

Early infectious diseases and the relation to emotional symptoms in child group day-care attendance

A 4-year population-based cohort study

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symptoms in child group day-care attendance:
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Abstract

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Background: Children attending group day-care have an increased risk for infectious diseases. Entry between the age of two and three years could be a “window of vulnerability” where children can strengthen their immune system due to early exposure, but to date there is little or no research on the potential psychological implications of long-term exposure to infectious diseases in group day-care. **Objectives:** To determine if there is a decline in severity and frequency over time of common infectious diseases in group day-care and whether infectious diseases can be associated with emotional adjustment. By this, it is possible that young children with infectious diseases could show more irritability as they have more difficulties explaining pain. **Method:** A 4-year population-based cohort study based on data from “*The Matter of the First Friendship*”. Participants ($N = 596$) were recruited from group day-care in a rural area in Norway. Parents answered questions each year about their child, family and day-care that included the Strengths and Difficulties Questionnaire (SDQ). **Results:** Linear regressions showed that overall frequency and severity of infectious diseases in group day-care decline over a 4-year period. Correlation analysis did not find infectious diseases in group day-care to be associated with emotional difficulties in the fourth year. **Conclusion:** This study supports the suggestion that early exposure to infectious diseases strengthens the immune system and does not have a negative effect on emotional adjustment.

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Table of contents

Introduction	2
What are the consequences of infectious diseases on development?	2
Definition of infectious disease and terminology	4
Definition	4
Infectious disease.....	5
Transmission.....	5
Infections during childhood	5
Emotional difficulties in childhood	5
Timing effects: “window of vulnerability”	6
Infections in group day-care	7
Variables associated with infectious diseases.....	10
Family covariates associated with infectious diseases.....	10
Child characteristics associated with infectious diseases	11
Emotional difficulties	11
Associations between infectious diseases and symptoms of emotional difficulties.....	12
Variables associated with symptoms of emotional difficulties.....	13
Aim of the study	14
Material and methods	15
Study design	15
Study subjects	15
Experimental procedure	16
Questionnaire design	16
Variables included	17
Infectious diseases.....	17
Emotional symptoms.....	18
Control variables	18
Child characteristics.....	18
Family characteristics	18
Research questions	19
A: Is the frequency of infectious diseases stable over time?	19
B: Do children with infectious diseases at T1, T3 or T4 show emotional difficulties at T4?	20
Preliminary analyses	20
Statistical analyses	20

Missing data.....	21
Results.....	22
Descriptive statistics of the study population	22
Associations between infectious diseases across T1, T3 and T4.....	23
Regression analyses.....	27
Discussion.....	33
Main findings.....	33
Decline in infectious diseases in group day-care.....	33
Confounders associated with infectious diseases	34
Infectious diseases and emotional difficulties	35
Confounders associated with emotional difficulties	36
Methodological considerations.....	36
Strengths.....	36
Limitations	37
Data collection.....	37
Rater bias.....	38
Future studies.....	38
Conclusion.....	39
References	40
Appendix	50

Introduction

There is increased focus on infectious diseases during childhood and potential long-term effects on somatic and psychological health later in life (Berkelman, Guinan, & Thacker, 1989; Bzostek & Beck, 2011). Physical health problems during early development have been associated with psychopathology and maladjustment later in life (Pine et al., 2001; Johnson et al., 2002). Severe infectious diseases are associated with both physical and mental health problems later in life. For instance, respiratory problems are associated with and predict depression, anxiety and post-traumatic stress disorder in adolescence and adulthood (Cohen, Pine, Must, Kasen, & Brook, 1998; Goodwin, 2011; Shears et al., 2007; Tedstone & Tarrier, 2003). In most studies focus has been on the impact of serious and chronic diseases, such as respiratory infectious diseases, which are linked to asthma, eczema and allergies (Dunder, Tapiainen, Pokka, & Uhari, 2013; Illi et al., 2001; Leadbitter et al., 1999; Nafstad, Brunekreef, Skrandal, & Nystad, 2005; Stick & Mutius, 2001), and the relation to later cognitive dysfunction (Steen & Campbell, 2008). In a review on the relation between early infectious diseases and later cognitive development, Steen and Campbell (2008) found that children with serious infectious diarrhoea diseases had lower academic performance and cognitive abilities later in life. Thus, severe infectious diseases may not only be a risk for later chronic somatic diseases, but may also be an important risk factor for later psychopathology and maladjustment.

What are the consequences of infectious diseases on development?

Several studies suggest that serious, acute and chronic infectious diseases are a risk for later development of psychopathology (Borge, Wefring, Lie, & Nordhagen, 2004; Goodwin, 2011; Shears et al., 2007). Chronic diseases, such as asthma or diabetes, are found to affect psychological adjustment due to prolonged stress both on child and family (Bennett, 1994; Calam et al., 2005; Klinnert et al., 2001). In the USA it is estimated that around 70% of all deaths can be associated with chronic diseases. A thorough understanding of the mechanisms behind common chronic diseases are important, as they represent a therapeutic challenge and a substantial burden to public health costs (Kockaya & Wertheimer, 2010). Chronic diseases may also have consequences for mental health throughout the life-course.

Infections during early childhood may have long-term mental consequences. Although disputed, it has been shown that prenatal infectious diseases may increase the risk for psychotic disorders in late adulthood (Brown, Cohen, Greenwald, & Susser, 2000) and panic disorder have been found related to early respiratory problems (Craske, Poulton, Tsao, & Plotkin, 2001; Verburg, Griez, Meijer, & Pols, 1995). Goodwin and colleagues (2011) studied the relation between severe infectious diseases during the first year of life, which required antibiotics, and psychiatric diagnoses later in life. They found increased risk of depression and anxiety disorders in child with severe infectious diseases during the first year, which required antibiotics. However, these findings have not been confirmed in studies investigating similar relations longitudinally.

Goodwin (2011) suggests three possible explanations for why infectious diseases in childhood might be a risk for psychopathology later in life. First, severe infectious diseases can result in functional impairment, which could cause psychopathology later in life. It has been shown that severe somatic diseases may be associated with post-traumatic stress disorder (Tedstone & Tarrier, 2003) and depression (Timonen et al., 2002). Second, early infectious diseases may be related to psychopathology and maladjustment as a result of biochemical and neurobiological changes in the immune system (Shanks & Lightman, 2001). Third, early infectious diseases and psychological problems in childhood may often share the same etiological factors, one of which may be associated with family characteristics (Connell & Goodman, 2002).

Divergent results exist on potential long-term effects of early infectious diseases. In some studies it has been shown that early infectious diseases may in fact be positive, whereas in other studies a negative effect on future health status has been found. There is no, or little support for a preventive effect of early-life respiratory infectious diseases on asthma (Nafstad, Hagen, Øie, & Jaakkola, 1999). In a 10-year longitudinal follow-up of the Oslo Birth Cohort Study, Nafstad et al. (2005), found that asthma and allergy in 10-year old children were related to exposure of respiratory infectious diseases in the first two years of life. An explanation may be that in vulnerable children early exposure to severe infectious diseases could impose a risk to develop chronic and atopic diseases later in life (Dunder et al., 2013). In contrast, some data support positive effects of early infectious diseases on asthma (Rothers et al., 2007). Long-term preventive effects against asthma may be a function of the immature immune system being repeatedly exposed to multiple mild infectious diseases (Côté et al., 2010; Illi et al., 2001).

Although the mechanisms are still unclear, data suggest that the risk of infectious diseases can have different developmental consequences depending on the frequency, severity and type of infectious diseases. Most of the research has focused on severe and chronic infectious diseases, whereas there are only a few studies on common and milder infectious diseases. According to Bradley (2003) different results and conclusions in the literature most likely also depend on differences in methodology between studies. Respiratory infectious diseases could have been registered differently (retrospective vs. prospective), and different informants have been used (caregivers, care providers, and clinicians). Also, different methods to recruit participants have been used (recruited at birth, at clinics, schools, different socioeconomic status, recent illness, or poor health), and lastly different control variables have been included.

Definition of infectious disease and terminology

Definition

Infections are caused by pathogens such as viruses, bacteria, parasites, fungi, protozoa or misfolded proteins called prions (Ryan, Ray, & Sherris, 2004). It can be difficult to distinguish between bacterial and viral infectious diseases as they both elicit similar types of symptoms. One important difference is that antibiotics can cure bacterial infectious diseases, whereas viral infectious diseases are resistant to antibiotics. Environmental toxins, exposure to radiation, diet, lifestyle, stress, and genetic disposition may affect the response to infectious pathogens.

An infection produces an abnormal condition in a body or organ that interferes with the anatomical and physiological state of homeostasis (Kanki & Grimes, 2013). Thus, infectious diseases disrupt the ability to maintain normal stability and balance and produces structural and functional changes that deviate from the normal state. Furthermore, infectious diseases are commonly classified as diseases when the aetiology of the condition is identified. The pathological symptoms and signs of the specific infection are also used in order to differentiate between types of infectious diseases. People who are infected report the symptoms they experience. An infection is often described as asymptomatic when symptoms do not occur early in the acute phase, but appear at a later stage (Williams & Nelson, 2007). Some infectious diseases attack the body in general, and typical symptoms are aches and pains, chills and night sweats, fevers, loss of appetite and weight and increased fatigue. Other

infectious diseases attack specific organs or a certain area of the body and result in runny nose, coughing or skin rashes.

