

Influence of Environmental Factors in Higher Risk of Sudden Infant Death Syndrome Linked With Parental Mental Illness

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Context: Since national risk reduction campaigns have been conducted, sudden infant death syndrome (SIDS) has become increasingly concentrated among disadvantaged families, including those affected by mental illness. However, causal mechanisms specific to this group are poorly understood.

Objectives: To estimate relative risk and compare risk factor prevalence in infants with and without parental psychiatric inpatient history, and to explore effect modification after the 1992 Swedish risk reduction campaign.

Design: National birth cohort. Parental psychiatric admissions, maternal prenatal smoking, obstetric and social risk factors, and cause-specific infant death were ascertained via linkage between national registers.

Setting: The Swedish population, 1978 through 2004.

Participants: All singleton live births (N=2.5 million).

Main Outcome Measure: Incidence of SIDS.

Results: Risk of SIDS was higher with a history of parental inpatient care, especially if both parents were admitted with any mental illness (odds ratio, 6.8; 95% confidence

interval, 4.7-10.0), or if the mother (6.5; 4.9-8.7) or both parents (9.5; 5.5-16.4) had an alcohol/drug disorder. A 2-fold higher risk was also seen if the mother or father was admitted with any psychiatric illness other than alcohol or other drug disorders. Elevated risk persisted even if the last maternal inpatient episode had occurred 5 or more years before the infant's birth. After the national campaign, risk factor prevalence (especially maternal antenatal smoking) remained high in this population, and relative risks therefore increased. During 1992 through 2004, smoking and individual social adversity measures jointly accounted for approximately half the excess risk linked with maternal psychiatric inpatient history, whereas the confounding effects of obstetric factors were minimal.

Conclusions: Tailored approaches are needed to ensure that standard safety advice is effectively communicated to these vulnerable families. In particular, mentally ill pregnant women should be encouraged and better supported to stop smoking. Families with 2 affected parents require particularly strong support. A clearer understanding is needed as to why high risk factor prevalence persists among these parents.

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SUDDEN INFANT DEATH SYNDROME (SIDS) designates a death during the first year of life that remains unexplained after autopsy, death scene investigation, and medical history review.¹ Despite substantial reductions in rates of SIDS during recent decades, it remains the leading cause of infant death beyond the perinatal period in developed countries. Known modifiable risk factors include parental smoking and the infant's sleeping position,^{2,3} and national risk reduction campaigns have successfully targeted these factors in the general population. Recent evidence from the United Kingdom indicates that SIDS has become highly concentrated among socially disadvantaged groups, so that up to three-quarters of all cases now occur among the 15% to 20% of poorest families.¹ The phenomenon is also associ-

ated with parental mental illness, but few studies have specifically examined these effects.⁴⁻⁸ Higher risk has been reported with maternal prenatal⁴ and postnatal^{5,6} depression, maternal schizophrenia,⁷ and severe parental mental illness per se; a recent Danish study reported a 7-fold elevation in risk if both parents had been admitted for psychiatric treatment.⁸ However, the causes of this excess risk are poorly understood. Adjustments for clinical factors (eg, smoking, previous pregnancies, gestational age)⁴⁻⁷ and social factors (eg, marital status, deprivation, ethnicity)^{5,6} have been made, but with arguably too few exposed cases to support comprehensive multivariate analyses: n=7,⁴ n=10,⁷ n=13,⁶ and n=15.⁵

National cohort studies are limited by a lack of detailed prospectively collected data concerning the antecedents and circumstances of these deaths. Nonethe-

less, linked Swedish registers enabled us to study SIDS risk with parental mental illness in the context of important clinical and social risk factors, such as maternal smoking, obstetric factors, and social adversity, using a larger and richer data set than previously available. We aimed to (1) replicate Danish findings of elevated risk with any maternal or paternal admission, particularly if both parents had been admitted for any psychiatric reason or the mother was diagnosed as having an alcohol/drug disorder⁸; (2) assess effects of time since last maternal inpatient episode before childbirth; (3) compare SIDS risk factor distributions among infants with and without parental admission history; (4) explore potential effect modification by period (1992-2004 vs 1978-1991); and (5) undertake multivariate adjustment for clinical and social risk factors.

We hypothesized that risk factors (particularly maternal smoking and social adversity) would be more common in this group, and that they would partly explain higher risks associated with parental mental illness. We predicted relative risks to be higher in the later years of the study period, in line with falling rates overall and an increasing concentration of risk factors and cases among disadvantaged families.¹ Finally, we expected higher risks among infants whose mothers had last received inpatient psychiatric care in the year preceding birth (indicating serious ongoing illness) rather than at some earlier time.

