $p_{mm} > p_{mf}$ and $q_{ff} > q_{mf}$, and consequently, $p_{MZ} > p_{mm} > p_{DZ}$ and $q_{MZ} > q_{mm} > q_{DZ}$. We can give formulae [1] and [2] different interpretations. Formulae [1] and [2] can be rewritten as

$$p_{mm} = \frac{(2n_{mm} - n_{mf})}{2n_{mm}} p_{MZ} + \frac{n_{mf}}{2n_{mm}} p_{DZ} \quad \text{and}$$

$$q_{ff} = \frac{(2n_{ff} - n_{mf})}{2n_{ff}} q_{MZ} + \frac{n_{mf}}{2n_{ff}} q_{DZ}$$

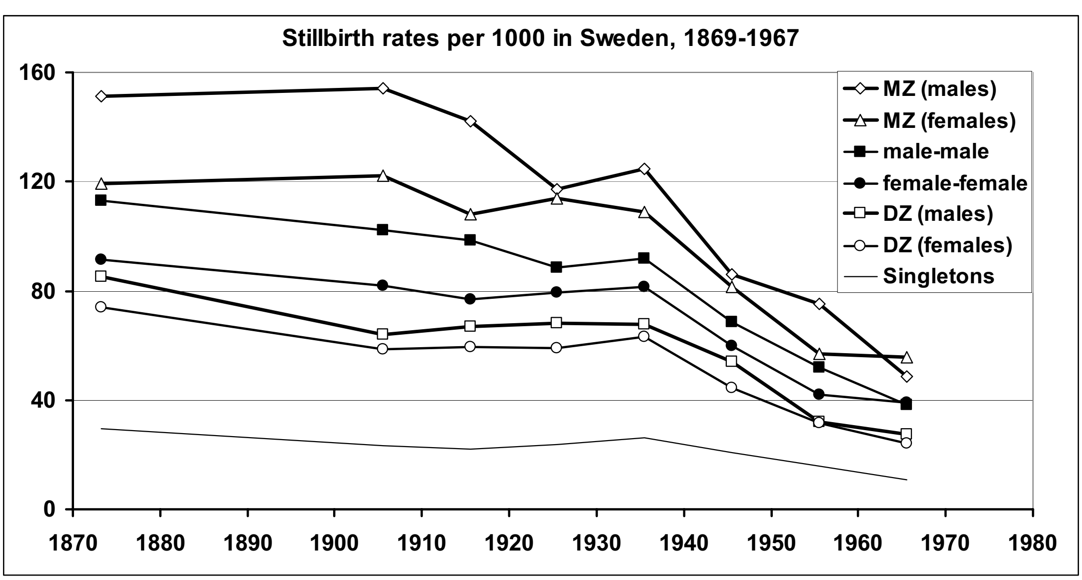

Figure 1

Estimated stillbirth rates per 1000 in Sweden.

Note: The decreasing trends for the SBRs among singletons, same-sexed and opposite-sexed twins have already been noted in Fellman and Eriksson (2006a) and Eriksson and Fellman (2006). Now, a similar decreasing trend for the SBR among MZ twins is observed.

Table 3

Ratios Between the Stillbirth Rates among Same-Sexed and DZ (Opposite-Sexed) Twins and Between the Stillbirth Rates Among MZ and DZ (Opposite-Sexed) Twins in Sweden

Period	n^1	p_{mm}/p_{DZ}	q_{ff}/q_{DZ}	p_{MZ}/p_{DZ}	q_{MZ}/q_{DZ}
1869–78	19,295	1.327	1.234	1.771	1.612
1901–10	20,508	1.590	1.403	2.401	2.087
1911–20	18,735	1.470	1.299	2.120	1.823
1921–30	15,564	1.300	1.348	1.718	1.932
1931–40	12,379	1.354	1.288	1.835	1.718
1941–50	15,561	1.266	1.347	1.587	1.827
1951–60	11,830	1.632	1.324	2.355	1.801
1961–67	8,115	1.378	1.629	1.758	2.329
All	121,987	1.392	1.314	1.902	1.800

Note: [1]Total number of twin pairs

This means that the SBRs for the SS twins are weighted means of the SBRs for the MZ and DZ twins. The weights, which add to one, are proportional to the number of MZ and DZ twins, males and females, respectively.