Infectious disease

In medical terms there is a difference between disease and illness/sickness. Disease is the identifiable cause or symptoms/medical signs of the dysfunctional condition, whereas illness and sickness constitute the subjective feeling of pain and discomfort (Emson, 1987).

However, these concepts are often used synonymously. The term disease is also used interchangeably with infectious disease. Infectious diseases are pathogenic microbiological agents that enter and grow in another organism and cause illness. Infections that do not cause illness are not classified as infectious disease (Ryan & Ray, 2004).

Transmission

Infectious agents spread from one host to another and survive by repeating the infection pattern in the new host (Bust et al., 2001). Transmission can occur by direct or indirect contact (Churchill & Pickering, 1997). Direct contact occurs through physical contact, such as touching, drinking or being bitten by a carrier and inhalation of agents that are released through sneezing and coughing. This form of transmission differs from indirect contact where the infectious agent is able to survive outside a host for a period of time, such as sticking to inanimate objects or contaminating food and fluids (Ryan & Ray, 2004).

Infections during childhood

Childhood infectious diseases is a term used for infectious diseases that are associated with children and not common in adults. Most infectious diseases are caused by viruses or bacteria and often require a consultation by a physician for medical treatment. In the first years of life common infectious diseases are typically lower respiratory tract infectious diseases, and viral infectious diseases (Brady, 2005). Common symptoms in children are rapid breathing, coughing, runny nose, poor peripheral perfusion and skin rash (Illie et al., 2001; Bruel et al., 2010).

Emotional difficulties in childhood

Emotional difficulties in early childhood are associated with a higher risk of psychopathology later in life, such as depression and anxiety. Symptoms of emotional problems in young

children can be hard to detect (Angold, Costello, & Erkanli, 1999; Wichstrøm et al., 2012). Some of the well-known symptoms can be that the child is unhappy, afraid, and worried (R. Goodman, 2001). Factors associated with emotional difficulties in childhood can be predicted from child characteristics (such as sex, birth complications) and family characteristics (such as parental distress, income, and education) (Berg-Nielsen, Vikan, & Dahl, 2002; Bhutta, Cleves, Casey, Craddock, & Anand, 2002; Côté et al., 2009; Lupien, McEwen, Gunnar, & Heim, 2009; Sanders et al., 2008). Early severe infectious diseases and medical problems are also associated with emotional problems in childhood (Bennett, 1994; Tedstone & Tarrier, 2003).

Timing effects: “window of vulnerability”

It has been shown that children in general have more infectious diseases during the first years of life and that the risk of infectious diseases decreases in the following years (Bradley, 2003; Brady, 2005; Côté et al., 2010). This is known as the “window of vulnerability” (Illi et al., 2001; Lupien et al., 2009). It is argued that children in the first years of life are especially vulnerable to infectious diseases as the immune system is immature and not completely developed (Krämer et al., 1998; Ball et al., 2000).

Rutter (2013) argues that brief exposures to pathogens, either through natural contexts or inoculation, allow the body to overcome the attacks and develop stronger resistance over time in relation to immunity and infection. Avoiding infectious diseases may have the opposite effect of increasing the likelihood of a more sensitive and vulnerable immune system (Bock & Whelan, 1991). It has been found that institutionalized and deprived children who were adopted before two years of age show less cognitive impairment and disinhibited attachment than children adopted after two years of age (Rutter & O’Connor, 2004). This supports the idea of a sensitive period in the first two-three years of life and that the risk of infectious diseases are balanced out when children are in the ages of four-five years old (Côté et al., 2010; Lu et al., 2004; Wefring, Lie, Loeb, & Nordhagen, 2001a).

Nevertheless, an increasing concern is the potential long-term effects of treating infectious diseases by antibiotics. In Norway, as in many other Western countries, the increase of group day-care attendance is followed by a major increase in antibiotic use for treatment of infectious diseases (Nordlie & Andersen, 2002). Progressive antibiotic treatment is suggested to increase bacterial resistance.

Infections in group day-care

The main focus of the present study was infectious diseases in group day-care. Overall, respiratory tract infectious diseases, gastrointestinal infectious diseases and ear infectious diseases are the most common infectious diseases in group day-care (Côté et al., 2010; Floret, 2000; Klein, 2013). Most studies have focused on respiratory infectious diseases that are often divided into upper and lower respiratory tract infectious diseases. Lower respiratory tract infectious diseases (e.g. bronchitis, pneumonia) are considered more severe than upper respiratory infectious diseases (e.g. common cold, cough, laryngitis). Upper and lower respiratory infectious diseases can give similar symptoms such as headache, fever, muscle/body ache, sore throat, etc. Gastrointestinal infectious diseases typically cause diarrheal illness in children. The most common form of ear problems is an infection in the middle ear, known as otitis media.

A common finding is that children who enter group day-care have higher rates of infectious diseases compared with children that are cared for at home. In a longitudinal study where children were followed from birth to 13 years of age it was reported that children who attended large group day-care centres (>six children) before the age of three, had less colds when they attended school (Ball, Holberg, Aldous, Martinez, & Wright, 2002). Similarly, Côté et al. (2010) found that children who attending large group day-care had less respiratory and ear infectious diseases when they entered school. These findings suggest that children attending group day-care may be protected from milder infectious diseases later in life. Thus, exposure to group day-care may have a positive effect on development, by improving immunity and resistance to pathogens causing common and mild infectious diseases (Illi et al., 2001). Overall, it seems that children attending group day-care are more prone to repeated infectious diseases as the group day-care environment poses an increased risk for infectious diseases compared to the home (Delour et al., 2006; Lu et al., 2004; Wald et al., 1988). However, early exposure to pathogens may have a preventive effect on infectious diseases when children grow older (Ball et al., 2002; Côté et al., 2010; Illi et al., 2001; Lu et al., 2004). Thus, although children attending group day-care in their first two years of life might be at risk for infectious diseases, they could gain a positive long-term effect.

In the majority of studies an increased risk of being subjected to infectious diseases when entering group day-care has been found and that the overall risk declines over time in group day-care. (Côté et al., 2010; Hardy & Fowler, 1993; Louhiala, et al, 1995; Wald et al., 1991). There are especially two factors related to an increased risk of infectious diseases

during the first years of group day-care. Firstly, the frequency of exposure, which is the more time (hours) children spend in group day-care, the higher the risk for infectious diseases (Thacker, Addiss, Goodman, Holloway, & Spencer, 1992). Secondly, the size of the day-care centre is related to infectious diseases. Studies have shown that frequency and severity of infectious diseases are higher among children entering large group day-care centres (>six children) compared to centres with less children (Bradley, 2003; Wald, Dashefsky, Byers, Guerra, & Taylor, 1988).

Floret (2000) examined group day-care centres in Paris and found that the size and type of day-care facilities influenced the spread of infectious diseases. The younger the children are when they enter group day-care, the higher the rates of infectious diseases. The infectious disease rates are highest early after the children have entered group day-care and thereafter gradually decreases. Wald et al. (1988) compared severity and frequency of infectious diseases over three years in home care and group day-care. They concluded that after three or four years the risk of infectious diseases in group day-care and home-care are balanced out and that the increase of infectious diseases can have preventive long-term effects. This argument was based on study on respiratory infectious diseases in group day-care by Olin (1979). These findings were also supported in a similar study performed by Denny, Collier, & Henderson. (1986). Wald, Guerra, & Byers (1991) conducted a three-year longitudinal follow-up study to investigate whether infectious disease rates differed between home-care, small group day-care (two–six children), and large group day-care (>six children). Data showed that children had most infectious diseases during the second year regardless of type of day-care. After three years in large group day-care there were no differences in infectious disease rate between the day-care groups. In a study by Wefring, Lie, Loeb, & Nordhagen (2001) found that the frequency of upper respiratory infectious diseases were higher among children in group day-care compared to children in home-care.

Time spent in group day-care and time in contact with other children are factors that potentially could affect the rate of infectious diseases. It has been found that children that stay many hours in group day-care have more infectious diseases than children who stay fewer hours (Kotch & Bryant, 1990). Gordon et al. (2007) found increased occurrence of ear infectious diseases between one and two years of age and increased occurrence of respiratory complications between one and three years of age for children who had a high frequency of group day-care hours. However, other studies do not support the hypothesis that time spent in group day-care increases the risk of infectious diseases (Bradley, 2001).

