

Articles

Sudden unexplained infant death in 20 regions in Europe: case control study

R G Carpenter, L M Irgens, P S Blair, P D England, P Fleming, J Huber, G Jorch, P Schreuder

Summary

Background After striking changes in rates of sudden unexplained infant death (SIDS) around 1990, four large case-control studies were set up to re-examine the epidemiology of this syndrome. The European Concerted Action on SIDS (ECAS) investigation was planned to bring together data from these and new studies to give an overview of risk factors for the syndrome in Europe.

Methods We undertook case-control studies in 20 regions. Data for more than 60 variables were extracted from anonymised records of 745 SIDS cases and 2411 live controls. Logistic regression was used to calculate odds ratios (ORs) for every factor in isolation, and to construct multivariate models.

Findings Principal risk factors were largely independent. Multivariately significant ORs showed little evidence of intercentre heterogeneity apart from four outliers, which were eliminated. Highly significant risks were associated with prone sleeping (OR 13.1 [95% CI 8.51–20.2]) and with turning from the side to the prone position (45.4 [23.4–87.9]). About 48% of cases were attributable to sleeping in the side or prone position. If the mother smoked, significant risks were associated with bed-sharing, especially during the first weeks of life (at 2 weeks 27.0 [13.3–54.9]). This OR was partly attributable to mother's consumption of alcohol. Mother's alcohol consumption was significant only when baby bed-shared all night (OR increased by 1.66 [1.16–2.38] per drink). For mothers who did not smoke during pregnancy, OR for bed-sharing was very small (at 2 weeks 2.4 [1.2–4.6]) and only significant during the first 8 weeks of life. About 16% of cases were attributable to bed-sharing and roughly 36% to the baby sleeping in a separate room.

Interpretation Avoidable risk factors such as those associated with inappropriate infants' sleeping position, type of bedding used, and sleeping arrangements strongly suggest a basis for further substantial reductions in SIDS incidence rates.

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Medical Statistics Unit, Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK (Prof R G Carpenter PhD, P D England PhD); **Medical Birth Registry of Norway, University of Bergen, Norway** (Prof L M Irgens PhD, P Schreuder BA); **Institute of Child Health, Royal Hospital for Children, Bristol, UK** (Prof P Fleming FRCPCH, P S Blair PhD); **University Hospital for Children and Youth, Utrecht, Netherlands** (Prof J Huber FRCP); **Clinic for General Pediatrics and Neonatology, University of Magdeburg, Magdeburg, Germany** (Prof G Jorch MD)

Correspondence to: Prof R G Carpenter, Medical Statistics Unit, Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK (e-mail: bob.carpenter@lshtm.ac.uk)

Introduction

The remarkable increase in sudden unexplained infant death (SIDS) rates recorded, especially in Norway¹ and in several other countries,^{2–4} towards the end of the 1980s prompted large scale case-control studies that were set up during 1992 in Scandinavia,⁵ Ireland,⁶ England, and Germany.^{7,8} The succeeding reduction in SIDS rates, led by the Netherlands,⁹ which occurred in some countries necessitated a reassessment of risk factors for the syndrome because, despite the reductions, SIDS was still a major cause of infant mortality after the first week of life. These investigations all included similar questions about most previously established risk factors. At the 1992 meeting of the European Society for the Study and Prevention of Infant Death, participants suggested the potential value of integrated data from these and other studies, which led to the founding of the European Union Concerted Action on SIDS (ECAS) in January, 1994. Our main aims were to combine data from across Europe and thereby establish risks currently associated with previously suspected risk factors, especially those associated with infant care practices, assess whether levels of risk vary across Europe, and investigate the extent to which risk factors interact.

Methods

In addition to continuing research, new studies that all followed the same ECAS protocol were set up in 12 centres, six of which were in eastern Europe. Therefore, data were derived from case-control studies of SIDS of varying duration done in 20 centres between September, 1992, and April, 1996. Denmark, Norway, and Sweden, which comprised the Nordic study, were counted as three centres, as were the three regions (Yorkshire, Trent, and South West) that made up the first 2 years of the Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI) study in England. SIDS was defined as sudden and unexpected postperinatal infant death that is unexplained by clinical history, details of the circumstances of death, and an adequate post-mortem examination as set out in an international protocol.¹⁰ Pathology conferences ensured agreement on the interpretation of post-mortem findings. Cases with pathological changes or clinical symptoms insufficient to explain death, or both, were included.^{11,12} In all centres, arrangements were made for the rapid notification of cases to the participating centre.^{5–8,13,14} Only cases who had had autopsies were included, consisting of on average 78% (IQR 64–91%) of registered cases of SIDS that arose in the defined area covered by the centre during the period of every study. All investigations were given ethics approval by the appropriate local authority committee, as was the pooling of the anonymised data.

We obtained incidence rates for all centres and established seasonal variation in incidence. For every case, two or more controls were selected from birth records,^{5,7,13,14} or clinic lists,⁸ to represent live infants of the same age, living in the same survey area at the time.

