Infants hospitalised with acute respiratory tract infections. Mapping, description, and evaluation of physiotherapy treatment methods including frequent changes in body position and stimulation of physical activity.

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LUND
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Abstract

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To examine current treatment and evaluation methods in Sweden, we constructed and distributed a digital survey. The survey consisted of questions with listed answer options—chosen from literature and expert experience—in addition to the possibility of answering in free text. The treatment methods were analysed with descriptive statistics and Chi2 tests. The survey showed that physiotherapists in Sweden use a wide range of treatment methods depending on the individual situation. The mostly used methods include frequent body position changes, stimulation of physical activity, and providing information to the parents.

To evaluate the effect of this treatment strategy, we planned and performed a randomised control trial (RCT) at two hospitals in southern Sweden. Infants aged 0–24 months without previous respiratory or cardiac diagnoses were included and individually randomised to a control group (standard care) or to one of two intervention groups (standard care with two varieties of additional interventions). Study procedures and design were thoroughly described in a study protocol. Furthermore, a safety analysis was performed in a feasibility study, showing no risk of harm. We also evaluated the feasibility of the study design, which enabled us to improve the analysis plan for the RCT. The feasibility study revealed some challenges about clinical research in acute hospital settings, including a low recruitment rate (19%) and more missing data than had been previously assumed. Scrutinising the data, we identified difficulties in utilising the intended primary outcome measure, which was consequently changed in the full RCT, and a new sample size calculation was performed.

The effect of the physiotherapy intervention was primarily analysed via Kaplan-Meier and an adjusted Cox regression model. No statistically significant differences were detected between the intervention group and the control group in the rate of improvement ($p = 0.46$; $p = 0.69$) or in the immediate changes in oxygen saturation, heart rate, or respiratory rate ($p = 0.28$–0.92). Both strategies were found to be equally effective and safe, indicating that the current recommendation of minimal handling for these infants should be reconsidered.

Key words physical therapy modalities, respiratory tract infections, bronchiolitis, pneumonia, infants, randomized controlled trial

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Table of Contents

Abstract

The overall aim of this thesis was to increase knowledge about physiotherapy treatment for infants with lower respiratory tract infections, which is the most common reason for infant hospitalisation worldwide. Physiotherapy treatment for these infants is debated, and there is no clear consensus regarding the best treatment strategy.

To examine current treatment and evaluation methods in Sweden, we constructed and distributed a digital survey. The survey consisted of questions with listed answer options—chosen from literature and expert experience—in addition to the possibility of answering in free text. The treatment methods were analysed with descriptive statistics and Chi^2 tests. The survey showed that physiotherapists in Sweden use a wide range of treatment methods depending on the individual situation. The mostly used methods include frequent body position changes, stimulation of physical activity, and providing information to the parents.

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Svensk populärvetenskaplig sammanfattning (Summary in Swedish)

Den vanligaste orsaken till att spädbarn läggs in på sjukhus över hela världen är akuta luftvägsinfektioner. Det är ofta en virusinfektion, exempelvis från det så kallade RS-viruset. Barnen får ofta mycket och segt slem som hindrar andningsfunktionen, och de kan snabbt bli allvarligt utmattade.

Genom åren har många olika behandlingar provats, men det är fortfarande inte känt vad som hjälper barnen bäst. Olika läkemedel rekommenderas inte standardmässigt och det finns ännu ingen botande behandling. Därför brukar barnen få stödjande vård som vätsketillförsel och syrgas på sjukhusen, och många får också andra åtgärder som extra luftflöde i näsan och inhalationer. I de allvarligaste fallen behövs andningshjälp med respirator. Fysioterapeuter arbetar i varierande grad i olika länder med dessa patienter enligt olika traditioner. Många olika metoder har provats, och målet har för det mesta varit att få bort slem från luftvägarna så att barnet kan andas lugnare, orka äta bättre och bli lite piggare. De flesta metoder som finns beskrivna innebär att fysioterapeuten trycker, vibrerar eller bankar med händerna på barnets bröstkorg när barnet ligger på rygg i sängen eller när barnet ligger i så kallade dränageställningar, ofta med huvudet nedåt. Det är också vanligt med beskrivningar där fysioterapeuten trycker på barnets luftstrupe för att stimulera till hosta.