Bradley and colleagues (2003), conducted a 4.5-year longitudinal study, investigating if there is a difference in frequency and severity of diseases in children over three years entering large group day-care (>six children). They found that these children had more respiratory tract diseases and gastrointestinal tract diseases compared to children who entered group day-care before three years of age. Furthermore, they compared children who entered group day-care prior to three year with children in home-care or smaller groups in day-care (<six children). They reported that children in home-care and small day-care groups (<six children) had fewer diseases. Thus, this and other studies have shown that there is an increased risk for infectious diseases when entering group day-care regardless of age (see e.g. Hurwitz, Pinsky, & Shonberger, 1991). In addition, studies from Norway have also found an increased rate of upper respiratory infectious diseases among children attending group day-care (Nafstad et al., 1999; Wefring, Lie, Loeb, & Nordhagen, 2001).

Using an 8-year prospective cohort Côté et al. (2010) examined the risk of gastrointestinal, ear and respiratory tract infectious diseases during child group day-care and school. The children were followed from the age of five months to eight years. The aim was to investigate how infectious diseases in the first years of life were related to child type of day-care (group or home-care) attendance and the potential association with age. They found that children, who enter group day-care with a group of six or more children before the age of 18 months have more respiratory and ear infectious diseases during group day-care, but fewer infectious diseases during their school years. The study controlled for maternal education, maternal immigration status, family income, and number of siblings. In line with these findings Ball et al. (2002) found that large group day-care centers had a positive long-term effect on the occurrence of later infectious diseases, while small group day-care did not have this positive effect. Furthermore, Côté et al. (2010) argued that this long-term preventive effect also applied to more severe infectious diseases, such as respiratory and ear infectious diseases and not just common cold as studied by Ball et al. (2002). These data support a “window of vulnerability” around two and a half years that can give positive long-term protective effect against infectious diseases.

Only two longitudinal studies exist, in which gastrointestinal, ear and respiratory infectious diseases have been investigated from group day-care throughout school (Ball et al., 2002; Côté et al., 2010). This is an interesting developmental period as the school is an arena where children come in contact with more children than in group day-care. The results from both these studies show that children exposed to infectious diseases at an early age had fewer

infectious diseases at school. Thus, these data indicate a protective effect for children in large group day-care with regard to later infectious diseases in school age.

Variables associated with infectious diseases

According to Rutter (2007) infectious diseases are probably one of the few types of diseases that are likely to be caused by a single agent. However, there are different features that influence the inoculation and development of infectious diseases. There can be child, family and other characteristics that are associated with an increased risk of being subjected to infectious diseases (Côté et al., 2009).

Family covariates associated with infectious diseases

There are potential family characteristics that have previously been shown to influence infectious diseases in children (Côté et al., 2009). Lu et al. (2004) found that child age and parental education are associated with the risk of common infectious diseases during group day-care. They investigated the frequency rate of upper respiratory and diarrhoea infectious diseases and compared children across three age groups. They found that younger children were subjected to more infectious diseases than older children. Parents with higher level of education had children with fewer infectious diseases compared with parents with less education. Children from low-income families are associated with a higher risk of exposure to upper respiratory tract, ear and gastrointestinal infectious diseases (Kotch & Bryant, 1990; Thacker et al., 1992). Parental employment and income and particularly work status of the mother have been found to be associated with child development (Url, Phillips, Voran, Kisker, & Whitebook, 1994; Votruba-drzal, Coley, Chase-lansdale, & Votruba-drzal, 2004) and are therefore important covariates for the occurrence of infectious diseases in childhood.

Solnit (1977) described the importance of parents during illness in young children, and reported that for ill children less than three years of age, the absence of parents can make the child more anxious. This is potentially due to the fact that the child has not developed object constancy, and that the physical pain is increased in stressful situations. According to Solnit the child has a unique and intimate bond to the parents, allowing the needs of the child to be met. As the child grows, it is increasingly able to explain discomfort and pain to others and to gain attention through communication. Solnit also argues that the ability of the child to express and communicate to others helps the child to develop self-regulation of emotions and the feeling of pain without the immediate comfort of a parent. The child in day-care is at the

developmental stage, according to Solnit, where it can imagine the “loved object” (the parent) in order to reduce pain and stress. However, in a group day-care setting it is plausible that, when away from their parents, children connect with high quality pre-school teachers who then become important caregivers (Côté et al., 2013; Essex, Armstrong, Burk, Goldsmith, & Boyce, 2012).

Child characteristics associated with infectious diseases

Child characteristics can also influence the rate of infectious diseases in children (Côté et al., 2009). Birth weight (Peterson et al., 2004) and poor health outcomes (Stein, Siegel, & Bauman, 2006; Thomas et al., 2011) are well-known biological risk factors associated with infectious diseases. It has also been shown that prematurity increases the risk of microbial infectious diseases due to an immature immune system (Clapp, 2006). Sex is another factor that influence the risk of infectious diseases (Berk, 2000). Boys are also more vulnerable to developmental difficulties and have higher death rates (Berk, 2000). Boys are also associated with low birth weight compared with girls (Johnson & Breslau, 2000).

Emotional difficulties

In the present study will also focus on the link between infectious diseases and emotional adjustment. Emotional difficulties in children have been linked to an increased risk of later anxiety and depression (Costello et al., 2006). Emotional problems that can be observed children are headaches, stomach-aches or sickness, worrying a lot, being unhappy, downhearted or tearful, being nervous in new situations, having many fears and being easily scared (R. Goodman & Scott, 1999; Theunissen, Vogels, de Wolff, & Reijneveld, 2013). In children with clinically significant mental health problems it is common that emotional problems and behavioural problems occur together, such as low self-esteem and poor peer relationships (Sawyer, 2000(Pedersen, Vitaro, Barker, & Borge, 2007). Family risk factors and the quality of parenting strongly influence the emotional development of children, such as low-income and parental mental health (Berg-Nielsen & Wichström, 2012; Bzostek & Beck, 2011). Berg-Nielsen, Vikan, & Dahl (2002) found that parental negativity was linked with child outcome. Also, the quality of group day-care has been linked to psychosocial development, especially for children from disadvantaged families (Clarke-Stewart & Miner, 2008; Geoffroy et al., 2006; Hagekull & Bohlin, 1995). As noted earlier, serious illness have been associated with mental health problems later in life (Goodwin, 2011). Symptoms of both

depression and anxiety have been associated with respiratory and ear infectious diseases (Calam et al., 2005; Clarke-Stewart & Miner, 2008; Cohen et al., 1998; Craske et al., 2001; Illi et al., 2001; Tedstone & Tarrier, 2003; Verburg et al., 1995). Thus, one may speculate if children with many infectious diseases may be more anxious, or irritable, or have other types of emotional problems.

Associations between infectious diseases and symptoms of emotional difficulties

Research indicates that child health and illness are predictors of health outcomes later in life (Case, Fertig, & Paxson, 2005). Studies show that cognitive development and mental health may be negatively affected by poor physical health in early life (Clarke-Stewart & Miner, 2008; Cohen et al., 1998; Geoffroy et al., 2010; Goodwin, 2011; Kaestner & Corman, 1995).

The majority of research on infectious diseases and later outcome has focused on the link between chronic illness and severe infectious diseases in early life and later emotional and behavioural difficulties (Khandaker, Zimbron, Dalman, Lewis, & Jones, 2012; Shears et al., 2007; Tedstone & Tarrier, 2003). Borge, Wefring, Lie, & Nordhagen (2004) found that four year old children with chronic illnesses, especially asthma, showed more aggressive behaviour. The researchers demonstrated how multiple factors might affect this relation. For example, children with language problems had higher risk for negative behaviour. However, children with language difficulties attending group day-care centres with 5-15 children had less aggressive behaviour. If children show emotional symptoms, it may be an early precursor for problems later in life. Although children are at elevated risk, early signs are not easily detected. It has been found through meta-analysis that children with chronic problems are not clinically depressed and that the depressive symptoms vary greatly (Bennett, 1994). However, few data exist on the influence of common infectious diseases on mental health in group day-care children. To this authors knowledge, there are presently no data showing that infected children are more irritable. It is possible that some children are more vulnerable to physical and emotional difficulties, and therefore more likely to develop psychiatric disorders. Accordingly, children with repeated ear infectious diseases (otitis media) may have difficulty to hear that can have a negative effect on speech and language development (Clarke-Stewart & Miner, 2008).

Variables associated with symptoms of emotional difficulties

Both child and parent characteristics have been found to influence child emotional adjustment (Côté et al., 2009; Berg-Nielsen & Wickström, 2012; Anthony, 2011). For instance, parents with poor parenting skills may have a negative effect on the emotional development (Peterson et al, 2004) and the social behaviour of a child (Guedeney, Marchand-Martin, Cote, & Larroque, 2012).

Parent and family stress can also affect development (Klein, 2013). In a study by Anthony et al (2011) on children with arthritis it was found that parents with high levels of depressive symptoms, stress and negative beliefs about their vulnerability of the child affected the psychological well-being of the child. Moreover, the level of pain and stress of the child was increased when parents were anxious. Also, the personality types of the parents have been associated with the mental health of the child (Berg-Nielsen & Wickström, 2012). Parents with inflexible coping styles may not be able take care of a sick child in a comforting manner. Wright et al. (2002) found that child wheezing was positively associated with caregiver stress. Thus, parent psychological adjustment is a factor that affects mental health in children.

