Multiple pregnancies among women engaged in agriculture in Norway, 1967-91

Petter Kristensen[1] and Lorentz M. Irgens[2]

[1] *National Institute of Occupational Health, N-0033 Oslo, Norway*
[2] *Medical Birth Registry of Norway, N-5021 Bergen, Norway*

Correspondence: Petter Kristensen, National Institute of Occupational Health, P.O. Box 8149 Dep, N-0033 Oslo, Norway
Telephone: + (47) 23 19 51 00 Telefax: + (47) 23 19 52 00 e-mail: petter.kristensen@stami.no

SUMMARY

Background. The worldwide occurrence of dizygotic (DZ) multiple pregnancies has increased since 1980 as a consequence of assisted fertilization techniques. An opposite influence by environmental factors yet unidentified has been a suspected explanation of decreased multiple pregnancies in several countries during 1960-1980. The aim of our study was to describe multiple, in particular DZ, pregnancy patterns in the Norwegian agricultural population between 1967 and 1991, and to investigate the hypothesis that grain production under climatic conditions favoring fungal growth causes a decline in DZ pregnancies.
Methods. By record linkage of national registers in Norway, we identified 246,043 farm holders and spouses born between 1925 and 1971 in agricultural censuses and the population register. In this population, 190,258 pregnancies were recorded in the Medical Birth Registry 1967-91. The prevalences of multiple pregnancy, subdivided in DZ and monozygotic (MZ) pregnancies, were examined in strata of several determinants. Exposure, defined as the combination of grain farming and categories of seasonal fungal warnings, was based on data on farm activity and on local fungal warnings in the growth seasons. Adjusted prevalence ratios (PR) served as estimates of association.
Results. We identified 2,131 (11.2 per 1,000) multiple pregnancies, 1,322 (6.9) were classified as DZ. The prevalence of DZ pregnancies was declining until the late 1970s, and increased thereafter. The agricultural population of Norway is heterogeneous along two dimensions, with a difference between farmers and non-farmers (mainly engaged in forestry), and a difference according to degree of maternal work input on the farm holding. Farmers, in particular active farmers, had more DZ pregnancies than non-farmers early in the study period; this ratio was reversed late in the study period. Non-farmers had a much higher temporal increase in the proportion of first-time mothers who were ≥30 years, and were more likely to undergo in vitro fertilization (IVF). Combined grain farming and seasonal late blight warnings did not influence the prevalence of DZ pregnancies. Unexpectedly, the same climate variable, in combination with horticulture, was negatively associated with DZ pregnancies (PR 0.3; 95% confidence interval 0.1–0.7).
Conclusion. Active Norwegian farmers seem to have a somewhat higher natural occurrence of DZ pregnancies than mothers in non-farming sectors of the agricultural population. After the late 1970s this situation was reversed, mainly because the latter group consisted of more older first-time mothers, and probably with a higher need of assisted fertility treatment. Interpretations are difficult concerning the inverse relation between DZ pregnancy and climatic conditions in horticulture.

INTRODUCTION

Throughout the world, prevalences of multiple pregnancies have varied considerably during the last decades.[1] Hormonal induction of ovulation and IVF have increased overall multiple birth rates since the 1980s.[2-7] In the decades preceding the use of these fertility treatment techniques, Western European and several other countries experienced a decline in dizygotic (DZ) twin rates.[8, 9] This was a matter of concern, because the decline was assumed to be a sign of declining fecundity. The causes of the observed DZ decline remained obscure; one hypothesis being that environmental factors disturb the hormonal regulation of ovulation.[9, 10] In Norway, the prevalence of multiple pregnancies was stable (about 10 per 1,000) between 1967 and the mid-1980s, but increased by 30% in the years to follow.[11]

In a study of perinatal outcomes in births to Norwegian farmers, delivery during gestational weeks 16-27 was associated with climatic conditions in grain farming favoring growth of field fungi and formation of mycotoxins.[12] Several mycotoxins prevail in grain farming in Norway,[13-15] of which some have immune and endocrine-modulating properties[16,17] that might influence DZ pregnancy tendency.

The purpose of the present study was twofold: to describe secular patterns of multiple, in particular DZ, pregnancies in the total Norwegian agricultural population and subgroups of this population, secondly, to pursue the hypothesis that conditions favoring fungal growth and mycotoxin formation in grain farming are inversely related with DZ pregnancies.