METHODS

STUDY COHORT

We obtained prior approval from the research ethics committees of the Karolinska Institutet, Stockholm, Sweden, and the University of Manchester, Manchester, England. The following national registers and databases, held by the National Board of Health and Welfare and Statistics Sweden, were linked by means of unique registration numbers: (1) Multigeneration Register and Population Register: dates of birth, death, immigration, and emigration, and infant-to-parent linkage; (2) Medical Birth Register: maternal prenatal smoking and obstetric factors for all births since 1973, and singleton vs multiple birth status; (3) National Patient Register: hospital discharges by diagnosis, with virtually complete national coverage of all public inpatient psychiatric care from 1973 (Swedish private inpatient psychiatric care is rare); (4) Cause of Death Register; and (5) Population and Housing Census (every 5 years, 1960-1990), Total Income Register (1985, 1990, 1995, and 2000), and longitudinal integration database for health insurance and labor market studies (1995 and 2000); these last two sources provided our social adversity measures.

Initially, we derived a cohort of all live births from January 1, 1978, through December 31, 2004 (N=2.69 million). Linkage to the Medical Birth Register was 99.4% complete and, as in other studies,⁷⁻¹⁰ we excluded multiple births (2.5%) because of lack of statistical independence among these sets. Infants who did not complete a full year of follow-up because of emigration (0.3%) were excluded to avoid survival-time bias in our logistic regression models. We excluded infants whose mother or father did not reside in Sweden during the entire 5-year period before December 31, 1977 (4.5%), to ensure that we had complete recent psychiatric inpatient histories for all parents. This approach, as opposed to excluding infants whose

parent or parents were born abroad, meant that immigrants were retained in the analyses to a representative degree. We conducted our final analyses on 2 480 320 live births.

EXPOSURES AND OUTCOMES

Psychiatric illnesses and cause-specific infant deaths were classified by means of the 8th, 9th, or 10th revision of the *International Classification of Diseases: ICD-8* (1969-1986),¹¹ *ICD-9* (1987-1996),¹² and *ICD-10* (1997-2005).¹³ On the basis of primary or secondary diagnoses entered in the National Patient Register, which also records physical diseases, the following codes were used to delineate psychiatric illnesses: (1) any psychiatric diagnosis: *ICD-8* codes 290 to 315, *ICD-9* codes 290 to 319, and *ICD-10* codes F00 to F99; (2) nonaffective psychoses: *ICD-8* codes 295, 297, 298.20 to 298.99, and 299.99, *ICD-9* codes 295, 297, and 298C-Z, and *ICD-10* codes F20 to F29; (3) affective psychoses: *ICD-8* codes 296.10 to 296.88, *ICD-9* codes 296C to 296W, and *ICD-10* codes F30.2, F31, F32.3, and F33.3; and (4) alcohol/drug disorders: *ICD-8* codes 291, 294.30, 303, and 304, *ICD-9* codes 291, 292, 303, 304, 305A, and 305X, and *ICD-10* codes F10 to F16 and F18 to F19.

We generated 2 broad mutually exclusive categories among the affected parents (history of admission with alcohol/drug disorders vs any psychiatric illness other than alcohol/drug disorders) to assess the extent to which any observed excess risk linked with parental admission could be explained by alcohol/drug disorders.

Follow-up was for 1 year from birth (up to December 31, 2005, for infants born on December 31, 2004, the final day of the cohort). We included only cases with an assigned underlying cause of death of SIDS^{10,14,15} by means of *ICD-8* code 795, *ICD-9* code 798.0, and *ICD-10* code R95. A small percentage (0.6%) of all births had no registered father. Paternal identity is automatically registered when Swedish married women give birth, but not so with unmarried mothers. The degree of missing paternal identity was much greater among SIDS cases (10.5%) and other infant deaths (18.0%) than among surviving infants.

COVARIATES

We categorized the 27-year birth cohort into 2 almost-equal periods, 1978 through 1991 vs 1992 through 2004, in line with the 1992 Swedish SIDS risk reduction campaign.^{16,17} Time period was assessed both as a potential confounder and as an effect modifier. Smoking at antenatal booking was recorded in the Medical Birth Register from 1983 as nonsmoker, 1 to 9 cigarettes per day, or 10 or more cigarettes per day, with 93.9% completeness. We had no measure of maternal smoking postpartum or of paternal smoking at any time. We also adjusted for obstetric factors recorded in this register: maternal age (<20, 20-24, or ≥25 years), parity (1, 2, or ≥3), premature birth (<37 weeks), low birth weight (<2500 g), small for gestational age (<2 SDs¹⁸), small head circumference (<32 cm¹⁹), and low Apgar score at 1 or 5 minutes (0-6 vs ≥7). Each was 99% to 100% complete during 1978 through 2004, except for small head circumference (96.4% complete).