Children from low-income families have been associated with poor socio-emotional development. In a study it was concluded that the more hours children from low-income families spent in group day-care, the better behaviour they exhibited in addition to improved calculation skills (Votruba-drzal et al., 2004). Group day-care quality has also been found to be an important factor regarding disadvantaged children. That is, good day-care quality reduces infectious diseases and differences between disadvantaged and advantaged children (Geoffroy et al., 2010; Zigler & Muenchow, 1986). This is also supported by a study on concerning early group day-care and later academic achievements by Geoffroy and colleagues (2010). In their study on day-care quality, children showed more positive emotions and less aggressive behaviour when their teachers gave them meaningful care and attention (Hestenes, Kontos, & Bryan, 1993). Accordingly, Hagekull & Bohlin (1995) found that children without problems before group day-care showed increased aggressive behaviour in low quality group day-care.

Preterm birth have also been found to have long-term effects on child development and have been associated with emotional difficulties (Bhutta et al., 2002; Bora, Pritchard et al., 2011). The developmental risk of low birth weight has also been shown to be associated with low-income and poor parenting (Landry et al., 2006; Dietrich et al., 2004). Language

and speech problems are associated with emotional problems, but high quality day-care may moderate this effect, and have a positive effect on development (Borge et al., 2004; Clarke-Stewart & Miner, 2008). Also, group day-care can be beneficial for children coming from disadvantaged families with low socio-economic status (Geoffroy, Borge, Larouche, Séguin, & Rutter, 2007).

Aim of the study

Studies show that the frequency of infectious diseases increase when children enter group day-care (Bradley, 2003; Côté et al., 2010; Illi et al., 2001; Wald et al., 1991). Entry between the age of two and three years could be a “window of vulnerability” where children can strengthen their immune system due to early exposure. Several studies conclude that early exposure strengthen resistance against infectious diseases. In contrast, there are also studies showing that an increased rate of infectious diseases at an early age may be a risk for more serious infectious diseases later in childhood (i.e. severe respiratory tract infectious diseases can pose a risk of developing chronic asthma). However, the relationship between infectious diseases in group day-care and later emotional symptoms has not previously been examined. This study is based on a cohort that answered questions about infectious disease over a 4-year period obtained from the study *The Matter of the First Friendship*. The focus of the study was to investigate the risk of infectious diseases over time in a group day-care setting, and the relation of early infectious diseases to emotional symptoms. If children show emotional symptoms, it may be an early precursor of problems later in life. For the majority of children it is likely that a high rate of infectious diseases do not show significant emotional symptoms. However, it might be that some children that are vulnerable show more irritability/emotional symptoms.

The first aim of the study was to investigate if there is a decline in severity and frequency over time of common infectious diseases in group day-care. The second aim was to investigate whether infectious diseases can be associated with emotional adjustment. By this we mean that young children with infectious diseases could show more irritability as they have more difficulties explaining pain.

Material and methods

Study design

The data material in this thesis belongs to the longitudinal and prospective study “*The Matter of the First Friendship*” (TMFFF) led by Professor Anne Inger Helmen Borge from the University of Oslo. Data was collected annually from 2006 to 2009. The purpose of the TMFFF-study was to examine the role of friendship in psychopathology of children. The study design is a multi-method, multi-informant approach, using questionnaires and interviews with data gathered from parents, teachers and children. The study was approved by the Regional Committee for Medical and Health Research Ethics in Norway and the Norwegian Data Inspectorate and was financed by the Norwegian Research Council.

This thesis is based on data sampled from the first year of day-care start-up in 2006 (first data sample - T1), two years later in 2008 (T3) and three years later in 2009 (T4). All children had attended group day-care for at least one year at the first data sample. The focus of this thesis is child health and infectious diseases.

Study subjects

The project aimed to include a representative sample of group day-care centres outside the larger cities in Norway. Subjects were recruited from two municipalities, Gran and Lunner, in Hadeland, Norway. In this area 28 out of 32 group day-care centres (both private and public) were included in the study. This size of the day-care centres varied from 4 to over 100 children.

In the first data sampling after one year in day-care (T1), the parents of 596 children approved that their children could participate in the study. This represented 60% of the children invited to participate. Two years later (T3) the study included 413 children (41%) and after three years (T4) 334 (34%) children were included in the study. The questionnaire at the second data sampling (T2) did not contain questions about infectious diseases, and therefore all data at T2 were excluded from the present study. The study subjects were primarily Caucasians as this part of Norway is known to be ethnically homogenous.

Experimental procedure

Parents were given written information about the purpose of the project, and signed a written consent form allowing their child to participate in the research project. Participation was voluntary, and they could withdraw their children from participation in the study at any time. All information about the children was anonymized. Parents answered questionnaires about the child, parenting, personal life and family life. Information was also gathered from the children by trained interviewers. The pre-school teachers reported on children's psychosocial functioning, including social skills and emotional regulation at the group day-care centres. They were paid for filling out the questionnaires. Day-care leaders were interviewed by telephone about the group day-care centre conditions. Schoolteachers were contacted when study subjects were old enough to go to school.

Questionnaire design

The questionnaire sent to the parents and teachers at the data sampling periods included questions about demographic characteristics, parenting skills, the mental health of the parents, family and couple relationship. There were also questions about child health and development. The Strengths and Difficulties Questionnaire (SDQ) (R. Goodman, 2001) was included in the questionnaires in order to gather information about child characteristics. SDQ is a brief behavioural instrument used to screen for child social and psychological adjustment. It is known to show high sensitivity for psychopathological diagnosis and subclinical difficulties, and it is used commonly used in research, clinical and educational settings in Norway (R. Goodman, 2000; Heiervang, Goodman, & Goodman, 2008). The SQD contains both positive and negative attributes. The SDQ version used in this study was informant-based and had 25 items on psychological attributes that were divided into five scales; emotional symptoms (5 items), conduct problems (5 items), hyperactivity/inattention (5 items) and peer relationships (5 items), and prosocial behaviour (5 items). Children were rated for each item according to three alternatives on a Likert scale: not true (1 point), somewhat true (2 points) and certainly true (3 points).

Variables included

Infectious diseases

The infectious diseases of the study subjects were used as the dependent variables in the present study. Data on infectious diseases were sampled at T3 (two years after first data collection) and at T4 (three years after first data collection). At T3 and T4 parents were asked nine questions about how often the specific types of infectious diseases had occurred in the past year. Also, at T3 parents had to retrospectively recall the same nine infectious diseases their child had been subjected the first year in group day-care (T1). Thus, data for infectious diseases concerning the first year in group day-care were not collected in the first year, but in the third year.

The nine infectious diseases were classified based on frequency and severity of the diseases. The classification was based on advises given by senior consultants and researchers. Three groups of infectious diseases (mild, moderate and severe) were defined. The first group (mild infectious diseases) consisted of cold, urinary tract and eye infectious diseases. The second group (moderate infectious diseases) contained throat and ear infectious diseases and gastric illness/diarrhoea. The third group (severe infectious diseases) consisted of laryngitis, bronchitis/RS-virus/lung infectious diseases, and fever convulsions.

The second step was to recode the values for the infectious diseases variables at the three time points (T1, T3 and T4). At each time point there were nine variables. Thus, in total 27 variables were recoded. The variables were recoded in SPSS by replacement of the category number with a new value (Appendix table A). Both severity and frequency of infectious diseases were taken into account by weighing infectious diseases depending on the classification of mild, moderate and severe and how often the children had been subjected to the infectious diseases. A severe infectious disease was given a higher value than a mild infectious disease. A high frequency of mild infectious diseases was added together and could give a higher total value than low frequency of severe infectious diseases.

The third step was to compute new continuous variables for each of the time points (T1, T3 and T4). This was achieved by summarising all the nine infectious disease variables into one total sum of scores. Thus, the extent of infectious diseases was estimated for each subject as the sum of the scores.

Emotional symptoms

Another dependent variable in this study is emotional symptoms at T4. This is a scale taken from the SDQ (Goodman, Lamping, & Ploubidis, 2010; Goodman, 2000). The emotional symptoms consist of five items (questions) about child behaviour that parent's rate. These items are *often complains of headaches, stomach-aches or sickness; often seems worried; often unhappy, downhearted or tearful; nervous or clingy in new situations, easily loses confidence; many fears, easily scared*. Each item is rated either *not true* (scored 0), *somewhat true* (scored 1) or *certainly true* (scored 2). Thus, the scores for the scale can range from 0 to 10 on a Likert scale if all five items are summarised, and at least three items have to be completed in order for the scale to be valid. The emotional symptoms scale scores can be classified as normal (0- 3 scores), borderline (4 scores) and abnormal (5-10 scores) in order to screen for psychopathology. In order to analyse the dependent emotional symptom items we created a continuous variable (sum of scores).