Country	Study region	Cases	Controls
Sweden	Sweden	117	430
Norway	Norway	72	269
Denmark	Denmark	55	170
E and W	Yorkshire	81	324
E and W	Trent	60	240
E and W	South Western	54	216
Ireland	Ireland	92	322
Germany	Nordrhein-Westfalen	76	150
Netherlands	Netherlands	31	61
Austria	Styria	17	34
Hungary	Hungary	17	56
Ukraine	Odessa	16	32
Spain	Catalunya	16	32
Italy	Milan	12	24
Russia	St Petersburg	9	18
Slovenia	Slovenia	9	18
France	Seine-Maritime	5	5
Belgium	Brussels	3	6
Poland	Bialystok	2	2
E and W	Cambridge	1	2
		745	2411

E and W=England and Wales.

Table 1: Country, study region, and number of cases and controls

Closely similar epidemiological questionnaires were completed for cases and controls with comparable methods.^{5,7,8,13,14} To keep recall bias to a minimum, questions relating to terminal history of the case were

replaced by corresponding questions for controls relating to the same time of the day before the interview. The median interval from death to interview for cases was 15 days (IQR 6–32). The median interval between the death and the control interview was 18 days (4–38).

In addition to date of birth, death, and interview; and the centre and numbers identifying each case and its controls; data relating to 56 variables representing potential risk factors were extracted from the five data sets (ie, Nordic, UK, Irish, Nordrhein-Westfalen, and remaining centre studies) and were merged into one set for analysis. Data for 32 of these variables were mostly complete. Data for the other 24 were not recorded by some centres. For clarity of effect, continuous variables other than age were categorised. Unconditional logistic regression methods (STATA version 5.0) were used to estimate odds ratios with 95% CIs associated with all these variables or their combinations considered in isolation—ie, unifactorial analyses—and to manually build up multivariate models based on the almost complete variables. To avoid exclusion of cases, missing data for these variables were entered separately for cases and controls to the values predicted by the most closely related variables. Because the number of controls per case varied between centres, adjustments were made for centres in all analyses.

	Cases	Controls	Unifactorial ORs*	Multivariate ORs* (95% CI)
Risk factor				
Position last left†				
Side vs supine	250 (35.6%)	894 (37.6%)	1.65	1.31‡ (0.93–1.85)
Prone vs supine	268 (38.2%)	269 (11.3%)	8.31	13.1 (8.51–20.2)
Mothers smoking and bed-sharing on last occasion				
Mother did not smoke or bed-share	249 (34.6%)	1621 (67.8%)	1	1
Mother did not smoke but shared bed‡	32 (4.5%)	139 (5.8%)	1.61	1.56 (0.91–2.68)
Mother smoked <10 cigarettes per day but did not bed-share	133 (18.5%)	328 (13.7%)	2.87	1.52 (1.10–2.09)
Mother smoked >10 cigarettes per day but did not bed-share	194 (27.0%)	247 (10.3%)	5.64	2.43 (1.76–3.36)
Mother smoked less or more than 10 cigarettes and bed-shared‡	111 (15.4%)	56 (2.3%)	14.8	17.7§ (10.3–30.3)
Others in household smoked after birth				
None	259 (41.8%)	1465 (66.0%)	1	1
1–9 cigarettes per day	64 (10.3%)	215 (9.7%)	1.72	1.07 (0.71–1.61)
10–19	131 (21.2%)	297 (13.4%)	2.82	1.54 (1.11–2.14)
20–29	110 (17.8%)	203 (9.1%)	3.44	1.73 (1.21–2.48)
30+	55 (8.9%)	41 (1.8%)	8.81	3.31 (1.84–5.96)
Dummy used ever vs not used	394 (62.5%)	1492 (66.9%)	0.84	0.74 (0.58–0.95)
History of ALTE: yes vs no	79 (11.2%)	73 (3.0%)	4.27	2.76 (1.76–4.32)
Sex (excluding matched set) (male vs female)	260 (61.2%)	683 (49.1%)	1.63	1.49 (1.11–1.99)
Multiple birth vs singleton	47 (6.4%)	36 (1.5%)	5.08	2.40 (1.27–4.52)
Birthweight				
≥3500 g	212 (28.7%)	1174 (49.1%)	1	1
2500–3499	381 (51.6%)	1131 (47.3%)	1.89	1.44 (1.14–1.83)
2000–2499	84 (11.4%)	59 (2.5%)	8.25	3.36 (1.92–5.88)
<2000	61 (8.3%)	28 (1.2%)	15.0	4.83 (2.36–9.88)
Admitted to SCBU: yes vs no	160 (24.4%)	204 (9.2%)	3.55	2.19 (1.51–3.17)
Urinary tract infection in pregnancy: yes vs no	79 (11.2%)	152 (6.4%)	1.99	1.61 (1.08–2.41)
Mother's age:				
>30 years	166 (22.5%)	868 (36.2%)	1	1
26–30	224 (30.3%)	875 (36.5%)	1.36	1.64 (1.22–2.21)
21–25	228 (30.9%)	529 (22.1%)	2.44	3.21 (2.30–4.48)
19–20	75 (10.2%)	92 (3.8%)	4.75	6.91 (4.09–11.7)
≤18	46 (6.2%)	31 (1.3%)	9.16	11.0 (5.38–22.4)
Previous livebirths				
None	199 (26.9%)	999 (41.5%)	1	1
1	256 (34.6%)	862 (35.8%)	1.49	2.76 (2.06–3.70)
2	161 (21.7%)	372 (15.5%)	2.29	3.94 (2.76–5.63)
3	73 (9.9%)	122 (5.1%)	3.23	4.68 (2.89–7.58)
4+	50 (6.8%)	50 (2.1%)	5.15	10.6 (5.78–19.3)
Marital status				
Cohabiting vs married	219 (29.8%)	596 (24.8%)	1.79	1.46‡ (1.07–1.99)
Single vs married	126 (17.2%)	162 (6.7%)	4.03	1.63 (1.10–2.40)
Partner unemployed vs employed	197 (29.8%)	275 (11.7%)	3.76	1.85¶ (1.39–2.45)