MATERIAL AND METHODS

Statistics Norway conducted three agricultural and two horticultural censuses between 1969 and 1989. In total, 149,254 farm holders born after 1924 were identified in the censuses, and 104,370 spouses were identified after linkage with the Central Population Register. We linked the file of farmers and spouses to the Medical Birth Registry of Norway to identify their births. The establishment of the cohort and linking procedures are described in more detail elsewhere.[12]

Data sources

The Medical Birth Registry of Norway, comprising all deliveries from 16 completed weeks of gestation since 1967, provided data on multiple pregnancies. We identified 190,258 pregnancies (192,417 births) 1967-91, to 90,578 mothers (median year of birth, 1948) who were farm holders or spouses. Data on sex of the newborn, year of birth, maternal age and birth order were derived from the Registry. Year of birth was categorized into six periods, maternal age into four categories and birth order into four categories (Table 1). Pregnancies after IVF treatment are registered since the late 1980s by the Medical Birth Registry in cooperation with the IVF laboratories.[7] In the study population, 39 pregnancies (2.0 per 10,000) were to mothers who had been subject to IVF treatment.

Data on farm activity from the agricultural and horticultural censuses were linked to all pregnancy records. Dichotomous categories of types of farming were assigned to each pregnancy, dependent on information in the census closest in time to the conception: farming activities defined as animal farming (cattle, sheep/goats, pigs, poultry, horses), and cultivation of potato, grain, horticultural products (orchards, berries, greenhouses) or field vegetables (Table 1). Pregnancies of mothers on a farm with none of the above mentioned activities came almost exclusively from forestry holdings, and were classified as «no farming activity» pregnancies. Data on farm location (six geographical regions) and acreage (three categories), and maternal work input on the farm were derived from the censuses. Maternal work input was dichotomized into <500 and ≥500 annual hours, the occupational criterion for a farmer of Statistics Norway.[18]

The Norwegian Meteorological Institute has since 1958 provided daily fungal warnings in the growing season (mid June to mid September) as a tool against late blight growth in potato.[19] Warnings have been based on daily climate data at local weather stations. Criteria for a late blight warning applied for two consecutive days and remained unchanged until the 1990s: minimum temperature ≥10^0 C, maximum temperature 17-24^0 C, relative humidity ≥75%, and precipitation. Warning data during 1973-90 were computerized, and data from 46 stations were allocated to all study farms based on their location. The local warning count in a specific season was assigned to pregnancies conceived between June in the same season until May next year. Thus, only pregnancies conceived between June 1973 and May 1991 were classified on seasonal warnings.

Table 1. Items of personal data for pregnancies of 90,578 women in the agricultural sector, Norway 1967-91.

Item	Total	%
Total	190,258	100.0
Year of birth		
1967-70	49,824	26.2
1971-74	42,911	22.6
1975-78	31,469	16.5
1979-82	26,092	13.7
1983-86	21,281	11.2
1987-91	18,681	9.8
Maternal age (years)		
-24	56,997	30.0
25-29	65,368	34.4
30-34	43,032	22.6
35+	24,861	13.1
Birth order*		
First	59,147	31.1
Second	61,654	32.4
Third	40,597	21.3
Fourth or more	28,487	15.0
Geographical region		
East	65,482	34.4
South	11,051	5.8
Jæren	12,487	6.6
West	49,083	25.8
Trøndelag	23,955	12.6
North	28,200	14.8
Acreage (hectares)		
0-0.4	40,701	21.4
0.5-4.9	62,624	32.9
5.0+	86,933	45.7
Maternal work input ≥500 annual hours	65,052	34.2
Animal farming	119,933	63.0
Potato cultivation	110,613	58.1
Grain farming	49,957	26.3
Horticulture	11,190	5.9
Field vegetable cultivation	28,986	15.2
No farming activity†	37,973	20.0

* Missing information in 373 pregnancies.
† No cultivation of potato, grain, horticultural products or field vegetables, and no animal farming in the agricultural census closest in time to the conception.