Control variables

Child characteristics

Information was gathered from the parent questionnaires at T1. All variables of the study subjects that could potentially be associated with infectious diseases and emotional symptoms were initially tested for correlations. The variables that showed significant correlations were included in further analysis in addition to common control variables as age, birth weight, early birth, serious or long-term illness and speech or language problems. Child age and birth weight were treated as scale order. Early birth included children that were born more than three weeks pre-term and was categorized as yes (1) or no (0). Yes (1) or no (0) also applied to children that had suffered serious or long-term illness and to children who were referred to a specialist for language or speech problems.

Family characteristics

Family characteristics were also collected from the parent questionnaires at T1 and were used as control variables. Parents answered questions about marital status, siblings, income and education level and dwelling type. Marital status included a range of six different marital statuses that were recoded into a dichotomous variable of married or living together (1) and single, divorced/widow or other (0). The variable for sibling contained how many siblings the child had. The values for income and education level ranged from one to six in rank order

and were collected for both mothers and fathers. Income level ranged from no income (1) to higher than 500 000 NOK. Education level ranged from junior high school (1) to higher university degree (6). All variables were entered separately in a correlation analysis. Income- and education level of the father were not included in the regression analysis because these variables were not significantly associated with T1, T3, T4 infectious diseases or emotional symptoms. Characteristics of the mother showed significant correlations and were included in the regression analysis. Mental distress of the parents was also included and was measured by using questions similar to the Hopkins symptom checklist (HSCL-10). The HSCL-10 is a shortened version of the HSCL-25 (Strand, Dalgard, Tambs, & Rognerud, 2003) and includes 10 items about symptoms. The questionnaire in the study contained 9 questions: continuously fearful or uneasy; nervous, inner anxiety; feeling hopeless about the future; feeling blue, down; worry a lot or restless; feeling everything is an effort; feeling tense or keyed up; and suddenly scared for no reason. Each item was measured on a four-point scale from no distress (0) to very much distress (4).

Research questions

A: Is the frequency of infectious diseases stable over time?

Alternatives:

- 1) A high rate of infections at day-care start-up increases the risk for infections two years later. This alternative indicates that children who experience a high rate of infections during the first year of day-care have greater vulnerability, and thus a general increased risk for infections.
- 2) A high rate of infections in the first year of day-care is associated with a decrease in number of infections two and three years later. This alternative could indicate that children with infections the first years of group day-care increase their resistance against later infections.
- 3) There is no change in the rate of infections during the day-care period. This alternative may suggest high vulnerability for infections among these children. The children who experience a high number of infections during the first year of group day-care also experience a high number of infections during the following day-care period, with no changes in the overall number of infections.

B: Do children with infectious diseases at T1, T3 or T4 show emotional difficulties at T4?

This research question investigates the emotional symptoms and difficulties of children with infections. If children have a high rate of infections in the first years of day-care, one may/could hypothesise that these children will be more irritable and show more emotional symptoms. Thus, the present study wishes to examine whether children with more frequent and severe infections over time are more irritable than other children in day-care.

Preliminary analyses

To check for missing data and potential out-of-range values, frequency and other descriptive statistics of categorical and continuous variables were conducted. All variables were tested for normality using Shapiro-Wilks and Kolmogorov-Smirnov calculations and graphically by histograms (Tabachnick & Fidell, 2007, p. 81). Due to skewed distribution of T1, T3 and T4 infectious diseases, these variables were log-transformed before parametric analysis (Tabachnick & Fidell, 2007, p. 87). However, because there were no differences in the regression analyses when using non-transformed or transformed variables (data not shown), all analyses and data reported in this study are given by using non-transformed variables.

Statistical analyses

The analytic strategy followed four steps, using the statistical computer software IBM SPSS Statistics (20; SPSS Inc., Chicago, IL, USA). In the first part of the analyses descriptive statistics were performed. Frequencies and percentages were examined for all categorical data, while means and standard deviations were examined for continuous variables.

Descriptive statistics for infectious diseases were examined at all three time points.

The Friedman test (Pallant, 2007, p. 228-31) was computed to investigate any significant changes in infectious diseases over the three time points. Post-hoc paired samples *t*-tests using Wilcoxon signed rank sum test (Pallant, 2007, p. 223-5) with Bonferroni adjustment (Pallant, 2007, p. 206) were used to investigate significant changes between the three time points. Correlations between variables were analysed by computing the Spearman's Rho (Pallant, 2007, p. 126) and Kendall's Tau-b (Hinton, 2004).

In the third part of the analyses, three multiple hierarchical regression analyses were computed in order to examine associations between child infectious diseases during the

child's first year of day-care (T1) and two (T3) and three years later (T4). Multiple hierarchical regression analyses were used because of the longitudinal structure of the data, with multiple data points over time. Thus, first it was tested whether infectious diseases during T1 (independent variable) increased the risk for infectious diseases at T3 (dependent variable). The effects of each independent variable were examined by partial eta square. The hierarchical regression analyses were computed in three steps. In the first model, the main predictor, infectious diseases during T1 were entered. In the second step and third steps, child characteristics (sex, age, early birth, birth weight, serious or long-term illness) and family characteristics (dwelling type, number of siblings, referral to specialist for speech or language problems, and income and education of mother) were entered respectively to examine whether the association between T1 and T3 infectious diseases were robust after adjustments for potential confounders. The choice of control variables were based on whether they are known confounders previously found to be associated with infectious diseases, and whether they were associated with the main predictors and/or the dependent variables.

Next, the association between infectious diseases of T1 and T3 with T4 were examined. The hierarchical regression analyses were computed in four steps. In the first model the main predictor, infectious diseases at T3 were entered; in the second model infectious diseases measured at T1 were entered. Potential covariates of child characteristics were entered in step 3, and family characteristics were included in the fourth and final step.

Finally in the fourth step of the analyses, it was examined whether a high rate of infectious diseases at T1, T3 and T4 were associated with increased risk for irritability, measured by emotional symptoms at T4, using multiple hierarchical regression analyses. The hierarchical regression analyses were entered in three steps. In the first step the main predictors; infectious diseases at T4, T3 and T1 were entered. Potential covariates of child characteristics were entered in the second model, and family characteristics were included in the third model.

Missing data

Missing values in the analyses were handled with the option of excluding cases pairwise in SPSS. Statistical analyses were conducted with the population of girls and boys that had participated both at T1, T3 and T4. Therefore, some analyses include fewer children due to missing data on all three time points (T1, T3 and T4).

Results

Descriptive statistics of the study population

Descriptive characteristics for the study population are presented in table 1 that shows the distribution and frequencies for demographic, socioeconomic, child and family variables.

Table 1. Selected variables used in the study

Variables^a	N	Definition and description	Distribution
<i>Child characteristics</i>			
Age	596	Age in months when entering group day-care	52 (± 16)*
Sex	543	Boys	257 (47%)
		Girls	286 (53%)
Early birth	528	>3 weeks pre-term	42 (8%)
Birth weight	563	Grams	3564 (± 591)*
Speech/language problems ^b	394	Referred to specialist	33 (8%)
<i>Family characteristics</i>			
Dwelling type	413	House	309 (75%)
		Apartment	27 (7%)
		On a farm	77 (19%)
Siblings ^b	397	Most frequent number of siblings	1 (51%)
Mother's income ^d	572	No income or less than 200 000 NOK	216 (38%)
Mother's education	579	Junior high school	23 (4%)
		Some high school	62 (11%)
		Technical high school	116 (20%)
		Completed high school	106 (18%)
		College/university diploma or degree	200 (35%)
		Higher degree (Masters, PhD etc.)	72 (12%)

Notes: * Means and standard deviations (in parenthesis) are provided for continuous variables.

^a Variables taken from Time 1 unless specified.

^b Measured at Time 3.

^c Measured at Time 4.

^d Gross annual income in thousand and currency Norwegian kroner (NOK).

Table 2 shows descriptive statistics for infectious disease variables reported for the first year of day-care (T1), and two (T2) and three (T3) years later. The descriptive statistics are presented as continuous scores and indicates a decline in infectious diseases.

Table 2. Infectious disease variables

	<i>N</i>	<i>Min</i>	<i>Max</i>	<i>Mean</i>	<i>SD</i>
T1	297	0	10	2.3	1.7
T3	380	0.25	7.5	1.7	1.2
T4	294	0	6	1.3	1.0

Notes: Data presented as continuous scores.

Associations between infectious diseases across T1, T3 and T4

First, we investigated the distribution of each of the total scores measuring infectious diseases (Figure 1).

