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Daycare attendance and respiratory tract infections: a prospective birth cohort study

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Keywords: daycare, respiratory infections, children, the STEPS Study

Word count: 2499

Abstract

Objective. We explored the burden of respiratory tract infections in young children with regard to daycare initiation.

Design. Longitudinal prospective birth cohort study.

Setting and method. We recruited 1827 children for follow-up until the age of 24 months collecting diary data on respiratory tract infections and daycare. Children with continuous daycare type and complete data were divided into groups of centre-based daycare (n=299), family daycare (n=245), and home care (n=350). Using repeated measures variance analyses, we analysed days per month with symptoms of respiratory tract infection, antibiotic treatments, and parental absence from work for a period of 6 months prior to and 9 months after the start of daycare.

Results. We documented a significant effect of time and type of daycare, as well as a significant interaction between them for all outcome measures. There was a rise in mean days with symptoms from 3.79 (95% CI 3.04-4.53) during the month preceding centre-based daycare to 10.57 (95% CI 9.35-11.79) at 2 months after the start of centre-based daycare, with a subsequent decrease within the following 9 months. Similar patterns with a rise and decline were observed in the use of antibiotics and parental absences. The start of family daycare had weaker effects. Our findings were not changed when taking into account confounding factors.

Conclusions. Our study shows the rapid increase in respiratory infections after start of daycare and a relatively fast decline in the course of time with continued daycare. It is important to support families around the beginning of daycare.

Article summary

Strength and limitations of this study

- We prospectively collected detailed day-to-day diary data on respiratory tract infections and related outcomes from 0 to 2 years of age in a birth cohort population, and documented daycare type and starting date.
- The study design allowed us to analyze the time-dependent effects of centre-based daycare and family daycare on the days per month with symptoms of a respiratory infection in comparison with children of same age in home care.
- Different confounders were taken into account, but they did not change our findings of a peak in the rate of respiratory tract infections shortly after daycare initiation, and a clear decline thereafter.
- A limitation is that, due to strict requirements regarding detail in follow up and careful exclusion of missing data, we lost a substantial proportion of cases.

Introduction

In modern society a considerable proportion of children attend daycare from the age of less than two years. Respiratory tract infections (RTIs) in this age group constitute an important health problem. In addition to causing stress to children and families, they also affect transmission of pathogens to other age groups, parental absences from work with ensuing economic consequences, and rates of anti-microbial medication use with subsequent impact on resistance patterns.[1-3] Previous studies suggest that increased rates of infections may be a transient problem related to the beginning of daycare,[4-7] but results are conflicting. Few prospective cohort studies have examined the topic, and lose frequency of follow-up has limited chronological conclusions. Some studies have found a protective effect of starting daycare early with regard to RTIs later in life.[4, 8]

Families, child health care professionals, and daycare providers would benefit from more detailed knowledge about the burden of disease as a function of time before and after the start of daycare in the above mentioned age group. We examined this in a prospectively followed birth cohort.

Methods

Study population and conduct

We used the cohort of the observational 'Steps to the Healthy Development and Well-being of Children' Study (The STEPS Study), which consists of 1827 children from 1797 families.[9] Recruitment occurred in two stages from women with a live birth between 1 January 2008 and 31 March 2010 in the Southwest Finland Hospital District (n=9936). During the first stage, 1387 families were recruited through community midwifery services during pregnancy, and a further 410 families joined the study soon after the birth of their child. In this study we collected questionnaire-based data on family related factors and daycare arrangements at gestational week 20, and at ages 13 months, 18 months, and 24 months, as applicable. Families kept study diaries that recorded health related factors, the precise starting date of daycare, and data from physician visits. Parents documented the child's symptoms, antibiotic treatments, and parental absence from work on a day-to-day basis in these diaries. Parents were instructed to also mark symptom-free days in the diary. We differentiated missing from negative data by excluding follow-up with no diary markings.

Families attended our nurse-led study clinic when the child was 2 and 13 months of age. During RTIs part of the cohort (n=982) were also followed up by our physician-led study clinic. Recruitment of children to our study is shown in figure 1. Exclusion criteria for this study constituted discontinuous daycare during our follow-up, or insufficient information on daycare arrangements including missing knowledge on the exact time of start of daycare. The Ethics Committee of the Hospital District of Southwest Finland approved the study protocol. The parents of the participating children gave their written, informed consent.

Daycare attendance

Children were categorized into three different groups according to daycare arrangements: children cared for by parents or relatives (comparison group), children attending family daycare (FDC), and children attending daycare centres (DCC). In this study family daycare was defined as daycare provided by a trained carer in her or his home, or in the children's homes using a rotational system. According to local regulations, FDC group sizes included no more than 5 children. In rare cases, carers worked together forming a common nursery. Since group sizes tended to be relatively small in those nurseries, these children were included in the FDC group. Daycare centres were defined by larger-group, centre-based care provided by several professional carers. FDC and care in DCCs were provided either by the municipality or on a private basis.

Outcomes

The outcomes of the study were symptoms of RTIs (cough, rhinorrhea, fever, or wheeze), consumption of antibiotic medication, and parental absence from work as recorded on a day-to-day basis in the study diaries. Antibiotic medications prescribed for any reason were included, but the main indication was acute otitis media. Any parental absence from work due to the child's illness was recorded, and reasons were not limited to RTIs. Final outcome measures constituted days per month with RTI symptoms (sick days), antibiotic medication, and parental absence from work.

Confounding factors

The following potential confounders were taken into consideration: sex, siblings, season of year at start of daycare, asthma in the parents, pets (cats or dogs at home), and maternal post-secondary education.[10-12] There was only a small proportion of families with known smoking in parents (127 out of 1827), and since our results strongly indicated reporting bias, this variable was excluded from the analyses.

Statistical analysis

All statistical analyses were carried out using SAS version 9.4 (SAS, Cary, NC, USA). In all our analyses p values less than 0.05 were regarded as statistically significant. In the first step, outcome variables were calculated as days per month for each child and aligned in a time sequence relating to the beginning of daycare. Day-specific chronological follow-up included a time of 6 months previous to and 9 months after the beginning of daycare. Children commenced daycare at different ages, so that not all above defined data related to the fixed age frame of 0-2 years. Data from outside the agreed age frame were excluded from the analysis using the SAS MIXED procedure. Chronological data for the comparison group were obtained from children at equivalent ages not attending daycare. The equivalent age range was calculated using the mean age of starting daycare in the FDC and DCC groups. According to this mean age, follow-up of children within the comparison group included the age range of 9 to 24 months (6 months prior to and 9 months after the mean start of daycare at 15 months).

Data were analyzed by repeated measures variance analysis comparing all three groups for type of daycare and time, as well as their interaction. In a second step, chronological thresholds of significance were obtained by comparing all p values for the difference of least square means between all pairs of analyzed months. We determined the shortest time for any given trend with a $p < 0.05$. Although the distributions of monthly outcome variables (sick days, days with antibiotic treatment, and parental absence from work) were skewed in our analyses (coefficient of skewness up to 2.4 and kurtosis 7.6), the pairwise difference variables followed approximately a normal distribution.

In a third step, repeated measures variance analysis was repeated according to the previous model, but stratifying according to individual confounding factors.

Results

Figure 1 shows numbers of children within follow-up. Within our cohort of 1570 children in active follow-up, 276 (21.8%) of 1264 children with data on daycare arrangements at age 13 months attended daycare (11.7% in DCC, 10.1% in FDC) and 593 (55.0%) of 1079 children attended daycare at the age of 24 months (29.5% in DCC and 25.0 % in FDC). At all ages the vast majority of children in daycare spent over 5 hours per day at daycare (88.5% at age 13 months and 91.6% at age 24 months). Group sizes were clearly smaller for children attending FDC as compared to DCC, with 88.3% (at 13 months) to 82.7% (at 24 months) of families reporting a group size of less than 5 children per group. In DCC group sizes were variable with the following results for the ages of 13 months (and 24 months): less than 5 children for 2.0%, 5-15 children for 86.8%, over 15 children for 11.1% (less than 5 children for 1.4%, 5-15 children for 87.8%, over 15 children for 10.9%). Mean age at the beginning of daycare was 15 months (SD 4.1). Sex was evenly distributed throughout the daycare groups with 49.1% of boys in the comparison group, 50.6% in FDC, and 54.2% in DCC. Start of daycare (FDC or DCC) occurred in 38.2% of cases during fall-winter (October to March) and in 61.8% during spring-summer (April to September). Within the comparison, FDC, and DCC groups, 97.5% of children were born full-term (gestational age equal to, or over 37 weeks), with only 5/894 children (0.6%) having been born at a gestational age of less than 35 weeks.

There was a peak of mean sick days per month at 2 months after the start of daycare for both FDC and DCC (figure 2). The rise in sick days was stronger for the DCC group than for the FDC group. We observed increases from 3.53 mean sick days (95% CI 2.83-4.24) during the month prior to the start of daycare to 8.34 mean sick days per month (95% CI 7.25-9.43) for the FDC group, and from 3.79 (95% CI 3.04-4.53) mean sick days prior to the start of daycare to 10.57 (95% CI 9.35-11.79) mean sick days per month for the DCC group. For both of these groups, the rise of outcome measures was a transient phenomenon; sick days were comparable to the baseline group at 5 months after the start of daycare. Antibiotic use (figure 3) and parental absences from work because of children's illnesses (figure 4) rose and declined according to a pattern similar to that observed in sick days in relation to the start of daycare, although this decline was less pronounced compared to sick days.

