



The Monozygotic Twinning Rate: Is It Really Constant?

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Abstract. Weinberg's difference method, applied to twin birth statistics, usually shows a dependence of the MZ rate on maternal age, like a thin shadow of the DZ rate. Some of this MZ variation could be explained away by James' finding of more same-sex (SS) than opposite-sex (OS) DZ twins, the excess being mistakenly classified as MZ by Weinberg's assumption of equal numbers. By several methods one can extract a constant value for the MZ rate and a constant or nearly constant value for the DZ SS/OS ratio, but these "constants" are actually arbitrary and they vary between populations.

Key words: MZ twinning rate, Weinberg's rule

INTRODUCTION

Twin birth statistics analyzed under the Weinberg assumption of equal numbers of same-sex and opposite-sex pairs among dizygotics generally support the view that variation in twinning rates can be largely attributed to the dizygotic (DZ) component, while the monozygotic (MZ) component is relatively constant. This is most often illustrated in the contrasting effects of maternal age on the two types of twinning, but the contrast is found also for other variables, such as birth order and race.

The best U.S. data are for 1964 [4], based on 30,446 pairs of liveborn white twins and 7,798 pairs of liveborn black twins. In that year the total twinning rates for white and black races were 9.1 and 13.0 per thousand livebirths, but the MZ rates estimated by Weinberg's difference were both 3.6. The effects of maternal age are illustrated in Fig. 1 with white births for the same year. Here the MZ rate does not appear to be constant.