Analysis

Our observation unit was the pregnancy, conditional on birth after 16 weeks of gestation. The analyses were performed in the Epicure software package.[20] We computed multiple pregnancy prevalences per 1,000, that were divided into DZ and MZ pregnancies on the probabilistic assumption that twice the number of opposite-sexed twin pairs and 8/6 the number of unequal-sexed triplets are DZ (Weinberg's differential).[21] DZ pregnancy was the main study outcome. Assignments of DZ and MZ pregnancies were made on the group level, after stratification for all determinants in the covariate matrix, allowing full adjustment in analysis. We used prevalence ratio estimates (PR) as measure of association, computed in contingency tables that were stratified by the determinants listed in Table 1. We fitted Poisson regression models, controlling for these variables, and computed approximate 95% confidence intervals (CI).

The analysis of the effects of the main environmental exposure indicator, combined grain farming and seasonal late blight warnings, was restricted to the pregnancies with season-specific warning data and known gestational age. Using DZ pregnancies as main outcome in this analysis created a conceptual problem since it can be influenced by opposing forces. The natural DZ tendency could be an indicator of high fecundity[9,10] whereas DZ pregnancies caused by assisted fertilization procedures certainly is an indicator of low fecundity.[1-6] We tried to avoid combining natural and iatrogenic DZ pregnancies in one outcome category in the investigation of environmental influence, but, apart from the few IVF pregnancies, we had no data on assisted fertilization treatment. Therefore, we used two measures to minimize the influence of iatrogenic DZ pregnancies: restrict analysis to 1967-1982, when those fertilization techniques scarcely were used, and, exclude first-time mothers ≥30 years, supposedly the main high consumer group of fertility treatment.[1-3]

RESULTS

We registered 2,131 multiple pregnancies (2,103 twin, 28 triplet; 11.2 per 1,000); 1,322 (6.9) were classified as DZ and 809 (4.2) as MZ pregnancies. Figure 1 shows the crude temporal trend of multiple pregnancies. The prevalence was stable around 11.0 before 1980, but increased thereafter until a maximum of 14.2 during 1987-91. This trend was mainly influenced by DZ pregnancies: the prevalence declined from 6.5 (1967-70) to 5.6 (1979-82), followed by a maximum of 10.6 in 1987-91. By contrast, the MZ prevalence was rather stable during 1967-91.

Table 2 illustrates that the DZ prevalence increased considerably with year of birth, maternal age and birth order. Twelve out of 39 IVF pregnancies (307.7 per 1,000) were multiple (10 twin, 2 triplet). The DZ prevalence changed only moderately by geographical region, acreage and maternal work input on the farm. The adjusted model showed clearly that maternal age was a strong determinant whereas birth order scarcely had any independent effect. In the adjusted model, PRs changed little over time but were moderately increased for births during 1987-91. Type of farming was not associated with DZ pregnancies, with the exception of horticulture (PR 0.7; 95% CI 0.6–0.9).

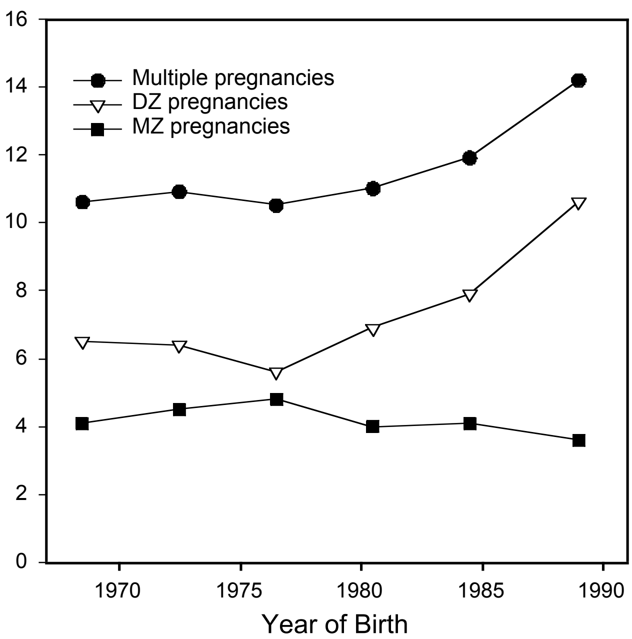

Figure 1. Crude prevalences (per 1,000 pregnancies) of multiple pregnancy, subdivided in DZ and MZ pregnancies, by year of birth, of women in the agricultural sector, Norway 1967-91.

Table 2. Prevalence of DZ pregnancies of women in the agricultural sector, Norway 1967-91, and associations with demographic and maternal variables, and type of farming.