När en del av dessa fysioterapimetoder har utvärderats har man inte kunnat se någon effekt av behandlingen, och i vissa fall har barnen fått negativa reaktioner som kräkningar, hjärt- och andningspåverkan som vid stress eller till och med brutna revben. Därför står det i många länders riktlinjer att fysioterapi inte rekommenderas, eller endast rekommenderas i vissa fall. En svårighet med att följa de här riktlinjerna är dels att uttrycket ”fysioterapi” egentligen omfattar många olika slags metoder, dels att utvärderingarna av fysioterapimetoderna har gjorts på många olika sätt. Därför är det svårt att som praktiserande fysioterapeut veta om och i så fall hur man ska behandla de här barnen för att hjälpa dem. I Sverige kan det upplevas särskilt svårt att förhålla sig till riktlinjerna, för de metoder som har utvärderats internationellt och som riktlinjerna bygger på liknar inte metoderna som vanligen används på sjukhusen här.

Det övergripande syftet med detta doktorandprojekt var att ta reda på mer om fysioterapibehandling för spädbarn som läggs in på sjukhus med akuta luftvägsinfektioner.

Den första studien gjordes för att ta reda på och beskriva vilka metoder som används i Sverige. En digital enkät spreds på olika sätt till fysioterapeuter som arbetar med barn under 2 år med akuta luftvägsinfektioner. Av de 52 svaren som uppfyllde kriterierna svarade 100% att de gav information till föräldrarna. 92% uppgav att de

studsade på en stor boll med barnen, och 94% att de gjorde lägesändringar med barnen. När de skulle beskriva sina tre vanligaste metoder, så innehöll de för alla fysioterapeuter de metoder som senare klassades som ”aktiva”, exempelvis stimulering till fysisk aktivitet, lägesändringar och arm- och benrörelser. ”Passiva” metoder som att trycka med händerna på bröstkorgen förekom också, men ingen fysioterapeut angav enbart metoder som sedan klassades som ”passiva” som sina vanligaste. Av resultatet i enkätstudien fick vi sammanfattningsvis veta att det användes en stor mängd behandlingsmetoder även i Sverige, och att de vanligaste inkluderade lägesändringar och stimulering av fysisk aktivitet och att samtliga gav information till föräldrarna.

De metoder som enligt enkäten används i Sverige hade inte tidigare beskrivits för den här patientgruppen och inte heller utvärderats vetenskapligt. Behandlingen påminner om behandlingen i Sverige för barn med cystisk fibros där den varit mycket gynnsam, och har också beskrivits för barn med sekundära andningsproblem vid multipla funktionsnedsättningar. Vi ville gå vidare och utvärdera effekten av den här behandlingen och startade därför en randomiserad kontrollerad studie. Upplägget i den studien är beskrivet i en artikel, ett studieprotokoll. Studien pågick vid Skånes universitetssjukhus i Malmö och Växjö Centrallasarett där 104 barn i åldern 0-2 år inkluderades. Alla barnen fick basal omvårdnad och de som lottades till kontrollgruppen fick enbart basal omvårdnad, och de som lottades till en intervention fick ett tillägg av lägesändringar, stimulering till fysisk aktivitet och kroppsrörelser utöver den basala omvårdnaden. Det förekom två behandlingsupplägg: antingen ett program lett av en fysioterapeut eller ett något reducerat program lett av vårdpersonal på avdelningen. Studieupplägget utvärderades i en separat studie, som bland annat visade att det gick långsamt att inkludera deltagare och att stort bortfall förekom i viss datarapportering. Genom att ändra analysmetoden stärktes studiedesignen och den kliniska studien kunde slutföras.

