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(Accepted 21 September 1992)

Tobacco and myocardial infarction: is snuff less dangerous than cigarettes?

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Abstract

***Objective*—To estimate the risk of myocardial infarction in snuff users, cigarette smokers, and non-tobacco users in northern Sweden, where using snuff is traditional.**

***Design*—Case-control study.**

***Setting*—Northern Sweden.**

***Subjects*—All 35-64 year old men who had had a first myocardial infarction and a population based sample of 35-64 year old men who had not had an infarction in the same geographical area.**

***Main outcome measure*—Tobacco consumption (regular snuff dipping, regular cigarette smoking, non-tobacco use) and risk of acute myocardial infarction.**

***Results*—59 of 585 (10%) patients who had a first myocardial infarction and 87 of 589 (15%) randomly selected men without myocardial infarction were non-smokers who used snuff daily. The age adjusted odds ratio for myocardial infarction was 0·89 (95% confidence interval 0·62 to 1·29) for exposure to snuff and 1·87 (1·40 to 2·48) for cigarette smoking compared with non-tobacco users, showing an increased risk in smokers but not in snuff dippers. Regular cigarette smokers had a significantly higher risk of myocardial infarction than regular snuff dippers (age adjusted odds ratio 2·09; 1·39 to 3·15). Smoking, but not snuff dipping, predicted myocardial infarction in a multiple logistic regression model that included age and level of education.**

***Conclusions*—In middle aged men snuff dipping is associated with a lower risk of myocardial infarction than cigarette smoking.**

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BMJ 1992;305:1252-6

Introduction

Dipping of moist snuff is traditional in many developing and industrialised countries.[1-3] In other countries, notably in North America, the use of smokeless tobacco has recently become common among young people.[4-6] Campaigns against smokeless tobacco have been launched in many countries. In the United States the Comprehensive Smokeless Tobacco Health Education Act was passed in 1986 and in Britain oral tobacco products were banned in 1990. This is difficult to reconcile with the continued permission to sell and advertise cigarettes; whereas there is a massive documentation of the many detrimental effects of smoking tobacco, knowledge about the health effects of smokeless tobacco is limited.[7,8]

Cigarette smoking kills by increasing the risk of various atherothrombotic disorders, in particular myocardial infarction.[9] Although smokeless tobacco has been implicated in the pathogenesis of circulatory disorders, including coronary artery disease, the evidence is mostly circumstantial.[7,8] We therefore estimated the risk of myocardial infarction among snuff dippers in northern Sweden, where the use of snuff is traditional in middle aged men—a group at considerable risk of myocardial infarction.

Subjects and methods

This case-control study was performed within the framework of the northern Sweden MONICA project (multinational monitoring of trends and determinants in cardiovascular disease). The World Health Organisation MONICA project tests the hypothesis that changes over time in commonly recognised cardiovascular risk factors such as hypercholesterolaemia, hypertension, and cigarette smoking affect incidence and mortality in acute myocardial infarction and stroke.[10] Thirty nine populations in 26 countries are being followed up for 10 years. The northern Sweden project covers the two northernmost provinces of Sweden, Norrbotten and Västerbotten, with a total population of 510 000 living in an area of 154 000 km^2.

We compared the pattern of tobacco consumption in patients with acute myocardial infarction with that of participants in a MONICA population survey of cardiovascular risk factors. Cases and controls were from the same population of 35-64 year old men. The prevalence of snuff dipping among women was too low to permit meaningful analysis.

During the period April 1989 to April 1991, 629 men aged 35-64 in northern Sweden had their first acute myocardial infarction. Case finding followed the structured MONICA procedures[10] and was based on reports from general practitioners and the nine acute care hospitals in the area, checks of computerised discharge registers, and screening of death certificates of all subjects who died in the two provinces. Uniform

WHO criteria for diagnosing and classifying acute myocardial infarction were used.[10,11] Surviving patients were interviewed about tobacco consumption by specially trained nurses. If the patient had died family members or "significant others" answered the same questionnaire as used in the population survey. Information on tobacco consumption was missing for 44 patients, and the results from the remaining 585 patients (93% of the target group) are reported here. The 28 day death rate in these 585 patients was 21·2% (122 patients including deaths out of hospital).