The shortest time for a significant rise of outcome measures was determined from the last month prior to starting daycare (month -1) and for a significant decline from the peak of each outcome variable. The rise in sick days (figure 2) and antibiotic use (figure 3) was more rapid among children starting DCC than in those starting FDC. Within the comparison group there were no significant findings in pairwise comparisons between months.

In repeated measures variance analyses there was a significant overall effect for time and type of daycare and their interaction for all outcome measures (table 1).

Table 1. P values* for the effects of daycare type and time on the rates of RTI symptoms (sick days), antibiotic treatments, and parental absence from work because of a child's illness

	Sick days per month, p	Days with antibiotic treatment per month, p	Parental absence from work, days per month, p
Time (month)	<0.0001	0.004	0.003
Daycare type	<0.0001	<0.001	0.02
Contrast: comparison - FDC groups	0.55	0.18	ND
Contrast: comparison - DCC groups	<0.0001	<0.001	ND
Contrast: FDC - DCC groups	<0.001	0.04	ND
Interaction: time and daycare type	<0.0001	<0.0001	0.003
Time (month) for comparison group	0.005	0.64	ND
Time (month) for FDC group	<0.0001	0.002	<0.0001
Time (month) for DCC group	<0.0001	<0.0001	<0.0001

ND, not determined; RTI, respiratory tract infection; FDC, family daycare; DCC, daycare centre.

*By repeated measures variance analysis.

This interaction showed the above described pattern of rise and decline, which was strongest for the DCC group and weaker for the FDC group. Within the comparison group there was no such pattern, but significant variation was observed in the frequency of sick days per month over time. When analyzing contrasts in sick days and antibiotic use between different types of daycare without the aspect of time, only the DCC group reached significance in comparison to the baseline group and FDC group.

The presence of older siblings in the family and higher post-secondary education in mothers were associated with a higher burden of disease (table 2).

Table 2. Effects of confounding factors on the rates of RTI symptoms (sick days) according to daycare type.

	Type of daycare							
	Comparison group		Family daycare		Daycare centre			
	n/N (%)	Sick days per month, mean (SD)	n/N (%)	Sick days per month, mean (SD)	n/N (%)	Sick days per month, mean (SD)	P*	P for interaction with mode of daycare
Older siblings							0.02	<0.0001
Yes	162/ 350 (46.3)	5.55 (3.72)	99 /245 (40.4)	5.26 (3.33)	132/ 299 (44.1)	5.10 (3.72)		
No	188/ 350 (53.7)	4.16 (2.95)	146/ 245 (59.6)	4.58 (3.59)	167/ 299 (55.9)	5.88 (4.31)		
Higher post-secondary education in mother							0.009	0.27
Yes	211/ 341 (61.9)	5.12 (3.53)	161/ 239 (67.4)	5.12 (3.72)	203/ 293 (69.3)	5.66 (3.75)		
No	130/ 341 (38.1)	4.40 (3.17)	78 / 239 (32.6)	4.23 (2.97)	90/ 293 (30.7)	5.45 (4.79)		
Start of daycare during fall-winter (October-March)							0.39	0.61
Yes	ND	ND	100/ 245 (40.8)	4.90 (3.15)	108/ 299 (36.1)	5.69 (4.21)		
No	ND	ND	145/ 245 (59.2)	4.82 (3.73)	191/ 299 (63.9)	5.45 (4.0)		
Asthma in parents							0.95	0.72
Yes	35/ 340 (10.3)	4.65 (3.26)	26/ 234 (11.1)	5.54 (4.0)	30/ 287 (10.5)	5.83 (4.25)		
No	305/ 340 (89.7)	4.86 (3.43)	208/ 234 (88.9)	4.76 (3.45)	257/ 287 (89.5)	5.56 (4.08)		
Cat or dog at home							0.31	0.23
Yes	94/ 295 (31.9)	4.43 (3.07)	80/ 196 (40.8)	4.83 (3.07)	57/ 219 (26.0)	5.80 (4.28)		
No	201/ 295 (68.1)	5.14 (3.48)	116/ 196 (59.2)	4.92 (3.14)	162/ 219 (74.0)	5.68 (3.66)		

n/N, number of children per number of those with data available; ND, not determined; RTI, respiratory tract infection.

*By univariate analysis, regardless of daycare type.

In repeated measures variance analyses stratified according to confounding factors, associations remained ($p < 0.0001$ for the effect of time and $p < 0.001$ for daycare type for all analyses, except for those with parental asthma, where $p = 0.004$ for daycare type). Online supplementary figures S1 and S2 illustrate the association of start of daycare with respiratory tract infections in children stratified according to the presence of siblings and maternal post-secondary education. For children without older siblings, the rise of sick days per month after start of daycare was more pronounced than for those with older siblings.

Discussion

In this study there was a strong but temporally limited effect of daycare initiation on the rate of RTIs. This was strongest for the DCC group and weaker for the FDC group. An effect of overall time in daycare,[4-7] as well as daycare type, on infections has been documented in previous studies.[5, 13-15] Our study specifically focused on RTI dynamics around the start of daycare.

We analyzed three main outcome measures. After showing a peak, the rate of sick days returned near to baseline within our 9-month follow-up period from the start of daycare; for antibiotic use there was more scatter with a less pronounced decline, and parental absence from work did not return to baseline, which was to be expected due to the fact that both parents tend to be at work after the start of daycare. Consideration of confounders did not change our findings. The effect of older siblings on infections in relation to daycare has been previously described,[7] and our findings are in line with previous results.

We obtained a small, but significant effect for overall time in our analysis for sick days also within the comparison group of children in home care. There was no consistent trend over time, but rather a random variation between different months in the comparison group. The effects of virus epidemics and season of year were minimized by the way the baseline group was formed, but they cannot be completely excluded.

We consider the main strength of our study the detailed follow-up on a day-to-day basis for a relatively large number of cases and in chronological relation to the start of daycare. Previous cohort studies mostly assessed data from follow-up with intervals of months or longer periods and without information on the exact starting point of daycare, such that detailed chronological analyses for the time around the start of daycare could not be carried out.[5, 6, 8, 12] Retrospective collection of data relating to symptoms poses problems in some other studies, since it strongly relies on parents' memories.

There are some limitations to our study. Follow-up time was relatively short albeit sufficient to demonstrate the above described effects. Outcome measures were based on self-reported data and are thus subject to bias. Daily diary-keeping demanded regular participation of families, although diaries were concise and easily completed. There were several indicators that, for the small number of families with known smoking, diaries were not completed as comprehensively as in the rest of the cohort, so that we had to exclude parental smoking as a confounder from our study. The group with more detailed follow-up during infections had access to our medical services free of charge, and thus may have been more motivated to accurately document all experienced events. Inclusion into this group was offered to all families without any selection criteria.

Due to strict requirements for comprehensive follow-up and careful exclusion of missing data, we lost a considerable proportion of cases. In order to screen for bias, a comparison of background variables was performed for non-responders and responders at 13 months of age, and there were only minor differences between groups.[9]

Our cohort children had less often older siblings than all eligible children, and their mothers had higher education and occupational status.[9] Otherwise our cohort represents the Southwest Finnish population well. Although lower socioeconomic class has traditionally been linked to an increased rate of infectious diseases,[16] a Swedish study found an association between low social status, smaller likelihood to be cared for in out-of-home care, and lesser consumption of medical services.[17] Within our cohort, social status, as indicated by maternal education, was also reflected by a higher rate of RTIs, but this did not affect our findings relating to daycare.

Conclusion

In this longitudinal cohort study, the respiratory infectious disease burden was clearly related to out-of-home care, but it decreased already within a short follow-up time of 9 months after the start of daycare. These findings have implications on a correctly focused approach when supporting families with small children. Families, daycare providers and pediatricians may be reassured of the transient nature of increased RTIs after the start of daycare.

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Footnotes

Competing interests. The authors have no competing interests.

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Data sharing statement: Enquiries regarding extra data can be emailed to Ville Peltola.

Contributors. LSH contributed to conception and design, the clinical follow-up and data collection, carried out data analyses, drafted the initial manuscript, and approved the final manuscript as submitted. LT and SK contributed to conception and design, the clinical follow-up and data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted. AK contributed to conception and design, coordinated data collection, carried out data analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted. VP conceptualized and designed the study, coordinated and supervised data collection and analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.

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Figure legends

Figure 1. Flow-diagram of the recruitment and follow-up of study children.

Figure 2. Means and 95% CIs (dashed lines) of sick days per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month).

Figure 3. Means and 95% CIs (dashed lines) of days with antibiotic treatment per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month). Dashed lines: transiently below the significance level.

Figure 4. Means and 95% CIs (dashed lines) of days with parental absence from work per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month). Dashed lines: transiently below the significance level.

