Determinants of acute respiratory infections in Soweto – a population-based birth cohort

Ines A Kristensen, Jørn Olsen

Background. Acute respiratory infections (ARIs) are an important cause of infant morbidity in both developing and developed countries, and they are the leading cause of death in poorer parts of the world. Respiratory viruses appear to be the most frequent microbiological pathogens, especially respiratory syncytial virus.

It has been suggested that factors such as being male, overcrowding, poor access to medical care, low level of maternal education, and passive smoking are associated with contracting ARIs.

Design. A fixed birth cohort of 571 children was followed from birth to 1 year of age. The children were monitored for symptoms of ARIs during regular home visits.

Setting. An urban low-income setting in Soweto, a township outside Johannesburg with an estimated 1.2 million inhabitants, including an estimated 45 000 children under 2 years of age.

Subjects. A total of 571 children were observed for 118 650 days.

Outcome measures. The incidence rate of ARIs. The determinants birth weight, breastfeeding, gender, crowding, passive smoking, indoor pollution, and sanitary facilities were analysed.

Results. A total of 489 episodes of coughing or coughing and nasal discharge combined were recorded. Only the father's level of education and the number of people living in the household remained significant in the multivariate analyses. The incidence of severe ARIs was reduced among breastfed infants.

Conclusions. Our study supports previous observations suggesting that crowding and communal living conditions are important determinants of ARIs. Breastfeeding seemed protective against severe ARI. The lack of association with well-described risk factors such as low level of maternal education, gender and passive smoking could be due to lack of statistical power in this rather uniform population.

S Afr Med J 2006; **96:** 633-640.

Acute respiratory infections (ARIs) are common in younger children worldwide, and are recognised as an important cause of morbidity and mortality.[1,2]

ARIs include a diverse group of diseases ranging from self-limiting illnesses to bronchiolitis and pneumonia that may require medical care. According to the World Health Organization (WHO),[3] they account for 20 - 40% of paediatric outpatient visits and 12 - 35% of hospitalisations.

The overall incidence of ARIs appears to be similar in developing and developed countries in the first year of life, with an average of 4 - 8 episodes per child.[2,4]

ARIs have been studied in many areas of the world in order to identify the environmental, socio-economic, immunological and genetic determinants.[5-8] By definition ARIs have microbiological causes, but what determines their incidence in the population is a function of complex causes that correlate with exposure to the infectious agent, such as size of the household, number and age of siblings, and sharing a bed with others, and factors of importance for individual and population susceptibility such as younger age, male gender, low birth weight, immunological factors, and short duration of breastfeeding.[9]

Published studies reveal geographical differences, but whether these are true differences or rather reflect methodological differences related to patient detection or study design is not clear. It is, however, expected that the large variance in determinants will be followed by a similar variance in occurrence of ARI.

Although most ARIs have a benign course, some children suffer from repeated episodes that may interfere not only with their health but also with their social and cognitive development. It is therefore essential to determine the external causes of an illness in order to understand, predict, and reduce the burden of the disease.

A longitudinal population-based birth cohort study of ARIs among children followed up to 1 year of age in Soweto, a township outside Johannesburg, was set up to identify the burden and determinants of disease in the study area. The study emphasised the roles of birth weight, breastfeeding, gender, age, maternal education, crowding, housing, and indoor pollution.

Skejby University Hospital/Viborg Hospital, Aarhus, Denmark
Ines A Kristensen, MD, PhD

Department of Epidemiology, UCLA, Los Angeles, USA
Jørn Olsen, MD, PhD

Corresponding author: *I A Kristensen (ines@dadlnet.dk)*

Subjects and methods

Study area

Soweto has an estimated 1.2 million inhabitants, including an estimated 45 000 children under 2 years of age. There is some movement in and out of the area because of links with more remote rural areas. Soweto is primarily a low-income area although all strata of society are represented, from shacks in squatter camps to modern houses in suburban areas.

The study was conducted in Soweto because it has a high population density and a well-organised health care system from primary to tertiary level. Health care and medication are provided free of charge by four health centres and Chris Hani Baragwanath Hospital in the study area.