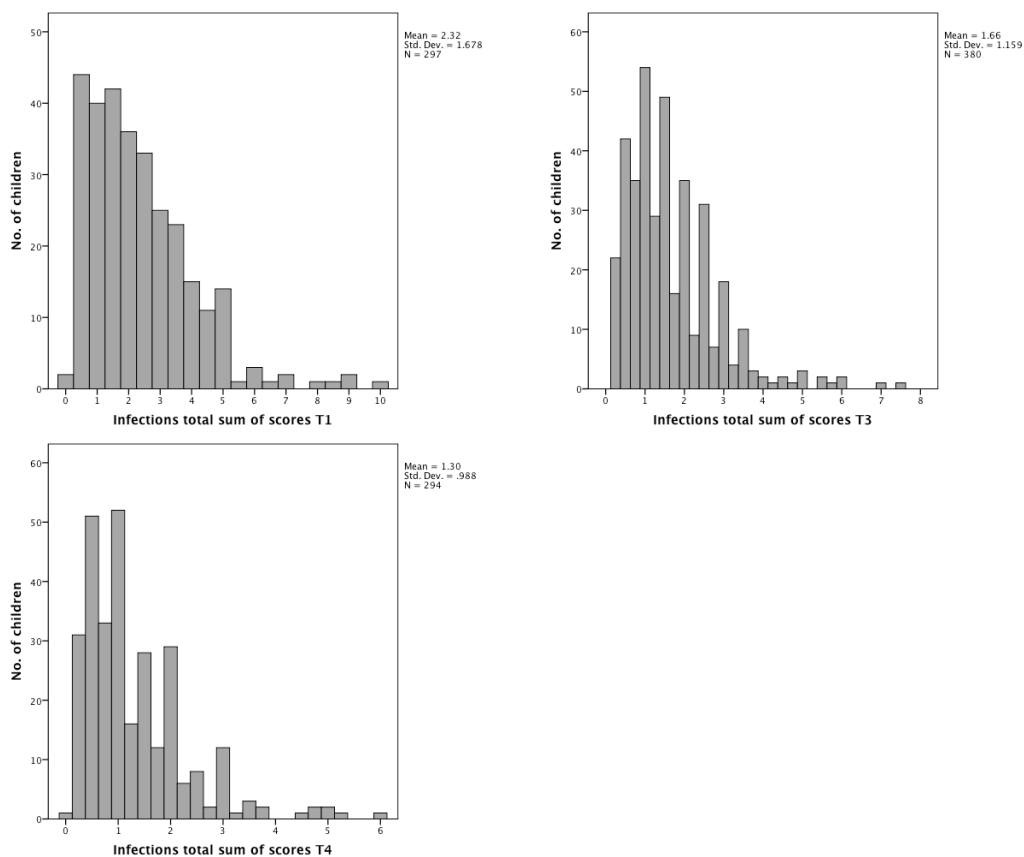


Figure 1: Distribution of data for T1, T3 and T4 infectious disease scores

The asymmetric distributions for T1, T3 and T4 infectious disease scores have similar positive skewness, with the majority of children having few infectious diseases. The distribution show that parents report children to have slightly more infectious diseases at T1 (drop in infectious diseases at 5-point value) compared to T3 (drop at the 3.5-point value) and T4 (drop at the 3-point value).

The continuous scores on infectious diseases measured at T1, T3 and T4 showed a significant reduction in infectious disease scores over time ($\chi^2(2) = 65.642, p < 0.001$). Table 3 shows a significant difference in the infectious diseases scores between T1 and T3 ($p < 0.001, r = -0.34$). Furthermore, there was a significant difference in the infectious disease scores between T1 and T4 ($p < 0.001, r = -0.42$); and between T3 and T4 ($p < 0.001, r = -0.29$).

Table 3: Comparisons of continuous infectious disease scores between T1, T3 and T4^a

Variable	<i>n</i>	<i>Mean</i>	<i>SD</i>	<i>p-value</i>
Time 1	179	2.4	1.61	<0.001 ^b
Time 3	179	1.6	1.08	<0.001 ^c
Time 4	179	1.3	0.92	<0.001 ^d

Notes.

^a Post-hoc pair-wise comparisons with Wilcoxon signed rank sum test and Bonferroni confidence interval adjustment.

^b Significantly different from T3 and T4.

^c Significantly different from T1 and T4.

^d Significantly different from T1 and T3.

Moreover, infectious diseases were moderately to highly correlated across the three time points. Pearson's bivariate correlations showed that infectious diseases at T1 was positively associated with infectious diseases at Time 3 ($r = 0.412, p < 0.01$), and T4 ($r = 0.147, p < 0.05$). Infections at T3 were positively associated with infectious diseases at T4, however this effect was small ($r = 0.268, p < 0.01$).

Table 4 shows the covariates significantly associated with infectious diseases at T1, T2 or T3 were age, weight, serious/long-term illness, number of siblings, dwelling type, and mother's

education and gross annual income, referral to specialist for speech/language problems, emotional symptoms, and parental distress, with correlation coefficients ranging from $r = -0.109$ to $r = 0.418$ (p range from < 0.001 to 0.048).

Table 4. Pearson's correlations between variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. T1 infections	-	0.42**	0.14	-0.02	0.09	0.06	-0.01	0.19**	0.04	0.06	0.01	-0.05	-0.08	-0.01	-0.11	0.07	-0.05	0.18**
2. T3 infections	0.42**	-	0.43**	0.20**	0.10	0.06	0.03	0.20**	0.05	0.01*	0.07	0.01	-0.07	0.02	0.11*	-0.08	-0.04	0.09
3. T4 infections	0.14	0.43**	-	0.00	0.03	-0.04	0.09	0.22**	0.25**	0.00	-0.01	0.07	-0.01	0.13*	-0.07	-0.04	-0.04	0.06
4. Age	-0.02	0.20**	0.00	-	0.04	-0.05	-0.01	0.04	0.12*	0.15**	0.02	0.04	0.01	0.09	-0.02	-0.04	-0.05	0.10*
5. Sex	0.09	0.10	-0.03	-0.04	-	0.08	-0.06	-0.05	0.08	-0.09	-0.02	-0.06	0.00	-0.04	-0.05	0.03	-0.02	-0.02
6. Birth weight	0.06	0.06	-0.04	-0.05	0.08	-	0.42**	0.08	0.01	-0.06	-0.10	-0.05	-0.01	0.09	0.08	0.03	0.06	0.01
7. Early birth	-0.01	0.03	0.09	-0.01	0.06	0.42**	-	-0.06	-0.04	0.10*	0.12*	0.12*	0.00	0.01	0.10*	0.01	-0.10*	0.04
8. Serious or long-term illness	0.19**	0.20**	0.22**	0.04	0.05	0.08	-0.06	-	-0.09	-0.07	-0.04	0.02	-0.01	0.01	-0.01	-0.02	-0.01	0.12**
9. Speech/language problems	0.04	0.05	0.25**	0.12*	0.08	0.01	-0.04	-0.09	-	0.08	0.04	0.01	0.04	0.09	-0.01	0.00	0.14**	0.05
10. T1 emotional symptoms	0.06	0.12*	0.00	0.15**	0.09	-0.06	0.10*	-0.07	0.08	-	0.45**	0.38**	0.17**	0.01	0.01	0.11**	-0.08	0.31**
11. T3 emotional symptoms	0.01	0.07	-0.01	0.02	0.02	-0.10	0.12*	-0.04	0.04	0.45**	-	0.41**	0.05	0.00	-0.02	-0.02	-0.02	0.25**
12. T4 emotional symptoms	-0.07	0.02	0.00	0.04	0.09	-0.06	0.10	0.02	0.03	0.39	0.42	-	0.07	-0.05	-0.01	-0.06	-0.06	0.30
13. Marital status	-0.08	-0.07	-0.01	0.01	0.00	-0.01	0.00	-0.01	0.04	0.17**	0.05	0.08	-	0.15**	0.01	0.13**	0.19**	0.13**
14. Siblings	-0.01	0.02	0.13*	0.09	0.04	0.09	0.01	0.01	0.09	0.01	0.00	0.03	0.15**	-	0.01	0.05	0.03	0.02
15. Dwelling type	-0.11	-0.11*	-0.07	-0.02	0.05	0.08	-0.10*	-0.01	-0.01	0.01	-0.02	-0.02	0.01	0.01	-	-0.02	0.10*	0.04
16. Mother's income	0.07	-0.08	-0.04	-0.04	0.03	0.03	0.01	-0.02	0.00	0.11**	-0.02	-0.07	0.13**	0.05	-0.02	-	0.32**	-0.07
17. Mother's education	-0.05	-0.04	-0.04	-0.05	0.02	0.06	-0.10*	-0.01	0.14**	-0.08	-0.02	-0.06	0.19**	0.03	0.10*	0.32**	-	0.02
18. Parent's mental distress	0.18**	0.09	0.06	0.10*	0.02	0.01	0.04	0.12**	0.05	0.31**	0.25**	0.30**	0.13**	0.02	0.04	-0.07	0.02	-

Notes: ** Significant at $p \leq 0.01$, * $p \leq 0.05$ (2-tailed).

Regression analyses

Multiple hierarchical linear regression analyses were used to assess the relationships between the infectious disease variables over time. The first set of analyses examined the association between infectious diseases measured at T1 and T3. Results are shown in Table 5. Infections at T1 predicted infectious diseases at T3, and this effect was stronger than the selected confounders entered in models 2 and 3. However, the association between T1 and T3 was reduced when child characteristics were entered in model 2, and in this model age was associated with infectious diseases at T3. Of the family characteristics entered in model 3, age, serious/long-term illness, and mother's income were significantly associated with T3 infectious diseases.