	Cases (No.)	Prevalence per 1,000	Prevalence ratio* (95% CI)
Total	1,322	6.9	
Year of birth			
1967-70	325	6.5	1 (reference)
1971-74	274	6.4	1.0 (0.8–1.1)
1975-78	177	5.6	0.8 (0.7–1.0)
1979-82	180	6.9	1.0 (0.8–1.2)
1983-86	167	7.9	1.1 (0.9–1.3)
1987-91	199	10.6	1.3 (1.1–1.5)
Maternal age (years)			
-24	228	4.0	1 (reference)
25-29	427	6.5	1.6 (1.4–1.9)
30-34	380	8.8	2.3 (1.9–2.7)
35+	287	11.6	3.0 (2.5–3.7)
Birth order†			
First	335	5.7	1 (reference)
Second	424	6.9	1.0 (0.9–1.2)
Third	333	8.2	1.0 (0.8–1.2)
Fourth or more	227	8.0	0.8 (0.6–1.0)
IVF treatment			
No	1,310	6.9	1 (reference)
Yes	12	307.7	27.2 (15.7–47.3)
Geographical region			
East	442	6.7	1 (reference)
South	65	5.9	0.9 (0.7–1.1)
Jæren	100	8.0	1.2 (1.0–1.5)
West	361	7.3	1.1 (0.9–1.3)
Trøndelag	148	6.2	1.0 (0.8–1.2)
North	206	7.3	1.1 (0.9–1.3)
Acreage (hectares)			
0-0.4	280	6.9	1 (reference)
0.5-4.9	433	6.9	0.9 (0.7–1.1)
5.0+	609	7.0	0.9 (0.7–1.1)
Maternal work input on the farm			
<500 annual hours	852	6.8	1 (reference)
≥500 annual hours	470	7.2	1.1 (1.0–1.2)
Animal farming	832	6.9	1.0 (0.8–1.1)
Potato cultivation	767	6.9	1.1 (1.0–1.2)
Grain farming	348	7.0	1.1 (1.0–1.3)
Horticulture	60	5.4	0.7 (0.6–0.9)
Field vegetable cultivation	194	6.7	1.0 (0.8–1.1)
No farming activity‡	258	6.8	0.9 (0.7–1.1)

* Adjusted for year of birth, maternal age, birth order, geographical region, acreage and maternal work input on the farm.

† Missing information in 373 pregnancies (including 3 DZ pregnancies).

‡ No cultivation of potato, grain, horticultural products or field vegetables, and no animal farming in the agricultural census closest in time to the conception.

The overall DZ prevalence in the «no farming activity» category did not deviate from the total prevalence. However, stratification by year of birth showed different trends in pregnancies according to farming activity (Table 3). Compared with no farming activity, farming activity mothers had DZ pregnancies more frequently during 1967-78 (PR 1.3, 95% CI 1.1–1.7). This relation was reversed during 1979-91, and the excess of DZ pregnancies in the no farming category compared with the farming category was highest in 1987-91 (14.4 and 9.3, respectively). The difference late in the study period could partly be explained by differences in IVF treatment (no farming activity, 18 IVF pregnancies, 4.7 per 10,000; farming activity, 21 IVF pregnancies, 1.4 per 10,000).

DZ prevalences stratified on maternal age (<30; ≥30) and birth order (first births, higher birth order) are shown in Figure 2. In pregnancies of first-time mothers aged ≥30 years the prevalence rose steeply from 6.0 in 1979-82 to 34.3 in 1987-91. The determinants of DZ pregnancy among first-time mothers ≥30 years of age were further investigated. Year of birth and IVF treatment were the only factors influencing DZ prevalences (Table 4), and none of the factors on farm size, maternal work input or farming activity had impact (data not shown).

Table 3. Prevalence of DZ pregnancies of women in the agricultural sector, Norway 1967-91, by year of birth and main type of agricultural activity.

	Cases (No.)	Prevalence per 1,000	Prevalence ratio* (95% CI)
Year of birth 1967-78			
No farming activity†	110	5.0	1 (reference)
Farming activity‡	666	6.5	1.3 (1.1–1.7)
Year of birth 1979-91			
No farming activity†	148	9.2	1 (reference)
Farming activity‡	398	8.0	0.9 (0.8–1.1)

* 1967-1978, adjusted for maternal age, birth order and geographical region; 1979-1991, adjusted for maternal age, birth order, geographical region, and IVF treatment.