In 1990 during the collection of cases with myocardial infarction, a population survey of cardiovascular risk factors was performed in Norrbotten and Västerbotten. A total of 2000 people were invited to participate. Within each age group (25-34, 35-44, 45-54, 55-64 years) 250 men and 250 women were randomly selected from continuously updated population records and invited by letter to an examination. Of 750 invited men aged 35-64, 609 (81·2%) participated. Twenty men who reported that they had had a myocardial infarction were excluded, leaving 589 men for comparisons with men who had had a first myocardial infarction. Limited data on cardiovascular risk factors were obtained by telephone interviews for 56 of the 141 men who did not participate.

Details of the survey procedures have been published.[12] Briefly, the participants were asked to complete a questionnaire with items on tobacco habits, social background, medical history, and drugs taken. The questionnaire was completed in local health centres throughout the area. The survey was conducted by two mobile teams. The team members also measured subjects' sitting blood pressure. Two measurements were taken with a mercury random zero sphygmomanometer.[13] Serum samples were taken after a minimum of four hours' fasting to measure lipid concentrations, and total cholesterol concentration was determined by an enzymatic method.

Based on reports from patients and control subjects, a regular cigarette smoker was defined as someone who smoked at least one cigarette daily. Other regular smokers included people who reported that they smoked over 5 g of tobacco a week in cigars, cigarillos, or a pipe and former smokers those who had previously been regular smokers but had now stopped. Non-smokers included people who had never been regular smokers or who reported occasional smoking (less than once daily). A regular snuff taker was defined as a person who used snuff at least once daily. A former snuff taker had previously taken snuff regularly but had now stopped. Non-tobacco users were people who did not smoke or take snuff regularly or reported occasional use of tobacco (less than once daily). In comparisons of risks of myocardial infarction those who used snuff and cigarettes concomitantly were excluded.

In dose-response evaluations, snuff dippers who consumed two or fewer cans ($\leq$100 g tobacco) were compared with those using more than two cans a week. This corresponds to the subdivision into light to moderate and heavy consumers proposed by Schroeder *et al.*[14] Among smokers, comparisons were made between those consuming fewer than 10 cigarettes (about $\leq$70 g tobacco) and more than 10 cigarettes a day.

Statistical analyses were performed with the SYSTAT software package and its LOGIT module supplementary program.[15] Odds ratios were calculated with their 95% confidence intervals. Data were adjusted for age based on the age distribution of patients with myocardial infarction in five year intervals. Independent predictors of myocardial infarction were estimated in a multiple logistic regression model.

The northern Sweden MONICA study has been approved by the research ethics committee of Umeå University and the data handling procedures by the National Computer Data Inspection Board.

Results

Table I shows the tobacco consumption pattern in men aged 35-64 with acute myocardial infarction compared with that in randomly selected men of the same age living in the same area. In all, 295 of the 585 (50%) men with myocardial infarction and 253 out of 589 (43%) control men regularly used some form of tobacco. Snuff was used more commonly by men who had not had a myocardial infarction than by men who had (118 (20%) *v* 91 (16%)). A similar proportion in both groups (about 5%) were both smokers and snuff dippers.

Former smokers were more common among patients with myocardial infarction than controls (178 (30%) *v* 154 (26%)), possibly because the men who had had an infarction were older (table I), whereas a significantly smaller proportion of the infarction group were former snuff dippers (22 (4%) *v* 82 (14%) controls; $p < 0{\cdot}001$ by χ^2 test). Change from smoking to snuff dipping was commonly reported. Thus, of the 59 non-smoking snuff dippers who had had a myocardial infarction, 33 (56%) had previously been smoking regularly. The corresponding proportion in the control group was 37 out of 87 (43%).

In further analyses, men who used both cigarettes and snuff were excluded because this group was too small to permit meaningful statistical analyses. The 35 men in the myocardial infarction group and 21 in the control group who used types of tobacco other than cigarettes and snuff were also excluded (table I). The remaining men were divided into three groups by their use of tobacco: regular cigarette smokers, regular snuff dippers, and non-tobacco users (including those who had stopped smoking or using snuff).