Ingen statistiskt signifikant skillnad visade sig mellan grupperna, och därför kan vi inte påtala någon effekt av fysioterapibehandlingen jämfört med den basala omvårdnaden. Inga biverkningar eller säkerhetsrisker kunde å andra sidan heller noteras. Därför kan vi genom studierna ifrågasätta den utbredda rekommendationen om ”minimal hantering” av de här barnen. Att hålla barn nära i famnen, och att vårda barn med akuta luftvägsinfektioner på mage eller med höjd huvudända av sängen har i andra studier visats har positiv effekt. Därför ser vi inte heller något hinder till att fortsätta den här utbredda behandlingen, och särskilt inte ifall man ser en annan klinisk effekt eller andra fördelar av behandlingen som inte har framkommit i det här arbetet. Fortsatta studier behövs för att få ytterligare kunskap om vad som bäst gynnar dessa små barn när de är allvarligt påverkade och inlagda på sjukhus.

Abbreviations

ALRI, Acute lower respiratory tract infections

CF, Cystic Fibrosis

CPAP, Continuous positive airway pressure

HFNC, High flow nasal cannula

HR, Hazard ratio

HS, hypertonic saline

ICF, International Classification of Functioning, Disability and Health

ICU, Intensive care unit

IQR, Interquartile range

MRC, Medical Research Council

pH, potential of Hydrogen

PT, Physiotherapist

RCT, Randomised control trial

RSV, Respiratory syncytial virus

WHO, World Health Organization

List of papers

I. Andersson-Marforio S, Hansen C, Ekvall Hansson E, Lundkvist Josenby A. A survey of the physiotherapy treatment methods for infants hospitalised with acute airway infections in Sweden. Eur J Physiother. 2021;23(3):149-56. https://doi.org/10.1080/21679169.2019.1663925

II. Andersson-Marforio S, Lundkvist Josenby A, Ekvall Hansson E, Hansen C. The effect of physiotherapy including frequent changes of body position and stimulation to physical activity for infants hospitalised with acute airway infections. Study protocol for a randomised controlled trial. Trials. 2020;21(1):803. https://doi.org/10.1186/s13063-020-04681-9

III. Andersson-Marforio S, Lundkvist Josenby A, Hansen C, Ekvall Hansson E. Physiotherapy interventions encouraging frequent changes of the body position and physical activity for infants hospitalised with bronchiolitis: an internal feasibility study of a randomised control trial. Pilot Feasibility Stud. 2022;8(1):76. https://doi.org/10.1186/s40814-022-01030-2

IV. Andersson-Marforio S, Hansen C, Ekvall Hansson E, Lundkvist Josenby A. Frequent changes in body position and stimulation of physical activity as effective as standard care for infants hospitalised with acute respiratory infections—a randomised controlled trial evaluating a physiotherapy intervention. *In manuscript.*

Description of contributions

Applications for ethical review were written by Sonja Andersson Marforio and Eva Ekvall Hansson. The sample size calculations were performed by statistician Helene Jacobsson and Sonja Andersson Marforio.

Paper I	
Study design	Eva Ekvall Hansson, Annika Lundkvist Josenby, Christine Hansen, Sonja Andersson Marforio
Data collection	Sonja Andersson Marforio
Data analyses	Sonja Andersson Marforio
Manuscript writing	Sonja Andersson Marforio
Manuscript revision	Annika Lundkvist Josenby, Eva Ekvall Hansson, Christine Hansen
Paper II	
Study design	Eva Ekvall Hansson, Annika Lundkvist Josenby, Christine Hansen, Sonja Andersson Marforio
Data collection	N/A
Data analyses	N/A
Manuscript writing	Sonja Andersson Marforio
Manuscript revision	Christine Hansen, Eva Ekvall Hansson, Annika Lundkvist Josenby
Paper III	
Study design	Eva Ekvall Hansson, Annika Lundkvist Josenby, Christine Hansen, Sonja Andersson Marforio
Data collection	Sonja Andersson Marforio
Data analyses	Sonja Andersson Marforio
Manuscript writing	Sonja Andersson Marforio
Manuscript revision	Eva Ekvall Hansson, Annika Lundkvist Josenby, Christine Hansen
Paper IV	
Study design	Eva Ekvall Hansson, Annika Lundkvist Josenby, Christine Hansen, Charlotta Webb, Sonja Andersson Marforio
Data collection	Sonja Andersson Marforio
Data analyses	Sonja Andersson Marforio
Manuscript writing	Sonja Andersson Marforio
Manuscript revision	Annika Lundkvist Josenby, Eva Ekvall Hansson, Christine Hansen