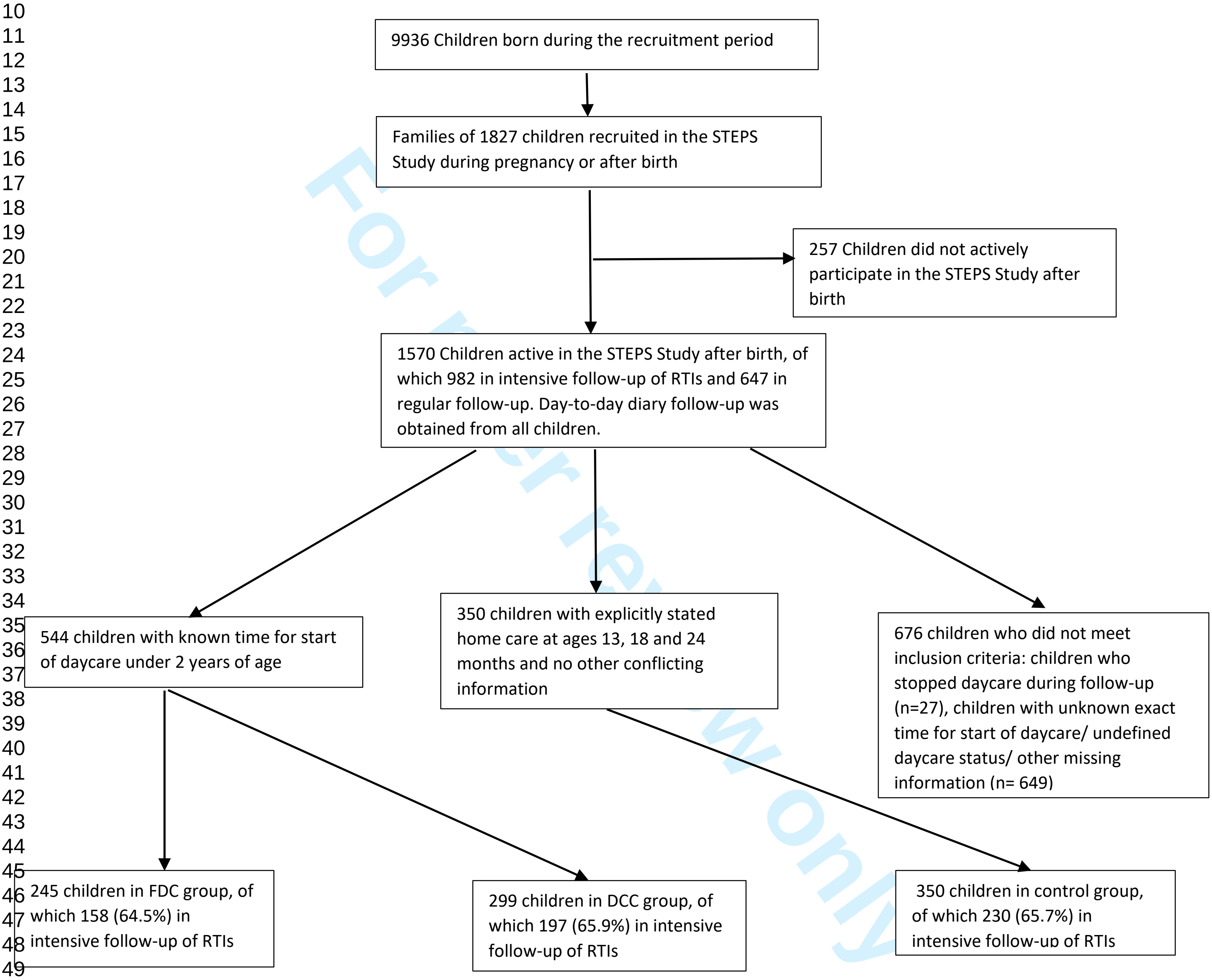

9936 Children born during the recruitment period
Families of 1827 children recruited in the STEPS Study during pregnancy or after birth
257 Children did not actively participate in the STEPS Study after birth
1570 Children active in the STEPS Study after birth, of which 982 in intensive follow-up of RTIs and 647 in regular follow-up. Day-to-day diary follow-up was obtained from all children.
544 children with known time for start of daycare under 2 years of age
350 children with explicitly stated home care at ages 13, 18 and 24 months and no other conflicting information
676 children who did not meet inclusion criteria: children who stopped daycare during follow-up (n=27), children with unknown exact time for start of daycare/ undefined daycare status/ other missing information (n= 649)
245 children in FDC group, of which 158 (64.5%) in intensive follow-up of RTIs
299 children in DCC group, of which 197 (65.9%) in intensive follow-up of RTIs
350 children in control group, of which 230 (65.7%) in intensive follow-up of RTIs

Figure 1

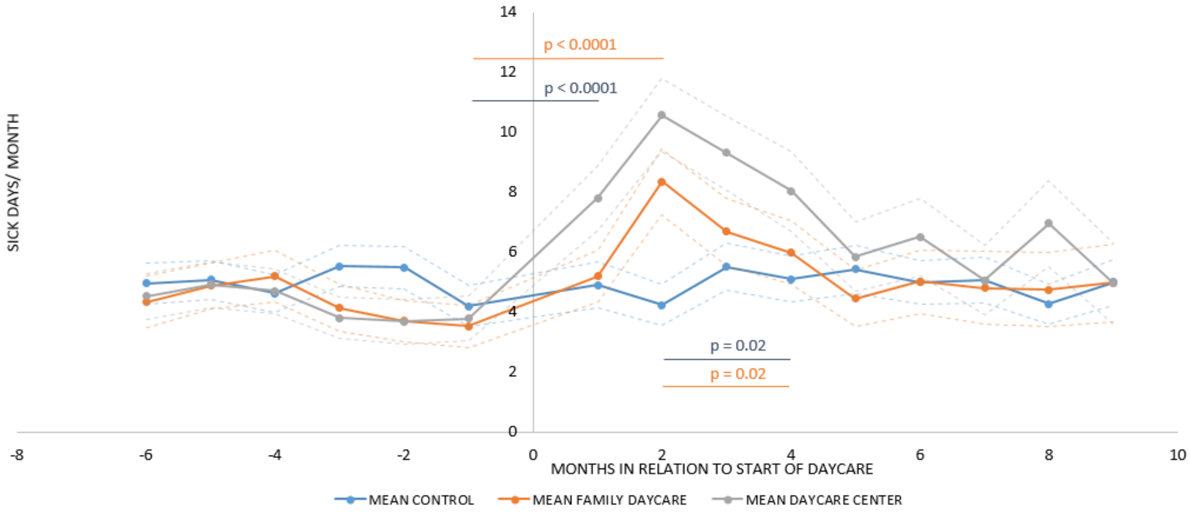

p < 0.0001
p < 0.0001
p = 0.02
p = 0.02
SICK DAYS/ MONTH
MONTHS IN RELATION TO START OF DAYCARE
MEAN CONTROL
MEAN FAMILY DAYCARE
MEAN DAYCARE CENTER

Figure 2

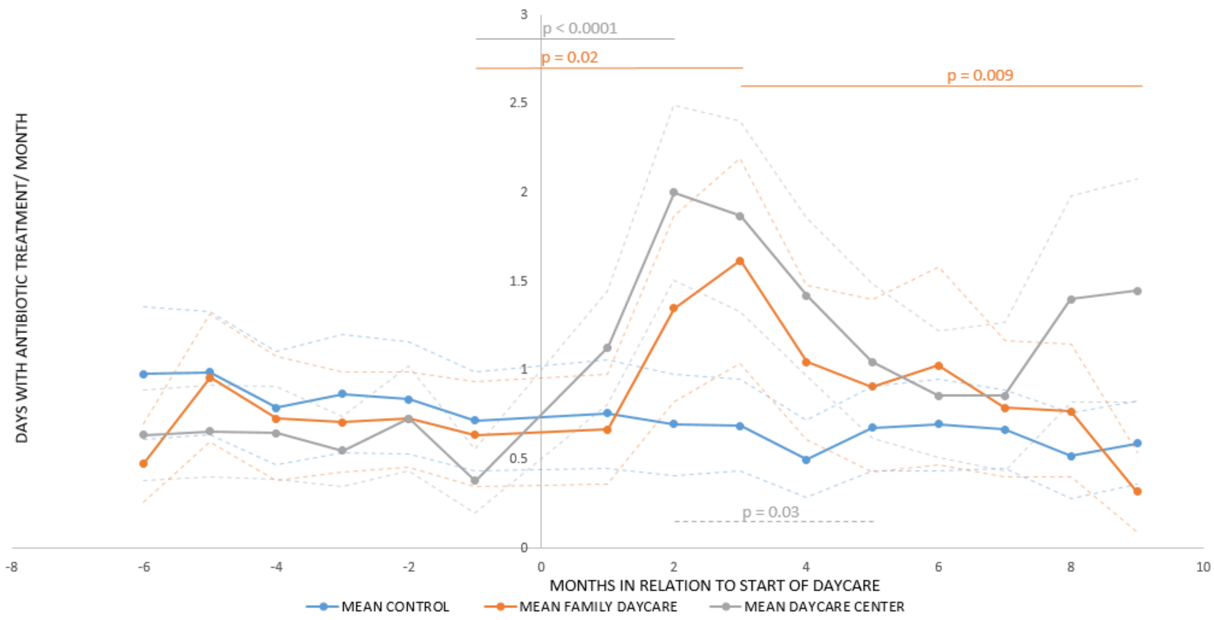

DAYS WITH ANTIBIOTIC TREATMENT/ MONTH
MONTHS IN RELATION TO START OF DAYCARE
MEAN CONTROL
MEAN FAMILY DAYCARE
MEAN DAYCARE CENTER
p < 0.0001
p = 0.02
p = 0.009
p = 0.03

