Infections in small children and their families - symptoms,consultations and antibioitcs

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Abstract

Infectious symptoms in infants and their families are common. With rising age the number of symptom day decreases, but increases again for the parents of infants. About one quarter of the symptom days lead to absence from daycare among the infants but the social remuneration system was used by the parents only in 1/3 of the absence days. Among the adults 12% of the symptoms days lead to absence from work and, here the social insurance system was used in 75% of the symptom days. A small proportion of the symptom episodes leads to a physician consultation and antibiotic prescription.

The differences in antibiotic prescription to small children between different communities in Sweden could not be explained by differences in reported infectious symptoms, differences in socioeconomic factors, daycare, "concern about infectious illness" in the family or physician consultations. This indicates that physicians' habits are of importance.

Infectious symptoms are more common among infants in daycare than among infants in home care. When infants in daycare are taken to consult a physician they are treated in the same way as infants in home care as regards antibiotic prescription

It is possible with little additional effort to inform and train personnel at daycare centres about infections and how they are spread, within the framework of ordinary preschool activities. There was a greater understanding of when a child should be kept at home and when a physician should be consulted. In the small interventional study there was a trend towards lower sickness absence, fewer physician consultations and fewer antibiotic prescriptions to the children.

Key words: preschool children, families, daycare, infectious symptoms, physician consultations, antibiotic prescription

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List of Publications

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IV Hedin K, Petersson C, Cars H, Beckman A, Håkansson A. Infection prevention in day-care centres: Feasibility and possible effects of intervention. Scand J Prim Health Care 2006;24:44-49.

Preface

Respiratory tract infections have been the focus of studies since the early twentieth century. I became interested in this topic in the mid-1990s. At that time I had worked as an "ST physician" for a few years and I met many parents who consulted me for small children's respiratory tract infections. I also had three little boys at home who contracted respiratory tract infections every now and then. During the winter season they almost always had runny noses, earaches and coughs and I wondered if that was normal.

The recommended treatment for otits media was antibiotics, and I think antibiotics also were given to many children with a common cold or cough. According to official statistics antibiotic prescriptions increased between 1980 and the early 1990s. In the mid-1990s there was a decrease in prescription rates. When looking at the statistics I also became aware that there were great differences in prescription rates to children ages 0–6 in different Swedish counties and municipalities. Kronoberg County had one with the highest prescription rates, almost twice as high as in the county of Dalarna.

As a mother I wondered if it was normal for small children to always have runny noses during the winter season. As a mother, I also wondered how often all these symptoms led to absence from daycare.

As a physician I wondered how often parents of children with respiratory tract symptoms made a physician consultation with their ill child. Antibiotic prescription and differences in antibiotic prescription rates between municipalities were of special interest to me.

A few years later, my "ST" supervisor encouraged me into this research field. Working with other interested physicians, we planed the studies being reported on here.

Background

Health problems expressed as symptoms of different kinds are an everyday part of most people' lives. For families with small children on 27% of all days some kind of symptom is reported in the family (Dahlquist et al., 1987) and on 49% of the days in children younger than 5 years (Cunningham-Burley and Irvine, 1987). On about 65% of these days some kind of action is taken (Bergström et al., 1985, Cunningham-Burley and Irvine, 1987). Many people do not consult a physician when they are ill, and it has been found that contact with the professional health care system was taken on only 7% of the symptom days (Cunningham-Burley and Irvine, 1987). The decision to consult a physician is not based only on the presence or severity of symptoms, but also on a number of non-medical factors (Campbell and Roland, 1996).

Morbidity in infectious diseases

Infections are the most commonly reported health problem among children and adults (Bergström et al., 1985, Dahlquist et al., 1987, Monto, 1994, Holme, 1995, Bruijnzeels et al., 1998b). In children, about 80% of the days with reported health problem are attributable to infections (Dahlquist et al., 1987, Hojer et al., 1987), which is more than reported in adults. Mothers reported having infectious symptoms on 37% of the days with a health problem and fathers on 53% (Dahlquist et al., 1987).

Among infections, respiratory tract symptoms are the most common cause of morbidity in both children and adults (Monto, 1994, Bruijnzeels et al., 1998b) and this has been known since the first population based study was conducted in the early twentieth century (Sydensticker, 1926). Since then, many studies have been conducted describing the patterns of RTIs. Both frequency (Lidwell and Sommerville, 1951, Buck, 1956) and seasonality (Frost and Gover, 1932) have been studied, as well as the importance of sex and age (Van Volkenburg and Frost, 1933, Tucher, 1952). In the late 1940s and early 1950s methods were developed making it possible to identify the agents involved (Monto, 1994).

Rhinovirus is the most common respiratory virus (Monto and Sullivan, 1993, Vesa et al., 2001). The best known and one of the latest studies is the prospective, population based Tecumseh study (Monto et al., 1971, Monto and Ullman, 1974).

Age and sex

The Tecumseh study found that respiratory tract infections (RTIs) are most common in the youngest children (Monto and Ullman, 1974). Between the ages of one and two, an average of 5 respiratory illness episodes were experienced (Monto and Sullivan, 1993). Until the age of nineteen the number of episodes falls gradually to around two per year (Monto and Sullivan, 1993).

An American retrospective population based telephone interview study found that 27% of the children younger than 36 months had had some upper RTI at any time during the two weeks before the interview, as compared with 20% of the children 36 months or older (Fleming et al., 1987). The mean number of days with cold, wheeze or cough was 16.3 per 100 child days at risk in a diary study in children up to two years (Holme, 1995).

In the age group 1 to 2 years, more respiratory illness episodes have been reported for boys than girls (Monto and Ullman, 1974). Thereafter, no differences were found between girls and boys until the age of around ten (Monto and Sullivan, 1993). Another study did not find any differences in reported RTIs among girls and boys below five (Fleming et al., 1987), but between the ages of ten and nineteen the differences between girls and boys become more prominent, with more respiratory illness among girls (Monto and Ullman, 1974, Monto and Sullivan, 1993, Monto, 1994).

Studies from other countries found that French and Italian children had 4.2 infectious episodes of RTIs per year (Saunders et al., 2003) and Australian children aged 12 to 71 months had 0.53 influenza-like episodes per child-month (Lambert et al., 2005).

Among young adults, a peak at about three mean annual respiratory illnesses is seen around the age of twenty to twenty-four in women (Monto and Ullman, 1974). For men, the peak comes little later, around the age of twenty-five to thirty, with a mean of around two respiratory illness episodes a year (Monto and Ullman, 1974). Until the age of 60 the number of episodes declines steadily in both women and men (Monto and Ullman, 1974, Monto and Sullivan, 1993) and the difference in respiratory illnesses between women and men were statistically significant until the age of 60 (Monto and Sullivan, 1993).

Factors of importance for morbidity

Socioeconomic status

Income and educational level have been used to characterize the socioeconomic status of the family (Monto et al., 1971). Reported rates of respiratory illness decreased in relation to family wealth, but increased with educational level of head of household (Monto and Ullman, 1974). This was confirmed for income when testing sera for antibodies against different respiratory agents, while for educational level the observed increase could not be confirmed when testing sera. This may be attributable to differences in what individuals perceive to be illness (Monto and Ross, 1977). Lower social class children presented with more colds and lower respiratory tract infections (van den Bosch et al., 1992) and in a more recent study parents with college educations reported more occurrences of mild upper RTI than parents with lower education, in children in daycare younger than five years (Lu et al., 2004). Another study also, found that mothers with higher education report more morbidity in their children (Hansen, 1993).

No importance of family income has also been found. On the other hand, this study found that upper RTIs were associated with living in crowded conditions for children below 36 months but not for children 36 months or older (Fleming et al., 1987).

Smoking in the family

Several large cohort studies from the 1960s found that young smokers had more respiratory tract infections than their non-smoking peers (Murin and Bilello, 2005). The adult smokers caught more colds (Cohen et al., 1993), and their colds were more serious than non-smoking adults (Bensenor et al., 2001, Murin and Bilello, 2005).The occurrence and duration of lower RTIs was higher in smoking young adults than in non-smokers (Aronson et al., 1982). It has also been found that smoking increases the risk of influenza infections, bacterial pneumonia and tuberculosis in adults (Murin and Bilello, 2005). Parental smoking or maternal smoking were independent risk factors for sore throat and upper respiratory tract infections in children younger than fifteen (Willatt, 1986, Fleming et al., 1987) (Peat et al., 2001). Swedish studies found no effects of smoking on numbers of RTIs (Harsten et al., 1990) or on sickness absence in preschool children (Rasmussen and Bondestam, 1992).

Number of children in the family

No importance has been found as regards number of children younger than five in relation to the occurrence of upper RTIs (Fleming et al., 1987). Another study found an increased risk for children with siblings (Douglas et al., 1994, Kvaerner et al., 2000). The importance of siblings to the occurrence of RTIs was different in children in daycare in different age groups. For children ages 6 weeks to 17 months, exposure to siblings was associated with an increased risk of RTIs, while for children ages 36 to 59 months older siblings were a protective factor against respiratory illness (Hurwitz et al., 1991). Another study found less illness among daycare children with siblings than among those with out siblings (Dales et al., 2004).

Daycare

A study conducted between 1966 and 1969 found 8.4 respiratory illnesses per child/year in children in daycare, from infancy to five (Loda et al., 1972). In those age groups the number of respiratory illnesses was found to be the same as for children in home care, although in this study data were compared with a general population (Loda et al., 1972).

In children under two, a Swedish study found a mean of five febrile respiratory illness episodes in children in daycare as compared with a mean of two febrile respiratory illness episodes in children in home care (Strangert, 1976). A peak of 10.4 respiratory illnesses a year was found in children ages six months to one year (Denny et al., 1986), and around eight RTIs in children ages one to two years (Schwartz et al., 1994). A prospective study, where mothers made daily health calendars and study nurses made structured telephone interviews every second week, found an average of 7.1 illness episodes among children up to 18 months in daycare and 4.7 for children in home care (Wald et al., 1988).

More RTIs were also found in Swedish children below three in daycare (Harsten et al., 1990, Petersson and Håkansson, 1990, Wald et al., 1991a), and for Norwegian children ages 4 to 5 (Kvaerner et al., 2000). Another Norwegian study found a mean of 2.9 common colds during a year in three-to-five-years-old children in daycare compared with 2.4 in children in home care (Nafstad et al., 1999).

Of children ages up to five in daycare, 32% had had an upper respiratory tract infection during the two weeks before the interview, as compared with 21% of children not in daycare (Fleming et al., 1987).An American cohort study found, in a telephone survey, the

occurrence of respiratory illness the previous two weeks to be about the same, for children younger than 18 months, 34% of the children in daycare had reported respiratory illness, as compared with 26% of the children in home care (Hurwitz et al., 1991).

Data on respiratory tract illnesses in children ages 4 to 36 months in different forms of care showed more respiratory tract illnesses among children in daycare. Of all days with nasal discharge, the daycare children accounted for 39% and the home care children for 28% of the days. The corresponding figures for cough were 49% and 27%, and for fever 52% and 22% (Ståhlberg, 1980). Around 90% of the infectious episodes among children in daycare and 80% of the episodes among children in home care have been found to be due to respiratory tract infections (Wald et al., 1988).

Children in daycare are at higher risk than children in home care of contracting a respiratory tract infection (Haskins and Kotch, 1986). Children up to 36 months at daycare centres have been found to have a mean excess risk of 0.79 (CI 95% 0.13-1.45) of more diagnosed infections than children in home care (Bell et al., 1989). Among one-year-old children in daycare the proportion of infections attributable to daycare attendance was 41% for common cold and 50% for otitis media (Louhiala et al., 1995). For children younger than 36 months, it was found that 30% of the respiratory tract infections were directly attributable to daycare exposure and for children older than 36 months the corresponding figure was 33%. The corresponding figures for ear infection were 64% for the young children and 68% for the older ones (Fleming et al., 1987). About the same attributable risk figures for respiratory tract infections were found in an American study (Hurwitz et al., 1991), while a Norwegian study found only 17% of the common colds to be attributable to daycare and 32% of the media otitis (Nafstad et al., 1999). A higher rate of absence attributable to infections was evident in all ages in Swedish children in daycare as compared with children in family daycare (Petersson and Håkansson, 1989).

The odds ratio for respiratory illness was 1.6 (CI 95% 1.1-2.4) in children in daycare as compared with children in home care, ages 6 weeks to 17 months. In children ages 18 to 35 months there were statistically significant differences between children in daycare and in home care only if the child did not have older siblings OR 3.4 (95%CI 2.0-6.0) (Hurwitz et al., 1991).

A recent study, although not population based, also found more infectious illnesses in children in daycare as compared with children in home care. For children ages up to 18 months the odds ratios were 3.61 for mild respiratory illness and 2.94 for severe respiratory

illness in children in daycare, and 1.98 for mild diarrhoea and 1.86 for severe diarrhoea. In older children no statistically significant differences were found (Lu et al., 2004).

On average, children in daycare ages two to three years were about twice as likely to have a respiratory tract illness and 1.5 times more likely to have a reported ear infection than children in home care (Bradley, 2003). In children ages 4 to 5 years, higher odds of 1.57 (CI 95% 1.12-2.21) were found for respiratory tract infections among children in daycare as compared with children in home care (Kvaerner et al., 2000)

Thus, data from both older and more recent studies show that children in daycare contract more respiratory tract infections than children in home care.

Gastrointestinal infections have also been found to be more common in children in daycare (Doyle, 1976) (Pickering et al., 1986, Holmes et al., 1996). For gastrointestinal illness, a 2-year prospective study found an overall rate of diarrhoeal illnesses of 1.02 cases per infant-toddler, among children in daycare up to 36 months of age (Bartlett et al., 1985) and 2.62 episodes per child/year in infants and toddlers some years later(Bartlett et al., 1988a). Another study found 0.44 episodes/person/year among children in daycare (Sullivan et al., 1984). Children in daycare were 1.4 times more likely to have a gastrointestinal tract illness than home care children (Bradley, 2003)

The higher frequency of infectious illnesses among children in daycare has been noted not only for respiratory tract infections and gastrointestinal infections but also for invasive bacterial infections such as hemophilus influence type b and streptococcus pneumoniae, herpes virus infections and probably the skin diseases impetigo, pediculosis and ringworm (Holmes et al., 1996).

An American study in children ages 3 months to 6 years in daycare found some protection against repeated infections after six months of attendance, even after adjustment for age (Collet et al., 1994). In a Swedish study a trend towards fewer infections in children in daycare were found when the child started daycare after 1years, as compared with staring before the age of 1 (Hagerhed-Engman et al., 2006). It is not clear whether or not repeated infections in younger years are protective against infections in later years. An American study indicates that children who attend large daycare centres in their preschool years have less risk of frequent colds at 6 through 11 years compared with children in home care before they start school and the same risk at the age of 13 (Ball et al., 2002).

Outdoor activity

The Swedish National Board of Health and Welfare recommends daily outdoor activity for every preschool child (Socialstyrelsen, 2001a). The effects of outdoor activity on preschool children's absenteeism from daycare due to infectious diseases have been very little investigated, but some small studies indicate that outdoor activity is of importance (Koefoed et al., 2002). A Danish study from 1988 at sixteen daycare centres indicates higher absence among children aged 0 to 2 years who are not outside every day at the daycare centre (Søe and Hammershøy, 1991).

In 1990 a Swedish cohort study at 476 municipal daycare centres with children ages 0 - 6, found a mean of 14.3% absenteeism among children who were outside less than five hours a week with their daycare group, as compared with 12.0% among children who were outside more than ten hours a week with their daycare group. However, this difference was not statistically significant OR 2.3 (95% CI 0.6 – 4.1) (Bondestam and Rasmussen, 1994).