Thesis at glance

	Paper I Survey study	**Paper II** Study protocol	**Paper III** Feasibility study	**Paper IV** Randomised control trial
Aim	To explore what treatment methods physiotherapists in Sweden use for hospitalised infants with ALRI, and to investigate possible differences in choice of treatment related to the background characteristics of the physiotherapists.	Describe a randomised control trial that aims to compare the effect of an individualised physiotherapy intervention, a nonindividualised intervention and a control group receiving standard care, in hospitalised infants 0–24 months of age.	To address uncertainties concerning the ongoing RCT and to determine whether the trial is feasible or not, or what adjustments to the protocol are needed.	To evaluate the effect of a physiotherapy treatment method including frequent changes in body position and stimulation of physical activity performed by health care staff and parents compared to standard care for infants aged 0–24 months hospitalised with ALRI.
Study population	PTs in Sweden, n=88	N/A	Infants with ALRI from 2 hospitals in southern Sweden, n=91	Infants with ALRI from 2 hospitals in southern Sweden, n=104
Main results	All answer options were marked at least once. Reported to be most frequently used: Bouncing on a big ball, change of position in arms, physical activity, passive arm and leg movements, information to parents. No differences in choice of method related to background characteristics of the PTs.	Description of a clinical RCT.	The recruitment rate was 19%. The data supply for the primary end point and for the primary outcome measure was lower than anticipated in the original sample size calculation. Difficulties concerning utilising the primary outcome measure were identified. The safety analysis detected no risks of harm related to participation in the study.	No statistically significant differences were found between groups in improvement rate or in immediate changes in oxygen saturation, heart rate, or respiratory rate. Not statistically significant, however, there was a higher improvement rate in the intervention group and an increased probability for improvement at the different times (HR).
Conclusions	A variety of treatment methods were used by the Swedish PTs. The most common methods involves frequent changes of the body position and stimulation of physical activity.The praxis in Sweden differed from the methods described in the international literature.	N/A	It was found feasible to continue the full RCT with modifications of the analysis plan. Participation in the study was not associated with any safety risks.	No effects of the interventions and no adverse effects were detected. Both strategies were found to be equally effective and safe, indicating that the current recommendation of minimal handling for these infants should be reconsidered.

Preface

Even at my very first job as a physiotherapist in the Department of Infectious Diseases in Lund in 1991, I found myself in respiratory care. At that time, I was also recruited to work with a patient with the lung disease Cystic Fibrosis (CF). Our team treated this patient for several hours every day in their home, and from that work I learned much about the compound treatment for a patient with this chronic diagnosis, as a complement to my work in the acute setting of the hospital. This is when I grounded my interest in respiratory physiotherapy. Changing jobs made me redirect my attention to other clinical fields, but I always kept my interest in respiratory difficulties. Having worked and educated myself for several years in musculoskeletal disorders of the neck and limbs, I returned to the field of respiration in 2004 as I worked with children and adolescents with CF in the team in Lund University Hospital. In 2008, in collaboration with a colleague, we started up a "respiratory centre" (in Swedish, "andningsmottagningen") for children with neuromuscular disorders and secondary respiratory symptoms. I worked with this patient group alongside children with other conditions, including disorders of the neck, which have also continuously interested me. Additionally, I met many infants hospitalised with bronchiolitis or pneumonia. We applied the same treatment principals for persons with CF and neuromuscular disorders as for previously healthy infants with acute airway infections, as the problem was often the same: increased mucus in the airways that affected respiratory function.