The HIV-1 prevalence rate was estimated at 17.1% (95% confidence interval (CI): 15.1 - 19.2, Stats 2000) of pregnant women presenting at the antenatal care clinics. There was no access to antiretroviral drugs at the time of the study, therefore 5 - 6% of birth cohorts were expected to have the virus transmitted from the mother, either *in utero* or perinatally, amounting to approximately 30 children in our cohort; of these, approximately 30% were expected to fall ill before their first birthday.

The infant mortality rate was 19/1 000 for HIV-negative infants, and 61/1 000 for HIV-positive infants. The climate is temperate with a short, dry winter with night temperatures down to 0 - 5 ℃.

Population

Pregnant women in gestational weeks 33 - 35, as assessed by nurses using the fundal height, were enrolled over a period of 4 months from May to September 2000. They were enrolled from four antenatal clinics covering three areas of Soweto, namely Diepkloof, Orlando East and Pimville. The inclusion criteria for participation in the study were residence in one of the three areas, pregnancy in gestational weeks 33 - 35, and an ability to communicate in Sesotho, Zulu or English. All women who gave false addresses so that they could utilise the health facilities in the area were excluded from the study. Most of these women came from rural areas within the province and from adjacent provinces.

Study approval was obtained from the Committee for Research on Human Subjects of the University of the Witwatersrand. Written consent for inclusion in the study was obtained from the women after a full explanation of the scope of the study had been given. The study was conducted in accordance with the Helsinki Declaration II for human clinical studies.

Surveillance method and case definitions

Seven field workers followed the fixed birth cohort of 572 infants biweekly from September 2000 to March 2001, and weekly from March to December 2001. The field workers were not medically trained but went through a training programme based on material from the WHO, including a video, and were supervised regularly throughout the study period.

The first home visit took place as soon as possible after the delivery of the child, preferably within 2 weeks of the birth. At this visit a delivery questionnaire was completed with information on the date of birth, gestational age, Wassermann reaction serology, and place of delivery, gender, ethnicity of the parents, birth measurements, and comments on any complications.

Information on the household, including the type of house, number of household members, number of persons sleeping in the same room and bed as the index child, sanitation facilities, cooking and heating facilities, refuse removal, household income, household assets, medical aid, educational level and employment of the mother and father or partner, siblings, pets, and smoking habits in the house, was obtained at this visit as well. The economy of the household was assessed in different ways, utilising either the assets or the income of the household as a measure.

Information was recorded on breastfeeding, bottle-feeding, weaning, solid food intake, immunisation status and milestones, as well as symptoms and treatment for asthmatic bronchitis and any history of asthma in the family. Measurements of weight, height and arm circumference of the child were done on a monthly basis.

For early detection of ARIs we monitored symptoms such as nasal discharge, coughing, wheezing, fever, and increase in respiratory rate at every visit.

One of the authors (IAK) received a daily report from each field worker on any infant with at least nasal discharge and coughing. The child was then visited by the registered nurse or the author the following day. A history of the illness was obtained and a full body examination performed. If the child had a minimum set of symptoms such as a nasal discharge and persistent cough, a nasal aspirate was taken. Together, episodes of upper and lower respiratory tract infection as defined by the WHO[10] were considered to constitute episodes of ARI.

In such cases the mother or guardian was encouraged to take the child to the local clinic, although many mothers had done so before our visit. Medical records from the clinics and hospital in the area follow the patient. This allowed us to record the symptoms, diagnosis and treatment from these visits and admissions. Furthermore, nurses from another study monitored the admission wards at the hospital 24 hours a day. These nurses recorded whether any of our children were admitted to the paediatric ward.

Episodes were counted in 7-day intervals. A symptom-free visit had to occur between the regular consecutive visits in order for a new episode to be counted. Days at risk for ARI

were counted as symptom-free days, which meant the days observed minus the number of 7-day intervals including 7 extra days in which the children were observed to still have an episode of ARI. If a child with reported symptoms was absent at a home visit undertaken between two regular visits this was counted as one long episode, which meant duration of at least 14 days.

If the child had left the study and then came back into the study again, the person time was calculated from 14 days before the first visit after the re-entrance.