Another small Swedish study comparing daycare centres that used a special outdoor method, "Rain and Shine" with traditional daycare centres, found 5.2% sickness absence among the daycare centres that focused on being outdoors, as compared with 7.4% among the traditional daycare centres. The difference was statistically significant but no confounding variables or cluster constellations were taken into account (Söderström and Blennow, 1998).

No effects of time spent outdoor were found in a Norwegian study of four-year-old children comparing daycare centres with traditional outdoor time with those spending most of the time outside each day (Wefring et al., 2001). Neither did a Danish study of 24 day nurseries find any statistically significant differences in sickness absence among children at daycare centres that spent more or less time outdoors in the winter (Rindel et al., 1992).A cross over study investigating the effects of enhanced outdoor time as a single intervention did not find any differences when the time spent outdoor was doubled for two months (Mygind et al., 2003).

A prospective five-year Swedish study found that the higher the numbers of hours of sunshine and the higher the outdoor temperature the lower was the frequency of illness-associated absence from daycare. This study also found that more cloudy days were associated with more sickness absence, while no correlation was found between the amount of precipitation and the frequency of sickness absence. Taking all the variables into account, the outdoor temperature was found to be significantly related to sickness absence (Sennerstam

and Moberg, 2004). Another longitudinal Swedish study also found that higher outdoor temperature and more hours of sunshine were correlated to lower sickness absence (Voss, 2003). Other positive outcomes of outdoor activity in the children are enhanced vigour, balance and flexibility (Grahn et al., 1997).

Daycare centres with an explicit outdoor pedagogy spend more time outside than traditional daycare centres, and traditional daycare centres that have a playground with trees and bushes spend more time outside during the summer and warm spring and autumn days than daycare centres without such a playground (Söderström et al., 2004) but the correlation to infections has not been studied.

Absence from daycare or work

Absence from daycare due to illness has been investigated in both more recent and older studies. Two-year-old Swedish children were found to be out of daycare 20% of their parents' work days as compared with about 7% for older children (Strangert, 1976) and during the nine winter months children ages 0 – 6 at daycare centres, had a mean of 6.3% absence days due to infectious diseases (Petersson and Håkansson, 1989). For children in daycare the number of illness days per year was found to be 96 as compared with 41 for children in home care (Wald et al., 1988).

In two Finnish studies the one found 4.9 absence days/person year at risk in children ages 0 - 6 (Uhari and Mottonen, 1999) the other 24 absence days or 8% of the days the child was expected to be present (Mottonen and Uhari, 1992). In Denmark a mean of 19 sickness days or 7.5% of the open days at the daycare centre during a year was found (Rindel et al., 1992). It has been found that families who have children in daycare lose around 13 days of work per year/family for all types of infections (Brady, 2005) and a Finnish study found that parents with children at daycare centres had 2.4 absence days per person/year because of having contracted an infectious disease themselves from their children (Uhari and Mottonen, 1999). The Swedish social insurance system enables a parent to stay at home to take care of an ill child with compensation for loss of earnings, for at least 60 days a year (Försäkringskassan). How often children's absence from daycare or parents' absence from work due to infectious morbidity results in the claiming of remuneration from the social insurance system has been very little investigated.

Physician consultations

Symptoms and consultations

Most parents manage their small children's symptoms without consulting the health care authorities and only consult a family physician in cases of severe illness. In one study no action was taken on 35% of the reported symptom days (Cunningham-Burley and Irvine, 1987). A recent diary study in children up to two, focusing on behavioural changes and non-specific symptoms, showed that parents deal with 67-99% of their children's symptoms without consulting a physician or health visitor (Holme, 1995).

In two recent Swedish studies a family physician was consulted by 45% of the total population in a neighbourhood during a year for any reason (Carlsson et al., 2004) (Andersson et al., 2004).

An older Swedish study in families with at least one child under the age of seven found that roughly 10% of all days with reported perceived health problems led to some contact with a physician during a four-week period (Dahlquist et al., 1984, Dahlquist et al., 1987). A study from Scotland found that 7% of the symptom days in children younger than 5 led to a consultation (Cunningham-Burley and Irvine, 1987). In a Dutch three-week diary study 15% of children aged up to five and 7% of children aged 10 - 14 years consulted a physician for any reason (Bruijnzeels et al., 1998b).

A Norwegian study found 2.6 contacts per child per year for any illness among children ages up to 5, with no differences between the sexes (Bruusgaard et al., 1993), and a prospective study found that until the age of 56 months, 97% of all children had seen a physician for any symptom (Hay et al., 2005).

The Tecumseh study showed that 25.4 % of all respiratory illnesses in the population led to a physician consultation (Monto and Sullivan, 1993) and another study found 46.7 consultations per 100 episodes in children up to 7 (Lambert et al., 2005). A Canadian study in children up to twelve found that 56% of children with respiratory tract infections consulted a physician during a 6-month period (Saunders et al., 2003).

Regarding appointments with a family physician, upper respiratory tract symptoms were more common in children 0 - 4 years than in other year cohorts and in the whole population these symptoms were more common in women than in men (103 vs 74 per 1000) (Hak et al., 2006).

Diagnoses at consultations

The most common diagnosis in primary care in all the Nordic countries is respiratory tract infection (Grimsmo et al., 2001, Tähepold et al., 2003) mainly the common cold (Andre et al., 2002, Engstrom et al., 2004). In Sweden about 18% of all diagnoses made in connection with a physician's appointment are respiratory tract infections (Grimsmo et al., 2001)

Fleming showed a reduction in the number of respiratory tract infections presenting to physicians by 43% based on sentinel reports during 1994-2000 (Fleming et al., 2003)and another British study found a reduction by 35% in the consultation rate for respiratory tract infections per year comparing 1994 with 2000 (Ashworth et al., 2004). Health Care Centres where physicians prescribe antibiotics to a smaller proportion of patients presenting with respiratory tract symptoms have lower consultation rates for this conditions. One explanation for the trend to lower consultation rates may be altered illness behaviour, which may be a response to previous consultation experience (Ashworth et al., 2005).

In a third British study in children up to fifteen , 40% of the diagnoses were infectious episodes and respiratory diseases (Saxena et al., 1999) and in the second Dutch National survey of general practice only 4% of the patient population consulting a family physician during a year had respiratory tract infection as the diagnostic label. But when taking all reported respiratory illness symptoms and diagnoses into account, 15% of the physician consultations were related to respiratory tract infections (Hak et al., 2006). This shows that the label the physician puts on the symptoms is of importance (Hutchinson et al., 2001).

The inconsistency in general practitioners' use of diagnostic labels for acute respiratory illness, has also been seen in American (Oeffinger et al., 1997) and European studies (Verheij et al., 1990, Fahey and Stocks, 1998, Stocks and Fahey, 2002) Therefore research into acute problems in primary care should probably be based on presenting symptoms rather than on disease categories (Stocks and Fahey, 2002).

Factors of importance for physician consultations

Symptoms

Symptoms are common, and sometimes result in physician consultations. Serious illness or severe symptoms in children are the strongest predictors for consultations (Campion and Gabriel, 1985, Wyke et al., 1990) which sound reasonable. An Australian four-week diary

study in children ages 11 to 26 months focusing on factors of importance for consultations found more consultations with a family physician if symptoms were recorded for fifteen days or more in a month (Osman and Dunt, 1995).

In children ages 2 months to 12 years with respiratory tract symptom the occurrence of earache or high fever as well as severe complaints or symptoms persisting more than 24 hours were independent predictors of consulting a physician (Saunders et al., 2003). Cough with no signs of improvement was the most common reason for a physician consultation in children younger than five (Cunningham-Burley and Irvine, 1987).

Other factors beyond symptoms have also been found to be of importance for physician consultations. Some of them are discussed below.

Socioeconomic status

Socioeconomic status may affect the help-seeking behaviour of parents of toddlers (Edwards and Pill, 1996) although contradictory results have been found regarding the importance of socioeconomic status in relation to physician consultation. Children of parents with low socioeconomic status and low education level were found to be high users of medical care in a Scottish study from the early of 1980s (Campion and Gabriel, 1984, Campion and Gabriel, 1985) and a recent Canadian study found that members over 12 in families with lower incomes were more prone to be frequent users of primary care (Dunlop et al., 2000). The importance of low socioeconomic status for higher use of medical care in children has also been found in Swedish studies (Petersson and Håkansson, 1996, Håkansson et al., 1996) and in one British study (Saxena et al., 1999).

Contradictory results regarding the importance of socioeconomic status were found in a later Nordic study, where the parents of lower class children ages two to seventeen used fewer phone calls to physicians and fewer specialist services (Halldorsson et al., 2002). There was only a small difference in the use of family physician's services in relation to socioeconomic factors. The largest difference, although not statistically significant, was found for education level of the mother in relation to seeking specialist care. (Halldorsson et al., 2002). Postsecondary parental education was the only independent predictor among parental factors predicting physician consultations in a later study. Here higher parental educational level led to four times higher odds for physician consultations in families with children ages 2 months to twelve years (Saunders et al., 2003).

No importance of socioeconomic status for consultation for any reason or respiratory tract symptoms in preschool children were found in other studies from both Sweden and the rest of Europe (Sundelin and Vuille, 1979, Wyke et al., 1990, Bruusgaard et al., 1993, Cooper et al., 1998) (Groholt et al., 2003). In school children, no importance of socioeconomic factors was found (Hjern et al., 2001).

Smoking in the family

In a Swedish study, mothers' smoking habits had no importance for the children's total health care utilisation (Håkansson et al., 1996) but in another, children of smoking mothers had more medical consultations both totally and for respiratory tract infections than children of non-smoking mothers (Petersson and Håkansson, 1996). A more recent study found fewer physician consultations among two-to-five-year-old children from smoking families (Forssell et al., 2001).

Number of children in the family

The number of children in the family in relation to physician consultations has been investigated. Mothers were found to be more likely to consult a physician for children's illness, the fewer children in the family (Campion and Gabriel, 1985). In another study in children up to 56 months, the odds of their mothers consulting a physician were 29% - 48% lower when the family had three or more children, as compared with mothers of one child (Hay et al., 2005). An older Swedish study also found more physician consultations during the first 18 months, by mothers of children without siblings (Håkansson et al., 1996). On the contrary, however the number of siblings was found to be of no importance in another study (Forssell et al., 2001).

Daycare

A Swedish retrospective study found that parents of 51% of children in daycare made at least one physician's consultation for an RTI during one year as compared with 40% of parents of children in home care (Petersson and Håkansson, 1990), and the relative risk of an acute infection was 1.43 (CI 95% 1.20-1.71) among the daycare children (Rasmussen and Sundelin, 1990). A more recent comprehensive Swedish study also found more physician consultations

for an acute infection during the last three months among children in daycare than among children in home care (24% vs 18% aOR 1.4 (CI 95% 1.1-1.8)) (Hjern et al., 2000). Even higher odds ratios for consulting a physician among children ages 2 - 5 years in daycare were found in another retrospective Swedish study, aOR 2.78 (CI 95% 1.34-5.78) (Forssell et al., 2001). There are concordant findings from an American study, where children with daycare outside the home were more likely to consult a physician than children in home care, aOR 2.8 (CI 95% 1.0-7.9) (Silverstein et al., 2003).

Concern about illness

Parents' concern about their children's health may be expressed in terms of 'worry' or concern about threat of illness, and it has been found that there are considerable variations in parents' concern about threat of illness in children below eight (Hansen, 1994). General anxiety in mothers of children younger than twelve is more correlated to a physician consultation for the child than reported symptom index, (Campion and Gabriel, 1985). In a Danish study, parents with high perceptions of general health threat reported high perceptions of the threat of illness in connection with the child's latest illness, and parents without experience of children's illnesses more frequently perceived an actual illness as a high illness threat than parents with previous experience of their children's illnesses (Hansen, 1994). However, this study did not correlate "concern about illness" to physician consultations. A study from Hong Kong in adults and parents of children below seventeen used the term "worry" and found worry about complications and worry about upper respiratory tract infections lasting too long being of importance in relation to physician consultation, but they did not define "worry" (Chan, 1996).

Antibiotic prescription

Variations in Europe

Antibiotic prescription for human being varies markedly among European countries (Cars et al., 2001, Mölstad et al., 2002, Odenholt et al., 2002, Vaccheri et al., 2002, Goossens et al., 2005, Ferech et al., 2006, Vander Stichele et al., 2006, Elseviers et al., 2006). Data shows that Sweden is one of the countries with the lowest prescription rates, with around 13 defined daily doses (DDD) per 1,000 inhabitants per day (TID) to outpatients (Cars et al., 2001,

Ferech et al., 2006). "The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults" and was originally developed by the Nordic Council in close collaboration with WHO (WHO Collaborating Centre for Drug Statistics Methodology, 2003). DDD is a relevant measurement unit for comparing antibiotic use among countries or regions (Monnet et al., 2004),

In Europe the prescription range varied from 36.5 DDD/TID in France to 8.9 in the Netherlands in 2001(Cars et al., 2001) and from above 30 DDD/TID in Grece to approximately around nine DDD/TID in the Netherlands 2003 (Ferech et al., 2006). Expressed as prescriptions per 1000 inhabitants and year the variation was from 1,350 in Greece to 390 in the Netherlands. The figures for Sweden were 458 prescriptions per 1000 inhabitants and year (Mölstad et al., 2002).

The trends regarding outpatient antibiotic use from 1997 to 2003 in Europe show the full range of patterns. Some countries had a continuous increase in antibiotic use, some an initial increase followed by a decrease, as for Sweden, and some an initial decrease followed by an increase and some had a stable pattern of use (Ferech et al., 2006). In the United States the prescription rates to children younger than fifteen decreased in the 1990s (McCaig et al., 2002) (Halasa et al., 2004).

Differences in prescription rates for upper respiratory tract infections among general practitioners within a country have also been found (Mazzaglia et al., 1998, Cucinotta et al., 2002).

A reduction in antibiotic prescription for RTIs by 45% was found from 1994 to 2000 in a British population. This reduction was partly attributable to physicians prescribing antibiotics less frequently in connection with a consultation, but mainly because there were fewer consultations for RTIs (Ashworth et al., 2004). One possible explanation is that patients had altered their illness behaviour, in which case previous consultation experience is of importance (Ashworth et al., 2005).

A recent British study concluded that one explanation for the declining prescription rates is a reduction in the general population in the incidence of respiratory tract infections presenting to the physicians rather than changing prescription thresholds for antibiotics per se (Fleming et al., 2003). Otters concluded that prescription rates by the physicians have remained quite constant, and the reduction in antibiotic prescription in children up to seventeen was part of a reduction in the population based prescription rate. Possibly the differences in population based and contact based prescription rates reflect a higher threshold for contacting a family physician (Otters et al., 2004a) (Otters et al., 2004b). A reduced

inclination of patients to present to their physicians with respiratory tract illness was found in another recent study from the Netherlands, which also found a shift in the diagnostic and coding practices of the physicians as a possible explanations for decreased antibiotic prescription rates in the general population (Kuyvenhoven et al., 2006). An American study in children ages 1-14 found that a decline in probability for a RTI consultation accounted for two-thirds of the reduction in antibiotic use for these conditions (Miller and Hudson, 2006).