ALTE=apparent life-threatening events. SCBU=special care baby unit. Data are numbers (%) *ORs are adjusted for age and centres. †ORs for age-dependent variables, position last left and bed sharing when mother did or did not smoke, are reported at modal age of 10 weeks. ‡Excluding OR for Sweden. §Excluding OR for Milan. ¶Excluding missing data for Ireland.

Table 2: Prevalence of multivariately significant potential risk factors for SIDS in cases and controls

Outlying ORs that were eliminated in analysis***Ireland**

Father unemployed: Data missing for 28% of cases and 2% of controls. Imputing missing to employed resulted in outlying OR, $p=0.00011$.

Milan

Mother smoked during pregnancy and shared bed on last occasion: High prevalence of smoking in controls (71% in Milan vs 26% in all other centres) resulted in an outlying low OR for Milan, $p=0.0008$.

Sweden

Last left on side: Only 8 (7%) cases in Sweden were last left supine, compared with 30% in all other centres, resulted in an outlying OR for last left on side, ($p=0.00001$), but not for last left prone.

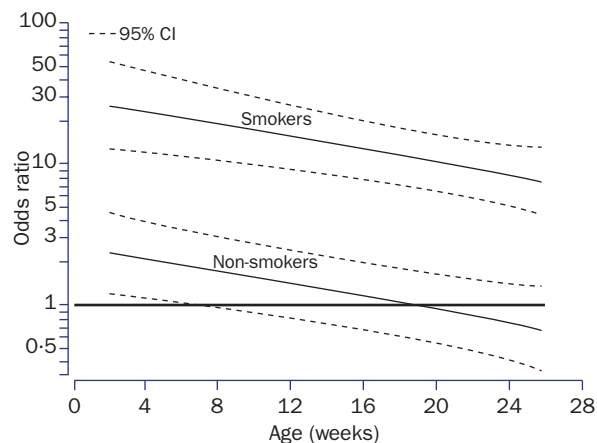
Cohabiting: 39% of cases and 52% of control parents were cohabiting in Sweden, compared with 28% and 19% in all other centres, p of outlying OR=0.00056.

*The effect of these outlying ORs was eliminated by modelling them with special parameters (see appendix 1; <http://www.espid.net>).

Risk factors are often inter-related, consequently ORs derived from unifactorial analyses are of little value. Therefore, we focused on the ORs of significant factors derived from multivariate analyses. Because these ORs are adjusted for the effects of all the other factors in the model, they describe the independent association of the factor with outcome. Agonal movement due to the terminal pathological process in the dying baby might have occurred. Therefore, data relating to position found were not initially included in the multivariate model. For the 24 incomplete variables, we obtained ORs adjusted for the variables included in the multivariate model, excluding position found. These adjusted odds ratios estimate their potential independent contribution to risk of SIDS.

Population attributable fractions (PAF; often called population attributable risk) reported as percentages,^{15,16} were derived for potentially modifiable factors from adjusted ORs and percentages (Results, tables 2, 3, and 4). These fractions estimate the expected percentage reduction of cases if a particular exposure were eliminated. PAFs are the percentage of cases exposed to factor (f) multiplied by its proportional excess risk $(OR_f - 1)/OR_f$. Numbers are not shown for estimated percentages.

Details of statistical methods are shown in appendix 1 (<http://www.espid.net>).



ORs (log scale) for SIDS and 95% CIs of bed-sharing by infant age and mother smoking or not during pregnancy

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

20 European centres assembled data for 745 cases of SIDS and 2411 controls (table 1). 12 new centres using the ECAS protocol contributed 138 (19%) cases. For the 20 centres, SIDS incidence rates at the time of the studies ranged from 0.17 per 1000 in Hungary to 1.3 per 1000 in Nordrhein-Westfalen (median 0.6 [IQR 0.4–0.7]). Seasonal rates varied by 13.6% (3.3%–26.1%) either side of the mean ($p=0.018$) with peak incidence close to the shortest day. Although frequency was higher at the weekend than at other times of the week, the rate did not vary significantly with day of the week ($p=0.230$). Incidence rates peaked at 10 weeks of age, and 57 (7.7%) cases occurred in babies younger than 1 month of age and 134 (18%) in those over 6 months. 471 (63%) were male.

The ORs and 95% CIs, for risk factors or combination of factors in isolation are available in appendix 2 (<http://www.espid.net>). Only four variables were not significant: immunised or vaccinated in the past 7 days; use of a hat usually or on the last occasion; and dummy (pacifier) ever used.

Table 2 shows the principal results of the multivariate analysis. Variables included in the table were more than 97% complete. Comparison of the unifactorial ORs based on recorded data and unifactorial ORs based on observed plus estimated missing data, showed a median difference of 1.3% (IQR –0.8 to 4.0%).