Sociodemographic variables were also assessed. From the Medical Birth Register we obtained an almost 100% complete measure of birth place (3 largest urban centers [Stockholm, Gothenburg, and Malmö] vs elsewhere) and parental noncohabitation at antenatal booking (93.7% complete, from 1983). Parents' country of birth (Sweden vs abroad) was taken from the Multigeneration Register (99%-100% complete). Low socioeconomic position was measured as an adult in the household receiving social welfare payment and by the mother's educational attainment, given at 5-year intervals from the Population and Housing Cen-

Table 1. ORs for SIDS Linked With Parental Psychiatric Admission by Diagnostic Group

| Diagnostic Group ^a | No. of Deaths | Risk per 1000 Live Births | Adjusted OR ^b (95% CI) |
|--|---------------|---------------------------|-----------------------------------|
| Maternal effects | | | |
| Mother not admitted | 1413 | 0.6 | 1 [Reference] |
| Admitted with any diagnosis | 118 | 1.7 | 3.1 (2.6-3.8) |
| Nonaffective psychoses ^c | 6 | 1.0 | 1.8 (0.6-3.9) |
| Alcohol/drug disorders | 49 | 3.3 | 6.5 (4.9-8.7) |
| All diagnoses other than alcohol/drugs | 69 | 1.2 | 2.3 (1.8-2.9) |
| Paternal effects | | | |
| Father not admitted | 1288 | 0.5 | 1 [Reference] |
| Admitted with any diagnosis | 82 | 1.3 | 2.5 (2.0-3.1) |
| Nonaffective psychoses ^c | 6 | 1.1 | 2.0 (0.7-4.4) |
| Alcohol/drug disorders | 46 | 1.5 | 2.8 (2.1-3.8) |
| All diagnoses other than alcohol/drugs | 36 | 1.1 | 2.1 (1.5-3.0) |
| Both parents | | | |
| Neither parent admitted | 1216 | 0.5 | 1 [Reference] |
| Admitted with any diagnosis | 27 | 3.4 | 6.8 (4.7-10.0) |
| Alcohol/drug disorders | 13 | 4.8 | 9.5 (5.5-16.4) |
| All diagnoses other than alcohol/drugs | 14 | 2.7 | 5.4 (3.2-9.2) |

Abbreviations: CI, confidence interval; OR, odds ratio; SIDS, sudden infant death syndrome.

^aDiagnostic groups are not mutually exclusive (except that alcohol/drug disorders + all diagnoses other than alcohol/drugs = any psychiatric diagnosis).

^bOdds ratios are adjusted for period of birth: 1978 through 1991 vs 1992 through 2004.

^cModels are not adjusted for period of birth owing to sparse data and exact CIs are applied, and we could not estimate effects with both parents admitted for nonaffective psychoses.

sus, the longitudinal integration database, and the Total Income Register. To eliminate potential reverse causality bias,²⁰ we extracted these data according to the earliest available measurement year before the infant's birth, and we derived variables only for mothers who reached 20 years of age in that year to ensure their complete eligibility for the measure. Social welfare data were applied to births from January 1, 1986, onward (96.8% complete), and maternal educational data were applied to births from January 1, 1992 (93.9% complete), with a low level defined as failure to complete upper secondary schooling. In the early 1990s, approximately 70% of the Swedish population completed this level (reaching 80% by 2000).

STATISTICAL ANALYSES

Statistical analyses were performed with Stata software, version 10 (StataCorp, College Station, Texas). Exposure was defined stringently so that first maternal/paternal admission must have occurred before the infant's birth. Risks were calculated as number of deaths at 0 to 364 days by number of live births per 1000. We fitted unconditional logistic regression models because, with rare outcomes, the odds ratios derived are equivalent to relative risk estimates.²¹ Multiple SIDS events per family were very rare (0.5% of all cases in the cohort). Nonetheless, standard errors were corrected for any sibship-clustering effects by means of the Huber-White estimator.²² For effect estimates calculated with sparse data (≤ 10 exposed deaths), we applied conservative exact confidence intervals.

RESULTS

SIDS RISKS BY PARENTAL ADMISSION HISTORY AND DIAGNOSTIC GROUP

From 1978 through 2004, the prevalence of parental psychiatric admission before the infant's birth was 2.8% for mothers, 2.6% for fathers, 4.8% for 1 parent only, and 0.3% for both parents. Among the 69 995 mothers with admission histories, 21.0% received diagnoses of

alcohol/drug disorders; 8.3%, nonaffective psychoses; and 3.2%, affective psychoses. The equivalent percentages among the 65 092 admitted fathers were 47.7%, 8.4%, and 3.1%, respectively. The other diagnoses resulting in parental admission consisted mostly of nonpsychotic depression, neurotic and stress-related conditions, childhood psychoses, autism, behavioral (and other developmental) disorders, and personality (and related) disorders.

A total of 1531 SIDS cases occurred in the whole cohort at a rate of 0.6 per 1000 live births. In 11.2% of all cases there had been at least 1 parental psychiatric inpatient admission before the birth (with almost half of this group having been admitted for alcohol/drug disorders). There were 118 cases (1.7 per 1000 live births) with maternal admission histories and 82 cases (1.3 per 1000 live births) with paternal admission histories. Our analyses excluded the few cases in which first parental admission occurred between the infant's birth and death (maternal, 6 cases; paternal, 3 cases).