Figure 1(a) shows the age adjusted odds ratio and 95% confidence interval for myocardial infarction in regular cigarette smokers compared with non-tobacco users. The odds ratio and its 95% confidence interval was above 1 in the 35-54 year age range, showing a significantly increased risk of myocardial infarction in smokers. In the 55-64 year old age group the odds ratio was lower and the 95% confidence interval included 1—that is, the possibility that smoking did not confer an increased risk of myocardial infarction. Taking all men aged 35-64 together, smoking was associated with a significantly raised risk.

When snuff dippers were compared with non-tobacco users the age adjusted odds ratio for myocardial infarction was not significantly different from 1 in any age group (fig 1(b)). In comparisons between cigarette smokers and snuff dippers (fig 1(c)) snuff dippers had a significantly lower odds ratio for

TABLE I—*Tobacco consumption among 35-64 year old men who had had a myocardial infarction and 35-64 year old men participating in the northern Sweden MONICA population survey for cardiovascular risk factors. Percentages in parentheses*

	35-54 years		55-64 years		All subjects	
	Myocardial infarction	Control	Myocardial infarction	Control	Myocardial infarction	Control
Total No of subjects	218	396	367	193	585	589
Regular smokers (non-snuff dippers):						
Cigarette users	81 (37)	76 (19)	88 (24)	38 (20)	169 (29)	114 (19)
Other	14 (6)	11 (3)	21 (6)	10 (5)	35 (6)	21 (4)
All	95 (44)	87 (22)	109 (30)	48 (25)	204 (35)	135 (23)
Regular snuff dippers (non-smokers)	22 (10)	69 (17)	37 (10)	18 (9)	59 (10)	87 (15)
Concomitant smokers and snuff dippers	17 (8)	23 (6)	15 (4)	8 (4)	32 (6)	31 (5)
Former smokers	52 (24)	107 (27)	126 (34)	47 (24)	178 (30)	154 (26)
Former snuff dippers	8 (4)	62 (16)	14 (4)	20 (10)	22 (4)	82 (14)
Not presently using tobacco regularly*	84 (39)	217 (55)	206 (56)	119 (62)	290 (50)	336 (57)
Never used tobacco	29 (13)	107 (27)	89 (24)	70 (36)	118 (20)	177 (30)

*Including subjects who reported occasional smoking or occasional snuff dipping (less than once daily).

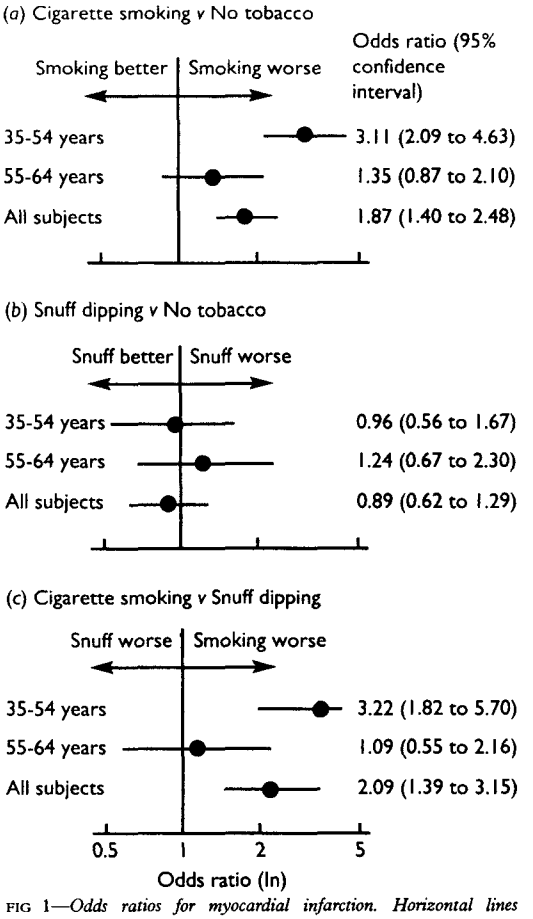

FIG 1—*Odds ratios for myocardial infarction. Horizontal lines indicate the 95% confidence intervals. Calculations are based on figures given in table I and are adjusted for age*

myocardial infarction in the 35-54 year age group, even the lower 99·9% confidence limit of the odds ratio being above 1. Among 55-64 year old men there was no significant difference between smokers and snuff dippers. When all men in the 35-64 year age range were taken together the difference in favour of the snuff dippers was significant.