Initially the intercentre variation of the multivariate ORs in table 2 was significant ($p=0.003$). However, further analysis revealed that this heterogeneity was due to four outliers (panel). After elimination of these outliers (appendix 1; <http://www.espid.net>), there was no evidence of more than random intercentre variation in the ORs ($p=0.272$). Further tests showed that ORs for combinations of factors shown in table 2 could be estimated by multiplication of the corresponding multivariate ORs (data not shown).

In table 2, multivariate ORs for previous livebirths are appreciably larger than the unifactorial ORs, because this variable is negatively correlated with mother's age. After adjustment for other factors, the OR for dummy (pacifier) ever used became significantly protective. Many of the ORs associated with other factors were reduced in the multivariate model. In particular, the multivariate ORs associated with others in household smoked after birth, although highly significant, were substantially reduced compared with the unifactorial ORs.

Risks associated with low gestational age and small for dates represented by z scores in the unifactorial analysis (see appendix 2; <http://www.espid.net>) were multivariately accounted for by birthweight and other factors. Subdivision of birthweight 2.500–3.499 kg into two equal groups gave ORs of 1.19 (0.92–1.55) for the 3.0–3.499 kg group and 2.20 (1.59–3.05) for the 2.500–2.999 kg group. The OR for birthweights lower than 1.5 kg was 4.87 compared with 4.83 for weight less than 2.0 kg (table 2). Eight cases and two controls had birthweights lower than 1000 g.

The effects of the multivariate risks associated with sleeping arrangements were tested and three significant interactions were identified. First, the OR associated with last left prone diminished by 3.8% per week ($p=0.003$). At 4, 10, and 26 weeks, the adjusted ORs for last left prone were 16.5 (9.63–28.4), 13.1 (8.51–20.2) (table 2),

	Risk factor	Records	Cases	Controls	Unifactorial ORs*	Multivariate ORs† (95% CI)	
	Baby found with head covered	Yes vs no	2662 (84.3)	154 (25.0%)	69 (3.4%)	11.9	12.5 (6.47–24.1‡)
	Evidence of sweating when found	Yes vs no	1578 (50.0)	83 (22.7%)	123 (10.2%)	2.76	2.69 (1.75–4.14)
	Duvet used on last occasion	Yes vs no	1774 (56.2)	191 (48.1%)	375 (27.2%)	2.95	1.82 (1.30–2.58)
	Dummy used in last sleep	Yes vs no	1545 (49.0)	130 (36.2%)	653 (55.1%)	0.50	0.44 (0.29–0.68)
	Room shared usually (not bed sharing)	Yes vs no	1773 (56.2)	180 (46.8%)	816 (58.8%)	0.56	0.48 (0.34–0.69)
	Room shared in last sleep (not bed sharing)	Yes vs no	1397 (44.3)	93 (28.0%)	474 (44.5%)	0.40	0.32 (0.19‡–0.55‡)
	Interval since last birth < 12 months	Yes vs no	1337 (42.4)	47 (13.4%)	39 (4.0%)	3.73	2.36 (1.18–4.71)
	Mother's alcohol consumption in last 24 h		2457 (77.8)				
	None			468 (84.1%)	1654 (87.2%)	1	1.00
	1–2 drinks vs none			50 (9.0%)	193 (10.2%)	0.92	1.00 (0.63–1.57)
	3+ drinks vs none			39 (7.0%)	53 (2.8%)	3.18	2.33 (1.28–4.21)
	Mother used illegal drugs after birth	Yes vs no	2508 (79.5)	21 (3.7%)	21 (1.1%)	4.87	1.92 (1.00–3.70)
	Moved house since birth:	Yes vs no	2488 (78.8)	54 (9.5%)	96 (5.0%)	2.72	1.69 (1.05–2.74)

Data are number (%). *Adjusted for age and centres. †Also adjusted for all risk factors included in the multivariate model presented in table 2. ‡CIs adjusted for more than random variation between the ORs for the centres.

Table 3: **Multivariately significant potential risk factors for SIDS not recorded by all centres**

and 7.1 (4.89–10.2), respectively. Second, the adjusted OR associated with bed-sharing, defined as all-night bed-sharing with an adult, was progressively greater for younger infants whether or not the mother smoked, the increase being 5.2% per week in both groups ($p=0.002$). The figure shows the multivariately-adjusted relation and 95% CIs for mothers who did and those who did not smoke during pregnancy. The ORs for the smokers was 11.3 times greater than that for the non-smokers, and ranged from 27.0 (13.3–54.9) at 2 weeks to 7.5 (4.3–13.2) at 26 weeks. For non-smokers, the risk was significant only at less than 8 weeks.

Of the 24 variables with incomplete data, ten were significant after adjustment for the variables included in the multivariate model (table 3). The adjusted OR for baby found with its head covered was the largest. Also, the multivariately adjusted ORs for dummy used in last sleep and for room sharing were more protective than unifactorial ORs. Other ORs were reduced.

Dummy ever used was correlated with dummy used in last sleep. When these variables were combined, it emerged that it was only when the dummy was used and used for the last sleep that the adjusted OR was significantly less than 1 (table 3). Similarly, only infants who usually shared the parents room (but not the bed) and did so on the last occasion were at greatly reduced risk (table 3). Duvet used on the last occasion had a significant adjusted OR. The ORs associated with duvet use were much the same whether the baby was bed-sharing or not, and conversely, risks associated with bed-sharing did not change significantly whether a duvet was used on the last occasion or not.