Figure 3

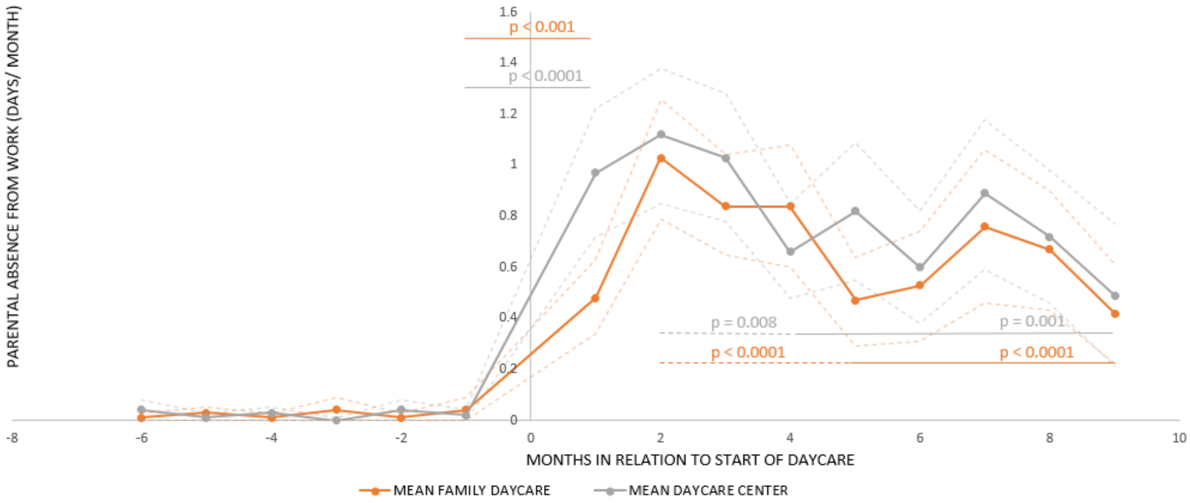
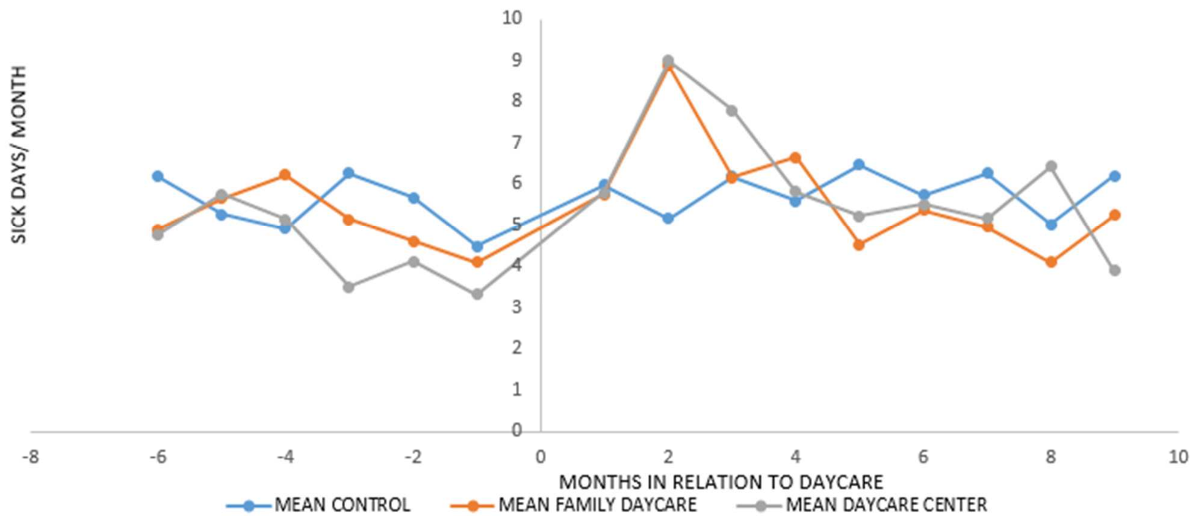

PARENTAL ABSENCE FROM WORK (DAYS/ MONTH)
MONTHS IN RELATION TO START OF DAYCARE
MEAN FAMILY DAYCARE
MEAN DAYCARE CENTER
p < 0.001
p < 0.0001
p = 0.008
p = 0.001
p < 0.0001
p < 0.0001

Figure 4

Supplemental material: figures S1 and S2.

A



B

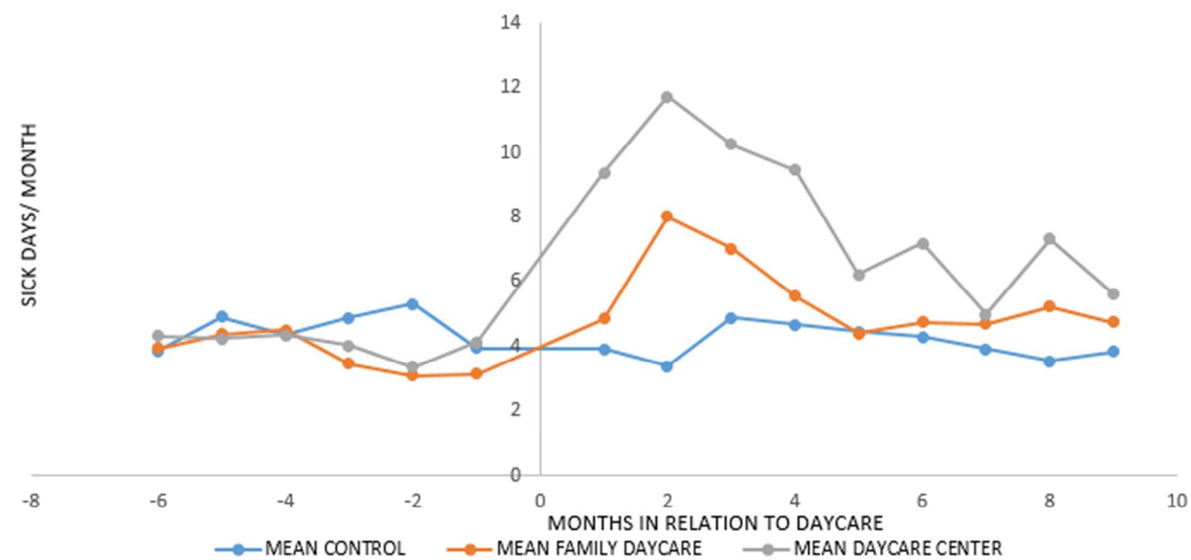


Figure S1. Mean sick days per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Data are shown for children with older siblings (A) and for children without older siblings (B).

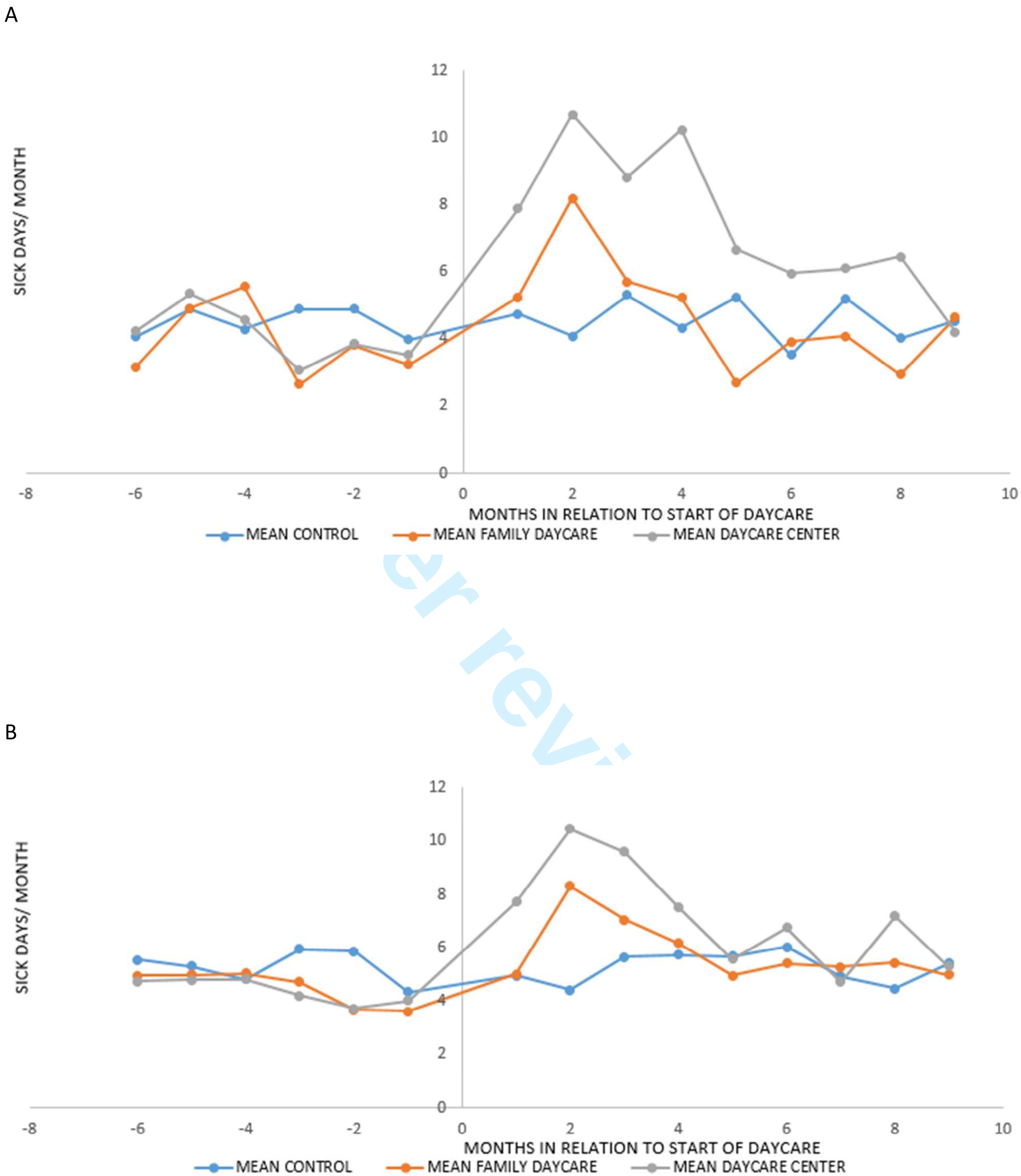


Figure S2. Mean sick days per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Data are shown for children of mothers with lower (A) and higher (B) post-secondary education.