General trends in Sweden

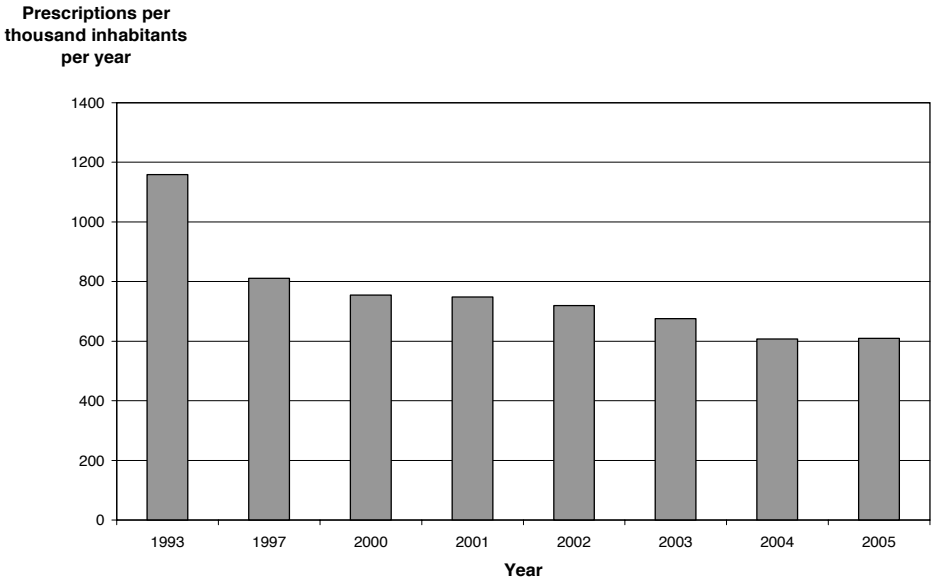
Data on antibiotics prescribed for outpatients have been available in Sweden since 1974, and during the period before 1986 antibiotic utilisation was relatively stable, approximately 12 DDD/TID. An increase in the antibiotic consumption to 18 DDD/TID was seen between 1986 and 1993 (Cars and Ekdahl, 2001), followed by a reduction in consumption to around 13 DDD/TID until 2004 (Cars and Olsson Liljequist, 2004). Most of this reduction took place between 1993 and 1997 (Cars and Ekdahl, 2002).

For children 0 - 6 years there was also an increase in antibiotic prescription rates between 1980 and 1993 (Mölstad and Cars, 1999). Then the prescription rate declined from 13.5 DDD/TID in 1993 to 7.2 DDD/TID in 2004 (Cars and Ekdahl, 2002, Cars and Olsson Liljequist, 2004). Since the prescribed daily doses for children are lower than the DDDs, it is important also to look at the numbers of prescriptions/1000 inhabitants/year in this age group. The number of prescriptions decreased from 1,159 prescriptions/1,000 inhabitants in 1993 (Cars and Ekdahl, 2001) to around 607 prescriptions/1,000 inhabitants in 2004 and 2005 (Cars and Olsson Liljequist, 2004, Cars and Olsson Liljequist, 2005) and Figure 1.

Geographical variations in Sweden

There is wide variation in total antibiotic prescriptions between counties in Sweden (Cars and Ekdahl, 2001). In 2001 and 2002 the differences between the county with the highest and lowest prescription rates was around 5 DDD/TID (Cars and Ekdahl, 2001, Cars and Ekdahl, 2002). These differences are also apparent for children 0 - 6 years within counties (Mölstad and Cars, 1999), municipalities (Melander et al., 2000) and within a city (Henricson et al., 1998). The differences between the counties seem to be quite stable over time (Strama, 2005).

Figure 1. Antibiotic prescriptions to children ages 0 - 6 years 1993-2005



Antibiotic prescription in primary health care

Antibiotic prescribing habits regarding respiratory tract infections vary between family physicians in different countries (Bjerrum et al., 2004), physicians at different health centres (McGavock, 1988) as well as among individuals (Howie et al., 1971, Howie, 1976, Howie, 1983) (Watson et al., 1999).

In Sweden 90% of all antibiotics are prescribed to outpatients (Cars and Olsson Liljequist, 2004) and the most common reason for antibiotic prescription in primary health care is RTI (Lundborg et al., 2002). Of all the antibiotics sold in Sweden, 57% have been prescribed for RTIs (Mölstad et al., 1990) and most of this prescribing, both for children and adults, is for viral conditions for which antibiotics are not actually indicated (Gonzales et al., 1997, Nyquist et al., 1998).

Of all patients seeking for respiratory tract infections in primary care in Sweden, 56% were prescribed antibiotics (Andre et al., 2002). Almost all patients who were given the diagnoses streptococcal tonsillitis, acute otitis media and acute sinusitis were prescribed antibiotics as compared with <10% of patients with common colds and acute pharyngitis (Andre et al., 2002). In the Netherlands, with a traditionally low prescription rate, 46% of respiratory tract diagnoses and 13% of respiratory tract symptoms led to an antibiotic prescription in the total population (Akkerman et al., 2004). Counting episodes, 19.7

antibiotic courses were prescribed/100 influenza-like episodes to Australian children 12-71 months (Lambert et al., 2005).

According to a Danish study, antibiotic prescription is most common for children 1 – 2 years, with 945 prescriptions/1000 children/year, falling to 582 prescriptions /1000 children /year for 3-to-6-year-olds and to 284 prescriptions/1,000 children/year for 7-to-10-year-olds (Thrane et al., 1999).The same trend was found in Dutch children (Otters et al., 2004b). No differences in antibiotic prescriptions were found between girls and boys (Forssell et al., 2001).

Factors of importance for antibiotic prescription

Symptoms

Symptoms, particularly purulent nasal discharge, purulent sputum, persistent fever for more than three days, looking unwell, exudates on the throat, inflamed eardrums, and cervical lymphadenopathy are clinical findings that influence antibiotic prescription according to a questionnaire study (Lam and Lam, 2003b). Another observational study found that the analysed predictors coated tonsils, fever, fatigue and yellow sputum explained 70% of the variance in antibiotic prescriptions (Fischer et al., 2005). However, the medical literature emphasizes that antibiotics provide little benefit for upper respiratory tract infections (Rosenstein et al., 1998, Williams et al., 2003, Arroll and Kenealy, 2005). In addition to symptoms, other factors are also of importance with regard to antibiotic prescription. Some are described below.

Socioeconomic status

In Sweden, high median family income and high employment rates were found in an ecological study, to be associated with more antibiotic prescriptions to children (Henricson et al., 1998). The importance of educational level has also been investigated, and in families where the responding parents had only primary education, antibiotics were less often prescribed to preschool and school age children, than in children in families where the parents had post-secondary education (Hjern et al., 2000) (Hjern et al., 2001) (Melander et al., 2003).

The opposite, a negative correlation between antibiotic utilisation and educational level, was found among Danish families with preschool children. Children less than two years of age from families where the mother had only compulsory education had a higher risk of more antibiotic prescriptions than children with mothers with higher education (Thrane et al., 2003), and the same trend was found for the Danish children in the ecological study among children ages 0-6 years (Melander et al., 2003). Lower parental income also increased the likelihood of children receiving an antibiotic prescription (Thrane et al., 2003). The same relationship of parental income to antibiotic prescription to children was seen in a Canadian study in children of all ages (Kozyrskyj et al., 2004).

No importance of socioeconomic factors was found in a Swedish study where the question of mothers being blue or white collar workers was found to be of no significance with regard to antibiotic prescriptions to infants (Håkansson and Petersson, 1992) as well as in another Canadian study where mothers' education and family financial situation were found to be of no significance for antibiotic prescription in 1.5-5-year-old children (Dubois and Girard, 2005).

Smoking in the family

A Swedish study found more antibiotics prescribed to children up to 18 months in smoking families than in non-smoking families (Håkansson and Petersson, 1992) but more recent Swedish studies of children up to five, found no significance of smoking in the family in relation to antibiotic treatment (Hjern et al., 2000, Forssell et al., 2001).

Number of children in the family

The relationship between the number of children in the family and antibiotic prescription rates is only occasionally mentioned in articles focusing on infectious symptoms. In one Swedish paper, the number of siblings was found to be of no importance (Forssell et al., 2001).

Daycare

A retrospective Swedish study found that children ages 1 - 3 years in daycare were more often prescribed antibiotics for respiratory tract infections than children in home care OR 1.35 (CI 95% 1.04-1.76) (Petersson and Håkansson, 1990). Another Swedish study from the same

period had approximately the same findings (Rasmussen and Sundelin, 1990). Also two recent Swedish studies in preschool children up to five years confirmed the results with aOR 1.5 (CI 95% 1.2-1.9) and aOR 2.73 (CI 95% 1.38-5.43), respectively, for prescribing antibiotics to children in daycare as compared with children in home care (Hjern et al., 2000, Forssell et al., 2001).

Studies from other countries have also found that preschool children in daycare ages up to five were more likely to be prescribed antibiotics than children in home care aOR 2.8 (1.2-6.1) (Silverstein et al., 2003). None of these studies took the number of symptom days into account.

Concerns about illness

As mentioned above, concern about illness may influence parents' decisions about physician consultations, although the expression "concern about illness" has not been correlated to antibiotic prescription. It may be assumed that it correlates to antibiotic prescription in the same way as physician consultations.

Parents' expectations.

Minor symptoms are common and most of them are handled by the families themselves (Dahlquist et al., 1987).One study showed that parents often waited four or five days before consulting their doctor for symptoms which could be regarded as "normal" for the child, such as some respiratory conditions, although fever resulted in a consultations on the second day, on average (Holme, 1995).

More than 70% of patients over 18 years and parents with children younger than five years believed that antibiotics are needed for green or yellow nasal discharge, indicating that there is a confusion about the implications of this symptom (Mainous et al., 1997, Belongia et al., 2002). The importance of symptoms has also been studied in Dutch studies. Here adult patients considered respiratory tract symptoms more serious and less self-limiting and they thought there was more need for antibiotics in case of respiratory tract symptoms than general practitioners (van Duijn et al., 2002). Personnel at the health care centre adopted a middle ground between the general practitioners and the adult patients (van Duijn et al., 2006). Adults who believed in antibiotics as treatment for viral infections had more often taken

antibiotics for upper RTIs during the previous year, according to an American study (Wilson et al., 1999).

About 65% of adult patients (Hamm et al., 1996, Britten and Ukoumunne, 1997) and 50% of parents of children ages 2 - 10 (Mangione-Smith et al., 1999, Mangione-Smith et al., 2001) expected antibiotics prior to the consultation for an upper respiratory tract infection. Another study found a higher (71%) expectation of antibiotics although this study included older people seeking for lower respiratory tract infectious symptoms (Macfarlane et al., 1997). In 40-75% of the adult patients (Hamm et al., 1996, Britten and Ukoumunne, 1997, Cockburn and Pit, 1997) and in about 40% of parents of children ages 2-10 (Mangione-Smith et al., 1999) the expectation of an antibiotic prescription was perceived by the physician. This implicate that the physician underestimate the expectations. Physicians also prescribes antibiotics to patients who did not expect antibiotics before the consultation (Hamm et al., 1996, Cockburn and Pit, 1997, Britten and Ukoumunne, 1997) and patients and parents apparently do not expect antibiotics as often as doctors think they do (Hamm et al., 1996, Cockburn and Pit, 1997, Britten and Ukoumunne, 1997, Mangione-Smith et al., 1999, Macfarlane et al., 1997). Only in 1% of the consultations did parents of children ages 2-10 make a direct verbal request for antibiotics (Mangione-Smith et al., 2001).

A more recent study found that 25% of the parents who consulted a physician with children ages 3 months - 6 years, for upper respiratory tract infections expect to be prescribed antibiotics. Younger parental age and higher education were associated with lower expectations of receiving antibiotics in this study. Previous antibiotic treatment and the thought that antibiotics help in upper respiratory tract infections were associated with greater expectations about antibiotics (Shlomo et al., 2003). In another study, caregivers with high scores regarding antibiotic knowledge were less likely to demand antibiotics (Parimi et al., 2004).

The strongest predictor of both likelihood of utilization and belief in the effectiveness of antibiotics was previous use of antibiotics for an upper respiratory tract infection, in an American study in adults (Mainous et al., 1997).In another American study, physicians failure to fulfil parental expectations during the consultation for children ages 2-10 was the only significant predictor of parental satisfaction, while failure to prescribe the expected antibiotics was not a predictor (Mangione-Smith et al., 1999). On the other hand, a British study found that adult patients who did not receive an expected antibiotic prescription were much more likely to express dissatisfaction than patients receiving an antibiotic prescription and those patients also reconsulted twice as often (Macfarlane et al., 1997).

A Swedish study found that general patient satisfaction and general practitioners' taking time to listen were factors of importance for variations in antibiotic prescription rates between different primary care centres. Adult patients at primary care centres with higher prescription rates of antibiotics were more satisfied with the consultations, based on all consultations. However, adult patients' were more satisfied with the amount of time the physician spent listening to their problems at primary care centres with lower prescription rates (Lundkvist et al., 2002).

Physicians' habits

The choice of antibiotics is also determined by the habits of the consulting physicians (Mölstad et al., 1990, Butler et al., 1998b) (De Sutter et al., 2001, Odenholt et al., 2002). Social, psychological and other non-medical factors have been found to influence the physicians' prescribing habits (Howie and Bigg, 1980, Howie, 1983, Lam and Lam, 2003a).

Adult patients who expected antibiotic treatment were nearly three times more likely to be prescribed it, and when the general practitioner thought the patient wanted a prescription, the patient was ten times more likely to receive it (Cockburn and Pit, 1997). Higher odds of receiving a prescription when the patient expected it was also seen in a more recent questionnaire study (Watkins et al., 2003). The doctors' perceptions of their patients' expectations (Britten and Ukoumunne, 1997) and of parents' expectations (Mangione-Smith et al., 1999) were the strongest predictors of the decision to prescribe, but the doctors seemed to overestimate the actual pressure to prescribe and seldom asked directly what the adult patient expected (Altiner et al., 2004).

Physicians sometimes felt that their adult patients urged them to prescribe antibiotics (Macfarlane et al., 1997, Coenen et al., 2002), although only a minority of patients ask for antibiotics and patients do not want antibiotics as often as their doctor thinks they do (Cockburn and Pit, 1997). A qualitative analysis of audio taped consultations found that general practitioners use a set of readily identifiable skills for managing the consultation without prescribing antibiotics. There was little evidence of either conflict or overt pressure from parents to prescribe. The word antibiotic was seldom mentioned and the clinicians did not elicit the parents' of children younger than 10 years expectations of receiving antibiotics (Rollnick et al., 2001).

In contrast, another study in children and adults seeking for RTI focusing on the interaction, found that patients were observed to put pressure on physicians for antibiotics. In

this study different patterns in the consultation situation were observed as leading to antibiotic prescription; "direct request, candidate diagnosis (a diagnosis suggested by the patient) implied candidate diagnosis (a set of symptoms specifically indexing a particular diagnosis), portraying severity of illness, appealing to life world circumstances and previous use of antibiotics". In 68% of these consultations antibiotics were prescribed and of those 80% were determined to be unnecessary according to the Centres for Disease Control and prevention guidelines (Scott et al., 2001). When urged to prescribe antibiotics general practitioners, frequently complied with their adult patients' expectations, probably in order to avoid conflict (Butler et al., 1998b). According to a questionnaire study even when they have not urged, the physicians thought that the desire to satisfy the patients would make them likely to over-prescribe antibiotics (Lam and Lam, 2003a).

The physicians' experience from previous consultations affects their decisions of whether or not to prescribe (Coenen et al., 2000).They also were observed to rationalize their antibiotic prescriptions by reporting medically acceptable reasons and diagnoses both to children and adult patients (Verheij et al., 1990, Scott et al., 2001).They were also 7% more likely to make a bacterial diagnosis and 21% more likely to prescribe antibiotics when they perceived that antibiotics were expected by parents of children ages 6 months - 10 years (Mangione-Smith et al., 2004).

In adults satisfaction with the consultation is not necessarily related to being prescribed antibiotics (Butler et al., 1998b), and satisfaction without an antibiotics prescription is achieved when the physician provides a treatment plan to parents of children ages 2 to 10 years (Mangione-Smith et al., 2001). Often there is a shortage of information from the physician to the parents regarding diagnosis, use of drugs and side effects (Akici et al., 2004).When a parent questions the plan, this increases the physician's perception that antibiotics are expected, leading to increased inappropriate antibiotic prescription (Mangione-Smith et al., 2006).