The adjusted OR for use of illegal drugs by the mother after birth was significantly raised. Mother's consumption of more than three alcoholic drinks in the past 24 h was associated with an increased risk of SIDS (table 3). The alcohol consumption of both parents increased significantly at weekends for both cases and controls, but the ORs for mother's alcohol consumption did not vary significantly with day of the week ($p=0.840$). Partner's consumption of alcohol was correlated with that of the

mother ($r=0.52$, Spearman's rank correlation), but did not add further to risk of SIDS. Further analysis revealed that risks associated with mother's alcohol consumption were confined to infants who bed-shared all night. For these infants, the OR increased by 1.66 (1.16–2.38) per drink. Because 28 (35%) of 81 mothers who smoked and bed-shared had also consumed alcohol, compared with eight (19%) of 44 controls, alcohol partly accounted for the high ORs for bed-sharing and smoking. By contrast, mothers who bed-shared and had not smoked, had consumed very little alcohol. When the analysis was confined to mothers who had neither smoked nor taken alcohol, the ORs for bed-sharing non-smokers were slightly more significant than those shown in the figure—ie, 4.23 (1.71–10.4) at 2 weeks and 2.07 (1.05–4.12) at 10 weeks.

Tea and coffee consumption during pregnancy was significantly correlated with the amount mother smoked (Spearman's rank correlation $r=0.45$, $p<0.0001$). Consequently, although three or more cups of tea or coffee per day during pregnancy was a significant risk factor in isolation, this variable was not multivariately significant. Immunisation or vaccination in the past 7 days was not a significant risk factor either by itself or multivariately.

When the position last left (table 2) was replaced in the multivariate model by a composite variable—position last left and last found—54 (8%) cases who turned from back to front and the 82 (12%) who turned from side to front on the last occasion formed two new categories and were associated with very high ORs. This modification of the multivariate model tended to increase the ORs of the other variables including those for bed-sharing. However, the OR for multiple births was reduced to 1.4 (0.68–2.7). Also the ORs for sleeping position (table 4) did not change significantly with age, including the OR for being placed prone. Infants who turned prone on the last occasion, but did not usually do so, were at 4.3 (2.1–8.7) times greater risk than were those for whom this behaviour was usual. Those who usually turned from the side position to

		Cases	Controls	Unifactorial ORs*	Multivariate ORs† (95% CI)
Position last left and last found					
Last left	Last found				
Supine	Supine or side	128 (18.6%)	1150 (48.4%)	1	1
Side	Supine or side	159 (23.0%)	848 (35.7%)	1.32	1.07 (0.72‡–1.58‡)
Prone	Any position"	267 (38.7%)	267 (11.3%)	13.1	13.9 (8.86‡–21.6‡)
Supine	Prone	54 (7.8%)	67 (2.8%)	16.6	20.1 (8.48‡–47.5‡)
Side	Prone	82 (11.9%)	42 (1.8%)	26.7	45.4 (23.4–87.9)

Data are numbers (%). *Adjusted for age and centres. †ORs and their CIs are adjusted for all factors other than position last left in the multivariate model presented in table 2. ‡95% CIs adjusted for more than random variation between ORs for the centres. §95% of cases and 90% of controls last left prone were found prone.

Table 4: **Change in sleeping position on last occasion of cases and controls with ORs**

	Attributable fraction as percentage of cases	
	Per item	Total (IQR)
Where slept last*		
Slept other room vs parent's room (not bed)	35.9	..
Shared bed vs parent's room (not bed)	15.9	51.8 (40.4–64.4)
Positioning		
Left prone vs left supine	35.9	..
Left on side and turned prone vs left supine	11.6	47.5 (25.8–70.0)
Mother smoked in pregnancy	..	36.9 (21.7–42.2)
Baby not always put down with dummy	..	35.7 (18.6–38.1)
Others in household smoked after birth	..	21.9 (11.7–25.7)
Head covered	..	23.0 (0.0–36.1)
Duvet used	..	21.6 (17.5–39.4)

Table 5: PAFs for avoidable risk factors for SIDS derived from adjusted ORs, in order of magnitude, with intercentre IQRs

supine were at reduced risk (OR=0.16 [0.081–0.31]). Since there was no significant interaction between position last left and found and mother smoked during pregnancy or bed-shared on last occasion, their effects were independent.

Table 5 shows the percentage of cases attributable to potentially modifiable factors. The prevalence of some factors varied considerably across the centres, but since the ORs were not significantly heterogeneous, the excess risk of those exposed ($[\text{OR}-1]/\text{OR}$) applied generally. In this table, IQRs show intercentre variation due to variation in the proportions of exposed cases. The largest PAF was for sleeping place. This PAF was 35.9% because, on average, 53% of cases were last left in another room (range 18–88% across the 15 centres for which this information was available) and 68% of the risk was attributable. Additionally, the PAF for bed-sharing was 15.9%, so the data suggested that 52% of cases might have been prevented had the baby slept in the parents' room but not in their bed.