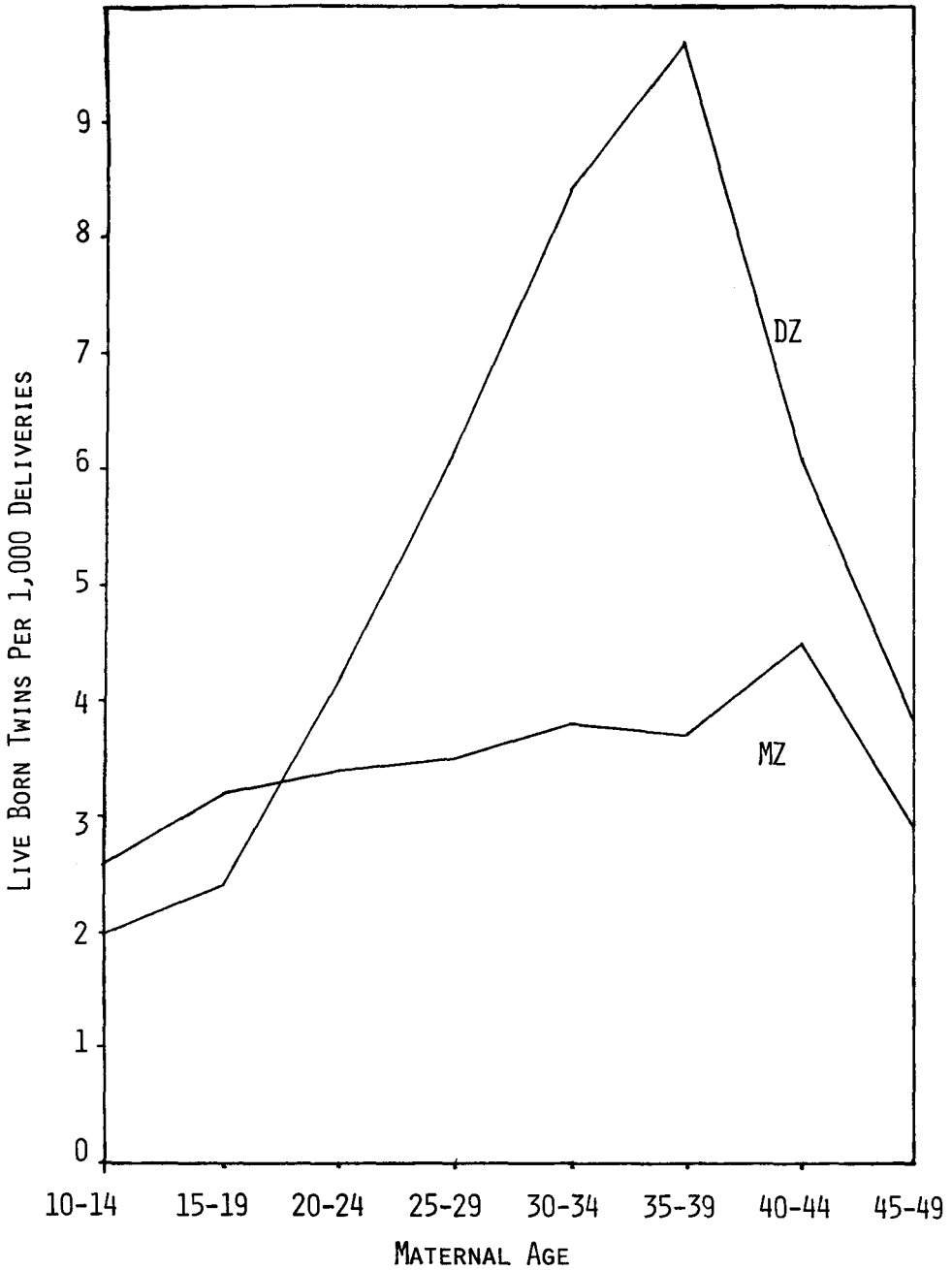


Fig. 1. Population frequencies of dizygotic and monozygotic twinning in six maternal age groups, as inferred by use of Weinberg's difference method. U.S. white mothers, 1964 [4].

Both types of twinning increase over most of the range of maternal ages and decline at the end. The age-changes in MZ twinning are relatively small, but the difference between white mothers under and over 30 is statistically highly significant; from Bulmer's [3] formula for the standard error, $t = 3.4$, $p < 0.01$. Except for an incongruity in the 40-44 maternal ages, one could obtain a flat curve for MZ twinning, ie, a constant MZ rate over all maternal ages, by including a correction factor in Weinberg's difference [1,6]. This is in fact supported by independent evidence [2,5] for an excess of same-sex (SS) pairs among DZ twins. If that excess is real, the usual Weinberg difference method would classify the extra SS pairs erroneously as MZ.

Twin statisticians have depended so long on Weinberg's rule that they are reluctant to abandon it, but if the MZ twinning rate were constant, the rule would not be needed. Moreover, it should be easy to find the constant value of MZ twinning if there is one. In this report we explore the possibility that the MZ twinning rate is a true constant that can be estimated by adjusting the DZ same-sex/opposite-sex (SS/OS) ratio.

Constants for Both the MZ Rate and the DZ SS/OS Ratio

The simplest approach to the problem is to assume constant values for both the MZ twinning rate and the SS/OS ratio among DZ twins. With two unknowns, all one needs is two sets of data involving the variables in order to solve the simultaneous equations. The equation for Weinberg's difference is

(1) $MZ = SS - OS$

where MZ, SS, and OS are either numbers or population frequencies of the respective kinds of twin deliveries. If one uses actual numbers of deliveries (confinements), and introduces the variables *a* for the MZ twinning rate, *b* for the DZ SS/OS ratio and P for all deliveries in the cohort, the equation one has to solve, the adjusted Weinberg difference, is

(2) $a \cdot P = SS - b \cdot OS$

Table 1 shows the results of substituting pairs of data sets into this equation and solving. Notice that, in all but the last line, the MZ rate is nearly constant and considerably lower than the 3.5 to 4.0 usually found for MZ twinning. In the same lines the SS/OS ratio is close to the 19% excess of SS pairs reported by James [5]. However, in the last line, where the two equations to be solved are based on data for the two races, respectively, the result is very different, *a* = 3.4, coincidentally almost the same as by Weinberg's difference method, 3.6. This casts doubt on the proposed estimates.

Table 1 - Constants estimated for the MZ twinning rate and the DZ SS/OS ratio by simultaneous solution of equation 2 for paired data sets based on maternal age or race. Data for U.S., 1964 [4].

Race	Criterion	MZ rate per 1000 live births	SS/OS ratio
White	< 30, > 30	2.89	1.23
White	< 25, > 25	2.95	1.21
Black	< 30, > 30	2.75	1.18
Black	< 25, > 25	2.76	1.18
Both	White, Black	3.42	1.04

Large discrepancies appear *within* each race when solutions are obtained for overlapping pairs of 5-year age groups (not shown): 15 - 19 \times 20 - 24, 20 - 24 \times 25 - 29, etc. Not only do both a and b drift over a wide range of values, but some of the solutions for the black population are quite impossible. These anomalies can hardly be attributed to sampling errors because the numbers are large.