The longer the general practitioner had practised, the more frequently they prescribed antibiotics, especially in combination with little medical knowledge in RTIs, or when the general practitioner felt she did not have enough time per patient (Akkerman et al., 2005).

Older physicians, more senior physicians or physicians in private practice were more likely to think antibiotics were useful for upper respiratory tract infections and to prescribe them (Lam and Lam, 2001) (Kozyrskyj et al., 2004) and a multilevel analysis found that older physicians as well as those working in urban or private practices prescribed more antibiotics to adults than their counterparts. (Huang et al., 2005b). Children of a physician were less

likely to receive antibiotic treatment in a Taiwanese study, but children of nurses had the same likelihood of receiving a prescription as children with non-medical personnel as parents (Huang et al., 2005c).

It has also been found that physicians with high prescribing costs are more likely to see drug company representatives, and to prescribe newly available drugs more frequently (Watkins et al., 2003). These physicians also report frustration about lack of time in the consultation and feeling unsatisfied when a consultation ended up with advice only (Watkins et al., 2003).

It has also been found that it is not time-saving to prescribe antibiotics (Linder et al., 2003) and those physicians who prescribed the most antibiotics had up to 30% more return visits than low prescribers (Watson et al., 1999).

How to prevent infections

Vaccinations

Vaccinations are widely and routinely administered around the world based on the common sense principle that "it is better to keep people from falling ill than to treat them once they are ill" (WHO, 2005). Vaccinations have been shown to be one of the most important medical contributions today as well as one of the most cost-effective health investments (Socialstyrelsen, 2001b, WHO, 2005). Many of the diseases we vaccinate against today can lead to potentially fatal illness, disability and death (Demicheli et al., 2005) (Greenberg and Caro, 2005).Vaccinating small children, not only achieves protection of the children, but also protection of all adults in the surroundings, leading to reduced numbers of illness days. Vaccination reduces the risk of transmission from children to adults and then back to children again (McIntosh, 2005). The Morbilli-Mups-Rubeola (MMR) vaccination is associated with lower incidence of upper respiratory tract infections (Demicheli et al., 2005), as is conjugate pneumococcal vaccination for children in daycare centre (Dagan et al., 2001).

Sweden has an established vaccination programme for children (Socialstyrelsen, 1996) and since 2005 another dose of pertussis vaccination is recommended to ten-year-old children (Socialstyrelsen, 2005). Swedish Institute for Infectious Disease Control now also recommends that Sweden begin vaccinating against pneumococci (Smittskyddsinstitutet, 2006).

Daily routines

As mentioned above there are various external factors of importance in relation to infectious symptoms in children. These are factors potentially possible to influence.

Today most children have daycare outside the home (Skolverket, 2005) where they are with many other children and are exposed to many infectious agents. It is therefore an important task to influence the transmission of the infectious agents in daycare so the increased risk of morbidity stays as low as possible. In Sweden, the National Board of Health and Welfare has made recommendations about how to handle infectious diseases in daycare and when to keep an infected child at home (Socialstyrelsen, 2001a).

In a review, the purpose of exclusion is summarised as twofold .One purpose is to provide for the child's comfort and well-being. These criteria should focus on needs of the child. Another purpose can be to prevent the spread of infections to other children. Most experts questions whether any policy for the exclusion for mild infections will have any substantial impact on infections among children in daycare (Shapiro et al., 1986). Asymptomatic children may transmit infections, and symptomatic children often shed infectious particles both before the onset and after the resolution of symptoms (Shapiro et al., 1986, Brady, 2005). The incidence of infectious illness among children who attend daycare is not substantially affected by stringency of the policies for excluding children (Loda et al., 1972, Strangert, 1976, Shapiro et al., 1986). Good hygiene practices however are found to affect the incidence (Huskins, 2000).

In the general population, soap and hand washing reduces the risk of respiratory tract infections by about 15% (Rabie and Curtis, 2006), gastrointestinal infections by 42-47% (Curtis and Cairncross, 2003) and pneumonia by 50% (Luby et al., 2005).

At daycare centres, numerous intervention studies about preventing respiratory tract and gastrointestinal infections have been conducted (Black et al., 1981, Bartlett et al., 1988b, Van et al., 1991, Kotch et al., 1994, Holaday et al., 1995, Uhari and Mottonen, 1999, Carabin et al., 1999, Roberts et al., 2000a, Roberts et al., 2000b, Pönkä et al., 2004). Some investigated the efficacy of specific interventions (Black et al., 1981, Van et al., 1991, Holaday et al., 1995) and some were multiinterventional oriented programs (Bartlett et al., 1988b, Kotch et al., 1994, Niffenegger, 1997, Ladegaard and Stage, 1999, Uhari and Mottonen, 1999, Carabin et al., 1999, Roberts et al., 2000a, Roberts et al., 2000b, Pönkä et al., 2004).

Careful hand hygiene as a specific intervention or as part of multiinterventional oriented programs has effects on all kinds of infectious episodes (Uhari and Mottonen, 1999, Ladegaard and Stage, 1999, Pönkä et al., 2004), gastrointestinal infections (Black et al., 1981, Kotch et al., 1994, Pönkä et al., 2004) and respiratory tract infections (Niffenegger, 1997, Carabin et al., 1999, Roberts et al., 2000b). Of these studies, only three were analysed with multilevel techniques (Carabin et al., 1999, Roberts et al., 2000b, Roberts et al., 2000a). The design, intervention method, measure method and results of studies focusing on hand washing, separately or in a multifaceted interventional program are summarised in table 1. The effect of a waterless alcohol based hand rinse has not yet been evaluated as a single intervention (Huskins, 2000).

In a Finnish study, the reduction in numbers of infectious episodes was found to be 9% for children ages three or younger and 8% for those over three. Physician consultations were reduced by 21% and antibiotic prescriptions by 24% as a result of multiintervention (Uhari and Mottonen, 1999). Another Finnish study found that a hygiene training program was effective in reducing absence due to any infectious illness by 26% among children under three (Pönkä et al., 2004).

Approximately the same reduction in incidence of respiratory tract infections was found in a Canadian study in children ages 18 - 36 months. The comprehensive hygiene training program reduced upper respiratory tract infections by 25% but no significant reduction was found for diarrhoea (Carabin et al., 1999). In an Australian study the reduction in respiratory tract infections in the intervention group was at about the same level in children 24 months of age and younger compared with the control group, and when compliance was good the reduction in episodes was 17% (Roberts et al., 2000b). An effect on diarrhoeal episodes was also found in this study in children over 24 months of age. The intervention, including training for the child care staff about transmission of infections and training in hand washing, reduced the number of episodes by 50% (Roberts et al., 2000a).

Table 1. Intervention studies focusing on hand washing separately or in combination with other activities.

Author	Country	Design	Intervention method	Measure methods	Results
Black -81	4 DCC Atlanta, USA	Controlled trial No cluster analysis	Hand washing schedule Bars of soap, paper towels	Daily reports by personnel	Diarrhoea 6 – 17 months significant reduction of diarrhoea 1½ -2½ years no significant difference
Bartlett -88	22 DCC Arizona USA	Randomised Controlled trial No cluster analysis	Personnel: information about hand washing, contagion, and diaper changing	Daily reports by personnel and weekly visits by study nurse.	Diarrhoea No effect but in daycare centres previously not informed the odds ratio of diarrhoea was 4.88 as compared with home care. Continuous registration resulted in fewer gastrointestinal infections
Kotch 94	24 DCC North Carolina	Randomized controlled trial No cluster analysis but controlling for confounders	Personnel: training in hand washing, diaper changing, hygiene routines repeated every fifth week Soap, paper towels	Telephone interviews of the parents ever second week	Diarrhoea Reduction of severe diarrhoea but not of light diarrhoea, respiratory tract symptoms or mixed symptoms
Niffenegge r 97	2 DCC Indiana USA	Controlled trial No cluster analysis No control for confounders	Hand washing of personnel and children.	Report by personnel and parents once a week	Respiratory tract infections No increase in RTI in the winter season during the intervention
Ladegaard, -99	8 DCC Denmark	No cluster analysis No control for confounders	Personnel: informed about contagion Training in hand washing, outdoor activities Children: training in hand washing, sing a song Parents: written information about hand washing, contagion	Reported by parents after sickness absence	Sick leave was reduced by 34% from 3.25 days to 2.22

Uhari -99	20 DCC Oulo Finland	RCT Paired DCC	Multiintervention Child: the personnel trained the children in hand washing Personnel: 1 hour training about contagion, alcohol based disinfectant for hand washing, washing schedule for toys, diaper changing routines Parents: Information at parents' meetings about the study design	Diary reported by parents every month	≤3 years reduction of all infectious episodes by 9% >3 years reduction of infectious episodes except diarrhoea by 8%
Roberts – 00 a	23 DCC Australien	Cluster RCT	Personnel: 3 hour training in hand washing, how to a handle runny nose, training during the study Children: taught by personnel Parents: no intervention	Telephone interview every second week with the parents	11% reduction in respiratory tract infection and when compliance high 17% ≤24 months the higher compliance the better >24 months no effect
Roberts – 00 b					50% reduction in diarrhoea in children >24 months
Carabin -99	47 DCC Montreal Canada	Cluster RCT	1 day hygiene training: washing schedule for toys, cleaning of the playground area, written information	Daily absence reports	37% less diarrhoea only by registration 25% reduction of upper respiratory tract infections by intervention
Pönkä -04	60+228 DCC Helsinki Finland	CT cluster analyse, Paired T-test No individual child data	Multiintervention for personnel and chidren: more hand washing, paper towels, diaper changing routines, cleaning of playing areas, washing of toys every second week, food hygiene, sick children stay at home Parents: written information	Parents reported to personnel about the reason for absence	Intervention 0≤3 years: 26% reduction in absence in RTI and diarrhoea 3-6 years no significant effects

Aim

As evident from the background the occurrences of everyday illnesses and infectious symptoms have been studied in several studies. However, since the well-known population based telephone interview study was conducted in Tecumseh, in the 1970s, no large population based study charting all the infectious symptoms occurring in families with small children has been made.

Physician consultations and antibiotics prescriptions in connection with reported infectious symptoms has not recently been studied. Regarding factors of importance for physician consultation and antibiotics prescription "concern about infectious illness" or "knowledge about antibiotics", have not previously been studied

Antibiotic prescription rates vary between countries, counties and municipalities. No research has focused on possible differences in infectious symptoms between municipalities as a reason for different prescription rates.

Infectious symptoms are more often reported in children in daycare than in children taken care of at home, and children in daycare have more physician consultations and consume more antibiotics than children in home care. However, no population based studies have compared physician consultations and antibiotics prescription among children in daycare and children in home care taking infectious symptoms, family and socioeconomic factors as well as "concern about infectious symptoms" and "knowledge about antibiotics" into account.

The possibility of reducing the occurrence of respiratory tract infections and gastrointestinal infections at daycare centres has been studied in intervention-oriented studies from other countries. However, no such studies have been made in Sweden and no research has focused on training parents and personnel.

The general aim of this thesis was to study infectious symptoms occurring in small children and their families as well as their consequences with special focus on factors influencing antibiotic prescription.

The specific aims were to

- describe infectious morbidity in 18-month-old children and their families (Paper I),
- investigate use of social insurance, utilisation of health care and prescription of antibiotics (Paper I),
- study factors of possible importance for regional differences in antibiotic prescription to children (Paper II),
- study, from a population-based point of view, study how infectious morbidity differs between 18-month-old children in daycare and children with home care (Paper III),
- study, from a population-based point of view, study how health care utilisation and antibiotic prescription rates differ between 18-month-old children with daycare and children with home care, taking infectious morbidity into account (Paper III),
- study the possibility of educating daycare centre personnel and parents about infectious illness and contagion, within the framework of ordinary preschool activities (Paper IV),
- study the possibility of decreasing absence due to infectious diseases, physicians' consultations and antibiotic prescription through education- oriented interventions in daycare (Paper IV).

Setting

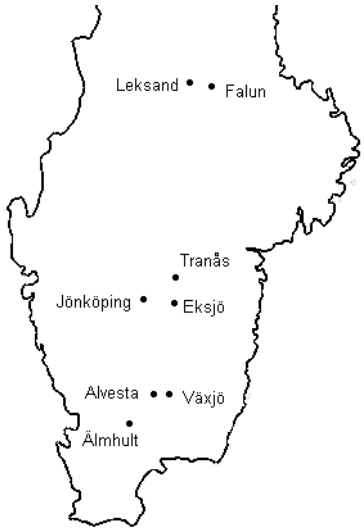
Studies I to III were conducted in the municipalities of Alvesta and Älmhult in the county of Kronoberg, in Jönköping, Eksjö and Tranås in the county of Jönköping and in Falun and Leksand in the county of Dalarna. These municipalities had had either high or low antibiotic prescription rates for children during 2000 and 2001. One rural and two urban municipalities were chosen as a convenient sample among those municipalities in the highest quartile of antibiotic prescription rates and one urban and three rural municipalities among those in the lowest quartile of antibiotic prescription rats for children ages 0 to 6.

The differences in the prescription rates between the high and low prescription areas remained during the study period. According to official statistics from the National Corporation of Swedish Pharmacies, antibiotic prescription rates for children aged one to two years from 1 July 2002 until 30 June 2003 in the municipalities in the two groups were 1,073 prescriptions/100, 000 inhabitants and 615 prescriptions/100, 000 inhabitants, respectively. The municipalities are located in the southern and the central parts of Sweden (Figure2) and they are similar in socioeconomic (demographic) structure, according to The Swedish Association of Local Authorities and Regions (SALAR). Jönköping and Falun belong to the category other large towns and the others to other municipalities 12,500 – 25,000 inhabitants. Other characteristics of the municipalities are shown in table 2 (SCB, 2005).

Table 2. Characteristics of the municipalities in 2002 according to Statistics Sweden SCB

	Low prescription area				High prescription area		
	Falun	Leksand	Eksjö	Tranås	Jönköping	Alvesta	Älmhult
Number of inhabitants	54,841	15,301	16,761	17,718	118, 581	18,930	15,444
Post-upper secondary education (%)	10.8	7.3	8.8	5.8	9.6	5.1	6.0
Mean income in families (in SEK 100,000)	224.7	201.8	204.6	196.4	219.2	199.5	206.2

Figure 2. Geographical setting. Map of southern and central Sweden



In Sweden 10% of the population has completed post-upper secondary education and the mean annual income is SEK 224,900.

Paper IV was conducted in the urban municipality of Växjö, with about 77,000 inhabitants located in the county of Kronoberg, in southern Sweden (Figure 2). The districts participating in Paper IV are quite close to the centre of Växjö, and all have similar socioeconomic structure and the same type of day-care arrangements.

Study population (Papers I, II, III)

The nurses at the 30 child health clinics, in the seven municipalities were informed by the authors about the study and they were all willing to take part. The nurses gave written and oral information about the study, to parents who came for routine checkups with an 18-month-old child. The families were included consecutively from 1 October 2002 until the 11 April 2003. The families who agreed to take part were asked to give their written informed consent.

Families that did not master the Swedish language, in the judgement of the nurses at the child health clinic, were excluded. The distribution of dropouts and reasons for dropout in the high and low prescription area are presented in table 3. A total of 638 families were included in the high prescription area and 316 in the low prescription area.

Table 3. Reasons for dropping out in the families in the prescription areas.

	Percentage	
Families with children of 18 months	High prescription area (N=800)	Low prescription area (N=385)
Families who did not attend the child health clinic	0.9	0
Families not invited owing to language difficulties according to exclusion criteria	4.0	1.6
Families who declined without stating any reason	13.0	13.0
Families who declined due to a difficult social situation	2.1	3.4
Families who moved away during the study	0.2	0
Families included (n=)	79.8	82.0
	100.0	100.0

A total of 13.0% in the high prescription area and 12.3% in the low prescription area did not submit complete logbooks. This means that 555 and 276 families respectively completed the study. The number of children participating was 570 and 278, respectively.