Daycare attendance and respiratory tract infections: a prospective birth cohort study

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Daycare attendance and respiratory tract infections: a prospective birth cohort study

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Abstract

Objective. We explored the burden of respiratory tract infections in young children with regard to daycare initiation.

Design. Longitudinal prospective birth cohort study.

Setting and method. We recruited 1827 children for follow-up until the age of 24 months collecting diary data on respiratory tract infections and daycare. Children with continuous daycare type and complete data were divided into groups of centre-based daycare (n=299), family daycare (n=245), and home care (n=350). Using repeated measures variance analyses, we analysed days per month with symptoms of respiratory tract infection, antibiotic treatments, and parental absence from work for a period of 6 months prior to and 9 months after the start of daycare.

Results. We documented a significant effect of time and type of daycare, as well as a significant interaction between them for all outcome measures. There was a rise in mean days with symptoms from 3.79 (95% CI 3.04-4.53) during the month preceding centre-based daycare to 10.57 (95% CI 9.35-11.79) at 2 months after the start of centre-based daycare, with a subsequent decrease within the following 9 months. Similar patterns with a rise and decline were observed in the use of antibiotics and parental absences. The start of family daycare had weaker effects. Our findings were not changed when taking into account confounding factors.

Conclusions. Our study shows the rapid increase in respiratory infections after start of daycare and a relatively fast decline in the course of time with continued daycare. It is important to support families around the beginning of daycare.

Article summary

Strength and limitations of this study

- We prospectively collected detailed day-to-day diary data on respiratory tract infections and related outcomes from 0 to 2 years of age in a birth cohort population, and documented daycare type and starting date.
- The study design allowed us to analyze the time-dependent effects of centre-based daycare and family daycare on the days per month with symptoms of a respiratory infection in comparison with children of same age in home care.
- Different confounders were taken into account, but they did not change our findings of a peak in the rate of respiratory tract infections shortly after daycare initiation, and a clear decline thereafter.
- A limitation is that, due to strict requirements regarding detail in follow up, we lost a substantial proportion of cases.

Introduction

Daycare has been known to be a major risk factor for respiratory tract infections (RTIs) in children for over 30 years.[1-4] A considerable proportion of children in modern society attend daycare from the age of less than two years. RTIs in this age group constitute an important health problem. In addition to causing stress to children and families, they also affect transmission of pathogens to other age groups, parental absences from work with ensuing economic consequences, and rates of anti-microbial medication use with subsequent impact on resistance patterns.[5-7]

Within the daycare setting, factors reflecting contact rates with other children have consistently been identified as important determinants of infection risk. These factors include group sizes, or size and type of the daycare facility,[8-12] as well as weekly exposure time.[13] A number of studies have shown children of young age to be particularly vulnerable to daycare-related effects regarding transmission of respiratory virus infections,[8, 13-17] and early daycare has also been linked to more severe or long-term health problems, such as recurrent acute otitis media (AOM), high numbers of antibiotic medications during early childhood, an increased lifetime risk of asthma, and an increased risk of invasive pneumococcal infections.[18-20] In their cross-sectional study, Hurwitz et al. were the first to specifically demonstrate a lower daycare-attributable risk of RTIs with increased time after daycare initiation, and thus provided data to suggest that daycare-related infection risks were not exclusively linked to the absolute age of a child.[17] A large register-based study assessing RTI-related hospitalizations in under-school aged children confirmed a decrease of hospitalizations with an increased time in daycare of over 6 months.[14] Only a few larger-size longitudinal studies have assessed the effects of overall exposure time to daycare in relation to RTIs,[15, 16, 21] and lose frequency of follow-up has limited the conclusions of chronological variations. Some studies have found a protective effect of starting daycare early with regard to RTIs later in life.[16, 21]

Given the discrepancy between potential risks and benefits of early daycare in children under the age of 2 years, detailed longitudinal studies assessing the burden of disease as a function of time before and after the start of daycare are needed. Families, child health care professionals, and daycare providers would benefit from more detailed knowledge about the daycare-related impact of RTIs on this vulnerable age-group over time. We examined our hypothesis of a time-limited effect of daycare on RTIs in a prospectively followed birth cohort.

Methods

Study population and conduct

We used the cohort of the observational 'Steps to the Healthy Development and Well-being of Children' Study (The STEPS Study), which consists of 1827 children from 1797 families.[22] Recruitment occurred in two stages from women with a live birth between 1 January 2008 and 31 March 2010 in the Southwest Finland Hospital District (n=9936). During the first stage, 1387 families were recruited through community midwifery services during pregnancy, and a further 410 families joined the study soon after the birth of their child. In this study, follow-up included an age frame of 0-2 years, until March 2012. We collected questionnaire-based data on family related factors and daycare arrangements at gestational week 20, and at ages 13 months, 18 months, and 24 months, as applicable. Families kept study diaries that recorded health related factors, the precise starting date of daycare, and data from physician visits. Parents documented the child's symptoms, antibiotic treatments, and parental absence from work on a day-to-day basis in these diaries. Parents were instructed to also mark symptom-free days in the diary. We differentiated missing from negative data by excluding follow-up with no diary markings.

Families attended our nurse-led study clinic when the child was 2 and 13 months of age. During RTIs part of the cohort (n=982) were also followed up by our physician-led study clinic.[23] Recruitment of children to our study is shown in figure 1. Exclusion criteria for this study constituted discontinued follow-up before daycare initiation, insufficient information on daycare arrangements, or a lack of information on home care. The Ethics Committee of the Hospital District of Southwest Finland approved the study protocol. The parents of the participating children gave their written, informed consent.

Daycare attendance

Children were categorized into three different groups according to daycare arrangements: children cared for by parents or relatives (home care group), children attending family daycare (FDC), and children attending daycare centres (DCC). In this study family daycare was defined as daycare provided by a trained carer in her or his home, or in the children's homes using a rotational system. According to local regulations, FDC group sizes included no more than 5 children. In rare cases, carers worked together forming a common nursery. Since group sizes tended to be relatively small in those nurseries, these children were included in the FDC group. Daycare centres were defined by larger-group, centre-based care provided by several professional carers. FDC and care in DCCs were provided either by the municipality or on a private basis.

Outcomes

The outcomes of the study were symptoms of RTIs (cough, rhinorrhea, fever, or wheeze), consumption of antibiotic medication, and parental absence from work as recorded on a day-to-day basis in the study diaries. Antibiotic medications prescribed for any reason were included, but the main indication was AOM. Any parental absence from work due to the child's illness was recorded, and reasons were not limited to RTIs. Final outcome measures constituted days per month with RTI symptoms (sick days), antibiotic medication, and parental absence from work.

Confounding factors

The following potential confounders were taken into consideration: sex, siblings, season of year at start of daycare, asthma in the parents, pets (cats or dogs at home), maternal post-secondary education, and family monthly net income.[24-26] There was only a small proportion of families with known smoking in either one of the parents (127 within the home care, FDC and DCC groups), and since our results indicated reporting bias, this variable was excluded from the analyses.

Statistical analysis

All statistical analyses were carried out using SAS version 9.4 (SAS, Cary, NC, USA). In all our analyses P-values less than 0.05 were regarded as statistically significant. In the first step, outcome variables were calculated as days per month for each child and aligned in a time sequence relating to the beginning of daycare. Follow-up included a time of 6 months previous to and 9 months after the beginning of daycare. Since children commenced daycare at different ages, this meant that not all data of individual follow-up related to the fixed age frame of 0-2 years. Data from outside this age range were excluded from the analysis using the SAS MIXED procedure. For the home care group the equivalent age range of follow-up was calculated using the mean age of starting daycare in the FDC and DCC groups (mean starting age at 15 months), and resulted in a follow-up period from 9 to 24 months (6 months prior to and 9 months after the mean start of daycare at 15 months).

If a child finished daycare during follow-up for any reason, data after discontinuation of daycare were selectively excluded by the SAS MIXED procedure.

After comparisons using independent sample t-tests and variance analyses, data were analyzed by repeated measures variance analysis comparing all three groups for type of daycare and time, as well as their interaction. In a second step, we compared the difference of least square means between all pairs of analyzed months and determined the shortest time intervals during which statistically significant differences in our outcome measures could be observed. The shortest time for a rise of outcome measures was determined from the last month prior to starting daycare and for a decline from the peak of each outcome variable. Although the distributions of monthly outcome variables (sick days, days with antibiotic treatment, and parental absence from work) were skewed in our analyses (coefficient of skewness up to 2.4 and kurtosis 7.6), the pairwise difference variables followed approximately a normal distribution.

In a third step, repeated measures variance analysis was repeated according to the previous model, but stratifying according to individual confounding factors.

Sensitivity testing was performed by additional variance analyses excluding all data from children who finished daycare during follow-up.