Table 1 shows relative risks of SIDS estimated as odds ratios. An elevated risk was seen for maternal and for paternal admission with any psychiatric diagnosis, and there was an approximate 7-fold increase if both parents were admitted. Table 1 also presents relative risks linked with specific parental diagnostic groups. There was no significant evidence of higher risk with maternal or paternal nonaffective psychoses. We also examined parental affective psychoses (results not presented), but there were too few SIDS cases for relative risk estimation (maternal, 2 cases; paternal, 1 case). Significantly higher risks were seen with parental alcohol/drug disorders (with a 6.5-fold higher risk linked to maternal admission). The greatest risk (4.8 per 1000 live births) was seen if both parents were admitted with alcohol/drug disorders: a 9.5-fold increase vs the general population. There was also a 2-fold elevated risk among infants with mothers or fa-

Table 2. ORs for SIDS Stratified by Number of Years Since Last Maternal Psychiatric Inpatient Episode Before Birth

| Diagnostic Group and Years Since Last Inpatient Episode | No. of Deaths | Risk per 1000 Live Births | Adjusted OR ^a (95% CI) |
|---|---------------|---------------------------|-----------------------------------|
| Admitted with any diagnosis | | | |
| <1 | 12 | 1.8 | 3.3 (1.9-5.8) |
| 1-4 | 46 | 1.8 | 3.1 (2.3-4.1) |
| ≥5 | 60 | 1.6 | 3.1 (2.4-4.1) |
| Alcohol/drug disorders | | | |
| <1 | 8 | 5.2 | 9.0 (4.5-18.1) |
| 1-4 | 25 | 3.6 | 6.9 (4.6-10.2) |
| ≥5 | 16 | 2.6 | 5.4 (3.3-8.8) |
| All diagnoses other than alcohol/drugs | | | |
| <1 | 4 | 0.8 | 1.4 (0.5-3.9) |
| 1-4 | 21 | 1.1 | 1.8 (1.2-2.8) |
| ≥5 | 44 | 1.4 | 2.7 (2.0-3.7) |

Abbreviations: CI, confidence interval; OR, odds ratio; SIDS, sudden infant death syndrome.

^aOdds ratios are adjusted for period of birth: 1978 through 1991 vs 1992 through 2004.

thers admitted for any psychiatric diagnosis other than alcohol/drug disorders. If both parents had admission histories without alcohol/drug disorders, a more than 5-fold higher risk was seen.

RISKS STRATIFIED BY YEARS SINCE LAST MATERNAL INPATIENT EPISODE BEFORE BIRTH

Among infants with mothers admitted for any psychiatric diagnosis, an elevated risk of 1.8 per 1000 live births was found with last maternal episode within a year and 1 to 4 years of the infant's birth, with risk falling only slightly to 1.6 per 1000 live births if the last episode was 5 or more years before the birth (**Table 2**). With adjustment for period effects, the relative risk was at least 3 in each time stratum. Categorizing maternal admissions into 2 broad diagnostic groups (alcohol/drug disorders vs all other psychiatric illnesses) produced divergent trends in relative risk by timing of the last episode. For infants whose mothers were admitted with alcohol/drug disorders, risk was highest if the last episode was within a year of the birth and lowest if it was 5 years or more previously, and vice versa among infants whose mothers had been admitted with other types of psychiatric illness. Although neither diagnostic group-specific test was significant, the interaction term indicated differential trends in risk over time since last episode between these groups ($P = .05$).

RISK FACTOR PREVALENCE BY EXPOSURE GROUP

Table 3 shows prevalence across the study period (or for all years with available data). Risk of SIDS was no higher among infants whose mothers or fathers were born abroad, or for those born in the 3 largest cities, and so these variables were discounted as risk factors in this cohort. There was a somewhat higher prevalence of

obstetric risk factors with parental mental illness compared with the general population. The prevalence of having at least 1 obstetric risk factor was 21.8% in infants with mothers admitted for any psychiatric reason and 24.8% in those with 2 admitted parents, compared with 15.9% among infants with neither parent admitted. There was a markedly higher prevalence of maternal smoking at antenatal booking and of social adversity, especially with both parents admitted (or with maternal alcohol/drug disorder). We also assessed maternal smoking rates at booking among infants whose fathers had been admitted (results not shown in Table 3); maternal smoking was almost as prevalent in this group (38.6%) as in the all maternal admissions group (41.1%). Among infants with 2 admitted parents (and with mothers admitted for alcohol/drug disorders), smoking at booking was approximately 3 times more common than in the general population, and prevalence of adverse social circumstances (parents not cohabiting at booking, low maternal educational attainment, social welfare receipt) was between 4 and 7 times higher. With such a large sample size, the prevalence was significantly higher ($P < .001$) among the exposed groups (mother admitted or both parents admitted) than the unexposed groups (mother not admitted or neither parent admitted) for each of the risk factors shown in Table 3, with the exception of male infant sex.