Figure 2 compares low to moderate and high consumers of tobacco with non-tobacco users. Only the group with high cigarette consumption (over 10 cigarettes per day) had an odds ratio for myocardial infarction significantly above 1. When high consumers of tobacco (>10 cigarettes a day or ≥100 g snuff a week) were compared the odds ratio for myocardial infarction in smokers versus snuff dippers was 1·93 (95% confidence interval 1·17 to 3·20).

Former smokers who did not take snuff had a significantly raised risk of myocardial infarction compared with snuff dippers who had never been regular smokers (odds ratio 1·80; 95% confidence interval 1·04 to 3·11) and with non-smoking former snuff dippers (odds ratio 4·50; 2·72 to 7·47).

Patients who had had a myocardial infarction differed from controls in two possible confounders of tobacco habits: they were more likely to have had nine years' education (415/585 (71%) *v* 247/589 (42%) or less and they were older (mean age 55·9 years *v* 44·9 years). In a logistic regression model including both cases and controls myocardial infarction was the dependent variable. Table II shows that the level of education, age, and regular cigarette smoking were highly significant independent predictors of myocardial infarction, whereas snuff dipping was not. When other cardiovascular risk factors were compared in cigarette smokers and snuff dippers in the control population, similar age adjusted serum concentrations of cholesterol (mean 6·61 *v* 6·59 mmol/l) and blood pressure (mean 131/83 *v* 133/86 mm Hg) were observed, and the age adjusted prevalence of diabetes was about the same (6% *v* 5%).

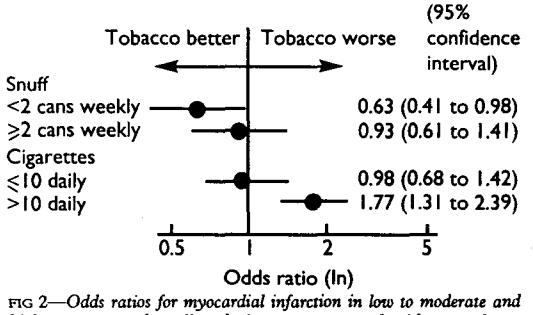

FIG 2—*Odds ratios for myocardial infarction in low to moderate and high consumers of snuff and cigarettes compared with non-tobacco users. Horizontal lines indicate 95% confidence intervals*

TABLE II—*Summary of multiple logistic regression model with myocardial infarction as the dependent variable and tobacco habits and possible confounders as independent variables*

Variable	Parameter estimate	Standard error	p Value
Regular cigarette smoking	0·79	0·17	<0·01
Regular snuff dipping	0·01	0·22	NS
Low level of education (≤9 school years)	0·93	0·15	<0·01
High age	0·95	0·10	<0·01

Data on tobacco use were missing in 44 men who had a myocardial infarction (41 who died and three who survived). Of these, 76% (33) were married, a proportion similar to that in other patients (77%). No other data on background variables were available in this group. Data on tobacco use were available from telephone interviews in 56 of the 141 (40%) men who did not participate in the population survey. Tobacco use tended to be more common in non-participants than in participants and there was a significantly higher proportion of former smokers among non-participants (table III).

TABLE III—*Tobacco consumption among 35-64 year old men selected for screening but not participating in the population survey compared with the participants. Percentages in parentheses*

	Non-participants (n=56)	Participants (n=589)
Regular cigarette smokers*	18 (32)	145 (25)
Regular snuff dippers†	13 (23)	87 (15)
Former smokers	26 (48)‡	154 (26)§
Former snuff dippers	7 (13)	82 (14)
Not presently using tobacco	25 (45)	336 (57)
Never used tobacco	20 (36)	177 (30)

*Including subjects who were both smoking and using snuff.
†Excluding subjects who were also smokers.
‡Data missing in two subjects.
§$p<0·01$ By χ^2 test.

Discussion

The high prevalence of snuff dipping among middle aged men in northern Sweden facilitates population based studies of the possible health hazards of snuff dipping. In our study detailed data on tobacco consumption were available in 93% of all patients who had had a first myocardial infarction and in 81% of the randomly selected control population. A telephone survey of non-participants showed that the pattern of tobacco consumption in non-participants was similar to that of participants, and we conclude that the pattern of tobacco consumption in participants was representative of that of the total background population of 35-64 year old men. The low proportion of missing data on tobacco consumption in patients with

myocardial infarction is unlikely to have affected other results. Even if all the 41 men who had a fatal infarction on whom information on tobacco use was missing had been non-smokers, differences now presented as significant would remain so.