Respiratory virus identification

A nasogastric tube (FG 8 10 cm in length, Ven Medical Products, Cape Town, South Africa) attached to a 5 ml syringe was used. Three millilitres of normal saline were injected into the nasopharynx, aspirated immediately, and placed into a viral transport medium, which was stored at 4˚C and transported to the laboratory within 2 hours. Specimens were centrifuged, and the pellet was spread on a slide and fixed. Initial screening was performed using a direct pooled immunofluorescent test for respiratory viruses[11] and respiratory syncytial virus (RSV) alone, as this was the main virus under study.

Pools testing positive samples were then tested for RSV, again using mouse anti-RSV monoclonal fluorescein antibody (Chemicon International Inc, Temecula, California). Specific monoclonal fluorescein conjugated antibodies were used for the other 6 respiratory viruses, namely influenza viruses A and B, parainfluenza 1-3, and adenovirus.

Statistical methods

Incidence ratios and 95% (CIs) were used as measures of relative risk (RR). Incidence was calculated as the number of episodes divided by the time at risk.

The number of episodes and days at risk were calculated on a weekly basis. The model had to account for the possible correlation between episodes from the same child. Therefore, a model accounting for larger variation than the Poisson model had to be applied to the data. Furthermore, the Poisson model is based on the assumption that events occur at random independently of each other. The negative binomial regression model was used in cases where the Poisson model was not appropriate. Each risk factor was analysed separately using a univariate model, and based on these results multivariate analyses were carried out.

All analyses were carried out for the two different outcome measurements. Episodes defined by any symptom of ARI recorded by the interviewers and the risk factors for these episodes were analysed using the negative binomial regression model. The episodes defined by at least the combination of nasal secretion and cough and seen by the nurse or doctor in the study were analysed using the Poisson regression model.

All analyses were adjusted for gender, time of entry into the study (in days) and season of birth. We did not adjust for the interviewers. Given the structure of the study, they were not all employed for the same timespan, which in itself would result in a difference in the number of episodes recorded.

Results

Five hundred and seventy-nine children were eligible for the surveillance programme. Ninety-eight of these children (17%) were followed up for less than 100 days, primarily because they moved out of the study area. Eighty per cent were enrolled before they reached 1 month of age. Eight children seen only at the first visit did not contribute any person time.

The cohort of 571 children was observed for a total period of 118 650 days. Maximum follow-up time was 1 year. During this time the field workers recorded 489 episodes of coughing or a combination of coughing and nasal discharge with or without fever. The time of risk for the whole group was 114 356 days. This resulted in an incidence of 1.56 per child year.

We recorded 330 episodes of nasal discharge and 121 episodes of diarrhoea as the only symptoms respectively and they did not count in the time of risk for ARIs.

Sixty-one per cent of the children in the cohort were born between June and August, and 75% of the episodes occurred between February and August, which is defined as the RSV season in the study area.

We went on 374 visits to 266 children; 185 children (240 visits) were found to have signs of URTI. The latter children were all eligible for nasal aspirate, but often the symptoms had resolved or we did not obtain enough secretion during the procedure. This resulted in 87 nasal aspirates from this group being analysed for respiratory viruses.

Eleven children were RSV-positive (12.6%), 3 were infected with parainfluenza 3 (3.4%), with 1 co-infected with RSV and 1 co-infected with adenovirus. One was positive for influenza A (1.1%), 1 had adenovirus (2.3%) and 1 was positive for parainfluenza 1 (1.1%).

Six children were HIV enzyme-linked immunosorbent assay (ELISA)-positive and 1 had symptoms of being HIV-positive, but the mother refused testing. They were all detected in the small group of children attending the hospital during the surveillance period.

Twelve children in the cohort died during the study period, 6 of whom died of AIDS-related illnesses. This gave an infant mortality rate of 26/1 000 (95% CI: 13.9/1 000 - 44.2/1 000). The 456 children included in the cohort from birth constituted the denominator.

The distribution of risk factors is presented in Tables I - III together with univariate analyses.