Table 5. Linear regression analysis with T3 infections as dependent variable

Variable	Model 1 ^a			Model 2 ^b			Model 3 ^c		
	β	B	Part r	β	B	Part r	β	B	Part r
T1 infections	0.288***	0.417***	0.417	0.264***	0.382***	0.373	0.264***	0.383***	0.369
Age			0.014***	0.189***	-	-0.187	0.014***	0.196***	-0.192
Sex			0.112	0.048	0.048	0.048	0.114	0.049	0.048
Birth weight			0.000	0.059	0.053	0.053	0.000	0.064	0.056
Early birth			0.272	0.062	0.055	0.055	0.255	0.058	0.051
Serious or long-term illness			-0.438	-0.11	-0.107	-0.107	-0.464*	-0.117*	-0.113
Speech/language problems			0.209	0.05	0.049	0.049	0.22	0.053	0.051
Marital status							0.113	0.03	0.03
Siblings							0.052	0.041	0.039
Dwelling type							-0.112	-0.076	-0.075
Mother's income							-0.165*	-0.14*	-0.131
Mother's education							0.027	0.031	0.029

Notes: ^a Unadjusted. ^b Adjusted for child characteristics. ^c Adjusted for family characteristics. * Significant at $p \leq 0.05$. ** $p \leq 0.01$. *** $p \leq 0.001$.

Table 6 presents T4 infectious diseases as the dependent variable. Model 1 shows that infectious diseases during T3 predicted infectious diseases a year later on T4, and this effect was stronger than the selected confounders. The association between T3 and T4 was reduced when T1 infectious diseases were entered in model 2, although T1 infectious diseases were not significantly associated with infectious diseases at T4. In models 3 and 4, referral for speech/language problems was the only covariate significantly associated with infectious diseases at T4.

Table 6. Linear regression analysis with T4 infections as dependent variable

Variable	Model 1 ^a			Model 2 ^b			Model 3 ^c			Model 4 ^d		
	β	<i>B</i>	<i>Part r</i>	β	<i>B</i>	<i>Part r</i>	β	<i>B</i>	<i>Part r</i>	β	<i>B</i>	<i>Part r</i>
T3 infections	0.364***	0.427***	0.427	0.38***	0.445***	0.405	0.373***	0.437***	0.383	0.367***	0.431***	0.371
T1 infections				-0.026	-0.044	-0.04	-0.037	-0.062	-0.056	-0.034	-0.058	-0.051
Age							0.004	0.065	0.063	0.003	0.055	0.053
Sex							-0.175	-0.088	-0.087	-0.166	-0.084	-0.083
Birth weight							0.000	-0.02	-0.017	0.000	-0.03	-0.027
Early birth							0.192	0.051	0.046	0.168	0.045	0.04
Serious or long-term illness							-0.426	-0.126	-0.121	-0.429	-0.127	-0.122
Speech/language problems							0.799***	0.224***	0.22	0.774***	0.217***	0.21
Marital status										0.030	0.025	0.024
Siblings										0.107	0.099	0.096
Dwelling type										-0.033	-0.026	-0.025
Mother's income										-0.008	-0.008	-0.007
Mother's education										0.014	0.019	0.018

Notes: ^a Unadjusted. ^b Adjusted for infections. ^c Adjusted for child characteristics. ^d Adjusted for family characteristics. * Significant at $p \leq 0.5$. ** $p \leq 0.01$. *** $p \leq 0.001$.

Emotional symptom is the dependent variable in the regression models shown in Table 7. In the unadjusted model 1 and the multiple-adjusted models 2 and 3, T1, T3, and T4 infectious diseases did not predict emotional symptoms at T4. In model 2 that included child characteristics, child emotional symptoms at T1 and T3 significantly predicted emotional symptoms at T4. In model 3, child emotional symptoms at T1 and T3 still predicted emotional symptoms at T4 after adjustments for family characteristics. Also in this model, parent's mental distress predicted child emotional symptoms at T4.

Table 7. Linear regression analysis with emotional symptoms at T4 as dependent variable

Variable	Model 1 ^a		Model 2 ^b		Model 3 ^c	
	β	Part r	β	Part r	β	Part r
T4 infections	0.087	0.078	0.138	0.104	0.126	0.095
T3 infections	0.003	0.003	-0.062	-0.051	-0.06	-0.049
T1 infections	-0.042	-0.063	-0.03	-0.041	-0.052	-0.068
Age			-0.001	-0.01	-0.002	-0.024
Sex			-0.027	-0.012	-0.025	-0.011
Birth weight			0.000	0.023	0.000	0.016
Early birth			0.254	0.056	0.218	0.047
Serious or long-term illness			0.193	0.048	0.225	0.056
Speech/language problems			-0.16	-0.038	-0.178	-0.042
T1 emotional symptoms			0.219***	0.224***	0.182**	0.18**
T3 emotional symptoms			0.255***	0.261***	0.232***	0.234***
Marital status					-0.004	-0.003
Siblings					0.019	0.015
Dwelling type					-0.038	-0.026
Mother's income					-0.012	-0.01
Mother's education					-0.030	-0.033
Parent's mental distress					0.093*	0.167*

Notes: ^a Unadjusted. ^b Adjusted for child characteristics. ^c Adjusted for family characteristics. * Significant at $p \leq 0.5$. ** $p \leq 0.01$. *** $p \leq 0.001$.

Discussion

Main findings

- This study shows that overall frequency and severity of infectious diseases in group day-care decline over a 4-year period.
- Infectious diseases in the first year of group day-care were associated with and predicted infectious diseases in the third year, but not the frequency of infectious diseases after 4 years.
- A high rate of infectious diseases in the third year of group day-care was positively associated with a high rate of infectious diseases after four years.
- Infectious diseases in the first, third and fourth year of group day-care were not associated with emotional difficulties in the fourth year.

Decline in infectious diseases in group day-care

The results show that infectious diseases in group day-care declined over a four year period. This is in accordance with previous studies that showed a decrease in infectious diseases over time (Ball et al., 2002; Côté et al., 2010; Illi et al., 2001; Rothers et al., 2007). Infectious diseases during the first year of group day-care were positively associated with infectious diseases after three years (T3), but not after four years (T4). These data indicate a change in the pattern of infectious diseases over time. Thus, a high rate of infectious diseases seems to increase the risk for infectious diseases after three years, but then decrease after four years, when most of the children have transitioned into school. One possible explanation for this finding may be that the youngest children have a higher risk for infectious diseases, but that their immune system is strengthened over a period with high exposure to pathogens, such as during the first year of group day-care (Ball et al., 2002; Côté et al., 2010; Illi et al., 2001; Wefring, Lie, Loeb, & Nordhagen, 2001b). The data were consistent, as they were not qualitatively altered when controlled for age, which was associated with a high rate of infectious diseases, that is, older children had fewer infectious diseases at T3. Thus, it may be that attending group day-care in the first two years of life, and being exposed to multiple pathogens, is important for strengthening children's immune system and protect children against infectious diseases later when entering school.

In short, this study shows an increase of infectious diseases, and then a decrease. This further supports the proposed “window of vulnerability” where children are especially vulnerable for infectious diseases when they are under three to four years of age (Denny et al., 1986; Illi et al., 2001; Wald et al., 1991; Wefring et al., 2001b). Age was associated with infectious diseases at Time 3, when the mean age where four years, but not when the children were older at Time 4.

Confounders associated with infectious diseases

Known confounders associated with infectious diseases were controlled for. Overall, the results showed that children with infectious diseases had more chronic (serious or long-term) illness than subjects without infectious diseases. This is in accordance with previous research where serious, acute or chronic infectious diseases are associated with higher risk of developing chronic illness (Dunder, Tapiainen, Pokka, & Uhari, 2013; Illi et al., 2001; Leadbitter et al., 1999; Nafstad, Brunekreef, Skrondal, & Nystad, 2005; Stick & Mutius, 2001). Thus, children with chronic illness are also at greater risk for common infectious diseases in group day-care in addition to severe infectious diseases. However, this effect was not present in the fourth year follow-up. It may be that the association between chronic illness and common infectious diseases is due to timing effects of the “window of vulnerability” and disappears with age. A speculation is that children with both chronic illness and high rates of infectious diseases could be vulnerable for severe physical health problems later in life (Cohen et al., 1998; Nafstad et al., 2005). However, more research is needed in order to fully understand how these children develop, and whether they are at risk. If they are at risk it is important to understand why and how these risks may influence their development later on.

In the present study, as others also have found, children with a high rate of infectious diseases at Time 4, also had increased risk for language and speech problems. However, further research is needed in order to understand whether this might be a confounding factor. Previous studies have found speech and language problems to be associated with severe and repeated infectious diseases, such as ear infectious diseases (Hardy & Fowler, 1993). However, others have not supported this result. For instance, in a large national study on early child infectious diseases in the USA no effect of high rate of infectious diseases on

language development were found (Bradley, 2003). Additionally, a meta-analysis by Roberts and colleagues (2004) including 11 studies on the link between otitis media with effusion and language problems showed no significant relation in early childhood and pre-schoolers (Roberts, Rosenfeld, & Zeisel, 2004). Thus, it is still uncertain whether high rate of infectious diseases can be considered a risk for poor language development. One possibility is that children with severe infectious diseases or chronic infectious diseases, spend less time at school, or group day-care, and, thus, have less opportunity to practice language skills. However, further studies focusing on infectious diseases during early development and later language development are needed to understand these relations.