Results

When these methods were applied to the Swedish data we obtain the results in Table 2 and Figure 1. For comparison we have included the SBRs among singletons (Fellman & Eriksson, 2006a). The decreasing trends for SBRs among same-sexed and opposite-sexed twins have already been noted in Fellman and Eriksson (2006a) and Eriksson and Fellman (2006). Now, however, a similar decreasing trend for the estimated SBR among MZ twins is obtained. The relative decrease varies between 53 and 68%, which can be compared with 64% among singletons. The rather constant relative decreases noted in Fellman and Eriksson (2006b) and Eriksson and Fellman (2006) seem to hold also for MZ twins.

In Table 3 and Figure 2 we present for Sweden the ratio between the SBRs among MZ and DZ twins and the ratio between the SBRs among SS and DZ twins. The ratios for the total data set are 1.90 for MZ males, 1.80 for MZ females, 1.39 for male–male and 1.31 for female–female twins.

We present in Tables 4 and 5 the corresponding results for the data from Åland, from Saxony and from England and Wales. We obtained varying results. Especially for Åland the ratios are low, but for England and Wales, they are high. One observes that for Åland the general formulae $p_{MZ} > p_{mm} > p_{DZ}$ and $q_{MZ} > q_{mm} > q_{DZ}$ do not hold, resulting in the low ratio values in Table 5.

In order to summarize our results concerning the ratios between SBRs for MZ, SS and DZ twins we combined all the data. Based on the total data set we applied the simple regression model $p_{MZ} = \beta_{MZ} p_{os} + \varepsilon$ for MZ twins and $p_{ss} = \beta_{ss} p_{os} + \varepsilon$ for SS twins. We estimate the coefficients by ordinary least squares and include no intercept in our models. We obtain β_{MZ} = 1.75 with *SE* = 0.092 and β_{ss} = 1.31 with SE = 0.037. We consider these estimates as common estimates for all data. There are good agreements between these average values and the values obtained for Sweden and Saxony. England and Wales show higher values and Åland shows lower.

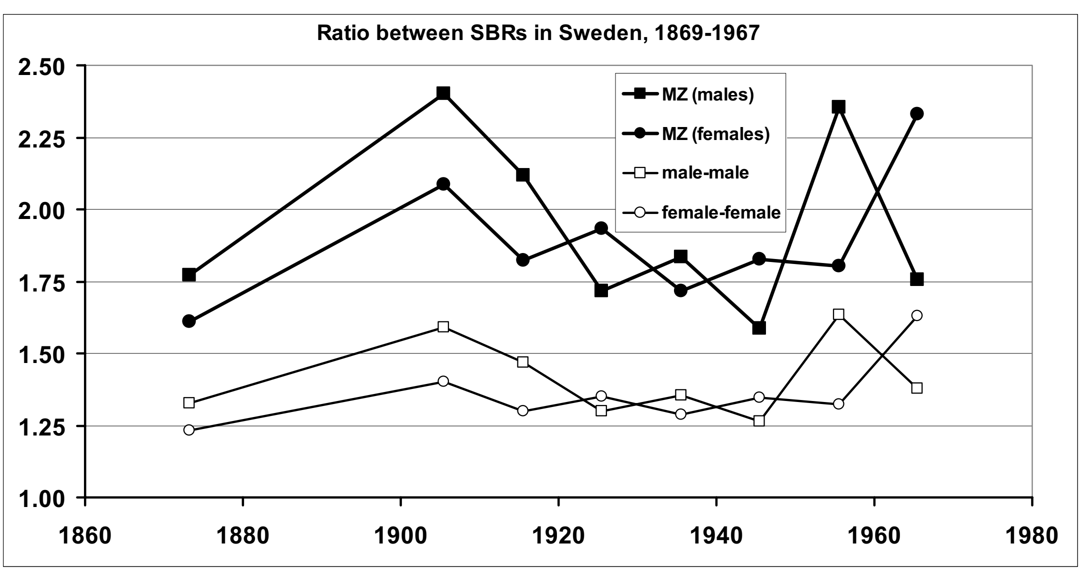

Figure 2

The ratios between the stillbirth rates for MZ and DZ (opposite-sex) twin pairs and between the stillbirth rates for same-sexed and DZ (opposite-sexed) twin pairs in Sweden.

Note: The ratios for the total data set are 1.90 for MZ males, 1.80 for MZ females, 1.39 for male–male and 1.31 for female–female twins.