A number of factors within many of the item groups showed a significantly increased risk for ARIs; namely level of maternal

Table I. Gender, birth and social factors as risk factors for acute respiratory infections in 571 Sowetan children

Risk factor	All episodes of acute respiratory infections					Moderate to severe acute respiratory infections				
	No. of children	Days at risk	No. of episodes	Relative risk	95% CI	No. of children	Days at risk	No. of episodes	Relative risk	95% CI
Gender (*N* = 571)										
Boys	285	59 158	265	1		285	59 306	141		
Girls	287	56 331	224	0.87	0.70 - 1.07	287	57 323	99	0.72	0.55 - 0.96
Birth weight (*N* = 558)										
1 700 - 2 499	42	8 268	51	0.98	0.63 - 1.52	42	8 848	23	0.76	0.45 - 1.29
2 500 - 3 499	413	84 512	362	1		413	85 001	186	1	
3 500 - 4 200	104	20 120	84	0.97	0.74 - 1.28	104	20 577	35	0.74	0.49 - 1.11
Mother's age (yrs) (*N* = 569)										
16 - 19	89	19 574	75	0.94	0.67 - 1.31	89	19 829	42	1.10	0.74 - 1.66
20 - 24	149	29 720	130	1.08	0.81 - 1.45	149	30 248	77	1.35	0.93 - 1.97
25 - 29	173	32 073	134	1		173	32 681	63	1	
30 - 34	110	22 277	105	1.14	0.84 - 1.55	110	22 753	40	0.94	0.61 - 1.46
35 - 42	49	11 332	44	0.98	0.67 - 1.43	49	10 605	17	0.85	0.45 - 1.60
Education, mother (*N* = 570)										
Matric	247	49 795	175	1		247	50 432	100	1	
Standard 8 - 9	174	37 322	173	1.35	1.05 - 1.73	174	37 322	79	1.10	0.79 - 1.52
Standard 6 - 7	86	16 690	95	1.64	1.24 - 2.16	86	17 136	44	1.29	0.87 - 1.91
None - standard 5	64	11 514	44	1.10	0.77 - 1.57	64	11 514	15	0.63	0.39 - 1.04
Education, father (*N* = 410)										
Matric	224	46 647	160	1		224	47 317	86	1	
Standard 8 - 9	89	17 257	89	1.53	1.15 - 2.02	89	17 663	38	1.22	0.82 - 1.80
Standard 6 - 7	44	8 924	34	1.19	0.78 - 1.81	44	8 057	18	1.28	0.72 - 2.25
None - standard 5	54	9 479	56	1.80	1.28 - 2.53	54	9 808	18	1.02	0.59 - 1.77
Number of siblings (*N* = 570)										
No siblings	252	52 347	213	1	-	252	53 237	110	1	-
1 sibling	186	35 322	155	1.08	0.84 - 1.39	186	36 031	74	1.01	0.73 - 1.42
2+ siblings	133	27 652	119	1.07	0.83 - 1.37	133	27 193	54	0.98	0.69 - 1.38

and paternal education, toilet facilities, number of smokers in the household, and night-time crowding. There were 1 or more smokers in 48% of the households, and only 25 of the mothers reported smoking. Gender and housing showed borderline significance. Factors such as maternal age, number of siblings, size of household, night-time crowding with other children, and type of fuel used for cooking did not show any association with ARIs. The same applied to season of birth and age at entry into the study. Analyses for the more restricted definition of the outcome measure only showed significant association within a few item groups, such as gender and housing.

The final multivariate analyses performed using negative binomial and Poisson regression models, respectively, consisted of the following variables: gender, birth weight, paternal education, type of housing, toilet facilities, night-time crowding, and size of household (Table IV).

Only level of paternal education remained significant for both outcome measures, and size of household for the more severe episodes of ARIs, when adjusting for several covariates.