When examining the associations between infectious diseases during the first year with the rate of infectious diseases three years later, this effect was robust over and above potential confounders. Although these findings were robust, they were moderated by maternal income. That is mothers who reported low income were also the mothers who reported that their children had a high rate of infectious diseases. This finding might suggest that children growing up in a family with low economic status are at risk. In Norway this should not be a direct effect on availability for health care, as the health care system is free of charge for children.

Furthermore, when controlling for child and family characteristics there were no effects of length of gestation, low birth weight, siblings, and education of mother in relation to infectious diseases. Hence, in this study these control variables did not influence infectious diseases over time.

Infectious diseases and emotional difficulties

In this study there were no significant relationship between infectious diseases in group day-care and emotional difficulties. Therefore, the hypothesis that children with a high rate of infectious diseases would show more irritability was not supported. This is in contrast to others who have found that illness can be associated with aggressive behaviour (Borge et al., 2004) and emotional problems (Anthony, Bromberg, Karen, & Schanberg, 2011; Bennett, 1994; Cohen et al., 1998; Garralda, 1994). It may be that children with infectious diseases are not sad or show significant emotional symptoms and that the emotional problem SDQ does not measure irritability adequately. Nevertheless, the results suggest that common and

communicable infectious diseases in group day-care, such as respiratory, ear, and gastrointestinal infectious diseases, differ from chronic infectious diseases. Future studies should be designed to use multiple scales, such as peer problems and other types of behaviour problems. Small children may have difficulties with explaining precisely what type of pain they experience. For instance, children might say they have stomach-aches, which can be understood as an expression for infectious pain, but it could also be a symptom of sadness, as stomach-ache might also reflect emotional problems (R. Goodman, 2001).

To the knowledge of this paper's author, there are no previous reports on the link between infectious diseases in group day-care and emotional difficulties. No such link was found in the present study. This finding suggests that exposure to increased risk of infectious diseases in group day-care does not have negative effect on emotional well-being. The implication of this is that children in group day-care have more common and communicable infectious diseases, without having more emotional difficulties.

Confounders associated with emotional difficulties

In the present study the distress of parents predicted emotional difficulties in children and previous emotional difficulties predicted emotional difficulties in the fourth year. This is in accordance with other studies (Bekkhus, Rutter, Barker, & Borge, 2011; Berg-Nielsen et al., 2002; Bzostek & Beck, 2011; Connell & Goodman, 2002; Hagekull & Bohlin, 1995).

Methodological considerations

Strengths

The present study is the first in Norway to longitudinally examine how frequency of infectious diseases during the first year of group day-care influence frequency of infectious diseases after three and four years, and examining the association with emotional difficulties while controlling for potential confounders. In this study there was a large sample size with 596 participants at T1, and of these 297 participants reported infectious diseases at T1. Thus, type 2 error (failure to reject null hypothesis) should not be an issue as the sample size is above 100 (Stevens, 2009). Also, the quality of the infectious diseases data in this study was high as the questionnaire contained nine questions about respiratory, ear, and gastrointestinal infectious diseases. The grouping of the questions was based on research and quality

assurance by a medical professional in order to weigh both frequency and severity of the infectious diseases into a total score. This “infectious disease index” differ from previous research that has investigated the frequency of respiratory, ear, and gastrointestinal infectious diseases (Bradley, 2001; Louhiala et al., 1995; Nafstad et al., 2005).

Limitations

Some limitations need to be considered when interpreting these results. The study subjects were from a rural area in Norway. Data from larger cities might be different, as both the population and climate might be different. Additionally, pollution is substantially more present in urban areas, which may affect the frequency of infectious diseases in children. Another important aspect is the lack of a control group with subjects not attending group day-care. Thus, it is impossible to conclude if the data in this thesis are valid to children overall or only to children attending group day-care.

The participation rate of the study was 50% in the first year, 38% in the third year and 31% in the fourth year. Selective attrition effects are of concern in longitudinal studies, implying that there are differences between the participants and the dropouts that may cause bias. In the present study there were no associations between control variables and infectious diseases, except for the income of the mother of the child. There were also measures of association between emotional difficulties and control variables, mental stress of the parents, and previous emotional symptoms of the child. However, in other longitudinal studies, it has been found that even though there can be a selection bias that affects the prevalence, it has little implication for the association measures (Nilsen et al., 2009; Wolke et al., 2009).

A study by Bekkhus, Rutter, Maughan, & Borge (2011) showed that Norwegian parents with high maternal education and family income are more likely to have their children in group day-care. This differs from the USA where families with high socioeconomic status are more likely to participate in studies, and children with low quality day-care are associated with families of low socioeconomic status.

Data collection

Infection data in the first year was collected retrospectively in the third year, as the study had not included questions about infectious diseases in the first and second years. Retrospective

reports on data are not as robust as prospective reports (Maughan & Rutter, 2009). There is the potential problem that participants do not remember correctly. However, the main concern is that participants tend to underreport retrospectively (Maughan & Rutter, 1997). Therefore, it is possible that the effect of infectious diseases in the first year of group day-care would have been stronger, and this could potentially explain why infectious diseases in the first year did not predict infectious diseases in the fourth year.

Another important limitation of the study is that data pregnancy risks were not collected. Factors during pregnancy could influence vulnerability to infectious diseases, such as prenatal smoking (Difranza, Aligne, & Weitzman, 2004) and prenatal alcohol consumption (Gauthier, Drews-Botsch, Falek, Coles, & Brown, 2005; O'Connor et al., 2002). Additionally, data on smoking (Holberg, Wright, Martinez, Morgan, & Taussig, 1993) and family pets (Hesselmar, Aberg, Aberg, Eriksson, & Björkstén, 1999), variables that are associated with increased risk of infectious diseases, were not available.

Rater bias

There is a potential bias when parents rate their own children. In a study on psychosocial problems in Norwegian 4-year olds by Berg-Nielsen, Solheim, Belsky, & Wichstrom (2012) it was found that teachers would rate children lower on internalizing problems than parents on the SDQ (R. Goodman, 2000). Similar results were found in a Danish birth cohort study where group day-care (kindergarten) teachers reported fewer emotional problems than parents (Elberling, Linneberg, Olsen, Goodman, & Skovgaard, 2010). They conclude that either it is difficult to detect problems in group day-care or group day-care quality is good and, thus, there are few problems.

Future studies

Future studies should be designed to investigate differences between subjects living in rural vs. urban areas. As outdoor day-care centres are becoming increasingly popular in Norway the effect of outdoor hours should included. Future research should also measure behavioural difficulties in examining emotional problems in children. Finally, future large scale longitudinal studies should investigate whether there is a relationship between infectious diseases in group day-care and later infectious diseases and relate the early rate of infectious diseases to psychological health in school, adolescence and later as grown-ups. However,

such longitudinal studies might be difficult to perform in the future due to the increasing changes of all facets in the modern society.

Conclusion

This study shows that the overall frequency and severity of infectious diseases in group day-care declines over a four-year period. A high rate of infectious diseases seems to increase the risk for infectious diseases after three years, but then decrease the risk after four years, when most children have transitioned into school. This supports the proposed “window of vulnerability” where children are especially vulnerable for infectious diseases when they are under three to four years of age. To the knowledge of the author, this thesis is the first in which a possible link between infectious diseases in group day-care and emotional difficulties has been investigated. No significant relations between infectious diseases in group day-care and emotional difficulties were found. This finding suggests that exposure to infectious diseases in group day-care does not have negative effects on emotional well-being. Thus, children in group day-care have more common infectious diseases, without having more emotional difficulties.

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Appendix

Table A. Recoded infectious disease values

No. of infectious diseases	Infection classification		
	<i>Mild^a</i>	<i>Moderate^b</i>	<i>Severe^c</i>
0	0	0	0
1	0.25	0.5	1
2	0.5	1	1.5
3	1	1.5	2
>4 ^d	1.5	2	2.5

Notes.

^a Mild infectious diseases: cold, urinal tract, and eye infectious diseases.

^b Moderate infectious diseases: throat, and ear infectious diseases and gastric illness/diarrhoea.

^c Severe infectious diseases: laryngitis, bronchitis/RS-virus/lung infectious diseases, and fever convulsions.

^d Children with four or more infectious diseases.

Table A shows the recoded infectious disease values. This was done in order to adjust for both illness severity and illness frequency. The infectious diseases were weighed by a giving a higher number depending on frequency and severity. As an example, three mild infectious diseases was given the same value as one sever infectious disease. Thus a high frequency of mild infectious diseases would also reflect severity.