When planning to write clinical guidelines on treating infants with acute respiratory infections in hospitals, I became aware of the conflicting scientific evidence on physiotherapy for this patient group. I also did not find anything in the international literature about the treatment that my colleagues and I had used for years, and which we experienced as having a good effect for many patients. Accordingly, I started to look more systematically into the best practice to guide my clinical work. I began to develop my research questions when I discovered (together with two students who performed a literature review) that there were clear gaps between clinical practise and scientific evidence. Consequently, the foundation of my doctoral studies are clinical questions for which I genuinely wanted answers. Clinical application has thus been a major motivating factor for me throughout the work of this thesis, apart from my enjoyment in the stimulating world of research itself.

Introduction

In this thesis, the focus is on physiotherapy treatment for infants hospitalised with acute respiratory infections, which is the leading cause of morbidity and the most common reason for hospitalisations of infants below 24 months worldwide (1). The Introduction section starts with a brief discussion of the human respiratory system, specifically that of infants. Next, follows an introduction to acute airway infections in infants, followed by an outline of the most common treatment modalities. Finally, perceived gaps in scientific evidence and disparities between guidelines and clinical practise are presented, to clarify the context of this thesis.

The respiratory system

This section is primarily dedicated to the process of moving air in and out of the lungs, which is sometimes expressed as 'pulmonary ventilation' (2). The term 'respiration' additionally includes the gas exchange that occurs between the lungs and the blood, the transport of respiratory gases, and the diffusion of oxygen and carbon dioxide between the peripheral cells and the blood (3). Respiration is autonomous, and mostly unconscious, being governed from the medulla oblongata and the pons in the brain stem, but it can also be controlled by will (4,5). The main function of respiration is to oxygenate the blood in order to supply mitochondria in the cells with oxygen for metabolism and remove excess carbon dioxide, keeping blood gases and pH levels balanced (3).

Upper and lower respiratory airways

The respiratory tract is an entity commonly described as consisting of two parts: the upper and the lower airways. The upper airways contain the nose, the mouth, and the pharynx. Passing through the nose, inspirated air is humidified and heated. The lower airways start with the trachea, which has a cartilaginous (albeit flexible) wall. The trachea divides into two bronchi, which lead to the left and the right lungs, and these tracts continue to divide into smaller airways, bronchiole, for approximately 23 generations (6). Gas exchange takes place in the most peripheral parts of the lungs, the alveoli, where oxygen and carbon dioxide permeate through cell

membranes between the alveoli and surrounding capillaries (2,7). See Figure 1 for an outline of the lower respiratory airways.

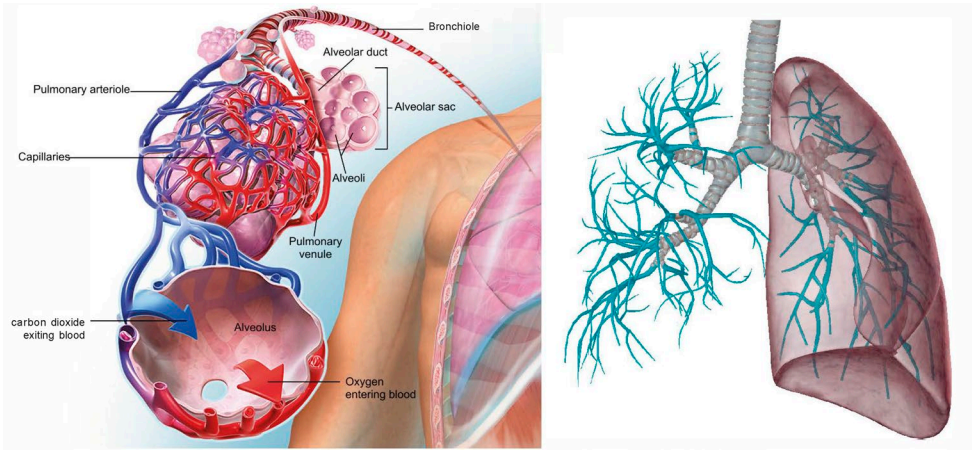


Figure 1. A general outline of the lower respiratory airways with bronchiole and alveoli in more detail. Lung anatomy (8). Reproduced with permission

The immune system in respiratory airways works both mechanically and chemically. The walls of the upper airways and the bronchi are lined with mucosa and contain cilia, whose regular movements assist in clearing inhaled particles, including viruses and bacteria, from airways (2). In the distal airways and alveoli, white blood cells like lymphocytes and leukocytes fight lung infections together with macrophages that engulf foreign matter. These cells are eventually transported to lymphatic cells or to the terminal bronchioles where they—together with mucus—are cleared from the peripheral airways (7).