† No cultivation of potato, grain, horticultural products or field vegetables, and no animal farming in the agricultural census closest in time to the conception.

‡ Cultivation of potato, grain, horticultural products or field vegetables, or animal farming in the agricultural census closest in time to the conception.

Table 4. Prevalence of DZ pregnancies among 7,558 first-time mothers, aged ≥30 years, in the agricultural sector, Norway 1967-91, and associations with year of birth and IVF treatment.

	Cases (No.)	Prevalence per 1,000	Prevalence ratio* (95% CI)
Total	95	12.6	
Year of birth			
1967-70	8	6.1	1 (reference)
1971-74	8	6.4	1.0 (0.4–2.8)
1975-78	12	9.2	1.5 (0.6–3.7)
1979-82	7	6.0	1.0 (0.4–2.7)
1983-86	15	13.0	2.2 (0.9–5.1)
1987-91	45	34.3	4.3 (2.0–9.4)
IVF treatment			
No	86	11.2	1 (reference)
Yes	9	375.0	19.6 (9.9–38.8)

* Model including year of birth, IVF treatment, geographical region, acreage and maternal work input on the farm.

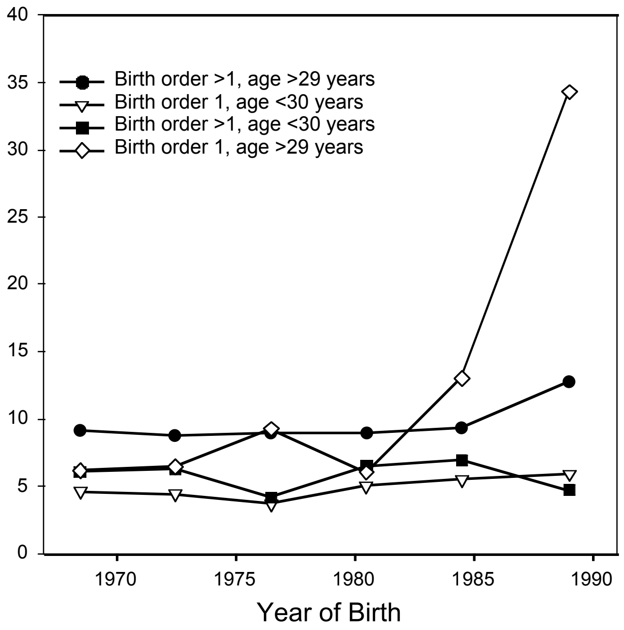

Figure 2. Prevalences (per 1,000 pregnancies) of DZ pregnancy by year of birth, in categories of maternal age and birth order, of women in the agricultural sector, Norway 1967-91.

The maternal age and birth order distribution in the population obviously had an influence on DZ prevalence. Therefore, we made a closer examination of the proportions of total pregnancies which were to first-time mothers ≥30 years (Table 5). This proportion increased almost three-fold during the study period, was highest in the eastern region, among residents on small farms and mothers in the no farming activity category. Low proportions were found in animal farming and potato cultivation, and particularly in pregnancies of mothers with ≥500 annual work-hours on the farm (2.7%). The increasing trend of first births to women ≥30 years was more moderate in the high work input category, from 2.2% to 4.1% between 1967-70 and 1987-91, compared with the low work input category (from 2.9% to 8.0% between 1967-70 and 1987-91).

Table 6 data show the association between combined grain and seasonal climate data, and DZ pregnancy. Analysis was restricted to pregnancies conceived between June 1973 and May 1991, first-time mothers ≥30 years of age were excluded. DZ prevalences declined slightly in pregnancies conceived in a season with >1 late blight warning, but this was not restricted to grain farms. Accordingly, there was no apparent association between combined grain farming and warnings, and DZ pregnancies. Due to the negative association with horticulture, the effect of horticulture was investigated in combination with late blight warnings, revealing that DZ pregnancy was negatively associated with combined horticulture and fungal warnings. On farms with horticultural cultivation and any seasonal warnings, 6 DZ pregnancies were observed (2.1 per 1,000; PR 0.3; 95% CI 0.1–0.7). Results of analyses in all pregnancies con-

Table 5. Proportions of pregnancies which were to first-time mothers ≥30 years of age, in the agricultural sector, Norway 1967-91, and relations with demographic variables and type of farming.