Results

Figure 1 shows numbers of children within follow-up. Within our cohort of 1570 children in active follow-up, 276 (21.8%) of 1264 children with data on daycare arrangements at age 13 months attended daycare (11.7% in DCC, 10.1% in FDC) and 593 (55.0%) of 1079 children attended daycare at the age of 24 months (29.5% in DCC and 25.0 % in FDC). At all ages the vast majority of children in daycare spent over 5 hours per day at daycare (88.5% at age 13 months and 91.6% at age 24 months). Group sizes were clearly smaller for children attending FDC as compared to DCC, with 88.3% (at 13 months) to 82.7% (at 24 months) of families reporting a group size of less than 5 children per group. In DCC group sizes were variable with the following results for the ages of 13 months (and 24 months): less than 5 children for 2.0%, 5-15 children for 86.8%, over 15 children for 11.1% (less than 5 children for 1.4%, 5-15 children for 87.8%, over 15 children for 10.9%).

Missing knowledge regarding the exact time of start of daycare, or earlier discontinuation of the study, led to a drop-out of a large part of cases, but these drop-outs occurred mostly before the start of daycare (figure 1). Baseline characteristics and mean (SD) values of outcome measures of children included in the analysis are shown in table 1. Mean age at the beginning of daycare was 15 months (SD 4.1). Start of daycare (FDC or DCC) occurred in 38.2% of cases during fall-winter (October to March) and in 61.8% during spring-summer (April to September). Over the whole follow-up period during daycare, children in DCC had only slightly more sick days per month (mean 5.54, SD 4.07) compared to children in FDC (mean 4.85, SD 3.49) or home care (mean 4.80, SD 3.39). There was no significant difference in days with antibiotic treatment. Parental absences from work could not be compared to the home care group, since the stay-at-home parent was not employed, and could therefore not be absent from work. Discontinuous daycare was observed in only a minority of children (11 children in FDC and 13 children in DCC). The results remained consistent in analyses performed without data from children who finished daycare during follow-up.

Table 1. Comparisons of baseline variables and outcome measures according to daycare type

	Type of daycare			
	Home care (n = 350)	Family daycare (n = 245)	Daycare centre (n = 299)	P
Age at the beginning of daycare, mean (SD)	NA	1.24 (0.37)	1.28 (0.35)	0.25*
Sex				
Males, number (%)	172 (49.1%)	124 (50.6%)	162 (54.1%)	0.4†
Born preterm (<37 gestational weeks), number (%)	18 (5.0%)	7 (2.9%)	14 (4.7%)	0.38†
Sick days per month, mean (SD)	4.80 (3.39)	4.85 (3.49)	5.54 (4.07)	0.03‡
Days with antibiotic treatment per month, mean (SD)	0.74 (1.41)	0.82 (1.36)	0.93 (1.14)	0.21‡
Days with parental absences from work per month, mean (SD)	NA	0.31 (0.38)	0.36 (0.45)	0.17*

NA, not applicable.

*Independent sample t-test

†Chi-square test

‡Unadjusted variance analysis

There was a peak of mean sick days per month at 2 months after the start of daycare for both FDC and DCC (figure 2). The rise in sick days was stronger for the DCC group than for the FDC group. We observed increases from 3.53 mean sick days (95% CI 2.83-4.24) during the month prior to the start of daycare to 8.34 mean sick days per month (95% CI 7.25-9.43) for the FDC group, and from 3.79 (95% CI 3.04-4.53) mean sick days prior to the start of daycare to 10.57 (95% CI 9.35-11.79) mean sick days per month for the DCC group. For both of these groups, the rise of outcome measures was a transient phenomenon; sick days were comparable to the home care group at 5 months after the start of daycare. Antibiotic use (figure 3) and parental absences from work because of children's illnesses (figure 4) rose and declined according to a pattern similar to that observed in sick days in relation to the start of daycare, although this decline was less pronounced compared to sick days.

The rise in sick days (figure 2) and antibiotic use (figure 3) was more rapid among children starting DCC than in those starting FDC. Within the home care group there were no significant findings in pairwise comparisons between months.

In repeated measures variance analyses there was a significant overall effect for time and type of daycare and their interaction for all outcome measures. This interaction showed the above described pattern of rise and decline, which was strongest for the DCC group and weaker for the FDC group. Within the home care group there was no such pattern, but variation was observed in the frequency of sick days per month over time. When analyzing sick days and antibiotic use between different types of daycare without the aspect of time, levels of these outcome measures were higher in the DCC group in comparison to the home care group ($P < 0.001$ for both measures) and FDC group ($P < 0.001$ and $P = 0.04$, respectively). There were no significant differences between the FDC and home care group.

The presence of older siblings in the family, higher post-secondary education in mothers, and higher family income were all associated with a higher burden of disease (table 2).

Table 2. Effects of confounding factors on the rates of RTI symptoms (sick days) according to daycare type

	Type of daycare							
	Home care		Family daycare		Daycare centre			
	n/N (%)	Sick days per month, mean (SD)	n/N (%)	Sick days per month, mean (SD)	n/N (%)	Sick days per month, mean (SD)	P*	P for interaction with mode of daycare
Older siblings							0.02	<0.001
Yes	162/ 350 (46.3)	5.55 (3.72)	99 /245 (40.4)	5.26 (3.33)	132/ 299 (44.1)	5.10 (3.72)		
No	188/ 350 (53.7)	4.16 (2.95)	146/ 245 (59.6)	4.58 (3.59)	167/ 299 (55.9)	5.88 (4.31)		
Higher post-secondary education in mother							0.009	0.27
Yes	211/ 341 (61.9)	5.12 (3.53)	161/ 239 (67.4)	5.12 (3.72)	203/ 293 (69.3)	5.66 (3.75)		
No	130/ 341 (38.1)	4.40 (3.17)	78 / 239 (32.6)	4.23 (2.97)	90/ 293 (30.7)	5.45 (4.79)		
Family net income under 2000 euros per month							0.005	0.37
Yes	83/ 343 (24.2)	4.15 (3.28)	33/ 239 (13.8)	3.43 (2.75)	56/ 294 (19.0)	5.29 (3.39)		
No	260/343 (75.8)	5.03 (3.43)	206/ 239 (86.1)	5.04 (3.57)	238/ 294 (81.0)	5.64 (4.23)		
Start of daycare during fall-winter (October-March)							0.39	0.61
Yes	NA	NA	100/ 245 (40.8)	4.90 (3.15)	108/ 299 (36.1)	5.69 (4.21)		
No	NA	NA	145/ 245 (59.2)	4.82 (3.73)	191/ 299 (63.9)	5.45 (4.0)		
Asthma in parents							0.95	0.72
Yes	35/ 340 (10.3)	4.65 (3.26)	26/ 234 (11.1)	5.54 (4.0)	30/ 287 (10.5)	5.83 (4.25)		
No	305/ 340 (89.7)	4.86 (3.43)	208/ 234 (88.9)	4.76 (3.45)	257/ 287 (89.5)	5.56 (4.08)		
Cat or dog at home							0.31	0.23
Yes	94/ 295 (31.9)	4.43 (3.07)	80/ 196 (40.8)	4.83 (3.07)	57/ 219 (26.0)	5.80 (4.28)		
No	201/ 295 (68.1)	5.14 (3.48)	116/ 196 (59.2)	4.92 (3.14)	162/ 219 (74.0)	5.68 (3.66)		

n/N, number of children per number of those with data available; NA, not applicable; RTI, respiratory tract infection.

*By univariate analysis, regardless of daycare type.

In repeated measures variance analyses stratified according to confounding factors, associations remained ($P < 0.001$ for the effect of time and $P < 0.001$ for daycare type for all analyses regarding sick days, except for those with parental asthma, where $P = 0.004$ for daycare type). Online supplementary figures S1 and S2 illustrate the association of start of daycare with respiratory tract infections in children stratified according to the presence of siblings and maternal post-secondary education. For children without older siblings, the rise of sick days per month after start of daycare was more pronounced than for those with older siblings.

Discussion

In this study there was a strong, but temporally limited effect of daycare initiation on the rate of RTIs. This was strongest for the DCC group and weaker for the FDC group. An effect of overall time in daycare,[14, 15, 17] as well as daycare type, on infections has been documented in previous studies.[8, 10, 11, 13] Our study specifically focused on RTI dynamics around the start of daycare.

We analyzed three main outcome measures. After showing a peak, the rate of sick days returned near to baseline within our 9-month follow-up period from the start of daycare; for antibiotic use there was more scatter with a less pronounced decline, and parental absence from work did not return to baseline, which was to be expected due to the fact that both parents tend to be at work after the start of daycare. Consideration of confounders did not change our findings. The effect of older siblings on infections in relation to daycare has been previously described,[17] and our findings are in line with previous results. The effects of virus epidemics and season of year were minimized in our study setting, but they cannot be completely excluded.

We consider the main strength of our study the detailed follow-up on a day-to-day basis for a relatively large number of cases and in chronological relation to the start of daycare. Previous cohort studies mostly assessed data from follow-up with intervals of months or longer periods and without information on the exact starting point of daycare, such that detailed chronological analyses for the time around daycare initiation could not be carried out.[13, 15, 16, 26] Retrospective collection of data relating to symptoms poses problems in some other studies, since it strongly relies on parents' memories.

There are some limitations to our study. Exposure to daycare was documented as hours per day only. However, irregular daycare was rare and high daily exposure can be extrapolated to high weekly or monthly exposure. Follow-up time was relatively short albeit sufficient to demonstrate the above described effects. Outcome measures were based on self-reported data and are thus subject to bias. Daily diary-keeping demanded regular participation of families, although diaries were concise and easily completed. There were several indicators that, for the small number of families with known smoking, diaries were not completed as comprehensively as in the rest of the cohort, so that we had to exclude parental smoking as a confounder from our study. The group with more detailed follow-up during infections had access to our medical services free of charge, and thus may have been more motivated to accurately document all experienced events. Inclusion into this group was offered to all families without any selection criteria.