We did a subanalysis of breastfeeding for those

Table II. Housing, sanitary facilities and crowding factors as risk factors for acute respiratory infection in 570 Sowetan children

	All episodes of acute respiratory infections					Moderate to severe acute respiratory infections				
Risk factor	No. of children	Days at risk	No. of episodes	Relative risk	95% CI	No. of children	Days at risk	No. of episodes	Relative risk	95% CI
Type of house (*N* = 570)										
Single or double-storey family house	281	62 609	255	1		281	62 587	136	1	
Room/flat	69	12 927	39	0.74	0.52 - 1.05	69	13 130	17	0.60	0.36 - 1.00
Shack	212	38 567	187	1.19	0.95 - 1.49	212	39 491	83	0.97	0.71 - 1.32
Hostel	9	1 128	6	1.25	0.52 - 2.99	9	1 253	2	0.75	0.22 - 2.53
Toilet facilities (*N* = 567)										
In the house	92	18 180	46	1		92	18 327	28	1	
Out of the house	444	90 360	412	1.84	1.28 - 2.64	444	91 171	203	1.49	0.93 - 2.36
Communal/pit bucket	32	6 102	27	1.88	1.13 - 3.12	32	6 277	6	0.63	0.24 - 1.65
No. of persons in household (*N* = 570)										
2 - 3	139	25 088	101	1		139	24 536	42		
4	113	21 058	89	0.98	0.70 - 1.37	113	21 450	46	1.19	0.74 - 1.91
5 - 9	249	53 727	212	0.94	0.70 - 1.27	249	54 654	116	1.21	0.79 - 1.84
10+	70	15 448	85	1.30	0.93 - 1.82	70	15 821	34	1.22	0.74 - 2.02
No. of adults in same bedroom as the index child (*N* = 570)										
1	156	33 803	112	1		156	33 198	66		
2	366	71 550	317	1.31	1.03 - 1.67	366	73 057	144	1.00	0.74 - 1.38
3+	49	9 968	58	1.75	1.26 - 2.44	49	10 206	28	1.33	0.84 - 2.10
No. of adults sleeping in same bed as the index child (*N* = 569)										
1	372	76 327	325	1		372	76 678	160		
2+	198	38 868	162	0.99	0.79 - 1.24	198	39 657	78	0.96	0.71 - 1.30
No. of children in same bedroom as the index child (*N* = 570)										
None	403	80 570	322	1		403	80 579	165		
1	107	21 410	95	1.08	0.84 - 1.40	107	21 919	42	0.92	0.64 - 1.34
2+	62	6 124	72	1.35	0.98 - 1.84	62	6 238	33	1.17	0.78 - 1.78
No. of children sleeping in same bed as the index child (*N* = 569)										
None	524	105 483	439	1		524	106 385	218		
≥ 1	48	10 006	50	1.22	0.88 - 1.69	48	10 244	22	1.08	0.67 - 1.75

Table III. Indoor pollution and smoking as risk factors for acute respiratory infections

	All episodes of acute respiratory infections					Moderate to severe acute respiratory infections				
Risk factor	No. of children	Days at risk	No. of	Relative risk	95% CI	No. of children	Days at risk	No. of episodes	Relative risk	95% CI
Fuel used for cooking (N = 570)	485	100 361	419	1		485	101 102	217	1	
Electricity or gas	86	14 960	68	1.13	0.84 - 1.52	86	15 359	21	0.65	0.40 - 1.05
Paraffin/coal										
No. of smokers in household										
0	299	58 386	222	1		299	59 341	116	1	
1	214	44 404	196	1.17	0.93 - 1.48	214	44 281	87	0.99	0.72 - 1.35
2 - 8	57	12 468	68	1.45	1.08 - 1.94	57	12 776	34	1.37	0.95 - 1.98
Mother smokes										
No	545	109 954	457	1		545	110 940	222	1	
Yes	25	5 304	29	1.38	0.87 - 2.18	25	5 458	15	1.43	0.83 - 2.47
Partner smokes										
No	212	38 808	157	1		212	39 567	74	1	
Yes	166	33 048	166	1.29	0.99 - 1.68	166	32 921	66	1.06	0.74 - 1.52
Daily No. of cigarettes, father (N = 351)										
0	212	38 808	157	1		212	39 567	74	1	
1 - 9	108	22 569	114	1.33	0.99 - 1.77	108	22 171	48	1.16	0.78 - 1.75
10 - 25	31	5 485	32	1.43	0.86 - 2.39	31	5 679	8	0.73	0.38 - 1.40