Discussion

Across the centres, the ORs for sleeping prone was negatively correlated with the prevalence of this sleeping position.¹⁷ Thus, our OR was much higher than noted in earlier investigations when sleeping prone was much more common.

Adjusted OR for position the infant was last left in—side versus supine—was not significant. However, the side position was much less stable than the back position. During the controls' reference sleep, 61% who were left on their side moved compared with 12% controls left supine. The corresponding figures for cases' last sleep were 53% and 34%. The difference between cases and controls was that only 16% of controls who moved from back or side position turned prone, compared with 72% cases. Consequently, the estimated OR for turning from side to prone position (table 4) was 45.4, and if this position were not usual, the OR was nearly double. Thus, 12% of cases were attributable to placing infants to sleep on their side.

This concerted action made it possible to assemble one of the largest case-control data sets on SIDS. It spanned Europe from Norway in the north to Catalunya in the south, and from the Ukraine in the east to Ireland in the west. All pathologists attended conferences to ensure agreement on which cases should be included. Contamination by cases of infanticide, which sometimes have been misclassified as SIDS,¹⁸ was discussed. It was suggested that a characteristic of such cases is the one of occurrence of previous infant deaths. There had been a previous infant death in 26 cases and 39 controls. After adjustment for the number of previous livebirths and

centres, the difference was not significant, $p=0.13$. Therefore, there was no evidence of significant contamination by cases of infanticide.

Despite limitations and problems of recall bias,¹⁹ case-control studies have been highly effective in identification of key risk factors for SIDS—eg, risks associated with sleeping prone.^{2,20} In this investigation, we kept recall bias to a minimum by asking parents of controls about the reference period (ie, time of day when the corresponding case died) in the past 24 h. Variation of risk with day of the week, specifically that associated with parental alcohol consumption, could be examined because 12.6% (205 of 1631) control questionnaires, in which day of interview was known but not included in data sets, were completed at the weekend.

Univariately, the ORs for 44 (79%) of the 56 variables assessed showed no more than random variation between the centres. Accounting for intercentre variation, when present, increased the width of the CIs of the ORs by a mean of 10%. Multivariately, when the four outlying ORs had been eliminated from the model, there was no evidence of more than random variation in the odds ratios across the centres. And although three of the 15 ORs in the analyses (tables 3 and 4) showed more than random variation across the centres, no additional outliers were detected and the significance of the results was unaltered by adjustment for intercentre variation. These findings imply that the sets of risk factors for SIDS infants is consistent across Europe and that variation in the prevalence of risk factors accounted for much of the intercentre variation in incidence rates.¹⁷ These conclusions primarily relate to white infants. Although ethnic background was not a significant factor in the multivariate analysis (OR 1.64 [0.96–2.83]), numbers relating to non-white infants (37 cases) were too low to clarify the issue.

There have been many studies of SIDS.^{21,22} However, comparisons are hindered by the absence of agreement about definitions and how risk factors should be analysed (continuous or categorical and how categories are defined) and what variables should be included in the model. The ORs presented here are, therefore, inevitably different from those presented in other recent studies.^{5–8,23} Nevertheless, there is good overall agreement. Also, this large study allowed the examination of the effects of combinations of factors not otherwise possible.

When the concerted action was set up, participating centres agreed that the only measures of socioeconomic status likely to be meaningful across Europe were parental education and employment. However, in the multivariate model, partner's employment, mother's age, and the number of previous livebirths accounted for parental education and maternal employment. In multivariate analysis, there was no increase in risk of SIDS if both partners were unemployed.

As others have reported,^{14,24,25} a substantial proportion of cases was attributable to turning prone or getting the head covered, or both (table 5). However, moving was not more frequent in cases (29%) than in controls (30%). Hence, turning prone and getting the head covered were generally not the result of agonal movement. We concluded that risks associated with turning face down or getting the head covered, or both, were due to a similar mechanism to that causing increased risk in infants sleeping prone. If this were so, the data suggest that 62% of the deaths were attributable to being placed prone, turning prone, or getting the head covered. Therefore, risk of SIDS might be substantially reduced by putting infants to sleep supine with no bedding other than a jumper suit,

as recommended by the US Consumer Products Safety Commission,²⁶ or in a well fitting cotton or acrylic sleeping bag of not more than 2-tog. A bag could have the advantage of restricting movement in children younger than 6 months of age.¹⁴

This recommendation also prevents risks associated with the use of a duvet, and could reduce the risk due to overheating because found sweating was associated with found head covered.²⁷

Our data, in agreement with those of almost all studies,²⁸ showed substantial risk attributable to smoking by one or both parents (table 5). Smoking before, during, and after birth was highly correlated and was represented best in the multivariate model by the amount that the mother smoked during pregnancy and the amount others in the household smoked after the birth.

Bed-sharing is being advocated to encourage breast-feeding,²⁹⁻³¹ although we did not identify a significant association. Scragg and co-workers³² first described the risk associated with maternal smoking and bed-sharing. The consistency of finding a high OR for bed-sharing when the mother smoked across the centres in this survey, apart from Milan, suggested that this was a true risk. For these infants, risk declined significantly with age in the same way as when the mother bed-shared and did not smoke (figure), and is highly significant even at 6 months.