	No.	Per 100	Prevalence ratio* (95% CI)
Total	7,558	4.0	
Year of birth			
1967-70	1,309	2.6	1 (reference)
1971-74	1,255	2.9	1.1 (1.0–1.2)
1975-78	1,299	4.1	1.5 (1.4–1.6)
1979-82	1,213	4.7	1.7 (1.5–1.8)
1983-86	1,181	5.6	2.0 (1.8–2.2)
1987-91	1,301	7.0	2.4 (2.2–2.6)
Geographical region			
East	3,298	5.0	1 (reference)
South	469	4.2	0.8 (0.7–0.9)
Jæren	352	2.8	0.6 (0.5–0.7)
West	1,802	3.7	0.8 (0.7–0.8)
Trøndelag	745	3.1	0.7 (0.6–0.7)
North	892	3.2	0.6 (0.6–0.7)
Acreage (hectares)			
0-0.4	2,286	5.6	1 (reference)
0.5-4.9	2,166	3.5	0.8 (0.7–0.9)
5.0+	3,106	3.6	0.8 (0.7–0.8)
Maternal work input on the farm			
<500 annual hours	5,829	4.7	1 (reference)
≥500 annual hours	1,729	2.7	0.7 (0.7–0.7)
Animal farming	3,757	3.1	0.8 (0.8–0.9)
Potato cultivation	3,607	3.3	0.9 (0.9–1.0)
Grain farming	2,038	4.1	1.1 (1.0–1.1)
Horticulture	415	3.7	1.1 (1.0–1.2)
Field vegetable cultivation	1,041	3.6	1.0 (1.0–1.1)
No farming activity†	2,172	5.7	1.2 (1.1–1.3)

* Adjusted for year of birth, geographical region, acreage and maternal work input on the farm.

† No cultivation of potato, grain, horticultural products or field vegetables, and no animal farming in the agricultural census closest in time to the conception.

Table 6. Prevalence of DZ pregnancies of women in the agricultural sector, Norway 1973-91*, and associations with environmental exposure indicators.

	Cases (No.)	Preva-lence	Prevalence ratio† (95% CI)
Total	694	6.9	
Combined grain farming and seasonal late blight warnings			
No grain, 0 warnings	301	6.7	1 (reference)
No grain, 1 warning	145	7.4	1.1 (0.9–1.4)
No grain, >1 warning	74	6.1	0.9 (0.7–1.2)
Grain, 0 warnings	89	7.6	1.2 (0.9–1.6)
Grain, 1 warning	54	7.7	1.3 (0.9–1.8)
Grain, >1 warning	31	6.2	1.0 (0.7–1.5)
Combined horticulture and seasonal late blight warnings			
No horticulture, 0 warnings	368	6.8	1 (reference)
No horticulture, 1 warning	195	7.8	1.2 (1.0–1.4)
No horticulture, >1 warning	103	6.4	0.9 (0.8–1.2)
Horticulture, 0 warnings	22	8.7	1.2 (0.8–1.9)
Horticulture, 1 warning	4	2.4	0.3 (0.1–0.9)
Horticulture, >1 warning	2	1.7	0.2 (0.1–1.0)

* Analysis confined to 100,574 pregnancies conceived between June 1973 and May 1991, excluding first births to mothers aged ≥30 years.

† Adjusted for year of birth, maternal age, birth order, geographical region, acreage and maternal work input on the farm.

ceived in 1973-1991, or in corresponding births early in the study period (1973-1982) deviated little from the results in table 6, but the latter strategy resulted in a considerable reduction in pregnancies and unstable PR estimates (data not shown).

DISCUSSION

The population of this study comprises most of the people who were engaged in agricultural work in Norway.[12] The study provides evidence that the prevalence of multiple pregnancy declined in the Norwegian agricultural population between 1967 and the late 1970s, after which it increased until 1991. These time trends were due to changes in DZ pregnancies whereas MZ pregnancies showed a stable tendency.