still present in the study at their 1-year birthday, which included 453 children. Forty of these children did not live with their biological mothers, and the data did not reveal when they had stopped breastfeeding, leaving 413 eligible for the analysis. The effect of breastfeeding was analysed in a multivariate analysis adjusting for the variables given in Table IV. No significant protection was found for breastfeeding for 2 - 5 months (RR 0.87, 95% CI: 0.57 - 1.30) or 6 - 12 months (RR 0.92, 95% CI: 0.55 - 1.54), compared with being breastfed for less than 1 month or not at all, for all episodes of ARI. Limiting the analysis to the outcome measure of both nasal discharge and coughing, being breastfed for 2 - 5 months showed borderline significant protection (RR 0.55, 95% CI: 0.30 - 1.00), whereas there was no effect from breastfeeding for 6 - 12 months (RR 1.16, 95% CI: 0.64 - 2.10) compared with less than 1 month or not at all.

Discussion

The present study is the first population-based study of risk factors for ARI in children living in Soweto. We managed to follow up 571 children, of whom 17% were followed for less than 3 months. We expected to find a high incidence of ARIs in this population, but the incidence was lower than that found in other studies.

ARIs often appear and disappear within a few days and are of varying severity and duration. In addition, the incidence may change from one calendar year to another. Furthermore, given the structure of the surveillance method and the fact that our measurement of episodes was based on direct observation, we would have missed events that occurred between visits.

Interestingly, RSV prevalence in this study was similar to the rate (14.7%) found in a community study from Finland[12] of 2 - 24-month-old children, while in Mozambique[13] a 10.6% prevalence of RSV infections was recorded among children under 5 years of age. One explanation could also be the fact that only 3.5% of 1-year-old children attended a child care centre, which is known to be an important risk factor for contracting ARIs.[14-16]

We would therefore maintain that the surveillance was reasonably intensive and the rate of participation was acceptable, with 79% of the initial study population still present at the end of the study.

Girls tended to be better protected against ARIs than boys, although the difference was not significant. Many studies have shown male preponderance, especially for more severe ARIs.[17]

Low birth weight is known to be a risk factor especially for severe ARIs. This was not found in our study, probably because of lack of statistical power.

Night-time crowding disappeared in the multivariate analyses as a risk factor for ARIs, but the number of people living in the household became significant for more severe events. As such crowding may not only increase the incidence of respiratory illnesses, but it might also play a significant role in increasing severity of the illness where close interpersonal contact results in a large infecting dose of the viral agent.[18]

As a risk factor passive smoking is most closely related to

Table IV. Multivariate analyses for the following outcome measurements: (*i*) all episodes of acute respiratory infection; and (*ii*) ARI at least defined by nasal discharge and coughing

Risk factor	Relative risk	CI 95% (*i*)	Relative risk	CI 95% (*ii*)
Gender				
Boys	1		1	
Girls	0.87	0.68 - 1.12	0.74	0.53 - 1.03
Birth weight (g)				
1 700 - 2 499	0.59	0.51 - 1.31	0.59	0.31 - 1.12
2 500 - 3 499	1		1	
3 500 - 4 200	0.85	0.84 - 1.51	0.85	0.54 - 1.33
Education, mother				
Matric	1		1	
Standard 8 - 9	1.12	0.85 - 1.49	1.09	0.73 - 1.65
Standard 6 - 7	1.20	0.80 - 1.80	1.19	0.70 - 2.03
None - standard 5	0.81	0.50 - 1.31	0.64	0.33 - 1.24
Education, father				
Matric	1		1	
Standard 8 - 9	1.56	1.16 - 2.09	1.45	0.93 - 2.28
Standard 6 - 7	1.32	0.83 - 2.10	1.92	1.06 - 3.50
None - standard 5	1.82	1.22 - 2.72	1.32	0.69 - 2.53
Type of house				
Single or double-storey family house	1		1	
Room/flat	0.71	0.42 - 1.19	0.50	0.23 - 1.11
Shack	0.84	0.55 - 1.29	0.74	0.42 - 1.30
Hostel	1.658	0.60 - 4.12	2.34	0.88 - 6.23
No. of persons in household				
2 - 3	1		1	
4	1.08	0.70 - 1.67	2.10	1.10 - 4.00
5 - 9	0.97	0.61 - 1.55	1.67	0.91 - 3.08
10+	1.42	0.79 - 2.55	1.61	0.73 - 3.53
Toilet facilities				
In the house	1		1	
Out of the house	1.38	0.93 - 2.04	1.30	0.77 - 2.19
Communal/pit bucket	1.12	0.56 - 2.24	0.56	0.16 - 1.44
No. of adults in same bedroom as the index child				
1	1		1	
2	1.07	0.77 - 1.48	0.93	0.60 - 1.44
3+	1.43	0.88 - 2.31	1.41	0.73 - 3.53
No. of children in same bedroom as the index child				
None	1		1	
1	0.92	0.65 - 1.30	0.68	0.41 - 1.13
2+	1.08	0.73 - 1.58	0.97	0.56 - 1.68