Respiratory muscle function

When respiratory muscles expand the thorax, ambient air flows into the lungs because of reduced pressure in the thorax compared to the atmosphere. When the muscles relax, elastic forces in lung tissue and the thorax reduce the volumes, which increases intrathoracic pressure, and air is exhaled (7). Furthermore, during respiration, a reflex of the pharyngeal dilator muscles stabilises the pharynx and prevents collapse (2,9). The prime inspiratory muscle is the diaphragm, with the addition of the external intercostals. The diaphragm is innervated by the phrenic nerve (C3-C5). During exertion—or in disease—additional accessory muscles like the sternocleidomastoids, scalenes, serratus anterior, pectoralis major and minor, trapezius, and erector spinae may also be activated. These accessory muscles normally have other functions, such as stabilising the vertebral column, and they are more easily exhausted than the primary respiratory muscles. During forced

expiration, contraction of the abdominal muscles and the internal intercostals help to increase intrathoracic pressure and subsequently enhance expiration. Abdominal muscles are also active in coughing (7).

Infant respiratory systems

Humans typically have complex compensatory functions for regulation of respiration in health and in disease. Nevertheless, respiration is more vulnerable in infants below 12 months than in older children and adults, younger infants and pre-terms being especially vulnerable (10). Reasons for this are diverse but mostly connected with the respiratory system being under development, having different proportions, and its regulation being more fragile (11-13). Below, examples of these different aspects are highlighted.

Both alveoli and the blood vessels in the lungs continue to develop in numbers as well as size during the first years of life (14,15). This has a great impact on the regional distribution of ventilation and perfusion, that suffice in health but may easily become insufficient if parts of the lungs and alveoli responsible for gas exchange are obstructed. The lumens of the smaller airways in infants are sometimes no more than 1mm in diameter, and they are, moreover, more susceptible to collapse than the airways of older persons (16). The high compliance of the airways causes increased airway resistance, and stabilising cartilage does not reach its final distribution until after two months of age, after which it continues to grow in thickness (17). Additionally, nasal breathing causes increased airway resistance, which especially affects infants up to 6 months of age, who primarily only breathe through the nose (18).

The respiratory mechanisms of the chest also contribute to the narrow margins for infants who experience an increased respiratory load. Infants' ribs are more horizontal than they become later in life, and the sternum is more elevated. Because of this, the ability to expand the chest laterally and cranially is limited. Furthermore, infants have a more compliant—non-stabilised—chest wall than adults, which can compromise respiration when respiratory muscles exert more force. Movements of the chest may thus become inefficient, and result in high energy costs (19,20).

Respiratory muscle function in infants is more susceptible to fatigue than for older persons, mainly because of the following two reasons: first, infants basically use only the diaphragm for breathing, and not the intercostals or the auxiliary muscles on which adults rely when extra resources are needed. Second, infants' diaphragms are more easily exhausted, as there is a smaller proportion of endurable type 1 fibres. At full-term birth, the diaphragm only consists of 25% type I fibres, increasing to 40% at three months age. Not until the age of seven or eight months does the fibre composition resemble an adult's 50–55%. Infants are thus easily fatigued when

compensating for increased metabolism (21). In case of infection, metabolic costs increase and the relatively low oxidative capacity in infants is further challenged. They are especially vulnerable in this respect, as infants typically have a higher oxygen consumption/kg body weight than adults and also have smaller glycogen supplies in muscle tissue (12,22).