This register-based study has crude exposure indicators, and it is well known that the resulting misclassification may attenuate true associations. In this study, there is another potential problem in using DZ pregnancy as outcome. DZ pregnancy might be a manifestation of both decreased and increased fecundity.[1-6,9,10] Furthermore, the DZ computation is based on assumptions that may not be true: the sex ratio of DZ births may shift over time and region, and Dutch data suggest that the use of Weinberg's differential underestimated DZ rates in 1960-90.[22]

The declining trend in multiple pregnancies before 1980 is in accordance with other populations in the same period,[1,8,9,22] but not with the total Norwegian population who had a stable prevalence during 1967-85.[11] An increasing prevalence after 1980 has been reported in studies in several developed countries,[1-3,8,11,22] and is probably iatrogenic, caused by in vitro fertilization and other forms of assisted fertilization.[1-8,23] Results from East Flanders[3] suggest that this is the only significant explanation, a statement that has been disputed.[24] We had data on IVF treatment but not other methods of infertility treatment. However, the DZ prevalence increase was restricted to older mothers (Figure 2) and could not entirely be accounted for by IVF that is considered to be completely recorded in the Medical Birth Registry since 1988.[7] It is therefore reasonable to assume that further iatrogenic factors, not recorded in the present study, had a major impact on the trend during the later study years.

Twinning has been reported to be more frequent in rural than in urban populations in Sweden and Finland[25] but not in Denmark.[26] The crude prevalence of multiple pregnancies in Norway was about 10 per 1,000 deliveries during 1967-85 and increased to 13.0 in 1990,[7] being more than 10% lower than in the agricultural population. However, this difference could be explained by a higher maternal age distribution compared with all Norwegian births.[7] Nonetheless, DZ pregnancies to mothers who took part in farming activities were more common than in other sectors of agriculture during 1967-78, even after adjustment for maternal age.

The results demonstrate other interesting differences within the study population. The high DZ prevalence during the later study years among women who were not involved in farming activities, suggest that they were more commonly treated for infertility. This was the case for IVF treatment: during 1988-91, the overall proportion of IVF treatments was 33.0 per 10,000 pregnancies in Norway,[7] the corresponding proportions in the farming and no farming activity categories were 19.4 and 47.2, respectively. However, this cannot be interpreted as a difference in fecundity, but rather be explained by different proportions of older first-time mothers in the population subsets during the later study years. During 1987-91, only 5.9% of pregnancies in the «farming activity» category were to first-time mothers ≥30 years of age; the corresponding proportion for «no farming activity» pregnancies was 9.8%.

The study hypothesis that mycotoxin exposure in grain farming reduces the prevalence of DZ pregnancies was not confirmed. Thus, very preterm delivery[12] and certain hormone-dependent cancers among the mothers (Kristensen et al, unpublished results), both being associated with fungal warnings in grain farming, were not correlated with DZ pregnancies. Unexpectedly, a decrease in DZ pregnancies was associated with climatic conditions favoring fungal growth in horticulture. This result is interesting, since pesticides was a suggested cause of the widespread decline in DZ pregnancies during 1960-80.[9] Furthermore, the horticulture-climate combination is associated with solid tumors in infancy (Kristensen et al, unpublished results). However, the quality of data in this study make inferences difficult, in particular since the indicator of exposure is related to fungi and mycotoxins as well as fungicides and other pesticides. Besides, DZ pregnancy has since 1980 become an ambiguous outcome unless data on assisted fertility treatment is at hand and can be accounted for.

ACKNOWLEDGMENTS

We thank Leif Sundheim at the Norwegian Crop Research Institute for valuable suggestions concerned with the farm exposure data, Ole-Henrik Edland at the Medical Birth Registry of Norway and Anne Snellingen Bye at Statistics Norway for file preparation and linking, and Einar Førsund at the Norwegian Crop Research Institute for electronic preparation of the late blight warning data. The study was funded by the Research Council of Norway (grant no. 103542/110).