RISKS OF SNUFF DIPPING

We found that among 35-54 year old men snuff dippers had a lower risk of acute myocardial infarction than cigarette smokers. In fact, snuff dippers had no increased risk of myocardial infarction compared with non-tobacco users. In 55-64 year old men the risk of myocardial infarction was not significantly different among snuff dippers, cigarette smokers, and non-tobacco users. A small effect of tobacco use in this age group could have been missed because of lack of statistical power. The limited size of the study also precluded meaningful analyses of mortality from myocardial infarction by tobacco use. A preliminary report on the effects of tobacco use in 136 000 Swedish construction workers suggested that taking snuff is associated with a small but significant increase of the risk of death from cardiac disease (odds ratio 1·2), although the risk was much lower than in smokers.[16] Oral tobacco increases the concentrations of catecholamines in the blood and has immediate sympathomimetic effects.[17-19] In extended studies, we are considering the possibility that snuff dipping has acute arrhythmogenic effects causing sudden death.

Our findings support the contention that taking smokeless tobacco is associated with less serious health hazards than cigarette smoking. Oral tobacco has been shown to be carcinogenic.[20] However, the risk of gastrointestinal and urinary tract cancer is only moderately increased by the use of moist snuff,[7 8 18 21] and is clearly outweighed by the high risk of lung cancer and other respiratory disorders in cigarette smokers.[22] Smokeless tobacco may also increase the risk of peptic ulcer and fetal toxicity.[7]

EFFECTS OF SNUFF

A serious concern about the use of smokeless tobacco is that it may introduce people to cigarette smoking.[1 4 5 23] Oral tobacco gives a prolonged absorption of nicotine, and the overall nicotine exposure is as high or higher than that achieved by cigarette smoking.[24 25] It is, however, still controversial whether smokeless tobacco causes the same (or greater) degree of dependency as cigarettes.[23 26] In the United States the tobacco industry has been very aggressive in marketing smokeless tobacco to young people.[27] This has led to a large decrease in the use of oral tobacco among adolescents and college students[23 28] and it seems that taking smokeless tobacco is often a gateway to smoking in these groups.[5]

The situation may be different in populations where snuff dipping is traditional, as it is among Swedish men.[1] The population in northern Sweden has the lowest prevalence of smoking of all male populations in the WHO MONICA study, whereas women in northern Sweden (in whom snuff dipping is rare) have a high prevalence of smoking.[10] Our data showed that about half of the snuff dippers were former smokers. Together, these observations indicate that in Sweden snuff is often a substitute for smoking tobacco. Nevertheless snuff dipping has been increasing in young Swedish men who have never smoked.[1] The observation that significantly fewer of the cases than the controls had stopped using snuff may perhaps indicate a greater tobacco dependence among patients with myocardial infarction.

The use of smokeless tobacco causes an immediate rise in blood pressure.[17 18] However, in agreement with some[29] but not all[30 31] investigators, we were unable to show that the use of snuff is associated with permanently raised blood pressure. Eliasson *et al* have also shown that the cardiovascular risk factor profile is in other respects generally more favourable in snuff dippers than in cigarette smokers.[29] We recently observed that serum concentrations of antioxidants such as carotenes and ascorbic acid do not differ in snuff dippers and non-tobacco users, whereas they are reduced in cigarette smokers.[32] Possible dietary differences between snuff dippers and cigarette smokers may contribute to the differing risks of myocardial infarction in the two groups.

CONCLUSIONS

Our results may shed some light on the mechanisms underlying the association between cigarette smoking and myocardial infarction. In view of the high serum concentrations of nicotine reached by taking oral tobacco[24 25] our data support the suggestion that carbon monoxide or aromatic hydrocarbon toxicity has an important role in the development of coronary artery disease and myocardial infarction in smokers. These components of tobacco smoke may induce damage to vessel wall cells or enhance the probability of coronary thrombosis by inducing a hypercoagulable state.[33-35]

We have shown that regular snuff dipping is associated with a lower risk of myocardial infarction than regular cigarette smoking in 35-54 year old men. Although we were unable to show any increased risk of myocardial infarction among snuff dippers when compared with non-tobacco users, a considerably larger study than ours is needed to finally rule out any detrimental effects of snuff dipping on the risk of developing ischaemic heart disease and myocardial infarction.