For mothers who did not smoke in pregnancy, the risk associated with bed-sharing was only significant for infants younger than 8 weeks (figure). By 13 weeks—median age of CESDI cases—the OR was almost identical to that for non-smokers reported by Blair and colleagues³³ after adjustment for relevant factors including tiredness, the use of alcohol, duvet, and overcrowding (>2 adults per room). In the ECAS data, the slight risk was not explained by overcrowding or use of alcohol because only three mothers (one case and two controls) had had more than two alcoholic drinks in the past 24 h. We have no data for maternal fatigue, but mothers with young children are those who are most likely to be fatigued.

The mother had smoked in 111 (77%) cases of bed-sharing, thus showing that all-night bed-sharing should be discouraged for all mothers who smoke. An important finding was that the risks associated with mother's alcohol consumption in the past 24 h were only significant when the infants were bed-sharing. An unexpected finding was that the factor with the largest PAF was that associated with either the baby sleeping in another room or bed-sharing. On average, cases slept in another room 26 (11.3–41.5) days earlier than controls, but the OR did not change with age. Why the baby sleeping in the parent's room reduced the risk is unclear.

It is noteworthy that the ORs measure differences in the pattern of events on the last occasion for cases compared with the reference occasion for controls. PAFs are similarly hypothetical, but proved accurate predictors of the reduction in mortality that followed the reduction in the use of the prone sleeping position.^{9,34} As almost all studies have found, SIDS is associated with biological, (male sex, low birthweight, multiple birth), social (young unmarried mother with unemployed partner, etc), and environmental (parental smoking, overcrowding) factors. Nevertheless, the data suggested that, despite unavoidable disadvantages, most of these deaths might not have occurred had these infants been put down supine in a cot in the parent's room with light bedding that the baby could not get over its head.

Controlled trials of the effects of infant care practices on the incidence of SIDS are impracticable and probably unethical. Therefore, continuous monitoring of SIDS

cases and controls is imperative, as in Ireland and the Netherlands,^{13,35} to assess the penetration and effectiveness of preventive messages. Continuous case-control monitoring would also ensure that new ideas about baby care would be tested at the earliest possible stage.

Contributors

The authors were the ECAS Executive committee. L M Irgens proposed the project and actively chaired the Executive Committee. R G Carpenter co-ordinated the study, oversaw the preparation of protocols, data collection and first analyses, carried out the final analysis and drafted this paper. P D England was assistant to R G Carpenter and was responsible for the preparation of the project protocols, assembling data from the centres, identifying, standardising the coding and assembling the common data, preparing basic tabulations, and the preliminary multivariate analysis. P Blair put together a questionnaire that combined the questions of all four ongoing projects, which formed the basis of the ECAS questionnaire.

L M Irgens with P Schreuder's assistance led the NESS project. P Fleming chaired the CESDI planning and co-ordinating group to which P S Blair was the statistician. G Jorch directed the Nordrhein-Westfalen study. They advised and assisted with the integration of the data. J Huber's role was to ensure that the pathology of the cases was as consistent as possible through the holding of conferences and paediatric pathology workshops. He was also responsible for implementing the study in the Netherlands. All contributed to this report.

Participants and collaborators by country who were responsible for the studies in each centre

Western Europe—Austria: C Einspieler. Belgium: A Kahn, J Groswasser. Denmark: K Helweg-Larsen. France: E Mallet. Germany: G Jorch. Netherlands: J Huber, M L'Hoir. Italy: M Stramba-Badiale. Ireland: B Kiberd. Norway: LM Irgens, P Schreuder. Spain: F Camarasa, J Lucena, G Perez. Sweden: G Wennergren, B Alm. United Kingdom: C Morley; CESDI: P Fleming, P S Blair; E Taylor; C Bacon, I Smith, D Bensley.

Eastern Europe—Hungary: D Schuler, E Barko. Poland: M Kaczmarek. Russia: I Kelmanson. Slovenia: D Neubauer. Ukraine: N Aryaev.

Conflict of interest statement

None declared.

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References

- 1 Vege Å, Rognum TO, Løberg EM, et al. Diagnosis of sudden infant death in the Nordic countries since 1970, revised. In: Rognum TO, ed. Sudden infant death syndrome: new trends in the nineties. Oslo: Scandinavian University Press, 1995: 67–69.
- 2 Department of Health. The sleeping position of infants and cot death. London: HMSO, 1993.
- 3 National Sudden Infant Death Register. 1994 Report. Irish Sudden Infant Death Association, Dublin.
- 4 Naujoks M, Jorch G. Infant mortality figures in Germany: application of the "window technique" for evaluation of the SID-rate. In: Jorch G, ed. Prevention of Sudden Infant Death, European Workshop. Ministerium für Arbeit, Gesundheit und Soziales des Landes Nordrhein-Westfalen: Münster, 1995.
- 5 Nordic Council of Ministers. Sudden infant death in Nordic countries: results of the Nordic study of sudden infant death syndrome, 1990–1996. Nordisk Ministerråd, København, *TemaNord* 1997; 600.
- 6 National Infant Death Register. Annual report 1994–1998. National SIDS Register, George's Hall, Temple Street Hospital, Dublin, 1999.
- 7 Fleming P, Blair P, Bacon C, Berry J. Sudden unexpected death in infancy: the CESDI SUDI studies. London: HMSO, 2000.
- 8 Findeisen M. Prone sleeping position. In: Jorch J, ed. Prevention of sudden infant death: European workshop. Ministerium für Arbeit Gesundheit und Soziales des Landes Nordrhein-Westfalen, Münster, 1995.