ASSESSMENT OF EFFECT MODIFICATION BY TIME PERIOD AND BY FAMILY ENVIRONMENT

The prevalence of risk factors declined after the national risk reduction campaign. The maternal smoking rate at antenatal booking fell by almost half in the general population, whereas in the exposed groups, even from higher baseline rates, there was a smaller percentage reduction. The highest-risk groups saw the smallest percentage reductions between periods: for example, both parents admitted (18.5% reduction) compared with neither parent admitted (49.0%). Rates of maternal smoking and social adversity were high during both periods if 2 parents were admitted or if the mother was treated for an alcohol/drug disorder. Thus, in the period after the campaign, more than half of the mothers in these 2 high-risk groups reported smoking at booking.

Table 4 shows strong effect modification by period of birth. Among infants with any parental psychiatric admission history (mother, father, or both parents), the relative risk increased significantly after the campaign. Maternal and paternal effects showed a more than 4-fold higher risk in the later period. In the earlier period there had been a parental admission before the birth in 8.0% of all SIDS cases, whereas after the campaign this figure rose to 20.1%. The increase in relative risk was especially marked if both parents were admitted (with the odds ratio increasing from 3.9 to 14.8).

Parental mental illness and greater maternal burden may interact to produce even higher risk. For example, SIDS risk could be especially elevated with mentally ill single mothers or with those caring for more than 1 child. We therefore tested for effect modification (of the maternal admission effect) by parity greater than 1 and by

Table 3. Prevalence of SIDS Risk Factors by Parental Psychiatric Admission Status

| SIDS Risk Factors ^a | Risk per 1000 Live Births ^b | Prevalence of Risk Factors by Parental Admission Status, % ^c | | |
|---------------------------------------|--|---|--------------------------------|-----------------------------------|
| | | Neither Parent Admitted | Mother Admitted, Any Diagnosis | 2 Parents Admitted, Any Diagnosis |
| Births, 1978-2004 | | (n=2 339 659) | (n=69 995) | (n=7901) |
| Male infant sex | 0.7 | 51.4 | 51.1 | 50.7 |
| Parity >1 | 0.8 | 58.0 | 60.5 | 62.3 |
| Maternal age <20 y | 1.5 | 2.6 | 4.6 | 4.5 |
| Premature birth | 1.4 | 4.9 | 7.9 | 9.4 |
| Low birth weight | 1.9 | 3.2 | 5.6 | 7.6 |
| Small for gestational age | 1.5 | 2.6 | 4.0 | 5.4 |
| Small head circumference | 1.2 | 6.9 | 9.5 | 11.9 |
| Low Apgar score at 1 or 5 min | 0.7 | 4.3 | 5.5 | 5.6 |
| ≥1 Obstetric risk factor ^d | 1.0 | 15.9 | 21.8 | 24.8 |
| Births, 1983-2004 | | (n=1 933 831) | (n=61 748) | (n=6821) |
| Smoking at antenatal booking | 1.5 | 19.1 | 41.1 | 62.1 |
| Parents not cohabiting at booking | 1.4 | 4.4 | 16.0 | 25.3 |
| Births, 1986-2004 ^e | | (n=1 543 474) | (n=48 368) | (n=5222) |
| Social welfare receipt | 1.1 | 7.3 | 28.0 | 50.5 |
| Births, 1992-2004 ^e | | (n=1 016 453) | (n=34 498) | (n=3456) |
| Low maternal educational status | 0.8 | 11.2 | 29.9 | 45.7 |

Abbreviation: SIDS, sudden infant death syndrome.

^aSIDS risk in the whole national birth cohort (by period of birth, according to data availability).

^bWith the exception of male infant sex, each of the SIDS risk factors presented had significantly ($P < .001$) greater prevalence in the exposed populations (mother admitted or 2 parents admitted) than in the respective reference groups (mother not admitted or neither parent admitted).

^cRisk factor data are 99% to 100% complete except for head circumference (96.4%), smoking (93.9%), parental noncohabitation (93.7%), social welfare receipt (96.8%), and education (93.9%).

^dAt least 1 of the following factors: maternal age younger than 20 years, prematurity, low birth weight, small for gestational age, small head circumference, and low Apgar score at 1 or 5 minutes.

^eData are restricted to maternal age 20 years or older in the year in which the risk factor was measured.