Due to strict requirements for comprehensive follow-up we lost a considerable proportion of cases. For all cases lost, missing data were collected before or at the time of daycare initiation, which means that the majority of drop-outs occurred before the critical follow-up after daycare initiation. This decreases the potential effect of exclusion-related bias on our results. In order to screen for bias, a comparison of background variables was performed for non-responders and responders at 13 months of age, and there were only minor differences between groups.[22]

Our cohort children had less often older siblings than all eligible children, and their mothers had higher education and occupational status.[22] Otherwise our cohort represents the Southwest Finnish population well. Although lower socioeconomic class has traditionally been linked to an increased rate of infectious diseases,[27] a Swedish study found an association between low social status, smaller likelihood to be cared for in out-of-home care, and lesser consumption of medical services.[28] Within our cohort, social status, as indicated by maternal education and family income, was also reflected by a higher rate of RTIs, but this did not affect our findings relating to daycare.

Conclusion

In this longitudinal cohort study, the respiratory infectious disease burden was clearly related to out-of-home care, but it decreased already within a short follow-up time of 9 months after the start of daycare. Our findings demonstrate a clearly limited temporal impact of daycare-related RTIs in early childhood, which has implications on a correctly focused approach when supporting families with small children. Families, daycare providers and pediatricians may be reassured of the transient nature of increased RTIs after the start of daycare.

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Footnotes

Competing interests. The authors have no competing interests.

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Data sharing statement: Enquiries regarding extra data can be emailed to Ville Peltola.

Contributors. LSH contributed to conception and design, the clinical follow-up and data collection, carried out data analyses, drafted the initial manuscript, and approved the final manuscript as submitted. LT and SK contributed to conception and design, the clinical follow-up and data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted. AK contributed to conception and design, coordinated data collection, carried out data analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted. VP conceptualized and designed the study, coordinated and supervised data collection and analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.

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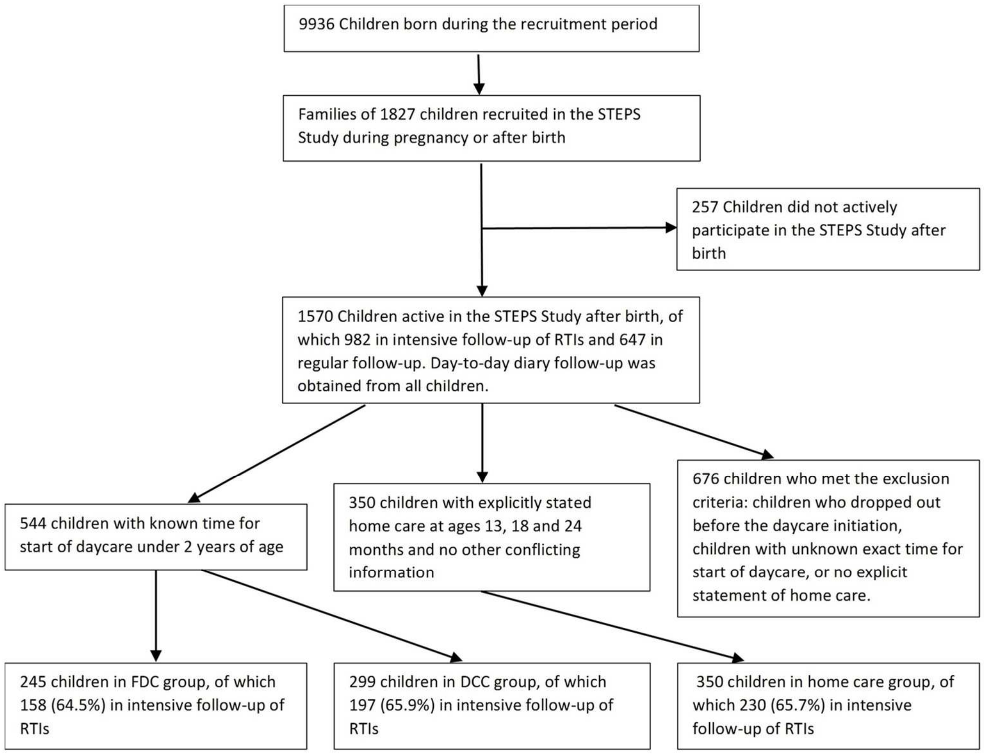
Figure legends

Figure 1. Flow-diagram of the recruitment and follow-up of study children.

Figure 2. Means and 95% CIs (dashed lines) of sick days per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month).

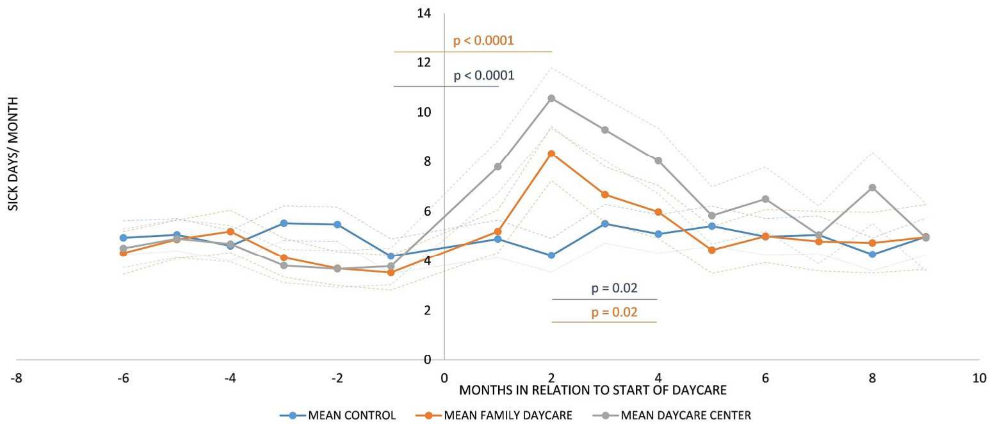
Figure 3. Means and 95% CIs (dashed lines) of days with antibiotic treatment per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month). Dashed lines: transiently below the significance level.

Figure 4. Means and 95% CIs (dashed lines) of days with parental absence from work per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month). Dashed lines: transiently below the significance level.



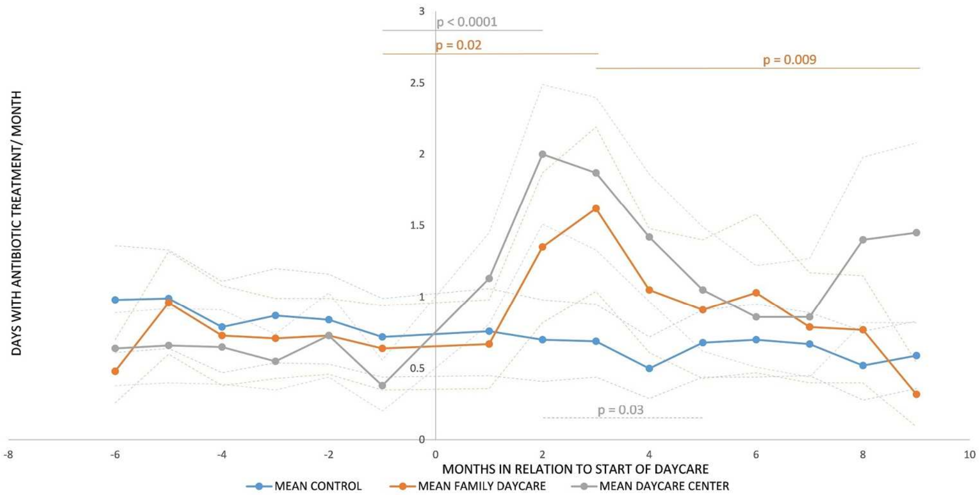
Flow-diagram of the recruitment and follow-up of study children.

66x50mm (600 x 600 DPI)



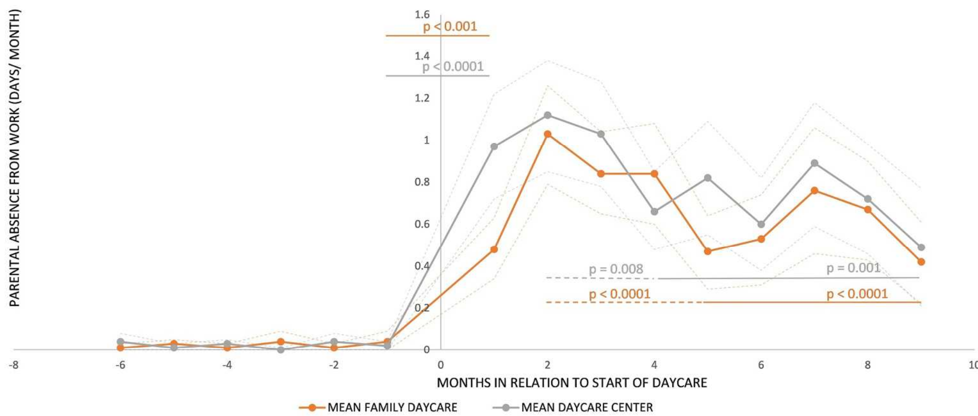
Means and 95% CIs (dashed lines) of sick days per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month).

173x86mm (300 x 300 DPI)



Means and 95% CIs (dashed lines) of days with antibiotic treatment per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month). Dashed lines: transiently below the significance level.

173x87mm (300 x 300 DPI)



Means and 95% CIs (dashed lines) of days with parental absence from work per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Horizontal lines indicate the shortest time for a significant rise (decline) from the last month prior to starting daycare (from the peak month). Dashed lines: transiently below the significance level.