There were more dropouts owing to language difficulties in the high prescription area which seems reasonable since there are more immigrants in the city of Jönköping than in the city of Falun (SCB, 2005).

In the 831 participating families there were 1152 children of whom 55% (848/1152) were 18 months old. There were 17 pairs of twins aged 18 months. In 58% (483/831) of the families there were siblings, of whom 26 were under 18 months age. These 26 were excluded from further analyses. The mean number of children per family was 1.9. Background data according to questionnaire for the families with 18-month-old children are presented in table 4 and characteristics of the family members are shown in table 5.

Table 4. Background data according to questionnaire for the 18-month-old children.

	Percentage n=848
Boys	51.9
Any siblings	57.5
Asthma	11.3
Other chronic illness	1.6
Daycare outside the home	66.9
Living in rental flat	23.5
Smoker in the family	13.0
Single parent	4.5
Mother without post-upper secondary education	58.4
Father without post-upper secondary education	67.8
Either parent unemployed	6.3
No one in the family with health care education	51.0
Both parents born outside the Nordic countries	6.6
Perceived as infection prone	17.3
High or medium level of concern about infectious illness	43.2
Inadequate expectations of antibiotics effects	57.8
Living in the high prescription area	67.2

Table 5. Background data in percentages for individuals in different age groups

	Percent						
	18 months		Siblings			Parents	
	Girls n=408	Boys N=440	19m – 3 y n=172	4-6 y n=272	7-17 y n=227	Mothers n=828	Fathers n=792
Born outside Scandinavia	0.7	1	1	1	5	7	7
In group daycare	67	68	75	93	0	-	-
Reported infection prone	15	18	7	6	6	2	3
Reported asthma or allergy	7	13	13	15	20	24	24
Other reported illness or disability	2	1	5	3	4	6	3

Methods (Papers I, II, III)

Questionnaire

Background data

All the members in the participating families answered a questionnaire given to them by the nurses, regarding socioeconomic status, ethnicity, smoking and occupation. The questionnaire also asked whether, in the opinion of the parents, the child had asthma/allergy or was prone to infections. The parents answered the same questions about themselves. The questionnaire also asked about what kind of daycare the children had.

Daycare

Daycare outside the home was defined as daycare at daycare centre or in family daycare, all other care was classified as home care.

Concern about infectious illness

Four statements, translated from English to Swedish, as described below were given to each family, about "Concern about infectious illness", each with four alternative answers. The statements were taken from the instrument "General Health Threat" (Hansen, 1994). The first statement was slightly modified from the original since we found the expression concern about infectious illness more relevant in this study. According to the answers three levels of concern about infectious illness were determined – low, medium and high (Hansen, 1994). The medium and high level of concern about infectious illness was then gathered to "high level".

The statements were:

1. "Your child's' infections worry you a lot."
2. "Each time your child is ill, you are afraid that it is something serious."
3. "Your child becomes ill more frequently than other children of the same age."
4. "You are often afraid that your child may become seriously ill.

The answers were

1. fully agree
2. partly agree
3. partly disagree
4. totally disagree

Antibiotics knowledge

The parent also answered two general questions about respiratory tract infections and antibiotic treatment. If the answers to both statements were "fully agree", their knowledge was classified as "adequate" otherwise "inadequate".

The statements were:

1. "Most respiratory tract infections in children go away without antibiotics".
2. "Most respiratory tract infections in adults go away without antibiotics".

The answers were

1. fully agree
2. partly agree
3. partly disagree
4. totally disagree

Logbook

During one month, the parents were asked to note all the family members' infectious symptoms in a diary according to preset alternatives. The alternatives were: runny nose, cough, earache, sore throat, temperature over 38º C, diarrhoea/vomiting, tiredness, and other symptoms. The symptoms were noted day by day. In the logbook the parents also noted whether they had been at home from daycare, school or work, if they had claimed for social insurance remuneration, if they had consulted a physician or received antibiotic treatment.

All families received a fridge magnet with a spring clip in which the logbook could be kept. Nurses from the child health clinic phoned the families twice during the study month to remind them about the registration and that the logbooks should be returned in the envelope with prepaid postage.

Definitions

A symptom day was defined as a day when one or more symptoms occurred. Respiratory tract symptoms were defined as at least one of the following: runny nose, cough, earache, sore throat, with or without tiredness and fever. Gastroenteritis was defined as diarrhoea or vomiting with or without tiredness and fever and without the occurrence of other symptoms. Mixed symptom s were defined as a combination of respiratory and gastrointestinal symptoms with or with out tiredness and fever.

A symptom episode was defined as occurrence of one or more infectious symptoms for at least one day. A new symptom episode was registered as starting when there were at least two days without symptoms since the previous episode.

Study population (Paper IV)

This study was conducted in six randomly chosen municipal daycare centres from three of the districts. The daycare centres were located in the same type of buildings in comparable residential areas, with similar outdoor environments. All centres consisted of one infant department and two departments with children aged 3 to 5. Three daycare centres were chosen at random for the intervention, while the others served as controls.

Children who started attending daycare later than one month after the study start were not included.

At the start of the study there were 154 children and 31 personnel in the intervention daycare centres and 157 children and 32 personnel in the control group. During the nine-month study (September to May), 10 and 9 children respectively left the centres owing to the birth of a new baby in the family.

Methods (Paper IV)

Questionnaire

At the study start all personnel at the daycare centres anonymously completed a questionnaire on guidelines for how to manage infectious diseases. At the end of the study they answered the same questionnaire again.

At the beginning of the study the parents of 140 (91%) of the children in the intervention group and of 145 (92%) in the control group completed a questionnaire concerning characteristics of the family.

At the same time 127 (82%) and 117 (74%) of the parents, respectively, also anonymously completed a questionnaire about the receipt of information concerning infectious diseases in children. This questionnaire was answered once more at the end of the study.

Sickness absence

After each episode of sickness absence, all the parents completed a special absence form concerning the reasons for the child's absence according to preset alternatives. Sickness absence from daycare were defined as absence as percentage of the expected presence. They also noted the length of the sickness episode, whether a physician had been seen or if antibiotics had been prescribed. The diagnoses otitis media, tonsillitis, and pneumonia had to be confirmed by a doctor. Otherwise the diagnoses were based on the parents' own reports. The parents' reports regarding the number of sickness absences were validated against the staff's own absence lists regarding the number of sickness episodes and absence days.

Intervention group

At the beginning of the study all personnel were made aware of the recommendations of the Swedish National Board of Health and Welfare (the provisional version by three of the authors) and each department was given a copy (Socialstyrelsen, 2001a). This book contains guidelines about how to handle infections and contagion in daycare.
In the course of the study, liquid soap and paper towels were used instead of terry towels and bars of soap. The personnel were urged to take the children outside as much as possible, but no exact numbers of hours was specified. A study day on outdoor pedagogy was arranged for the personnel. Posters with information on respiratory tract infections and contagion were placed near the entrances.

In connection with parents' meetings, one at the start of the study and one while the study was in progress, the authors informed the parents about infectious diseases and contagion. The use of antibiotics to cure infections in pre-school children was discussed as was the risk of developing resistance through overuse.

Control group

At the beginning of the study the parents and personnel were informed about the aims and the arrangements of the study. No other activities were undertaken.

Statistical methods

The distributions of the variables measured were calculated as proportions and means ± standard deviations (SD) and, where relevant, median (Md) with interquartile range (IOR) in each of the Papers I – IV. All statistical tests used in Papers I-IV were two-tailed since we did not have any preconceived ideas about the direction of the results. A p- value of <0.05 was regarded as significant. Version 13.0 or earlier of SPSS (Statistical package for social sciences) was used to run the analyses in Papers I- IV, except the multilevel analyses in Paper IV, which were performed with MlWin 1.1.

Mann-Whitney U-test

The non-parametric test, Mann-Whitney U-test was used to test for ranking location in discrete count data in two independent groups. Since we were handling count data, whole numbers with mostly a skewed distribution, the T-test was not applicable. Mann-Whitney U test does not make a distributional assumption (Petrie A and C, 2000) and was used in testing for differences in median number of symptom days, number of days per episode, number of physician visits and antibiotic prescriptions between the sexes and between different age groups (Paper I). It was used for comparing median number of symptom days in the high and low prescription areas respectively (Paper II) as well as in children with daycare outside the home and home care (Paper III). In paper III it also was used for comparing median number of episodes and days per episode and median number of days with different symptoms. The outcome symptom days in the month can also be handled in other ways (Paper I).

χ^2 –test

The χ^2 –test was used to test for differences in proportions on categorical variables between independent groups (Petrie A and C, 2000). This was applicable when comparing antibiotic prescription in the high and low prescription areas (Paper II). The χ^2 –test was used to compare the personnel's experience of infections at the study start as compared with the study end and to compare the parents' experience of information concerning infections in children at the study start as compared with the study end (Paper IV). Fischer's exact test was used to test for differences in proportions on categorical variables between groups when the expected value was less than five in any one cell (Paper IV) (Petrie A and C, 2000).

Logistic regression analyses

Logistic regression analysis was used to compute odds ratios (OR) and their 95% confidence intervals (95% CI) in both univariate and multiple variable analyses, when there were binary dependent variables and a number of explanatory exposure variables (Petrie A and C, 2000). Backward elimination of non-significant exposure variables was performed until all remaining variables were significantly related to the outcome (P-removal 10%) (Papers I, II, III). In paper II, prescription area was kept in the model irrespective of significance level since this was the main outcome. At first crude ORs were drawn u, then we adjusted for background variables (Model 1), knowledge about antibiotics, perceived infection proneness and concern about infectious illness (Model 2). In Model 3 infectious symptoms were added and, finally, physician consultations (Model 4). In paper III, the same type of logistic regression analysis was used but daycare was kept in the model irrespective of significance level. The variable chronic illness was also put into the models since this may be of importance for physician consultations. Models 1 to 3 were used when physician consultation was the main outcome and Models 1 to 4 when antibiotic prescription was the main outcome. To assess the impact of risk variables on the odds ratio (OR) we calculated the proportion of excess odds ratio accounted for by risk variable adjustment, $\frac{OR - OR_{adjusted}}{OR - 1}$ (Lynch et al., 1996). This was calculated for physician consultations and antibiotic prescriptions in paper III.

Anova

Anova is an applicable test when the dependent variable is normally distributed and the independent variables are categorical (Petrie A and C, 2000). This test was used for comparing symptom days in smoking and non-smoking families, at the same time controlling for sex (Paper III).

Multilevel analyses

The monitoring of the children was a form of repeated measure with individuals appearing several times since every child can have one or more absent episodes. Since the dependent variables were count variables they were not normally distributed but rather following a skewed distribution, indicated by a standard deviation (SD) close to the mean. Furthermore,

although the children were individuals, they were a part of collective (departments) that could be regarded as clusters above the individual level. This level could affect the behaviour of the children or the personnel. Ignorance of a hierarchical structure, i.e. oversimplification of a complex reality, could give unreliable results with incorrect standard errors and confidence limits. To make a correct statistical analysis of our material, we used multilevel Poisson regression analyses (Leyland, 2001, Goldstein et al., 2002, Snijders, 1999). Multilevel analyses provided an enhanced understanding of the potential heterogeneity behind the different departments and made it possible to analyze repeated measurements on the same individual. Multilevel analyses are therefore capable of disentangling between individual and contextual (surrounding) effects, i.e. can account for both between and withinsubject variation.

The analyses were performed using children at the first level and departments at the second level.

All computations were made using the four dependent factors in a given order: The analysis began with a so-called empty model (Model 1), i.e. individuals on level one and departments on level two and no explanatory variables, in order to detect any effects on level 2 (departments). Then the independent variables were introduced in the model (Model 2) and their effects and the effects on level 2 were observed (along with confidence intervals). A simple Wald test was used to test the significance of covariates.

Results

Infectious symptoms, social insurance and health care (Paper I)

The number of days with any reported symptom decreased with rising age and the older children reported the same levels of days without symptoms as the adults. The youngest children were those reporting most symptom days Table 6.

Table 6. Days with and without symptoms during a month in percent.

	Percent						
	18 months		Siblings			Parents	
	Girls	Boys	19m - 3 y	4-6 y	7-17 y	Mothers	Fathers
	n=408	n=440	n=172	n=272	n=227	n=828	n=792
0 days of symptoms	7	7	13	18	34	31	37
1 to 7 days of symptoms	29	28	43	52	45	39	42
8 to 14 days of symptoms	30	30	25	22	17	19	13
15 days or more of symptoms	34	35	19	8	4	11	8

Different constellations of symptoms could occur during one day but a runny nose as a single symptom was most frequent in all age groups, occurring in 26 to 30 percent of all symptom day. Any respiratory tract symptom was reported in about 80% and gastrointestinal symptoms in about 5% of all symptom days. Children aged 18 months had 1.6 infectious episodes as compared with 1.0 for older siblings, and more days per episode compared with older siblings (p<0.001). There were no statistically significant differences between the sexes.

The 18-month-old children had more physician consultations than siblings older than four years (p=0.001) and consumed more antibiotics than siblings older than seven (p=0.04) table. Mothers had 1.1 infectious episodes compared with 0.9 for the fathers (p<0.001) and

the mothers consumed more antibiotics per episode (p=0.04). The measures taken in symptom episodes are shown in table 7.

Table 7. Symptom episodes and measures taken, in different age groups.

	Mean (S.D)						
	18 months		Siblings			Parents	
	Girls	Boys	19m - 3y	4 - 6 y	7-17 y	Mothers	Fathers
Symptom episodes n	n=703	n=771	n=270	n=396	n=290	n=1139	n=984
Days per episode	5.7(4.6)	5.4(4.4)	5.1(4.1)	4.0(3.4)	3.8(2.7)	4.3(3.7)	3.9(3.3)
Physician consultations per episode	0.12(0.4)	0.15(0.4)	0.09(0.4)	0.08(0.3)	0.04(0.2)	0.05(0.2)	0.06(0.5)
Antibiotic prescriptions per episode	0.05(0.2)	0.07(0.2)	0.04(0.2)	0.05(0.2)	0.02(0.2)	0.03(0.2)	0.02(0.1)

On 23-30 % of the symptom days the children had to stay home from daycare or school, but social insurance was seldom claimed when the children were ill. When the parents were at home ill, mothers claimed their sickness remuneration from the social insurance authorities for 75% of their sickness days, and fathers for 77% (table 8).

Table 8. Percentage of days at home and utilisation of social insurance: Data are based on symptom days reported by all the individuals who had daycare outside the home.

	Percent						
	18 months		Siblings			Parents	
	Girls	Boys	19 m - 3 y	4 - 6 y	7 - 17 y	Mothers	Fathers
	n=3313	n=3911	n=1019	n=1514	n=901	n=4801	n=3429
At home	24	30	23	27	23	12	13
Use of social insurance	9	10	6	6	2	9	10

Differences in antibiotic prescribing (Paper II)

In the high and low prescription areas there were some differences in background data. In the high prescription area 70.7% of the children had daycare outside the home, as compared with 60.1% in the low prescription area, and 15.0% of the families had at least one smoker as compared with 8.8% in the low prescription area.

There were no differences in percentage of 18-month-old children (7%) whose parents did not report any symptoms during the registration month in the two groups. The median number of symptom days was 11.0 (interquartile range 6-17) and 10.0 (interquartile range 5-17), respectively, Mann-Whitney U-test p=0.38.

In the high prescription area 20.5% (117/570) of the children had had appointments with a physician. The corresponding figure in the low prescription area was 15.8% (44/278) OR 1.37 (95% CI 0.94-2.01). These consultation rates were not statistically different even after adjustment for socioeconomic factors, concern about infectious illness and infectious symptoms more than seven days, adjusted odds ratio (aOR) 1.40 (95% CI 0.88-2.23).