Table 4. Effect Modification by Period of Birth: Before and After 1992 National SIDS Risk-Reduction Campaign

| Maternal/Paternal Effects and Period of Birth | No. of Deaths | Risk per 1000 Live Births | OR (95% CI) | Effect Modification: Ratio of ORs (95% CI) [P Value] |
|---|---------------|---------------------------|-----------------|--|
| Maternal admission ^a | | | | |
| 1978-1991 | 63 | 2.1 | 2.5 (1.9-3.3) | 1.7 (1.2-2.6) [.005] |
| 1992-2004 | 55 | 1.4 | 4.4 (3.3-5.8) | |
| Paternal admission ^a | | | | |
| 1978-1991 | 37 | 1.2 | 1.6 (1.2-2.2) | 2.8 (1.8-4.5) [<.001] |
| 1992-2004 | 45 | 1.3 | 4.6 (3.3-6.2) | |
| Both parents admitted ^a | | | | |
| 1978-1991 | 11 | 2.9 | 3.9 (2.1-7.0) | 3.8 (1.8-8.4) [.001] |
| 1992-2004 | 16 | 3.9 | 14.8 (9.0-24.5) | |

Abbreviations: CI, confidence interval; OR, odds ratio; SIDS, sudden infant death syndrome.

^aParental admission with any psychiatric diagnosis.

parents not cohabiting, but in both cases the interaction term was not close to being significant ($P = .91$ and $P = .76$, respectively).

CONFOUNDING BY OBSTETRIC FACTORS, MATERNAL SMOKING, AND SOCIAL ADVERSITY

We assessed the obstetric factors separately, and each one had minimal confounding effect. However, maternal smoking at antenatal booking had a considerable confounding influence, and the strength of this effect was greater during 1992 through 2004 than during 1983 through 1991. The results presented in **Table 5** relate to maternal admissions only, but, during 1992

through 2004 and with both parents admitted, the adjustment for maternal smoking was stronger still: from an odds ratio of 14.1 to 5.6. Social adversity also had some additional confounding effect. We adjusted for maternal smoking plus 1 social adversity measure (parents not cohabiting, social welfare receipt, or low educational attainment) in the same model. In each case these combined adjustments reduced the odds ratio with maternal admission by around a half, from an approximate 4-fold to a 2-fold increase in risk. Additional multivariate analyses were fitted with combined adjustment for smoking, multiple social adversity measures, and low birth weight or at least 1 obstetric risk factor. These were flawed because of multiple zero cell

Table 5. Confounding Effects of Maternal Smoking and Social Adversity Factors by Period of Birth: All Maternal Psychiatric Admissions

| Period of Birth and Social Adversity Factors | No. of Infants Included in Models (% Complete) | OR (95% CI) | | | |
|--|--|-------------------|------------------------------------|------------------------------------|---|
| | | Unadjusted Effect | Adjusted for Maternal Smoking Only | Adjusted for Social Adversity Only | Adjusted for Social Adversity and Smoking |
| Before 1992 | | | | | |
| Parents not cohabiting at booking ^a | 791 932 (90) | 2.5 (1.8-3.4) | 1.9 (1.4-2.6) | 2.2 (1.6-3.1) | 1.8 (1.3-2.5) |
| Social welfare receipt ^b | 506 958 (91) | 2.7 (1.8-4.0) | 2.1 (1.4-3.1) | 2.1 (1.4-3.2) | 1.8 (1.2-2.7) |
| 1992-2004 | | | | | |
| Parents not cohabiting at booking ^a | 1 070 751 (91) | 4.3 (3.1-5.8) | 2.5 (1.8-3.4) | 3.6 (2.6-4.9) | 2.3 (1.7-3.2) |
| Social welfare receipt ^b | 985 178 (91) | 4.4 (3.1-6.2) | 2.5 (1.8-3.6) | 3.5 (2.4-4.9) | 2.2 (1.6-3.2) |
| Low maternal educational attainment ^c | 960 359 (89) | 4.1 (2.9-5.8) | 2.4 (1.7-3.5) | 3.1 (2.2-4.5) | 2.2 (1.5-3.2) |

Abbreviations: CI, confidence interval; OR, odds ratio.

^aData are available for births during 1983 through 2004 only.

^bData are available for births during 1986 through 2004 only (and restricted to maternal age ≥ 20 years in the year in which the risk factor was measured).

^cData are available for births during 1992 through 2004 only (and restricted to maternal age ≥ 20 years in the year in which the risk factor was measured).

counts with sparse event data, and sizeable proportions of missing data when several incomplete covariates were combined, and so they are not presented herein. However, as with the more robust models shown in Table 5, they suggest an adjusted odds ratio of approximately 2 in each case. Thus, even with multiple confounder adjustment, a considerable degree of residual confounding by unmeasured factors was indicated.