A more elegant estimation procedure uses data for all age groups at once. If one divides both sides of equation 2 by the population frequency, P , and rearranges, one obtains a simple regression equation, expressing the SS twinning rate as MZ twinning plus a function of the OS twinning rate. In this formulation SS' and OS' are rates among all deliveries, with the same dimensions as:

$$(3) \quad SS' = a + b \cdot OS'$$

In Fig. 2 this equation has been used to plot the white twinning rates of each 5-year maternal age group. Note the rationale. The X-axis now is not ordered by maternal age or parity, but by the rate of opposite-sex twinning in subgroups of deliveries, and the Y-axis measures the rate of same-sex twinning. The SS twinning rate includes the MZ rate, shown here as a , the Y-intercept. In any observed set of births the SS twins will also include a DZ increment that can be expressed as a ratio, b , times the number of OS pairs. When b is one, the number of DZ SS twins equals the number of DZ OS twins, giving the usual Weinberg estimate.

One can divide the data into any number of groups, for example by parity within age, and solve the regression equation by the method of weighted least squares. Table 2 shows the constants estimated by the regression method applied to 5-year maternal age groups in the 1964 U.S. data; first, for all whites and for all blacks, then for white male and white female infants separately. (In 1964 there were 10,793 male same-sex pairs, 10,330 female pairs, and 9,283 opposite-sex pairs of twins. To make the SS/OS ratios for separate sex comparable with those for combined sexes, the number of OS twins is halved).

The sex difference in the SS/OS ratio is reduced slightly in an alternative solution. One can use the MZ rate found above for combined sexes, 3.02, and solve for the DZ SS/OS ratio separately in each sex. The resulting ratios are 1.20 and 1.16 males and females.

The three figures for white births, in lines one, three, and four, are close to each other and only a little higher than the two values for whites in Table 1. The value for blacks, however, is lower than those in Table 1, and the difference between the races, if one applies Bulmer's standard error formula, is significant at $t = 2.45$, $p \approx 0.01$. A constant MZ rate thus eludes us, and the SS/OS ratio among DZ twins also is rather different between the sexes, though not significantly so. J. Fellman (personal communication) points out, however, that when values of the independent variable are estimated as here, least squares regression analysis is unreliable.

A Constant for MZ Twinning but not for the DZ SS/OS Ratio

Finding rather different SS/OS ratios for male and female infants suggests allowing the ratio to vary among maternal age groups when estimating the MZ rate. That makes too many unknowns and requires some limitation on the SS/OS ratio. One possibility is to