During the studied months 11.6% (66/570) of the children in the high prescription area and 4.7% (13/278) of the children in the low prescription area were prescribed antibiotics (Chi- Square=10.54, p=0.001). The crude odds ratio for antibiotic use was 2.67 (CI 95% 1.45-4.93) (table 9). When controlling for background variables (Model 1) as well as knowledge about antibiotics, perceived infection proneness and concern about infectious illness, the aOR, still remained significant (Model 2). When symptoms for more than seven days were added, the aOR did not change significantly (Model 3). Neither did it change appreciably when physician consultations were taken into account (Model 4). Thus, irrespective of which model we used, the differences in antibiotic prescription between the areas remained.

Table 9. Antibiotic treatment for the 18-month-old children.

Crude (univariate) odds ratio (OR) and adjusted odds ratios with 95% confidence intervals (95%CI). The variables in the last step are shown in the adjusted models. Adjusted odds ratios were calculated using multiple logistic regressions with backward elimination of all variables except prescription area.
Model 1 adjusting for social variables.
Model 2 adjusting for variables in model 1 and antibiotic knowledge and concern about infectious illness.
Model 3 adjusting for variables in model 2 and infectious symptoms more than seven days.
Model 4 adjusting for variables in model 3 and physician consultations.

	Crude		Adjusted							
			Model 1		Model 2		Model 3		Model 4	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
High prescription area	**2.67**	**1.45-4.93**	**2.50**	**1.27-4.95**	**2.44**	**1.19-4.99**	**2.55**	**1.23-5.32**	**2.61**	**1.14-5.98**
Being a boy	1.49	0.93-2.39								
Any sibling	1.23	0.76-2.00							**2.21**	**1.06-4.41**
Asthma	**2.28**	**1.20-4.32**	**2.62**	**1.35-5.07**			1.96	0.92-4.16		
Daycare outside the home	**2.43**	**1.34-4.41**	1.85	0.98-3.50						
Living in rental flat	1.44	0.86-2.41								
Smoker in the family	1.24	0.65-2.39								
Single parent	1.15	0.40-3.33								
Mother without post-upper secondary education	1.13	0.70-1.82								
Father without post-upper secondary education	0.90	0.55-1.49								
Either parent unemployed	0.81	0.28-2.32								
No health care education in the family	1.51	0.92-2.51								
Both parents born outside the Nordic countries	1.98	0.93-4.20	**2.59**	**1.07-6.28**						
Perceived as infection prone	**3.60**	**2.18-5.93**			**2.79**	**1.52-5.11**	**2.00**	**1.04-3.83**		
High or medium level of concern about infectious illness	**4.26**	**2.51-7.23**			**3.76**	**2.00-7.07**	**3.71**	**1.96-7.04**	**4.01**	**1.97-7.97**
Inadequate antibiotics knowledge	**1.82**	**1.08-3.05**								
Symptoms more than 7 days	**5.43**	**2.58-11.5**					**4.40**	**1.93-10.07**		
Physician consultations	**36.0**	**19.1-67.8**							**38.2**	**18.0-81.2**

Daycare, infectious symptoms, consultations and antibiotics (Paper III)

Paper III focuses on daycare attendance. When comparing background data in the daycare and home care group there were some differences. 15.5% of the children with daycare outside the home had at least one smoker in the family as compared with 7.9% among home care children. 46.6% of the families reported high or medium level of concern about infectious illness as compared with 36.6% among the home care children. For children perceived as infection prone the figures were 20.3% and 11.5%, respectively.

Infectious symptoms

During the study month the daycare children had more reported symptom days (Mann-Whitney U-test $p<0.001$) and more infectious episodes (Mann-Whitney U-test $p<0.001$) than the home care children. The daycare children had a median of 2 infectious episodes (range 0-3) during the studied month as compared with 1 episode (range 0-4) for the home care children. Among the daycare children there were more days with reported symptoms from the respiratory tract (Mann-Whitney U-test $p<0.001$) and more reported days with respiratory tract symptoms with fever (Mann-Whitney U-test $p<0.001$).

Physician consultations

Of the daycare infants 23.3 percent had seen a physician during the study month, as compared with 10.8 percent of the home care infants OR 2.49 (95% CI 1.63-3.82). When taking all data from the questionnaire into account, the daycare infants had more physician consultations than the home care infants (Table 10 Model 1 and 2). When adjusting for all data from the questionnaire and symptoms more than seven days during the month, the odds ratio for physician consultations decreased to 1.51 (CI 95% 0.92-2.47) (Table 10 Model 3). The excess odds ratio for physician consultations after questionnaire data variable adjustment was 42.3%.

Table 10. Physician consultations for the 18-month-old infants.

Crude and adjusted odds ratios (ORs) with 95% confidence intervals (95%CI). The variables in the last step are shown in the adjusted models. Adjusted odds ratios were calculated using multiple logistic regressions with backward elimination of all variables except daycare.

Model 1 adjusting for background data.

Model 2, adjusting for data in Model 1 and knowledge about antibiotics, perceived infection proneness and concern about infectious illness. Model 3 adjusting for data in Model 2 and infectious symptoms more than 7 days during the month.

	Physician consultations							
	Crude		Adjusted					
			Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Daycare outside the home	**2.49**	**1.63-3.82**	**2.03**	**1.27-3.23**	**1.86**	**1.14-3.03**	1.51	0.92-2.47
Being a boy	**1.43**	**1.01-2.02**			1.43	0.94-2.19		
Any siblings	0.76	0.54-1.08	**0.65**	**0.43-0.96**				
Asthma	2.95	1.80-4.84	**3.33**	**1.96-5.66**	**2.50**	**1.39-4.47**	**3.37**	**1.90-5.99**
Other chronic illness	2.76	0.89-8.56	**3.54**	**1.08-11.65**	**3.45**	**1.05-11.36**		
Living in rental flat	1.17	0.78-1.74						
Living in a large municipality	0.90	0.61-1.32						
Smoker in the family	0.76	0.44-1.31						
Single parent	1.34	0.62-2.89						
Mother without post-upper secondary education	1.06	0.74-1.50						
Father without post-upper secondary education	1.01	0.69-1.46						
Either parent unemployed	0.77	0.35-1.67						
No health care education in the family	0.97	0.68-1.38						
Both parents born outside the Nordic countries	1.46	0.78-2.75						
Perceived as infection prone	**2.61**	**1.74-3.91**			**1.73**	**1.00-2.98**		
High or medium level of concern about infectious illness	**2.25**	**1.58-3.20**			**1.74**	**1.13-2.69**	**1.98**	**1.29-3.03**
Inadequate antibiotics knowledge	**1.40**	**0.95-2.04**						
Symptoms more than 7 days during the month	**4.85**	**2.92-7.94**					**4.99**	**2.78-8.97**

Antibiotic prescription

Antibiotics were prescribed to 11.4 % of the daycare infants and 5.0 % of the home care infants, OR 2.43 (95% CI1.34-4.41). Daycare infants were prescribed more antibiotics after socioeconomic background data were taken into account (Table 11 Mode1), but not when all data from questionnaire were taken onto account (Table 11 Model 2). When all data from questionnaire and symptoms more than seven days during the month were taken into account (Table 11 Model 3), the odds ratio decreased to 1.45- (CI 95% 0.71-2.96) for antibiotic prescription. The excess odds ratio for antibiotic prescription after questionnaire data variable adjustment was 32.9%.

Table 11. Antibiotic prescriptions for the 18-month-old children.

Crude adjusted odds ratios (ORs) with 95% confidence intervals (95%CI). The variables in the last step are shown in the adjusted models. Adjusted odds ratios were calculated using multiple logistic regressions with backward elimination of all variables except daycare.

Model 1 adjusting for background data.

Model 2 adjusting for data in Model 1 and knowledge about antibiotics, perceived infection proneness and concern about infectious illness. Model 3 adjusting for data in Model 2 and infectious symptoms more than 7 days during the month

	Antibiotic prescriptions							
	Crude		Adjusted					
			Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Daycare outside the home	**2.43**	**1.34-4.41**	**2.06**	**1.09-3.91**	1.95	0.96-3.96	1.48	0.72-3.02
Being a boy	1.49	0.93-2.39						
Any siblings	1.23	0.76-1.98						
Asthma	**2.28**	**1.20-4.32**	**2.36**	**1.21-4.64**				
Other chronic illness	3.14	0.84-11.67	3.41	0.87-13.4	3.89	0.90-16.8		
Living in rental flat	1.44	0.86-2.41						
Living in a large municipality	0.67	0.41-1.11						
Smoker in the family	1.24	0.65-2.39						
Single parent	1.51	0.40-3.33						
Mother without post-upper secondary education	1.13	0.70-1.82						
Father without post-upper secondary education	0.93	0.55-1.49						
Either parent unemployed	0.81	0.28-2.32						
No health care education in the family	1.51	0.92-2.51						
Both parents born outside the Nordic countries	1.98	0.93-4.20	**2.63**	**1.08-6.40**				
Perceived as infection prone	**3.59**	**2.18-5.92**			**2.62**	**1.41-4.89**	**2.38**	**1.28-4.45**
High or medium level of concern about infectious illness	**4.26**	**2.51-7.23**			**3.71**	**1.96-7.00**	**3.78**	**2.00-7.15**
Inadequate antibiotics knowledge	**1.94**	**1.10-3.40**			3.44	0.82-14.4		
Symptoms more than 7 days during the month	**5.43**	**2.58-11.49**					**4.04**	**1.77-9.26**

Effects of intervention (Paper IV)

At the end of the study, more of the personnel at the intervention daycare centers thought that more children were at home long enough after an infection episode than at the start of the study. Also more parents in the intervention group felt informed about infectious diseases and when to keep an infected child at home.

The total absence for illness as a percentage of the expected presence was 6.6% in the intervention group and 6.8% in the control group.

The multilevel empty models showed significant variation on the department level which decreased with introduction of the individual variables but remained significant for absence in days. Although if there were no statistically significant differences, there was a consistent pattern in favour of the intervention with regard to sickness absence, physician consultations and antibiotic prescriptions (Table 12).

Table 12. Multilevel analysis of the effects of the intervention on sickness absence, physician consultations and antibiotic prescription**.**

	Sickness absence				Doctor consultations		Antibiotic prescriptions	
	Days		Episodes					
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Fixed effects								
Intervention vs control RR (95% CI)		0.95 (0.78-1.15)		0.90 (0.78-1.05)		0.81 (0.63-1.04)		0.70 (0.48-1.02)
Infection prone vs not infection prone RR (95% CI)		**1.48 (1.35-1.63)**		**1.36 (1.17-1.58)**		**2.80 (2.13-3.67)**		**2.99 (2.06-4.34)**
Asthma vs not asthma RR (95% CI)		**1.20 (1.09-1.31)**		1.09 (0.95-1.26)		1.10 (0.82-1.47)		0.94 (0.60-1.49)
Random effects								
Dept. variance (SE)	**0.09(0.03)***	**0.04(0.02)***	**0.04(0.02)***	0.01(0.01)ns	0.09(0.05)ns	0.00(0.00)ns	0.18(0.10)ns	0.02(0.05)ns
Median Mean Ratio	**1.33**	**1.21**	**1.33**	1.10	1.33	1.00	1.50	1.14

*p <0.05

ns. Not significant

Discussion

Methods

In Sweden, 99% of all families attend a child health clinic (Hagelin et al., 2001), which provides researchers with excellent opportunities to perform good population-based prospective cohort studies in young children (Paper I-III).

Logbooks

Using logbooks (Papers I-III) was a convenient way to capture a large amount of information at a low cost. The logbook method used gave us the opportunity to build a time dimension, which retrospective interviews not do. It also gave us the possibility of aggregating events over time and computing new variables, describing individual and family characteristics, as previously mentioned (Roghmann and Haggerty, 1972). We informed the parents that they were to report every symptom of infection they perceived during the month. We believe the parents found the logbooks easy to handle since the response rate was high and the logbooks were well filled in. The logbooks and questionnaire were not validated, but they were tested in a pilot study to see if they were manageable for the families.

Logbooks have previously been used to study morbidity and health care utilisation (Dahlquist et al., 1987, Hojer et al., 1987).(Holme, 1995, Bruusgaard et al., 1993, Bruijnzeels et al., 1998b). They give a more detailed picture of daily symptoms and measures than retrospective interviews, above all when it comes to minor and mundane events. Minor everyday events are only remembered for one to two days. In logbooks, such events will be noted (Roghmann and Haggerty, 1972) (Dahlquist et al., 1984). Contradictory results have been found, and more symptoms have been reported in interviews than in logbooks (Bruijnzeels et al., 1998a). The differences were most obvious in children of mothers with little education. These mothers reported fewer symptoms in their children than mothers with higher education. In that study the interviews were made from a checklist asking about the presence or absence of 42 different symptoms and the logbook they used consisted of open

questions about health status (Bruijnzeels et al., 1998a). The sensitivity was higher in interviews (0.84) than in logbooks (0.72) when estimating children's medical utilisation, but the specificity was higher in the logbooks (0.96) than in interviews (0.96) (Bruijnzeels et al., 1998c). Telephone interviews have also been compared with visits in the home, showing 1.8 times more reported illness episodes in the telephone interview than in the home group (Fox et al., 1972).

Symptom episodes

The definition of a symptom episode was one or more symptoms for at least one day (Paper I-III) as in other studies (Monto et al., 1971, Dahlquist et al., 1987). Also other definitions of symptom episodes have been used for example symptoms for more than one day (Wald et al., 1991b), as well as consecutive days with the same diagnose (Hojer et al., 1987, Bruijnzeels et al., 1998b). An episode was deemed to have commenced if there had been at least two symptom-free days before it as in the Tecumseh study (Monto et al., 1971) but three or more symptom-free days since the last episode have been used as the time frame by others (Lambert et al., 2005). When comparing data from different studies it is important to look at the definitions since this can result in major differences in number of episodes.

In Paper IV the parents of the children reported the reason for absence after every sickness period. It has been found that parents of children in daycare report more symptoms than daycare educators (Carabin et al., 2000). This leads to larger estimations of incidence rates, and parents' data are probably more valid than educators' data. The parents' reports of sickness absences were validated against the personnel's own absence lists as regards number of sickness episodes and absence days.

Study population

The high attendance rate at the child health clinic, and the fact that the nurses reminded the families twice, facilitated obtaining the satisfactory results that 73% completed the study (Papers I-III). The study population was chosen from areas with either very high or very low antibiotic prescription rates for children, in order to find explanations for differences in the prescription rates (among the two areas). No big cities were represented and the mean income and education level were a little below the means in Sweden. Families that did not master the Swedish language in the judgement of the nurses at the child health clinic, were excluded thus it may not be possible to generalise the results to the whole of Sweden.

In Paper IV the compliance with the study were high (91%), but we are aware that we had a small study population. The study was well conducted and analysed with the proper multilevel method. The results may be generalisabel to areas with similar characteristics in socioeconomics and daycare.

All the physicians in the regions where the study took place were unaware that the studies were being made (Papers I-IV). This reduces the risk of systematic bias.

Statistics

Multiple logistic regression analysis is used to describe associations between exposure or explanatory variables and a dichotomous outcome (Petrie A and C, 2000). The explanatory variables, one or more, influence the outcome. The model can be used to predict the outcome category into which an individual will fall, from values of the explanatory variables (Petrie A and C, 2000). In papers II-III we used different logistic regression models to be able to study the odds, taking one or more variables into account. We used the backward elimination procedure, meaning that explanatory variables of no importance were excluded one by one. The backward elimination procedure also enhances the possibility of finding multicollinearity. Finally, we obtained a well-fitting model for predicting the outcome. We also checked for interactions between independent variables particularly “concern about infectious illness” and “infection proneness” but did not find any interaction.

