By using the Wilcoxon test only the sign of the difference in birth weight is taken into account, i.e. twin pairs that differ 1 gram in birth weight are not differentiated from twin pairs who differ many hundreds of grams in birth weight. By using a correlation test, the size of the difference in birth weight is, however, also considered and hence the analysis becomes more powerful (i.e. increasing the chances of detecting an association).

Another disadvantage with the methods used by Poulsen et al. is the need to be able to separate the twins with respect to their birth weight. If the birth weight of the twins within a pair is equal, the data for these twins cannot be used. Therefore, in some of the analyses, Poulsen et al. had to drop 23 of their 109 twin pairs because of similar birth weights within pairs. This problem does not arise in a 'correct' analysis of the data.

To examine if Type II diabetic twins have a statistically significant lower birth weight than non-diabetic twins a correct analysis using the Wilcoxon test based on intra-pair differences (i.e. birth weight of the Type II diabetic twin minus birth weight of the non-diabetic co-twin) was carried out. Unfortunately, the method used to obtain intra-pair differences by always taking the Type II diabetic twin minus the non-diabetic twin also seems to have been used when calculating the correlation between duration of diabetes and birth weight.

When calculating the intra-pair differences, in duration of diabetes and birth weight, to be used in the correlation analysis, it is not necessary to be consequent in the meaning of always taking the Type II diabetic minus the non-diabetic twin or vice versa. It is correct and even more powerful to be inconsequent, i.e. taking the non-diabetic twin minus the Type II diabetic twin for one twin pair and vice versa for another twin pair. Which approach to be applied to which twin pair is decided by randomisation.

By always taking the Type II diabetic minus the non-diabetic twin we will only get positive differences in duration of diabetes. Therefore, the range of possible differences is restricted to only positive values. If we are inconsequent when calculating the intra-pair differences, we can obtain both positive and negative values and the range will be wider. This is important because the correlation coefficient is dependent on the variability in the sample. The larger the variability in the sample the stronger the correlation.

Hence, the procedure used by the authors to calculate intra-pair differences reduced the probability to find a significant relation.

Another approach to examine the relation between duration of diabetes and birth weight is to calculate the intraclass correlation [2, p. 273]. In this analysis each twin pair is used twice. Once taking the Type II diabetic twin minus the non-diabetic twin and once taking the non-diabetic twin minus the Type II diabetic twin. A third approach is to analyse the data by means of regression analysis [3]. Observe that the randomisation method described above is not suitable for small samples. For small samples the intra-class and the regression method is more suitable.

Our comments do not invalidate Poulsen et al's results, but stronger associations and even more interesting results could have been found if a better statistical analysis of the data had been done. How to analyse twin data in the best possible way is far from trivial. Poulsen et al. are not the first researchers using inefficient methods in the analysis of twin data [4, 5].

Yours sincerely,
J. Bring, L. Wernroth

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Evidence for an association between diabetes and birth weight still exists

Dear Sir,
We thank Bring et al. for their comments. We are pleased that our paper published in April 1997 continues to be of interest [1]. In our study we report the finding of lower birth weights in both monozygotic and dizygotic twins with Type II (non-insulin-dependent) diabetes mellitus compared with their non-diabetic co-twins. These results indicate an association between low birth weight and Type II diabetes mellitus independent of factors such as gestational age, maternal height, birth order and sex. The finding of lower birth weights in monozygotic twins with Type II diabetes compared with their genetically identical non-diabetic co-twins, furthermore, eliminates the possibility that the association can be due to a genotype causing both Type II diabetes and low birth weight.

In addition to the paired-twin approach (Type II diabetic twin vs non-diabetic twin) we carried out the non-parametric Wilcoxon test for paired data in the comparison of the group of twins with the heavier birth weight and the group of co-twins with the lighter birth weight to detect any differences. Furthermore, we did Spearman correlation analysis between birth weight and other variables.

Bring et al. suggest that a more powerful analysis of our data would be the correlation between intra-pair differences. We *did* perform these analyses (i.e. the "correct" analysis of data). The only significant correlation between intra-pair differences was the correlation between difference in birth weight and difference in 120-min post OGTT plasma glucose ($r = -0.26$, $p < 0.01$). This is mentioned on page 443, paragraph 3. We did not believe that the non-significant correlations between intra-pair differences added to the scientific content and we, subsequently, chose not to show the data.

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On request we have furthermore calculated intra-class correlations among the mentioned twin group. By doing this you double the number of pairs (which is an advantage with small samples) as described by Bring et al. The numeric value of the correlation coefficient is similar to the one described previously, however, the p value is smaller due to the larger sample size giving a significant correlation between difference in birth weight and difference in body weight ($r = 0.14$, $p < 0.05$), plasma fasting glucose ($r = -0.16$, $p < 0.05$) and 2 h-post OGTT plasma glucose ($r = -0.26$, $p < 0.001$).

We report the correlation between duration of diabetes and birth weight among the 14 monozygotic and 14 dizygotic twin pairs discordant for diabetes. Of the 28 Type II diabetic twins 9 twins were diagnosed at the time of the oral glucose tolerance test so the duration of their diabetes was 0 years. It is well known that patients can have diabetes several years before diagnosis so defining a diabetes duration in this case is very difficult. Considering this problem and the relatively small number of discordant twins, we did not, in this context, consider the relation between duration of diabetes and birth weight as a major point. It is true, however, that we consequently subtracted the non-diabetic twin from the Type II diabetic twin in the correlation calculations and the analysis would presumably have been more powerful by being inconsequent when calculating the intra-pair differences due to points raised by Bring et al.

Yours sincerely,
P. Poulsen, A. A. Vaag, K. O. Kyvik, D. Møller Jensen, H. Beck-Nielsen

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