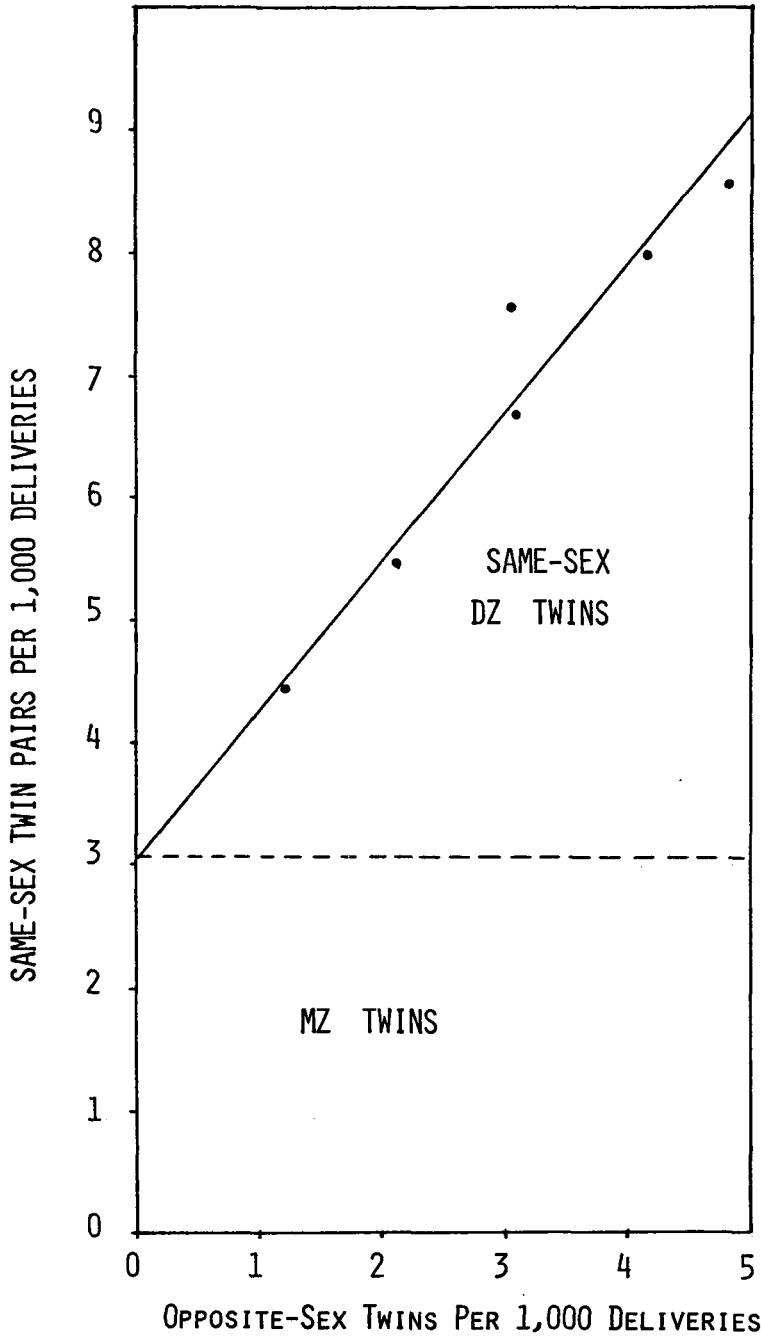


Fig. 2. Regression of same-sex twinning rate on opposite-sex twinning rate for six maternal age groups plotted by equation 3 and fitted by weighted least squares. Y-intercept = estimated MZ twinning rate; slope = estimated ratio of same-sex to opposite-sex pairs among DZ twins. U.S. white mothers, 1964 [4].

Table 2 - Constant for the MZ twinning rate and for the DZ SS/OS ratio estimated by weighted least squares regression analysis of SS and OS twinning rates in 5-year maternal age groups within race or within sex of infant. Data for U.S., 1964 [4].

Race	Births	MZ rate per 1000 live births	SS/OS ratio
White	All	3.02	1.18
Black	All	2.64	1.20
White	Male	2.99	1.21
White	Female	3.06	1.15

find the constant MZ rate that minimizes variance in the SS/OS ratio over maternal age groups, or whatever categories are used.

Table 3 shows the MZ rate and the SS/OS ratios obtained at the MZ twinning rate that gives the least variance in the ratios, first when births are divided by maternal age groups and second, when divided by birth order groups. The estimates of the MZ twinning rate obtained in these two operations are 3.00 and 3.14, a rather large difference considering that both estimates are based on the same data (excepting a very small number of twins classified by only one of the two maternal variables).

The method is applied in Table 4 to two different Caucasian populations, contrasting the 1964 USA data with McArthur's [7] data on 22,700 Italian twin deliveries for 1949-50. The MZ rates are 3.00 and 3.64, respectively, similar in both countries to those obtained by the regression method. The variation in SS/OS ratio between age groups is not very great, but the MZ rates are 3.00 and 3.64 respectively. If this is the best available method, it forces us to give up the search for a constant MZ twinning rate even for all Caucasian populations. If that is the case, there is no justification for applying any of these methods, since they are all predicated on a constant MZ rate.

One further approach suggests itself. If the differences in SS/OS ratio between age groups are real, and the differences within age groups between Italy and the United States are real, one might at least expect the same *relative* rates; that is, a similar profile for the six values. Fig. 3 shows very different profiles whatever solution one chooses. The two

Table 3 - DZ SS/OS ratios obtained with MZ rates that minimize variance among the ratios for maternal age groups or birth orders, respectively. Data for U.S. white mothers, 1964 [4].

By age group		By birth order	
MZ rate	SS/OS group	MZ rate	SS/OS ratios
3.00	1.20	3.14	1.13
	1.18		1.17
	1.18		1.12
	1.20		1.14
	1.15		1.17
	1.50		0.99
			1.23
			1.14

Table 4 - DZ SS/OS ratios obtained with MZ rates that minimize variance among the ratios for maternal age groups among U.S. white mothers or Italian mothers, respectively. Data for U.S., 1964 [4] and Italy 1949-1950 [7].

U.S.A.		Italy	
MZ rate	SS/OS ratios	MZ rate	SS/OS ratios
3.00	1.20	3.64	1.21
	1.18		0.90
	1.18		1.02
	1.20		1.00
	1.15		1.07
	1.50		1.09