This study was supported by grants from the Swedish Medical Research Council (27X-07192), the Heart and Chest Fund, King Gustaf V's 80th Anniversary Fund, King Gustaf V's and Queen Victoria's Foundation, the 1987 Stroke Fund, and the Joint Committee of the Northern Sweden Health Care Region.

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(Accepted 2 October 1992)

Risk of schizophrenia in adults born after obstetric complications and their association with early onset of illness: a controlled study

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Abstract

***Objective*—To determine whether obstetric complications occur to excess in the early histories of individuals who go on to develop schizophrenia when compared with controls, and to seek clinical correlates of any such excess.**

***Design*—Contemporaneous maternity hospital records were identified and extracted verbatim, and these extracts evaluated for obstetric complications by two independent assessors who were blind to subjects' status.**

***Subjects*—65 patients having an ICD-9 diagnosis of schizophrenia, the records of the previous same sex live birth being deemed to be those of a control subject.**

***Main outcome measure*—Presence of one or more obstetric complications recorded in maternity notes of patients and controls.**

***Results*—When two recognised scales for specifying obstetric complications were used the patients with schizophrenia were significantly more likely than controls to have experienced at least one obstetric complication (odds ratio 2·44, 95% confidence interval 1·08 to 6·03). Patients also showed a greater number and severity of and total score for obstetric complications, fetal distress being the only complication to occur to significant individual excess (present in five (8%) patients, absent in controls). There was a marked sex effect, male patients being more vulnerable (odds ratio 4·24, 1·39 to 12·90) to such complications. Obstetric complications in patients were unrelated to family history or season of birth but were associated with a significantly younger age at onset of illness (mean difference −4·5 years, −1·2 to −7·8 years).**

***Conclusions*—Patients with schizophrenia, particularly males, have an excess of obstetric complications in their early developmental histories, and such complications are associated with a younger age at onset of their disease. Though the data are not conclusive, they also suggest that obstetric complications may be secondary to yet earlier events.**

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BMJ 1992;305:1256-9

Introduction

The personal, social, and economic consequences of schizophrenia make it perhaps the most serious of all psychiatric disorders and are a public health problem of major significance. Though the aetiology of this illness remains obscure, recent evidence continues to point not to the period immediately before the onset of psychotic symptoms, typically in the late teens or 20s, but rather to considerably earlier events.[1] The neurodevelopmental hypothesis of schizophrenia contends that in fetal or immediate postnatal life the establishment of fundamental aspects of cerebral structure and function is subtly but critically disrupted. Diagnostic symptoms of the disorder are then posited to emerge some two decades later only on the full maturation of other physiological systems that are necessary for expressing the consequences of this early developmental perturbation.[2,3]

One element of this hypothesis is evidence that patients with schizophrenia may be more likely than other individuals to have experienced a problematic gestation or delivery and the attendant presumption that such obstetric complications might be one source of early cerebral insult. Were this to be the case the significance of such a putative course of events would be compounded by its evident implications for prophylaxis in terms of further improvements in obstetric and perinatal care. However, existing publications on the issue,[4-12] though provocative, are far from conclusive and are open to several serious methodological criticisms.[11,13] For example, widespread reliance on maternal recall as a retrospective source of information on obstetric complications has been considered prone to both inexactitude and artefact, though our own study[14] indicated it to be of considerably greater validity than had been recognised. Conversely, though "high risk" studies have utilised birth records, all of the subjects' mothers suffered from schizophrenia, so that it may not be possible to generalise to a typical patient population. The use in one study of the maternity records of a modest number of schizophrenic patients was confounded by the use of comparable records only for their "well" siblings, with attendant problems of generalisation to the population at large.[12]

Done and colleagues sought to identify psychiatric morbidity in a population for whom birth histories had been obtained in the 1958 British perinatal mortality survey. They found no evidence that "factors predicting perinatal mortality contribute significantly to causation of schizophrenic illness" among 57 patients and on that basis concluded that obstetric complica-