173x87mm (300 x 300 DPI)

Supplemental material: figures S1 and S2.

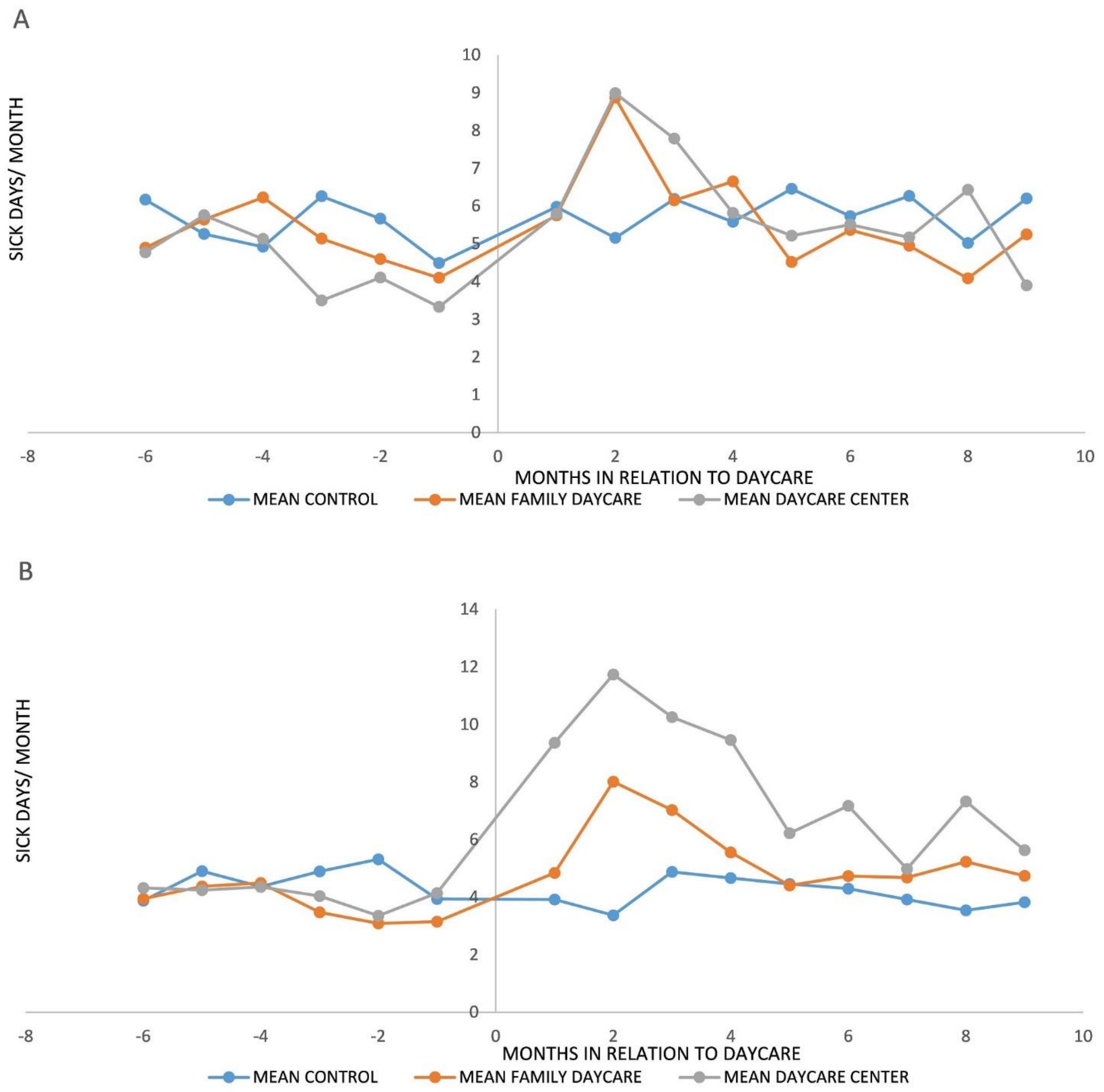


Figure S1. Mean sick days per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Data are shown for children with older siblings (A) and for children without older siblings (B).

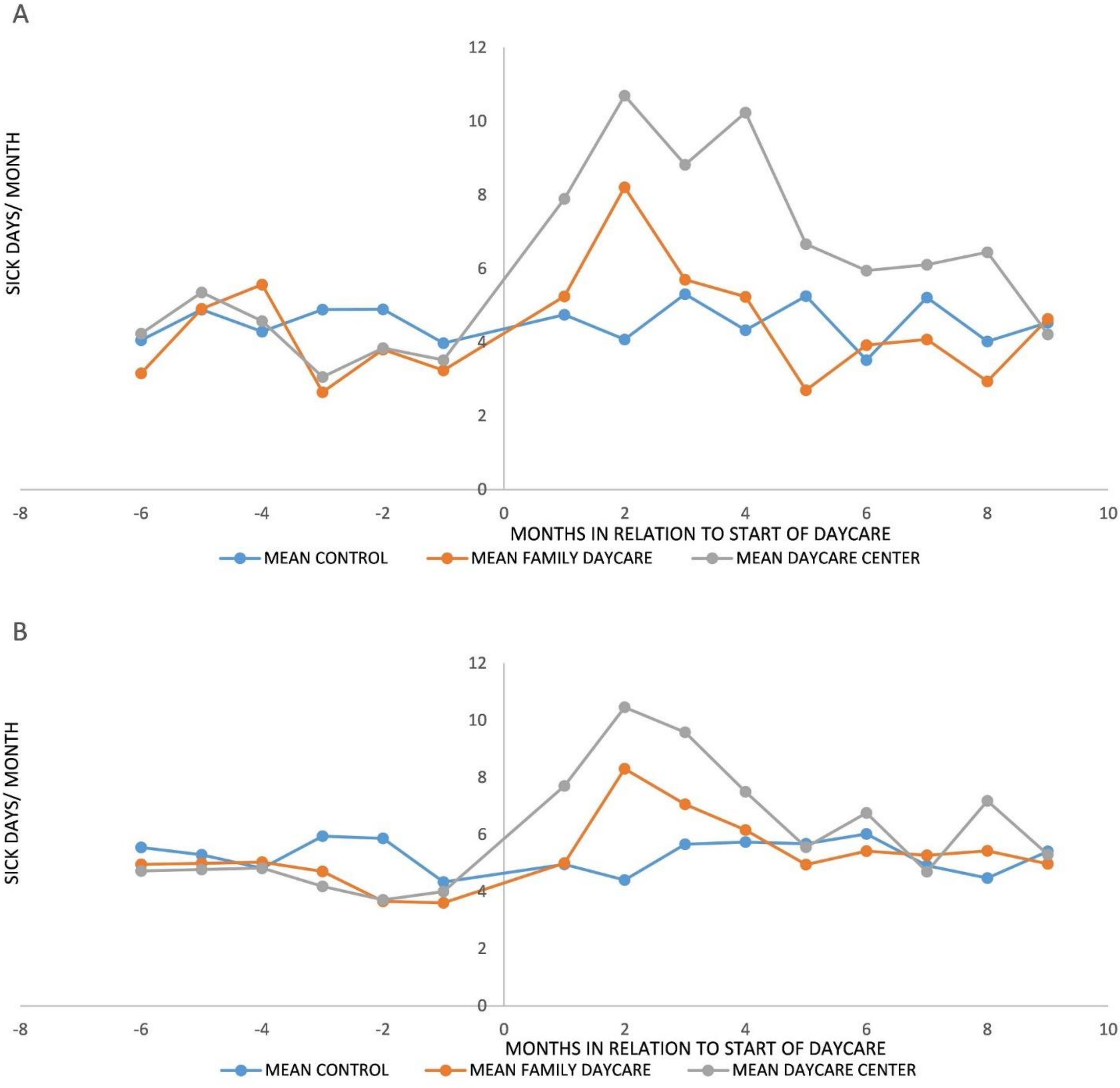


Figure S2. Mean sick days per month according to daycare groups in relation to start of daycare. Negative months denote the period prior to start of daycare. Data are shown for children of mothers with lower (A) and higher (B) post-secondary education.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Manuscript ID bmjopen-2016-014635, revision 1. Schuez-Havupalo L et al. Daycare attendance and respiratory tract infections: a prospective birth cohort study

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	p 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	p 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	p 4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	p 5
Methods			
Study design	4	Present key elements of study design early in the paper	p 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p 5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	p 5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p 6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	p 5-7
Bias	9	Describe any efforts to address potential sources of bias	p 8 (cf. results/ discussion)
Study size	10	Explain how the study size was arrived at	p 5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p 7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	p 7-8
		(*b*) Describe any methods used to examine subgroups and interactions	p 8
		(*c*) Explain how missing data were addressed	p 7-8 (cf. results/ discussion)

		(*d*) If applicable, explain how loss to follow-up was addressed	p 8, 9
		(*e*) Describe any sensitivity analyses	p 8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	p 8-9, fig 1
		(b) Give reasons for non-participation at each stage	fig 1
		(c) Consider use of a flow diagram	fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	p 8-10
		(b) Indicate number of participants with missing data for each variable of interest	p 8-9, fig 1
		(c) Summarise follow-up time (eg, average and total amount)	p 5, 7-8
Outcome data	15*	Report numbers of outcome events or summary measures over time	p 9, table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p 11-15, table 2
		(*b*) Report category boundaries when continuous variables were categorized	tables 1 and 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	p 8-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	p 15
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p 15-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	p 17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.