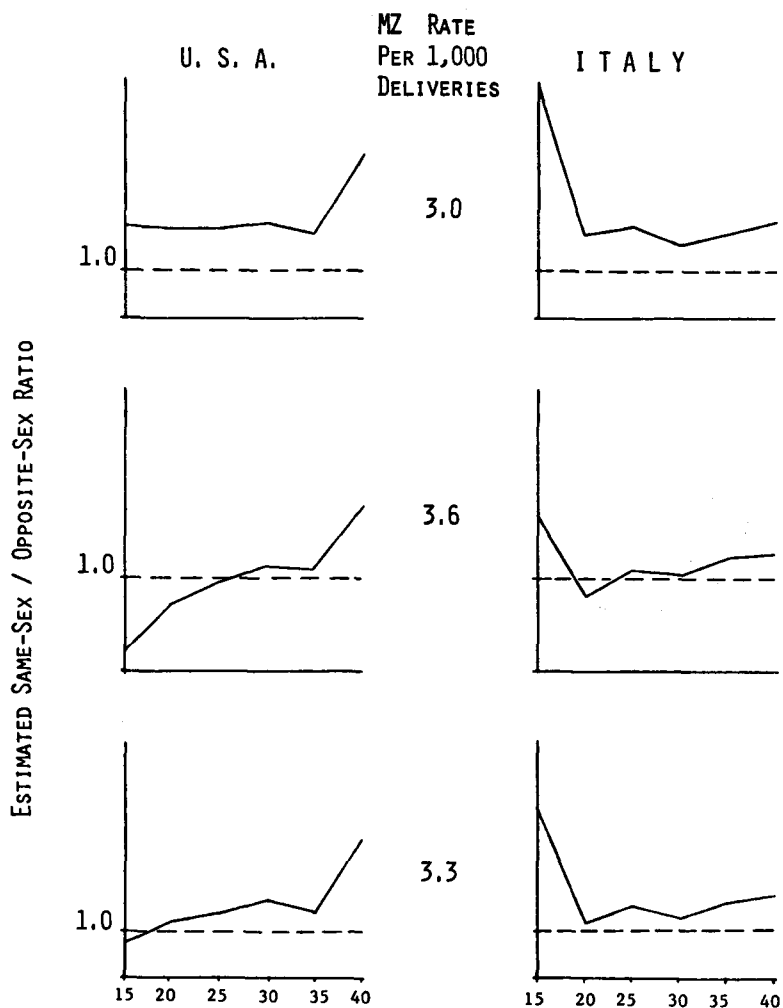


Fig. 3. Profile of the estimated dizygotic SS/OS ratio at six maternal ages for three trial values of the MZ twinning rate. U.S. white mothers, 1964 [4] and Italian mothers, 1949-1950 [7].

graphs at the top are for an MZ rate of 3.00, optimum for the U.S. data, and the next two are for 3.6, optimum for the Italian data. At the bottom are the results of a compromise MZ rate of 3.3, which might be expected to bring the profiles of the two populations close together, but there is still no resemblance.

Actually the estimates of the SS/OS ratio are not very stable, and the differences between these profiles might not be statistically significant. It is enough to test the largest difference, that for the youngest maternal age group. Precise confidence limits are difficult to define, but a conservative approach is to ignore the correlation between estimates of MZ and DZ twinning rates (both depend on the number of same-sex pairs in a sample). The 95% confidence intervals for the American and the Italian populations do not overlap. This seems to exhaust the possibilities of finding a constant MZ twinning rate.

Conclusion

If there is a true, constant value for the human MZ twinning rate, it is apparently not to be found in ordinary birth statistics by any obvious adjustment of the ratio of SS to OS DZ twins. The differential mortality of DZ twins by sex-concordance types [2] warns us to be skeptical of the Weinberg assumption of equality in the numbers. But the present data do not provide a fixed ratio to substitute for equality, nor even an independent confirmation of James' [5] estimate of a 15% to 20% overall excess of DZ SS pairs.

REFERENCES

1. Allen G (1981): Errors of Weinberg's difference method. In Gedda L, Parisi P, Nance WE (eds): *Twin Research 3. Part A: Twin Biology and Multiple Pregnancy*. New York: Alan R Liss, pp 71-74.
2. Boklage CE (1985): Interactions between opposite-sex dizygotic fetuses and the assumptions of Weinberg difference method epidemiology. *Am J Hum Genet* 37:591-605.
3. Bulmer MG (1970): *The Biology of Twinning in Man*. Oxford: Clarendon Press.
4. Heuser RL (1967): *Multiple Births, United States - 1964*. Washington; US Government Printing Office (Public Health Service Publication No. 1000, Series 21, No. 14).
5. James WH (1976): The possibility of a flaw underlying Weinberg's differential rule. *Ann Hum Biol* 3:549-556.
6. James WH (1984): Twins. *N Engl J Med* 311:58.
7. McArthur N (1953): The frequency of monozygotic and dizygotic twin births in Italy, 1949-1950. *Acta Genet Med Gemellol* 2:11-17.

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