Multilevel analysis is the correct analysis method for data in clusters that has affects at different levels (Twisk, 2006). Children in daycare are an example of this. Each child is nested with other children in departments and the departments are nested into daycare centres. The Median Mean Ratio is the median difference between the daycare departments expressed as an odds ratio (Larsen and Merlo, 2005). Many studies have been conducted at daycare centres but only a few more recent studies have taken cluster effects into account using the multilevel method (Carabin et al., 1999, Roberts, 2000 #60, Roberts et al., 2000b).

Results

Infectious symptoms

Infectious symptoms are common in 18-month-old children and 93% of the children had reported such symptoms during the month. As many as one third of the days during one

month had symptoms reported or expressed as episodes, 1.6 episodes during a month (Paper I). Other studies found 4 - 6 episodes a year (Monto and Ullman, 1974, Lambert et al., 2005). This could be explained by the fact that infectious symptoms are common at the age of 18 months. Another explanation may be that more symptoms are reported when using logbooks and that the study was in the winter season, when most infections occur (Monto et al., 1971, Monto and Ross, 1977, Monto and Sullivan, 1993).

As children mature, the number of symptom days decreases, to increase again in young adulthood (Paper I), as found in the Tecumseh study (Monto and Ullman, 1974, Monto and Sullivan, 1993). Like some other studies (Fleming et al., 1987, Monto and Sullivan, 1993) we did not find any clear differences between boys and girls, although more morbidity among boys younger than two and among girls older than ten has been found by other researchers (Monto and Ullman, 1974, Monto and Sullivan, 1993). The pattern with more symptom episodes in adult women than men (Paper I) was also apparent (Lidwell and Sommerville, 1951, Brimblecombe et al., 1958, Monto and Ullman, 1974, Monto and Sullivan, 1993).

Respiratory tract symptoms are the most common type of symptom in all age groups (Paper I) (Sydensticker, 1926, Monto, 1994). In daycare children, too, respiratory tract symptoms are the most common symptoms (Paper III). Infectious diseases account for at least 90% of sickness absence in children in daycare, and 60-70% of this sickness absence attributable to RTIs (Petersson and Håkansson, 1989, Pönkä et al., 1991).

Although the siblings and parents contracted fewer infectious episodes than the small children (Paper I), the total number of symptom days is numerous in families with small children. In families where the small children are in daycare, the number of symptoms and episodes are even higher, since children in daycare have more symptoms than children in home care (Paper III). This is in accordance with previous studies (Loda et al., 1972, Strangert, 1976, Wald et al., 1988, Petersson and Håkansson, 1990, Wald et al., 1991a)}(Churchill and Pickering, 1997, Nafstad et al., 1999, Kvaerner et al., 2000). This does not mean that the reported symptom days always resulted in restrictions in daily activities, absence from daycare or work, or contact with the health care system, but the families have to handle the symptom days some how.

In a winter month, almost every infant in daycare and most of the infants in home care had some reported symptom (Paper III). In contrast, an American retrospective study found that only 32% of preschool children in daycare and 21% of preschool children in home care had some reported symptom during a two-week period in the summer (Fleming et al., 1987). In paper III, children in daycare had a median of 2 infectious episodes and children in

home care a median of 1 infectious episode during a month. Other studies have found 6-14 episodes per child/year in children in daycare and 4-7 in children in home care (Wald et al., 1988, Flores Hernandez et al., 1999). The median duration of the episodes was 5 days (Paper III), as compared with around 8 days found earlier (Wald et al., 1991b, Flores Hernandez et al., 1999). The differences may be due to differences in the definition of an infectious episode and to the fact that logbooks were not used for data collection.

In concordance with previous results (Harsten et al., 1990, Rasmussen and Bondestam, 1992) we did not find any differences in infectious symptoms between infants from smoking and non-smoking families (Paper I). On the contrary parental smoking or maternal smoking has been found to be important in relation to reported infectious symptoms in children (Willatt, 1986, Fleming et al., 1987, Peat et al., 2001). We did not go into detail about this topic and smoking, was not the prime focus of the study.

No other factors of potential importance for infectious symptoms were studied further.

Absence from daycare or work

Roughly 25% of the symptom days for the children and about 13% of the symptom days for the parents resulted in absence from daycare or work (Paper I). The 18-month-old children had just above two absence days during the study month (Paper I) and the children in daycare had around ten days during the nine-month study (Paper IV). In Finland and Denmark children in mixed age groups in daycare had 14-24 absence days per year (Mottonen and Uhari, 1992, Rindel et al., 1992). For a family in the study the total number of absence days is around 4.4 in a winter month (Paper I) thus more than a recent American study found (Brady, 2005). For families with small children, this means many days of absence during a winter season.

In Sweden the social insurance remuneration is generous, i.e. parents can receive financial compensation if they have to stay at home with an ill child (Försäkringskassan). We found that social insurance remuneration was claimed only in a small proportion of the days the child had to be cared for at home (Paper I). This means that parents must have made arrangements for their ill children to be looked after in other ways despite the possibility of social insurance remuneration.

When we spoke to personnel at daycare centres we found that their feelings were concordant. Parents try to arrange for care of their ill children so they can handle their own

work in a reasonable way. Arrangements in the parents' working schedule and help from grandparents are ways the daycare personnel were familiar with.

When the parents are absent from work themselves due to infectious symptoms, they use the social insurance remuneration to a larger extent, which sounds reasonable. No previous studies have, to our knowledge, related the number of days one needs to stay at home from daycare or work due to reported infectious symptom, to the use of social insurance remuneration.

Physician consultation

We have not found any directly comparable population based study measuring the numbers of infectious symptom days leading to a physician consultation. Studies measuring any health problem, however, have found that 7–10% of the symptom days in families with small children led to a consultation (Dahlquist et al., 1987, Cunningham-Burley and Irvine, 1987) as compared to 1.7-4.0% of the infectious symptom days found in paper I. The difference may be explained by measuring all other health problems and diseases in those studies. If you count infectious episodes instead, 4-15% of the episodes resulted in a physician consultation (Paper I). This is in accord with a consultation rate of 11% for children ages 0–14 years and 16% for families with small children when counting the whole family, as previously found (Dahlquist et al., 1987, Bruijnzeels et al., 1998b). Other studies have found higher consultation rates, 46% in children aged 12-71 months and 23% in families with small children when counting the whole family (Monto and Ullman, 1974, Lambert et al., 2005). For most of the symptom days and episodes there was thus no need to contact health care, a pattern that has not changed noticeably over the last twenty years.

The 18-month-old children had more consultations than children older than four years (Paper I), as previously found (Bruijnzeels et al., 1998b, Saunders et al., 2003). Mothers made as many consultations as fathers for infectious symptoms (Paper I).

We did not focus on severity of symptoms or number of symptom days before a consultation but when parents decide to consult a physician, most parents make careful decisions based on what they see as objective criteria about the illness of the child. (Cunningham-Burley and Irvine, 1987, Wyke et al., 1990, Saunders et al., 2003). We chose a cut-off point of more than seven symptom days during the month, for the independent variable symptomdays, and this variable was found to be the strongest independent predictor for physician consultation in infants (Paper III). The importance of symptoms has previously

been described (Campion and Gabriel, 1985, Wyke et al., 1990) but not only the severity and duration of symptoms are of importance for physician consultation. There are several other factors that impact on the decision to have a physician consultation.

The importance of socioeconomic factors for physician consultations is not clear. Higher socioeconomic status (Halldorsson et al., 2002, Saunders et al., 2003) as well as lower socioeconomic status (Campion and Gabriel, 1984, Campion and Gabriel, 1985, Petersson and Håkansson, 1996) (Håkansson et al., 1996, Saxena et al., 1999) has been found to lead to more consultation. We found no effect of socioeconomic factors in our study when comparing infants in daycare with infants in home care (Paper III). No importance of socioeconomic factors in relation to physician consultations in preschool children has previously been described in Scandinavia and Great Britain (Sundelin and Vuille, 1979, Wyke et al., 1990, Bruusgaard et al., 1993, Osman and Dunt, 1995, Cooper et al., 1998, Groholt et al., 2003).

Siblings in the families were a protective factor, resulting in fewer physician consultations (Paper III), which is concordant with both Swedish and foreign studies (Campion and Gabriel, 1985, Håkansson et al., 1996, Hay et al., 2005). The experience of the parents from having older children provides them with strength, and with experience of children's illnesses. Consequently they less frequently perceive an actual illness as a threat (Hansen, 1994). The results in papers II and III are concordant. "Concern about infectious illness" was found to be an independent factor for more physician consultations.

Another factor of importance for more physician consultations is parents perceiving their children as infection prone (paper III). We do not know if these children in fact are more infectious prone or if this is a subjective perception of the parents.

From previous studies we know that children in daycare have more physician consultations than children in home care (Petersson and Håkansson, 1990, Hjern et al., 2000, Forssell et al., 2001, Silverstein et al., 2003), and the results from paper III are concordant with this. Since infectious symptoms are more common in infants in daycare, these infants are at higher risk of needing to consult a physician than infants in home care. After adjusting for socioeconomic data, "concern about infectious illness" and "infection proneness" excess odds for a consultation were 42% among the 18-month-old daycare children (paper III). When we also took reported symptom days into account the differences between children in daycare and children in home care as regards physician consultations was no longer statistically significant. This result is congruent with theories stating that higher occurrence of minor self-limited communicable illnesses explains the differences in physician consultations among children in daycare and children in home care (Silverstein et al., 2003).

Antibiotic prescription

Antibiotic use was more common among infants than among children older than seven years (Paper I). More antibiotic use among small children has also been found in Demark and the Netherlands (Thrane et al., 1999, Otters et al., 2004b). Among adults, mothers consumed more antibiotics per episode than fathers (Paper I), in contrast to other studies where no differences were found between men and women in terms of antibiotic prescriptions (Akkerman et al., 2004, Huang et al., 2005a).

Variation in antibiotic prescription to infants from different areas was found in paper II, and variations in antibiotic prescriptions to children has previously been found in Sweden (Henricson et al., 1998, Mölstad and Cars, 1999, Melander et al., 2000, Cars and Ekdahl, 2001, Cars and Ekdahl, 2002).

More than seven infectious symptom days during one month was one of the factors of greatest impact for antibiotic prescription (Paper II, III). No exactly comparable study was found, but the impact of symptoms particularly fever, fatigue, coated tonsils and yellow sputum on antibiotic prescription has been described by other researchers (Lam and Lam, 2003b, Fischer et al., 2005).

Socioeconomic status was of no importance in relation to antibiotic prescriptions (Papers II, III), but various effects have previously been found. No importance of socioeconomic status was found in a Swedish study (Håkansson and Petersson, 1992), but other Swedish studies found more prescriptions to be associated with higher socioeconomic status (Henricson et al., 1998, Hjern et al., 2000, Melander et al., 2003), and Danish and Canadian studies found less antibiotic prescription to be associated with higher socioeconomic status (Thrane et al., 2003, Kozyrskyj et al., 2004). Different patterns are seen in different countries indicating, that results cannot be generalised from one area to another (Melander et al., 2003). Neither siblings (Papers II, III) nor smoker in the family (Papers I,II,III) were of importance for antibiotic prescription. This is concordant with earlier studies of both siblings (Forssell et al., 2001) and smokers in the family (Hjern et al., 2000, Forssell et al., 2001). However a smoker in the family can also lead to higher antibiotic utilisation among children (Håkansson and Petersson, 1992).

18-month-old children in daycare received more antibiotic prescriptions than children in home care (Paper III) as already known for infants and other age groups in daycare (Rasmussen and Sundelin, 1990, Hjern et al., 2000, Forssell et al., 2001).

However, when adjusting for other relevant socioeconomic variables, “concern about infectious illness”, “infection proneness”, and reported symptoms more than seven days during one month, the odds for antibiotic prescription decreased and were no longer statistically significant (Paper III). It has been assumed that minor infectious morbidity makes the difference between the numbers of antibiotic prescriptions in children in daycare and children in home care (Silverstein et al., 2003) but no study has focused on this topic. When infants in daycare are taken to consult a physician they are treated in the same way as infants in home care as regards antibiotic prescription (Paper III).

The differences between the high and low prescription areas in terms of antibiotic prescriptions could not be explained by differences in reported infectious symptoms. Neither could it be explained by differences in socioeconomic factors, daycare arrangements nor concern about infectious illness in the family (Paper II).

Physicians’ habits

RTIs are not only common in the general population, but are also the most common diagnosis at health care centres (Grimsmo et al., 2001, Tähepold et al., 2003).This means that a lot of time and effort are required to handle these infections at health care centres. A physician must be aware of the parent's expectations about the consultation (although he does not necessarily have to acquiesce to them). This is a factor of great importance for parental satisfaction (Mangione-Smith et al., 1999). Expectations of the patients are seldom made clear during the consultation (Butler et al., 1998b, Altiner et al., 2004) and the physician often does not assess what the patient or parent expected correctly (Hamm et al., 1996, Britten and Ukoumunne, 1997, Cockburn and Pit, 1997, Mangione-Smith et al., 1999). Some parents may consult just to receive good advice and have confirmation that they are handling the situation in the right way. Others have the expectation of receiving antibiotics although only 1% make a direct verbal request (Mangione-Smith et al., 2001).

If the patient is not satisfied with the consultation she may have a greater symptom burden after leaving (Little et al., 2001). Parents who were given a contingency plan from the physician have higher mean satisfactory scores than parents not receiving such a plan (Mangione-Smith et al., 2001).

Patient and parent pressure to prescribe antibiotics leads to increased rates of over-prescribing (Vinson and Lutz, 1993, Hamm et al., 1996, Macfarlane et al., 1997, Mangione-Smith et al., 1999, Britten and Ukoumunne, 1997, Cockburn and Pit, 1997). What happens in

physician-parent interaction is important in relation to the prescribing of antibiotics (Hamm et al., 1996, Macfarlane et al., 1997, Cockburn and Pit, 1997, Butler et al., 1998b, Mangione-Smith et al., 1999). Our results indicate that physician prescribing habits are the most important factor for explaining differences between high and low prescription areas (Paper II). Inappropriate use of antibiotics may reinforce patients' perceptions that they should consult for similar complaints in the future (Butler et al., 1998a). If the physician provides the patient with an antibiotic prescription for a common cold the physician also confirms that it was right of the patient to make a consultation.

To reduce the over-prescribing of antibiotics, the cultural differences and attitudes towards use of antibiotics in parents and/or physicians have to change (Deschepper et al., 2002). If the attitude of the physician can be changed so as to involve the patient more in the management of the symptoms, this will provide a better platform for appropriate use of antibiotics (Pechere et al., 2002).

Since many patients do not know that upper respiratory tract infections are caused by viruses and that the infection can be handled without seeing a physician (Chan, 1996), this leads to misconceptions among parents or patients as regards indications for antibiotic use in treatment of RTIs (Belongia et al., 2002). Patient satisfaction with the consultation depends not only on antibiotics prescribing habits, (Butler et al., 1998b, Mangione-Smith et al., 2001) but also on time the physician spends listening (Lundkvist et al., 2002). Since consultations for RTIs are short, mean 7.3 minutes (Tähepold et al., 2003) a few minutes more might make it possible for the physician to elicit patient expectations for antibiotics and answer the parents' or patient's questions or concern about infectious symptoms in connection with the consultation.

It is possible to reduce the use of antibiotics considerably if the doctor is interested in doing so and has established a relationship with the patient (Petursson, 1996). For the physician it is important to focus on patients with severe symptoms in order to identify those who might benefit from antibiotic treatment (Mölstad, 2003). Clinical signs, for example abnormal auscultation when coughing are not always easy to handle (Hopstaken et al., 2006). C-reactive protein (CRP) is a useful but not always safe alternative distinguishing between viral and bacterial aetiology in adults (Melbye et al., 2004) and no studies have been conducted in children. Using CRP does not lead to reduced antibiotic prescriptions in adults with RTIs (Diederichsen et al., 2000).