Acute lower respiratory tract infections (ALRI)

In this thesis the focus is on infants who are afflicted by acute lower respiratory tract infections (ALRI), such as bronchiolitis or pneumonia. ALRI can have quite serious impacts on infants, along with other risk groups (elderly or adults with comorbidities). Older children and adults may certainly also be affected by ALRI, but they normally experience fewer symptoms (23).

Viral infections

The respiratory syncytial virus (RSV) is responsible for a majority of ALRI in infants, although there are other agents as well; for example, human rhinovirus, human bocavirus, human metapneumovirus, influenza A and B viruses, and parainfluenza viruses (24). Bacterial infections are not as common in infants as viral infections (25). The yearly RSV appears in the winter season in the Northern hemisphere. The virus is easily transferred either directly via drops into the mucosa in the eyes or nose, or by inhaled aerosols; or indirectly by touching surfaces and subsequent mucosa infection. Frequent handwashing and social distancing may reduce the spread of the infection. Parents of new-born infants are also commonly recommended to avoid indoor crowds and to restrict their contact to the closest family circle. It is assumed that after the age of two years, most people have been infected with RSV at least once, and infections may be repeated several times after that. The most severe symptoms of RSV, however, are experienced in younger infants or in individuals with comorbidities, as is the case in ALRIs in general (23, 25,26).

Epidemiology and clinical manifestations

Most infants with acute respiratory infections experience nose blockage and sometimes middle ear infection (otitis media). A minority of infants, 1-3% of the infants below 24 months of age, experience severe infection and need hospital care. Although this is only a small proportion of all infants, the individuals who require hospitalisation every year still constitute a very large group in society. ALRI is the most common reason for infant hospitalisation worldwide, which greatly affects

society resulting in high costs for families and health care systems, as well as the suffering it causes to individuals and families (1). In countries with lower socioeconomic levels this condition can be fatal, but in richer countries deaths are rare (23,27). Additionally, it is known that young age and premature birth may cause more severe symptoms, and male sex, exposure to tobacco smoke, hereditary backgrounds including asthma or atopic disease, and low socioeconomic status are positively correlated with infections leading to hospital admittance (1,23).

Bronchiolitis is an inflammation of the smallest airways, the bronchiole, in the respiratory system following an infection. Clinically, the symptoms and management of bronchiolitis resemble that of pneumonia, where the alveolar spaces and interstitial tissues (parenchyma) of the lungs are affected. The term bronchiolitis is still used extensively, even though an increasing number of sources advocate that it is normally not clinically relevant to define the exact location of the infection, which may require chest radiographs (23,25,26,28). In this thesis both conditions are referred to as ALRI.

Due the immunological response to infection, there is an inflammatory process resulting in mucosal oedema and increased mucus production, which reduce airway lumens. Smooth muscle hyperreactivity coincides (29), and wheezing or crackles may be auscultated (30). Excess mucus clogs the small airways which may reduce lung volume and the area for gas exchange: when alveoli distal to the clogged bronchiole collapse there is a mismatch in ventilation–perfusion. Following reduction of lung volumes and disturbed gas exchange, the respiratory pattern alters to compensate, initially through an increased respiratory rate. This increases the muscular work involved in maintaining adequate ventilation. The increased work of breathing can often be inspected as retractions in the chest wall and as nose flaring in severe cases. Typical retraction locations in the chest are illustrated in Figure 2.

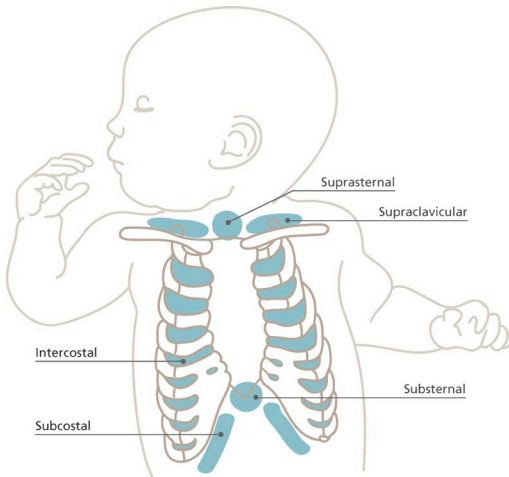


Figure 2. Typical locations of retractions in infants' chest. Illustration: Katarina Jandér

Dehydration may follow, as infection increases the demand for fluid, while feeding becomes more difficult because of the high respiratory rate (31). Unstable breathing or apnoea is also common (32). Furthermore, the ability to cough and efficiently clear mucus may be impaired due to viscous secretions and muscle fatigue. An infants' condition can deteriorate quickly, leading to respiratory failure, requiring treatment at an intensive care unit (ICU) (23, 30).