REFERENCES

1. Derom R, Orlebeke J, Eriksson A, Thiery M. The epidemiology of multiple births in Europe. In Keith LG, Papiernik E, Keith DM, Luke B, editors. *Multiple pregnancy: epidemiology, gestation and perinatal outcome*. New York: Parthenon Publishing Group; 1995. p. 145-62.
2. Westergaard T, Wohlfahrt J, Aaby P, Melbye M. Population based study of rates of multiple pregnancies in Denmark, 1980-94. *BMJ* 1997; **314**: 775-9.
3. Derom C, Derom R, Vlietinck R, Maes H, Van den Berghe H. Iatrogenic multiple pregnancies in East Flanders, Belgium. *Fertil Steril* 1993; **60**: 493-6.
4. Lamont JA. Twin pregnancies following induction of ovulation. A literature review. *Acta Genet Med Gemellol* 1982; **31**: 247-53.
5. Schenker JG, Yarkoni S, Granat M. Multiple pregnancies following induction of ovulation. *Fertil Steril* 1981; **35**: 105-23.
6. Hecht BR. The impact of assisted reproductive technology on the incidence of multiple gestation. In: Keith LG, Papiernik E, Keith DM, Luke B, editors. *Multiple pregnancy: epidemiology, gestation and perinatal outcome*. New York: Parthenon Publishing Group; 1995. p. 175-90.
7. Von Düring V, Maltau JM, Forsdahl F, Åbyholm T, Kolvik R, Ertzeid G, Steier A, Baste V, Irgens LM. Pregnancies, births and babies after in vitro fertilization in Norway, 1988-91 (in Norwegian, English summary). *Tidsskr Nor Lægeforen* 1995; **115**: 2054-60.
8. Murphy M, Hey K. Twinning rates (Letter). *Lancet* 1997; **349**: 1398-9.
9. James WH. Second survey of secular trends in twinning rates. *J Biosoc Sci* 1982; **14**: 481-97.
10. Tong S, Caddy D, Short RV. Use of dizygotic to monozygotic twinning ratio as a measure of fertility. *Lancet* 1997; **349**: 843-5.
11. Medical Birth Registry of Norway. Births in Norway through 30 years. Bergen: Medical Birth Registry of Norway; 1997.
12. Kristensen P, Irgens LM, Andersen A, Bye AS, Sundheim L. Gestational age, birth weight, and perinatal death among births to Norwegian farmers, 1967-1991. *Am J Epidemiol* 1997; **146**: 329-38.
13. Sundheim L, Nagayama S, Kawamura O, Tanaka T, Brodal G, Ueno O. Trichothenes and zearalenone in Norwegian barley and wheat. *Nor J Agric Sci* 1988; **2**: 49-59.
14. Langseth W, Stenwig H, Sogn L, Mo E. Growth of moulds and production of mycotoxins in wheat during drying and storage. *Acta Agric Scand, Sect B, Soil Plant Sci* 1993; **43**: 32-37.
15. Langseth W, Elen O. The occurrence of deoxynivalenol in Norwegian cereals – differences between years and districts. *Acta Agric Scand, Sect B, Soil Plant Sci* 1997; **47**: 176-84.
16. Kuiper-Goodman T, Scott PM, Watanabe H. Risk assessment of the mycotoxin zearalenone. *Regul Toxicol Pharmacol* 1987; **7**: 253-306.
17. Golden RJ, Noller KL, Titus-Ernstoff L, Kaufman RH, Mittendorf R, Stillman R, et al. Environmental endocrine modulators and human health: an assessment of the biological evidence. *Crit Rev Toxicol* 1998; **28**: 109-227.
18. Central Bureau of Statistics. Population and housing census. Volume 2. Industry, occupation, working hours, etc. Oslo: Central Bureau of Statistics of Norway, 1970; 1975.
19. Førsund E. Late blight forecasting in Norway 1957-1980. *EPPO Bull* 1983; **13**: 255-8.

20. Preston DL, Lubin JH, Pierce DA, McConney ME. Epicure. Seattle: Hirosoft International Corporation; 1993.
21. Weinberg W. Differenzmethode und Geburtenfolge bei Zwillingen. *Genetica* 1934; **16**: 282-8.
22. Orlebeke JF, Eriksson AW, Boomsma DI, Vlietinck R, Tas FJ, de Geus EC. Changes in the DZ unlike/like sex ratio in the Netherlands. *Acta Genet Med Gemellol* 1991; **40**: 319-23.
23. Parazzini F, Restelli S, Moroni S, Crosignani PG. Trend in legitimate and illegitimate multiple births. *Hum Reprod* 1994; **9**: 1784-5.
24. James WH. Are «natural» twinning rates continuing to decline? *Hum Reprod* 1995; **10**: 3042-4.
25. Eriksson AW, Fellman J. Differences in the twinning trends between Finns and Swedes. *Am J Hum Genet* 1973; **25**: 141-51.
26. Olsen J, Knudsen LB. Twinning rates by residence in Denmark 1978 to 1982. *Scand J Soc Med* 1986; **14**: 147-50.