Table 4

Estimated Stillbirth Probabilities for Åland, Saxony and England and Wales

Population	p_{mm}	q_{ff}	$p_{DZ} = p_{mf}$	$q_{DZ} = q_{mf}$	p_{MZ}	q_{MZ}
Åland	.0625	.0595	.0706	.0583	.0448	.0633
Saxony	.0831	.0700	.0595	.0516	.1175	.1014
England and Wales	.0208	.0181	.0117	.0086	.0301	.0281

Note: The notations of the stillbirth rates are defined in the Method section. When the probabilities are multiplied by 1000 one gets the SBRs per 1000 births. The origins of the data sets and the total number of twin pairs are given in Table 1. For Åland the general formulae $p_{MZ} > p_{mm} > p_{DZ}$ and $q_{MZ} > q_{mm} > q_{DZ}$ do not hold. These findings are discussed in the text.

Discussion

Male twins are at greater risk than females twins (Barr & Stevenson, 1961; Spurway, 1962; Potter, 1963). Butler and Alberman (1969) found that in SS twin males nearly one in ten pregnancies ended in the death of both babies in contrast to SS female pairs, where the death of both babies was less common than in any other group.

The results for Åland presented above deviate from the results in other populations, but Eriksson (1973) has stated that the SBR among male–male twin pairs was 62.5, among female–female 59.4 and among males–females 64.5 per 1000, indicating that the observed SBR among OS twins is somewhat higher than among SS twins. However, in comparison with the other data sets, the Åland series is small (cf. Table 5).

Boklage (1985) found that the mortality of SS DZs resembles that of MZs much more than that of OS DZs, and that OS twins enjoy a relative protection from stillbirths and neonatal deaths. Boklage (1987) analyzed the SBR among MZ and DZ twins, using WDR, but he assumed that the sex ratio may differ from 100. In fact, this improvement did not have discernible effects, because his data set was too small. He also assumed, as we did, that the SBR among SS DZ twins is the same as among OS DZ twins. He obtained a ratio of 2.29 between the SBR among MZ and DZ, which is higher than our finding (1.75). According to his data the ratio between SS and OS stillbirths is 1.80. This value is also rather high compared to ours (1.31). Boklage also applied alternative methods and obtained discrepancies between the results. Our impression is that these discrepancies may arise from his small data series. The total number of twin pairs was only 616. He concluded that fetal mortality (SBR) and neonatal mortality do not differ greatly with zygosity overall, but that same-sexed DZ mortality is much higher than that of OS twins and probably even higher than that of MZ twins. Furthermore, Boklage believed that MZ and DZ twinning share some of their causes.

Neefe (1877, p. 183) already observed that twin maternities with only males had the highest SBR while those with only females had the lowest SBR. Wedervang (1924) noted that the probability of both twins being stillborn was markedly higher among SS than among OS twins. He associated this difference with zygosity, noting that all OS twin pairs are DZ and all MZ are SS. Later similar results have been reported in the literature. There is a higher liability to stillbirth in males, particularly in male-male pairs, than in females, a liability difference also noted by Lowe and Record (1951). Males have a better chance of survival if the co-twin is a female rather than a male (Potter, 1963) and the lowest death rates in females occurred in those of OS pairs (Barr & Stevenson, 1961). These OS pairs have a better chance of survival than SS pairs (Potter, 1963, Klein, 1964 and Dunn, 1965). Salihu et al. (2004) stated that siblings within a plurality set are generally subjected to similar prevailing conditions in the womb and are equally affected by the same attributes that characterize the mother. It is logical to expect conditions leading to the stillbirth of a plurality set member to have affected the other siblings as well, although unexplained factors determining vulnerability may vary. In short, one has to consider both the intra-cluster variation, the variation between individual twins or triplets, and the inter-cluster variation, the variation between mothers (see also Fellman & Eriksson, 2006b).

Derom and Derom (2005) have observed that MZ monochorionic infants were at a considerably higher risk of stillbirth than DZ infants, whereas MZ dichorionic infants had the same risk as DZ infants. This suggests that stillbirth is much more a matter of chorionicity than zygosity, which is in agreement with the findings of other investigators (Machin, 2001).

Table 5

Ratios Between the Stillbirth Rates Among Same-Sexed and DZ (Opposite-Sexed) Twins and Between MZ and DZ (Opposite-Sexed) Twins

Population	pmm/pDZ	qff/qDZ	pMZ/pDZ	qMZ/qDZ
Åland	0.886	1.020	0.635	1.076
Saxony	1.395	1.357	1.973	1.964
England and Wales	1.781	2.113	2.578	3.287

Note: The populations are the same as in Table 4. Note the low values for Åland and high values for England and Wales. For discussions, see the text.

Acknowledgments

This work was supported by grants from The Finnish Society of Sciences and Letters. We also thank two anonymous referees for valuable comments and suggestions, but any remaining weaknesses are on our responsibility.

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