maternal smoking,[19,20] which could explain the lack of association in the multivariate analysis in our study, as very few mothers reported smoking.

Indoor pollution from use of paraffin and coal did not show any association, in contrast to a study in Cape Town,[21] where absence of electricity for heating purposes remained significant after adjustment for parental smoking, maternal education, crowding, sanitation facilities and refuse removal.

Another study from South Africa[22] failed to show any effect of indoor pollution, but the study suffered from lack of statistical power and good data on indoor pollution.

Maternal education, which probably operates as a proxy for many of the other factors, did not show any association with ARIs, whereas the level of the father's education did, although it was not consistent. This could be an indication of the father's role as a breadwinner.

Other studies have shown that breastfeeding does not seem to protect against ARIs.[23,24] The observed effect of breastfeeding was inconsistent in our study probably because of lack of statistical power, as most participants were largely breastfed and we observed too few severe cases of ARIs. However, our findings tend to support suggestions that breastfeeding might confer protection against the severity rather than the incidence of ARIs.

Although there is an emerging middle class in the area, Soweto is still primarily a low-income area with a relatively even distribution of the determinants under study, which could

influence the detection of significant results. Furthermore, children who had private medical insurance and who would be cared for in private clinics were not eligible for the birth cohort.

In conclusion, we found that crowding (number of persons in the household) and the father's level of education increased the risk of ARIs. Breastfeeding showed a tendency towards protection against more severe ARIs.

The main source of support for the study was the Danish Council for Development Research, Danida. Minor sources of support were the Dagmar Marshall Foundation, the Danish Epidemiology Science Centre, the Novo Nordic Foundation, and the National Research Foundation, South Africa.

The authors thank research assistants Lindiwe Hlomuka, Mpho Seliboane, Elizabeth Ndlovu, Nomalanga Nkos, Annette Kesi, Joy Tshabalala, Simangele Xulu, Lebohang Khunou and professional nurse Nkensani. They also thank laboratory technicians Tchaka Ndou and Nadia van Niekerk for valuable support in running the study smoothly, Dr Shabir Mahdi, Head of the Respiratory and Meningeal Pathogen Research Unit, University of the Witwatersrand, for valuable advice and logistical support, and the study participants for their willingness to open their homes to us.