COMMENT

KEY FINDINGS

In a 27-year national birth cohort, we found significantly higher SIDS risks among infants whose mothers or fathers had received psychiatric inpatient care. A particularly high risk was seen if both parents had been admitted for any psychiatric reason or if the mother, or both parents, had been diagnosed as having an alcohol/drug disorder. Additional analyses (not presented herein) showed that maternal, but not paternal, alcohol/drug disorders were also linked with elevated risk of infant death owing to all other natural causes, and of unnatural-cause death, albeit with smaller effect sizes. Furthermore, a 2-fold elevation in SIDS risk with parental psychiatric admission with illnesses other than alcohol/drug disorders was also indicated. Thus, there was no evidence of specificity in the association between parental alcohol/drug disorders and higher SIDS risk. We found no evidence of higher risk with parental affective or non-affective psychoses, perhaps because of a lack of power to detect modest effect sizes in these groups. In relation to all admitted mothers, a consistent 3-fold increase in risk was seen irrespective of whether the last inpatient episode had occurred within a year of the birth or some years previously.

As in other developed countries, Swedish national SIDS rates have declined in recent decades, but the relative risks linked with parental mental illness increased after the 1992 risk reduction campaign. In approximately a fifth of all cases after the campaign, at least 1 parent was admitted with psychiatric illness before the

infant's birth, and this proportion is likely to have been substantially higher if we had been able to include community-treated mental illnesses. During 1992 through 2004, with 3.4% of mothers having been admitted before the infant's birth and an odds ratio of 4.4, a population-attributable fraction of approximately 10% is indicated from our results. Therefore, the population impact of maternal mental illness on SIDS risk may be considerable. Inclusion of more common forms of mental illness, occurring before and after the infant's birth, suggests a much greater population impact. For example, a prospective study in New Zealand⁵ reported an odds ratio of 4 linked with postnatal depression (prevalence, 16%), indicating a population-attributable fraction of more than 30%. However, causality cannot be established from these study designs, and so these estimates should be treated cautiously.²³

Known SIDS risk factors in the general population, particularly maternal smoking in early pregnancy and social adversity measures, continued to cluster strongly in families with parental mental illness after the Swedish national campaign. Thus, rates of maternal smoking fell in all groups, but to a far lesser extent with maternal or paternal admission, and smoking prevalence remained high if both parents had been admitted or if the mother had an alcohol/drug disorder. In the later period, maternal smoking in early pregnancy and individual social adversity measures jointly accounted for approximately half the excess risk associated with maternal psychiatric admission. The confounding effects of obstetric risk factors, however, remained marginal throughout the study period. Our multivariate adjustments did not account for important unmeasured confounders, but there may also have been some over-adjustment if worsening social adversity and failure to quit smoking lie directly on a causal pathway between mental illness and higher SIDS risk.

These findings are only partially consistent with previous evidence. A national Danish study also reported higher risk with parental admission,⁸ and in both Denmark and Sweden there was a 7-fold elevation in risk if both parents had been admitted or the mother had an

alcohol/drug disorder. Denmark implemented its own national risk reduction campaign in 1991,²⁴ but, unlike in Sweden, there was no evidence of a subsequent change in relative risk with parental mental illness.⁸ This difference in results between neighboring countries may have occurred because maternal smoking rates remained generally high in Denmark after the campaign.^{24,25}

POSSIBLE CAUSAL MECHANISMS

Our study gives new insight into possible reasons for higher SIDS risk among infants with mentally ill parents. Our measures of social adversity, including single parenthood, low levels of educational attainment, and social welfare receipt, had some confounding influence. Consistent with our findings, a recent systematic review found that low socioeconomic position is an independent predictor of SIDS risk.²⁶ Our results show that relative social differences have an important confounding effect, even in an affluent country like Sweden.¹⁷ Socioeconomic position could act as a marker for unmeasured causal mechanisms in 2 ways. First, key health promotion messages may currently be communicated in such a way that they mainly reach better-educated parents.²⁷ Second, psychosocial stress may prevent parents from acting on key safety messages. For example, highly stressed parents may have difficulty coping if their infant's sleeping pattern becomes disrupted when placed in the supine position,^{28,29} and they may also find it harder to stop smoking. We assessed 2 potential markers of heightened maternal burden (caring for more than 1 child and single parenthood), but neither modified the effect of maternal admission in this cohort. Even if the last maternal psychiatric admission had been 5 or more years before the birth of the infant, we found that risk remained significantly elevated. This could mean that severe mental illnesses had not remitted among affected mothers experiencing long periods without inpatient care before the birth, or it could reflect more general psychosocial adversities encountered by these families. Thus, intractable social problems, rather than effects directly linked with acute psychopathologic factors around the time of childbirth, might underpin much of the elevated risk.