Adverse effects of antibiotics

Inappropriate antibiotic use is harmful since exposure to antibiotics in a population increases the risk that people will be carriers of resistant of bacteria (Klugman et al., 1986). Recent antibiotic treatment in a child also increases the risk that the child will be a carrier (Reichler et al., 1992, Arason et al., 1996, Melander et al., 1998) as does the overall use of antibiotics in society (Arason et al., 1996) (Melander et al., 2000).

There may be risk of complications, from using too little antibiotics and this topic has been very little investigated. A British study using large routine data sets investigated complications in RTIs in relation to antibiotic prescriptions. Increased penicillin use was associated with significant reduction in admissions for both quinsy and mastoiditis when demographic data were controlled for. But to save one admission with either quinsy or mastoiditis would require approximately 2000 extra items of antibiotics per year for a practice of 10,000 patients (Little et al., 2002). Another British study using data sets found ambiguous results and concluded that the subject would benefit from further studies (Majeed et al., 2004). A third British study in children younger than fifteen did not find an increase in hospital admissions for quinsy or rheumatic fever when antibiotic prescription rates were decreased. Ambiguous result were found for mastoiditis (Sharland et al., 2005)

Interventions to reduce infections

The intervention oriented program in paper IV found a pattern towards lower sickness absence. This lower absence has earlier been found in foreign multifaceted interventional studies (Bartlett et al., 1988b, Kotch et al., 1994, Niffenegger, 1997, Ladegaard and Stage, 1999, Uhari and Mottonen, 1999, Carabin et al., 1999, Roberts et al., 2000a, Roberts et al., 2000b, Pönkä et al., 2004), though multilevel analyse technique were used only in three studies (Carabin et al., 1999, Roberts et al., 2000a, Roberts et al., 2000b).

Proper hand washing as a single intervention has been found to be effective in reducing infections at day care centres (Black et al., 1981) and in the general population (Curtis and Cairncross, 2003, Luby et al., 2005, Rabie and Curtis, 2006). In our multifaceted interventional study (Paper IV), proper hand washing was one part of the intervention.

Our program also included spending as much time as possible outside, although no exact amount of time was recommended (paper IV). Outdoor activity every day has reduced sickness absence in a small study (Søe and Hammershøy, 1991), although the cluster effect was not taken into account. Daycare centres with special outdoor pedagogy also seem to have

lower sickness absence (Söderström and Blennow, 1998). On the other hand no effect of time spent outdoors was found in others studies (Wefring et al., 2001, Rindel et al., 1992, Mygind et al., 2003).

Training about infectious symptoms, consultations and antibiotics

Our model for training personnel and parents about how to handle infectious symptoms in preschool children was manageable (Paper IV). The meetings were hold in connection with the ordinary personnel and parents' meeting thus not taking more time for either personnel or parents. At the meetings, we all had the opportunity to discuss when to keep the children at home, when to go to a doctor, and when to prescribe antibiotics. Training about infectious diseases and contagion has earlier been used as part of multifaceted intervention programme at daycare centres. Some of the studies focused on training for personnel (Bartlett et al., 1988b, Kotch et al., 1994, Uhari and Mottonen, 1999, Ladegaard and Stage, 1999, Roberts et al., 2000a, Roberts et al., 2000b, Pönkä et al., 2004)and some gave written information to parents about the intervention (Uhari and Mottonen, 1999, Ladegaard and Stage, 1999, Pönkä et al., 2004). None of them had training for parents as the prime focal point (Huskins, 2000). The response we received from the personnel and parents was positive and almost all families participated. We think the contact with the personnel and the parents at ordinary parents' meetings with the possibility of providing training enhances the knowledge about infections and facilitates future contacts with the primary health care.

One study has found that personnel at daycare centres advised parents to seek medical care for discoloured nasal discharge and cough. The personnel sometimes also required antibiotics to be commenced before the child returned to daycare (Skull et al., 2000). This supports the need for training for daycare personnel. Another study has, however, found that parental knowledge is more important for consultation behaviour than daycare centres' polices (Friedman et al., 2003).

We saw a trend towards fewer physician consultations after the personnel and parental training (Paper IV). Another study found that educational programme for families in a community reduced consultations with a physician for minor respiratory illnesses (Roberts et al., 1983). It has also been found that more parental knowledge about upper respiratory tract infections was related to lower acute care-seeking for respiratory tract infections (Friedman et al., 2003).

Public knowledge regarding antibiotic is poor (Pechère, 2001, Belongia et al., 2002, Finch et al., 2004) Educational campaigns have been used to affect public attitudes to antibiotic prescribing but were not found to have influenced the attitudes (Parsons et al., 2004). Campaigns have to be designed differently to reach different target groups (Mangione-Smith et al., 2004) (Finch et al., 2004).

Multifaceted educational programs for parents and clinicians led to community-wide reductions in antibiotic prescribing, but among participating children in child daycare facilities there was no apparent impact on antibiotic use (Belongia et al., 2001). A trend towards lower antibiotic prescription rates was found in paper IV, and the effect would probably have been clearer if we had included more daycare centres.

As discussed, not only parents are important in trying to rationalise antibiotic prescription. Also the physicians' attitudes are of importance since they are the prescribers. Clinical decision support to the physicians was found in one study to reduce the overall antibiotic prescribing rate by about 10% and to improve the appropriateness of antibiotic prescribing for respiratory tract infections (Samore et al., 2005). According to a review, delayed prescription, that is when the patient was asked to wait a few days before picking up the prescription, is an effective way of reducing antibiotic use in respiratory tract infections in general practise (Arroll et al., 2003).Medical audits where the physicians register how they handle different infections may be another (Melander et al., 1999).

Problem oriented group education for prescribers may be a way of improving antibiotic prescribing in general practise (Ekedahl et al., 1995, Welschen et al., 2004), but it is unclear if the results from educationally oriented interventions based on prescribing feedback and management guidelines are maintained in the long term (Zwar et al., 2002). However, one study found that educational oriented group programme indicated effect also after five years follow up (Mölstad et al., 1994).

Implications for clinical practise and future research

The logbook study gave information about the occurrence of infectious symptoms and the measures taken. Infectious symptoms are common in families with small children and when the children have to stay at home only a small proportion of the absence days are claimed as social insurance remuneration. Apparently parents try to arrange care of their ill children so as to be able to handle their own work in a reasonable way. This should be borne in mind when

discussing the utilisation of the social remuneration system in Sweden. It would be valuable to study how the parents arrange for their children to be taken care of.

Most of the infectious symptoms are handled without consulting a physician, and when parents consult physicians for their small children, the prescription rate of antibiotics varies. The differences in antibiotic prescription rates between different areas cannot be explained by differences in socioeconomics, "concern about infectious illness", "infection proneness" or number of symptom days. The physician's habits and the interaction between the physician and the patient or parents during the consultation are of importance with regard to antibiotic prescription. Further research is needed to find out what makes the physician prescribe antibiotics and why the prescription rates differ between different areas in Sweden.

Since infectious symptoms are more common in children at daycare than in children in home care it is valuable to find ways reducing infectious symptoms in daycare centres. Although we did not find statistically significant differences after the multifaceted intervention, is seems important to have simple training in hand-washing and education about infection and contagion for parents and daycare personnel. Since we found the intervention manageable a larger study would be valuable.

Conclusions

In conclusion, we found that:

- infectious symptoms are reported in 93% of the 18-month-old children during one month and in about 34% of the parents,
- the social insurance is used in about 33% of the absence days for 18-month-old children and in 75% of the absence days for the parents,
- a physician consultation was made in 13% and antibiotics were prescribed in 6% of the infectious episodes in 18-month-old children, and more seldom among older siblings and parents,
- socioeconomics, “concern about infectious illness”, “infection proneness”, and number of symptom days could not explain regional differences in antibiotic prescription to children,
- 18-month-old children in daycare have more reported symptoms than children in home care,
- no differences in health care utilisation and antibiotic prescription were found in 18-month old children in daycare as compared with children in home care when taking socioeconomics, “concern about infectious illness”, infection proneness and number of symptom days into account,
- it is possible to educate daycare centre personnel and parents of children about infectious diseases and contagion, within the framework of ordinary preschool activities,
- there was a trend towards lower sickness absence owing to infectious diseases, physicians’ consultations and antibiotic prescription through education-oriented interventions in daycare.

Sammanfattning på svenska (Summary in Swedish)

Populationsbaserade studier från USA från 70-talet kartlade förekomsten av infektioner i barnfamiljer. Små barn hade flest infektioner och med stigande ålder hos barnen minskade antalet dagar då infektionssymtom förekom för att sedan åter öka hos vuxna med små barn. Någon aktuell svensk kartläggning av förekomsten av infektionssymtom hos barn, hur ofta man besöker läkare och hur ofta antibiotika ordineras finns inte. Det finns inte heller svenska studier som visar hur ofta infektionssymtom hos barn leder till att de stannar hemma från förskola eller skola och hur ofta föräldrarna använder ersättning från socialförsäkringen i samband med infektionssymtom i familjen.

Apoteksbolagets statistik visar sedan flera år att det finns stora geografiska skillnader i försäljning av antibiotika till barn när olika kommuner jämförs. Man vet inte om dessa skillnader beror på att barn är olika mycket sjuka, att de söker läkare i olika utsträckning eller att läkare förskriver antibiotika i olika omfattning i olika kommuner.

Sedan tidigare vet man att barn i förskola har mer infektioner, gör fler läkarbesök och använder mer antibiotika än barn som vistas hemma dagtid. Ingen har dock studerat om det är den ökade förekomsten av infektionssymtom som leder till fler läkarbesök och till högre antibiotikaförbrukning eller om detta kan förklaras av andra faktorer till exempel större benägenhet att söka läkare vid infektionssymtom.

Interventionsstudier där noggrann handtvätt har varit en del har visat att förekomsten av infektioner i förskolan kan minska. Ingen av dessa studier har fokuserat på att utbilda både personal och föräldrar med barn i förskolan om smitta och smittspridning.

Dagboksstudien (Artikel I-III)

Sju kommuner, som enligt Apoteksbolagets statistik, sedan flera år haft antingen hög eller låg försäljning av antibiotika till barn mellan 0 och 6 år valdes ut. Alla familjer som kom med ett 18 månader gammalt barn till BVC erbjöds delta i en prospektiv populationsbaserad dagboksstudie (Artikel I-III). Familjerna inkluderades konsekutivt från 1 oktober 2002 till 15

april 2003. Alla familjemedlemmar, noterade samtliga infektionssymtom och åtgärder i en dagbok.

Under en vintermånad hade 94% av barn som var 18 månader gamla haft infektionsrelaterade symtom (snuva, hosta halsont, ont i öronen , diarré, feber) (Artikel II). Antalet dagar med infektionssymtom minskade med stigande ålder. Av 18 månaders barnen gjorde 13% ett läkarbesök och 6% använde antibiotika vilket var mer än äldre syskon. Barnen stannade hemma från barnomsorgen i 27% av antalet dagar med symtom, medan socialförsäkringen endast utnyttjades i 10 % av dagarna med rapporterade symtom (Artikel I). Förvånade nog använder alltså föräldrarna socialförsäkringen i endast en tredjedel av alla dagar som 18 månader gamla barn behöver vara hemma.

Barnen från kommunerna med låg antibiotikaförskrivning hade lika mycket rapporterade infektionssymtom, och besökte läkare lika ofta, som barnen från kommuner med hög antibiotikaförskrivning (Artikel II). Oddsraten för att bli ordinerad antibiotika i en kommun med hög förskrivning var 2,67 (CI 95% 1,45–4,93) jämfört med en kommun med låg förskrivning. Om man tog hänsyn till skillnader i socioekonomi, oro för infektionssjukdom i familjen och rapporterade symtom mer än 7 dagar under en månad var skillnaderna fortfarande statistiskt signifikanta (OR 2,61; (CI 95% 1,14–5,98)) (Artikel II). Utifrån de faktorer vi studerat är det alltså svårt att förklara skillnaderna mellan olika kommuner men skillnader mellan olika doktorer i förskrivning av antibiotika spelar stor roll.

Barn i förskola hade signifikant fler infektionsepisoder än barn som vistades hemma (median 2 respektive 1 episod) (Artikel III). Av barnen i förskola gjorde 23 % ett läkarbesök jämfört med 11% av hemmabarnen (OR 2,49; (CI 95% 1,63- 3,82). För antibiotika var motsvarande siffra 11% respektive 5%. (OR 2,43; (CI 95% 1,34-4,41)). När vi tog hänsyn till bland annat skillnader i socioekonomi, oro för infektionssjukdom i familjen och mer än 7 dagar med rapporterade symtom under månaden var oddsraten för läkarbesök 1,51 (CI95% 0,92-2,47) och för förskrivning av antibiotika 1,48; (CI95% 0,72-3,02) inte längre signifikanta (Artikel III). Det tycks alltså vara den ökade förekomsten av infektionssymtom som gör att barn i förskola besöker läkare oftare och använder mer antibiotika än barn som är hemma

Interventionsstudien (Artikel IV)

Till interventionsstudien valdes sex förskolor med liknande karaktäristika ut. Alla förskolor hade en småbarnsavdelning och två syskonavdelningar (Artikel IV). Tre förskolor slumpades till interventionsförskolor och i dessa informerade vi personal och föräldrar om infektioner

och smittspridning. Vi informerade även om när barn bör vara hemma samt när läkarbesök och antibiotika kan vara aktuellt. Efter varje sjukdomsepisod hos barnen fyllde föräldrarna på alla förskolorna i en sjukfrånvarorapport, där sjukdomsorsaken och eventuell sjukvårdskontakt och antibiotikabehandling noterades.

På interventionsförskolorna var den totala sjukfrånvaron 6,6% jämfört med 6,8% på kontrollförskolorna (Artikel IV). Barnen på interventionsförskolorna gjorde i genomsnitt 0,8 läkarebesök under niomånadersperioden och barnen på kontrollförskolorna gjorde 1,1 läkarbesök. Motsvarande siffra för antibiotika förbrukning var 0,4 behandlingar/barn respektive 0,7 behandlingar/barn. För att titta på skillnader mellan grupperna användes multinivåanalys Även om det i denna lilla studie inte fanns statistiska skillnader sågs ett tydligt mönster med färre infektionsepisoder, färre läkarebesök och mindre antibiotikaförskrivning i interventionsgruppen.

Det var alltså möjligt att inom ramen för den ordinarie förskoleverksamheten utbilda personal och föräldrar om infektioner och smittspridning. Resultaten talar för att man kan minska frånvaron på grund av infektioner i förskolan, samt minska antalet läkarbesök och antibiotika behandlingar

Konklusion

Vi har gjort en omfattande svensk dagboksstudie som visar att infektionssymtom är vanligt i barnfamiljer och att de yngsta barnen har flest symtom. Oftast behöver inte barnen var hemma på grund av symtomen men när de är det så utnyttjar föräldrarna socialförsäkringen sparsamt. Vid ett fåtal tillfällen leder symtomen till läkarbesök och antibiotika förskrivs i ungefär hälften av läkarbesöken. Förskrivningen av antibiotika varierar mellan olika kommuner och detta förklaras inte av att barnen har olika mycket infektioner utan av att läkarna förskriver antibiotika olika. Däremot är det den ökade förekomsten av infektionssymtom som gör att barn i förskola söker läkare oftare och använder mer antibiotika än barn som är hemma.

Eftersom barn i förskolan har mer symtom än barn som vistas hemma är det angeläget att finna vägar att informera personal och föräldrar om infektioner och smittspridning samt på olika sätt minska antalet infektioner. Interventionsstudien visar att detta går att göra inom ramen för den ordinarie förskoleverksamheten men en större studie skulle var av värde för att visa att detta leder till minskad sjukfrånvaro och lägre antibiotika användning.

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