References

1. Berman S. Epidemiology of acute respiratory infections in children of developing countries. *Rev Infect Dis* 1991; **13:** Suppl 6, S454-462.
2. World Health Organisation. Division of Diarrhoeal and Acute Respiratory Disease Control. Integrated management of the sick child. *Bull World Health Organ* 1995; **73:** 735-740.
3. Graham NM. The epidemiology of acute respiratory infections in children and adults: a global perspective. *Epidemiol Rev* 1990; **12:** 149-178.
4. Borrero I, Fajardo L, Bedoya A, Zea A, Carmona F, de Borrero MF. Acute respiratory tract infections among a birth cohort of children from Cali, Colombia, who were studied through 17 months of age. *Rev Infect Dis* 1990; **12:** Suppl 8, S950-956.
5. Yun BY, Kim MR, Park JY, Choi EH, Lee HJ, Yun CK. Viral etiology and epidemiology of acute lower respiratory tract infections in Korean children. *Pediatr Infect Dis J* 1995; **14:** 1054-1059.
6. Saijo M, Terunuma H, Mizuta K, *et al*. Respiratory syncytial virus infection in children with acute respiratory infections in Zambia. *Epidemiol Infect* 1998; **121:** 397-400.
7. Chan P, Goh A. Respiratory syncytial virus infection in young Malaysian children. *Singapore Med J* 1999; **40:** 336-340.
8. Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980 - 1996. *JAMA* 1999; **282:** 1440-1446.
9. Koch A, Molbak K, Homoe P, *et al*. Risk factors for acute respiratory tract infections in young Greenlandic children. *Am J Epidemiol* 2003; **158:** 374-384.
10. World Health Organization. Programme for the Control of Acute Respiratory Infections. *Technical Bases for the WHO Recommendations on the Management of Pneumonia in Children at First Level Health Services*. Doc. WHO/ARI/91.20 Geneva: WHO, 1991.
11. Madhi SA, Schoub B, Simmank K, Blackburn N, Klugman KP. Increased burden of respiratory viral associated severe lower respiratory tract infections in children infected with human immunodefiency virus type-1. *J Pediatr* 2000; **137:** 78-84.
12. Vesa S, Kleemola M, Blomquist S, Takala A, Kilpi T, Hovi T. Epidemiology of documented viral respiratory infections and acute otitis media in a cohort of children followed from two to twenty-four months of age. *Pediatr Infect Dis J* 2001; **20:** 574-581.
13. Loscertales MP, Roca A, Ventura PJ, *et al*. Epidemiology and clinical presentation of respiratory syncytial virus infection in a rural area of southern Mozambique. *Pediatr Infect Dis J* 2002; **21:** 148-155.
14. Nafstad P, Hagen JA, Oie L, Magnus P, Jaakkola JJ. Day care centers and respiratory health. *Pediatrics* 1999; **103:** 753-758.
15. Hurwitz ES, Gunn WJ, Pindy PF, Schonberger LB. Risk of respiratory illness associated with day-care attendance: a nationwide study. *Pediatrics* 1991; **87:** 62-69.
16. Wesley AG, Loening WEK. Assessment and 2-year follow-up of some factors associated with severity of respiratory infections in early childhood. *S Afr Med J* 1996; **86:** 365-368.
17. Weber MW, Mulholland EK, Greenwood BM. Respiratory syncytial virus infection in tropical and developing countries. *Trop Med Int Health* 1998; **3:** 268-280.
18. Aaby P, Bukh J, Lisse IM, Smits AJ. Overcrowding and intensive exposure as determinants of measles mortality. *Am J Epidemiol* 1984; **120**(1): 49-63.
19. Fergusson DM, Horwood LJ. Parental smoking and respiratory illness during early childhood: a six year longitudinal study. *Pediatr Pulmonol* 1985; **1**(2): 99-106.
20. Ferris BG jun, Ware JH, Berkey CS, Dockery DW, Spiro A 3rd, Speizer FE. Effects of passive smoking on health of children. *Environ Health Perspect* 1985; **62:** 289-295.
21. Von Schirnding YER, Yach D, Blignault R, Mathews C. Environmental determinants of acute respiratory symptoms and diarrhoea in young coloured children living in urban and peri-urban areas of South Africa. *S Afr Med J* 1991; **79:** 457-461.
22. Wesley AG, Loening WEK. Assessment and 2-year follow-up of some factors associated with severity of respiratory infections in early childhood. *S Afr Med J* 1996; **86:** 365-368.
23. Golding J, Emmett PM, Rogers IS. Does breast-feeding protect against non-gastric infections? *Early Hum Dev* 1997; **49:** Suppl, S105-120.
24. Rubin DH, Leventhal JM, Krasilnikoff PA, *et al*. Relationship between infant feeding and infectious illness: a prospective study of infants during the first year of life. *Pediatrics* 1990; **85:** 464-471.

Accepted 8 December 2005.