With widespread adoption of the supine sleeping position for infants, maternal antenatal smoking is now the major SIDS risk factor in the general population.^{25,30,31} It had a major influence throughout our study period, although its confounding effect became stronger after the national risk reduction campaign. The campaign emphasized the importance of smoking cessation as well as sleeping position, but more than a third of women with psychiatric histories reported smoking in 1992 through 2004 (and the prevalence was higher still if both parents had been admitted or if the mother had an alcohol/drug disorder). Our only smoking measure was based on maternal self-report at antenatal booking. One study reported that only 30% of Swedish women stop smoking after their first antenatal visit,³² and so the increased prevalence we report may apply throughout pregnancy and infancy (albeit at a somewhat lower level). It is difficult to disentangle pre-

natal vs postpartum smoking effects because most infants are exposed during both periods. The Nordic Epidemiological SIDS Study indicated that the effect is specific to maternal smoking in pregnancy, and that infants' exposure to parental smoking after birth is unlikely to have a major influence.²⁵ Infants in that study had a 4-fold higher risk with prenatal or postpartum exposure to maternal smoking, but there was no effect of paternal smoking postpartum without maternal smoking in pregnancy (odds ratio, 0.8). Several mechanisms could explain the prenatal smoking effect, including reduced oxygen and nutrient availability to the fetus, altered ventilatory and awakening responses to hypoxia, decreased lung volume and compliance, poorer development of the neonatal airway, impairment of the immune system, and greater susceptibility to airway infections and other diseases.^{2,25,33} An estimated one-third of all SIDS cases might be prevented if in utero smoking exposure was eliminated.³⁴

STRENGTHS AND LIMITATIONS

Important strengths of our study include record linkage between multiple national registers, a large sample size for investigation of rare exposures and outcomes, absence of information or recall bias, and complete follow-up. In particular, the Swedish registers combined vital statistics data (births, deaths, and parent-infant linkage) with clinical data (obstetric and psychiatric) and sociodemographic measures. Assessment of all types of admitted parental psychiatric illnesses enabled us to conduct a comprehensive investigation of this rare outcome, compared with previous Swedish studies that have focused on parental schizophrenia but have lacked power to investigate SIDS as a specific cause of death.^{9,35}

The study had 2 main limitations. First, we were unable to measure some key modifiable risk factors, especially prone infant sleeping position³⁶ and infant bed sharing with parents who smoke or who are intoxicated with alcohol.³⁷ Important contextual factors like these are commonly missing from registry studies.³⁸ However, our findings concerning prenatal maternal smoking and social adversity suggest that the prevalence of the unmeasured risk factors may also be higher in these parents. Second, our measures were imperfect. We used a broad definition of parental mental illness (all inpatient admissions) including alcohol/drug disorders, but our results cannot be generalized to the far larger community-treated psychiatric population. Equivalent information is not available in Sweden, but a Danish validation study indicated that alcohol/drug disorders are significantly underdiagnosed in their national psychiatric register.³⁹ The social adversity covariates were measured at 5-year intervals only, and their confounding effects may therefore be underestimated. A greater concern is potential misclassification of cause of death⁴⁰ without retrospective verification. However, Swedish classification is comparatively accurate because virtually all infants dying outside of hospitals undergo forensic autopsy.²⁸ A previous national study reported that autopsies were performed on 97% of all babies with a SIDS diagnosis during 1983 through 1990,¹⁰ whereas

data for 1997 through 2004 (from the National Board of Health and Welfare) show a mean autopsy rate of 98%. In the United States⁴¹ and the United Kingdom,⁴² there is evidence of a growing reluctance to diagnose SIDS where co-sleeping with a parent is discovered. During 1997 through 2004 we also compared numbers of SIDS cases (ICD-10 code R95) against "other ill-defined and unspecified causes" (code R99.0). Only 10 infants were assigned that code (vs 215 SIDS cases), indicating no evidence of a similar trend in Sweden.

CONCLUSIONS

Standard SIDS risk reduction messages appear to be ineffective in reaching the most vulnerable families, including those with serious parental mental illness and especially those with alcohol/drug disorders. We recommend the delivery of tailored health education messages to mentally ill parents and parents-to-be, using client-focused approaches by trained staff. Professionals working in mental health, child health, and primary care should strive to provide continuing support to affected parents to help them take advantage of this advice. In particular, parents should be strongly encouraged and supported to stop smoking at antenatal booking and afterward. Families with 2 mentally ill parents will require particularly high levels of ongoing support. Smaller, but more detailed, retrospective case-control studies should be conducted to investigate the specific circumstances of death in families with parental mental illness, to further advance the findings from our large cohort study. Qualitative research is also needed to understand why risk factor prevalence remains so high among these parents.

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Correction

Error in Dosage and Degree. In the article "A Randomized Placebo-Controlled Clinical Trial of 5 Smoking Cessation Pharmacotherapies" published in the November issue of *Archives* (2009;66[11]:1253-1262), there was an error in the "Procedures" section. On page 1255, in the second and third lines of the right column, the dosage of bupropion SR should be "150 mg twice daily for 9 weeks total" instead of "150 mg twice weekly for 9 weeks total." In the byline, Michael C. Fiore was listed as having an MD and PhD. His actual degrees are an MD, MPH, and MBA.