- 9 Engelberts A. Cot death in the Netherlands: an epidemiological study. Amsterdam: VU University Press, 1991.
- 10 Kraus HF. The international standardized autopsy protocol for sudden and unexpected infant death. In: Rognum TO, ed. Sudden infant death syndrome: new trends for the nineties. Oslo: Scandinavian University Press, 1994: 81–95.
- 11 Taylor EM, Emery JL. A study of the causes of postperinatal deaths classified in terms of preventability. *Arch Dis Child* 1982; **57**: 668–73.
- 12 Gregersen M, Rajs J, Laursen H, et al. Pathologic criteria for the Nordic Study of SIDS. In: Rognum TO, ed. Sudden infant death syndrome: new trends for the nineties. Oslo: Scandinavian University Press, 1994: 50–58.
- 13 Mehanni M, Kiberd B, McDonnell M, O'Regan M, Mathews T. Reduce the risk of cot death guidelines: the effect of a revised intervention programme. *Irish Med J* 1999; **92**: 266–69.
- 14 L'Hoir MP, Engelberts AC, van Well GT, et al. Risk and preventive factors for cot death in the Netherlands, a low incidence country. *Eur J Pediatr* 1998; **157**: 681–88.
- 15 Hanley JA. A heuristic approach to the formulas for population attributable fraction. *J Epidemiol Community Health* 2001; **55**: 508–14.
- 16 Bruzzi P, Green SB, Byar DP, Brinton LA, Schairer C. Estimating population attributable risk for multiple risk factors using case control studies. *Am J Epidemiol* 1983; **122**: 904–14.
- 17 Report on co-ordinated case-control studies to determine ways of reducing sudden infant death (SIDS) rates in Europe. Page 65. Report to EU on Concerted Action, BMH1 CT93-1207. 1997.
- 18 Meadows R. Unnatural sudden infant death. *Arch Dis Child* 1999; **80**: 7–14.
- 19 Shapiro S, Rosenberg L. Bias in case-control studies. In: Armitage P, Colton T, eds. Encyclopedia of Biostatistics. Chichester: John Wiley and Sons, 1998: 313–22.
- 20 Beal SM, Finch C. An overview of retrospective case-control studies investigating the relationship between prone sleeping position and SIDS. *J Paediatr Child Health* 1991; **27**: 334–9.
- 21 Guntheroth WG. Crib death. The Sudden Infant Death Syndrome. 3rd edn. 1995. Futura, Armonk.
- 22 Sullivan FM, Barlow SM. Review of risk factors for Sudden Infant Death Syndrome. *Paediatr Perinatal Epidemiol* 2001; **15**: 144–200.
- 23 Mitchell EA, Taylor BJ, Ford RPK et al. Four modifiable and other major risk factors for cot death.: The New Zealand study. *J Paediatr Child Health* 1992; **28** (suppl): S3–8.
- 24 Mitchell EA, Thach BT, Thompson JM, Williams S. Changing infants' sleep position increases risk of sudden infant death syndrome. *Arch Pediatr Adolesc Med* 1999; **153**: 1136–41.
- 25 Li DK, Petitti DB, Willinger M, et al. Infant sleeping position and the risk of sudden infant death syndrome in California, 1997–2000. *Am J Epidemiol* 2003; **157**: 446–55.
- 26 US Consumer Product Safety Commission. Recommendations revised to prevent infant deaths from soft bedding. April 8, 1999.
- 27 Guntheroth WG, Spiers PS. Thermal stress in sudden infant death: is there an ambiguity with the rebreathing hypothesis. *Pediatrics* 2001; **107**: 693–98.
- 28 Golding J. Sudden infant death syndrome and parental smoking—a literature review. *Paediatr Perinat Epidemiol* 1997; **11**: 67–77.
- 29 Jackson D. Three in a bed. Why you should sleep with your baby. 1989. Bloomsbury, London.
- 30 United Nations Childrens Fund (UNICEF) Facts for Life File - Breast Feeding Apr 2002. www.unicef.org/ffl/04/3.htm
- 31 Ball HL. Breastfeeding, bed-sharing, and infant sleep. *Birth* 2003; **30**: 181–88.
- 32 ScraggR, Mitchell EA, Taylor BJ, et al. Bed-sharing, smoking and alcohol in the sudden infant death syndrome. *BMJ* 1993; **307**: 1312–18.
- 33 Blair PS, Fleming PJ, Smith IJ et al, and the CESDI SUDI research group. Babies sleeping with parents: case-control study of factors influencing the risk of sudden infant death syndrome. *BMJ* 1999; **319**: 1457–61.
- 34 Wigfield RE, Fleming PJ, Berry PJ, Rudd PT, Golding J. Can the fall in Avon's sudden infant death rate be explained by changes in sleeping position?. *BMJ* 1992; **304**: 282–83.
- 35 Jonge de GA, L'Hoir MP, Ruys JH, Semmekrot BA. Wiegendood, ervaringen en inzichten. [Cot death, experiences and understanding]. 2002. Stichting Wiegendood [Dutch Cot Death Foundation], Noorden.