The impact of ALRI on infants may vary, depending on personal and environmental factors. The World Health Organization (WHO) has modelled the relationship of different aspects of the manifestation of impairments in health conditions in the International Classification of Functioning, Disability and Health (ICF) model (33). The model has been described as "a biopsychosocial model designed to provide a coherent view of various dimensions of health at biological, individual, and social levels" (34 p. 1101). Interventions and assessments may also be performed and described on these different levels (33). Components of this multidimensional relationship in infants with ALRI are suggested in Figure 3.

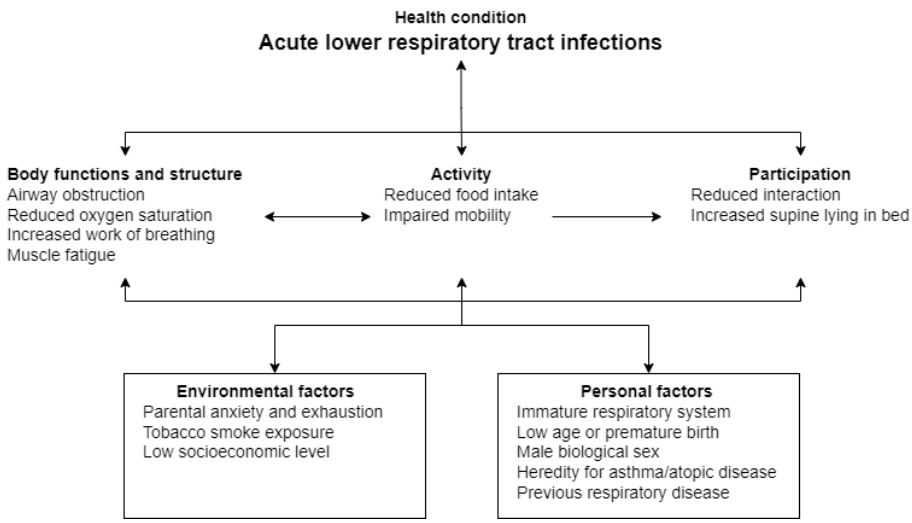


Figure 3. Application of the ICF-model (33) on infants with acute lower respiratory tract infections

We can see from this model that symptoms, disability and functioning are "viewed as outcomes of interactions between health conditions and contextual factors" (33 p.10).

Treatment of ALRI

As many infants with ALRI are seriously impacted, many treatment methods have been tried over the years. These treatment methods have been used to reduce symptoms, to cure the infection, or to prevent infection.

General treatment methods

To date, no definite consensus has been established on a general treatment strategy for infants hospitalised with ALRI, but supportive care, such as hydrogenation and oxygen supply, is most often advocated in guidelines (25,28,30,35-37). Moreover, high flow nasal cannula (HFNC) are frequently used (38), and some infants are treated with continuous positive airway pressure (CPAP), or may require care in an ICU (39).

Different medical treatments such as antibiotics, corticosteroids, bronchodilators, and antivirals have been attempted, and are not generally recommended (25,28). Inhalations of 3% hypertonic saline (HS), with the proposed effect of reducing mucosal swelling and enhancing mucus transportation, has been evaluated extensively with conflicting evidence as to its effect (40, 41). Vaccinations against RSV have been tried without success, but methods are still under development (42).

Physiotherapy treatment methods

In many countries, different physiotherapy treatment modalities are used in infants with ALRI in addition to supportive care (43-53). The main aims of these treatment methods are to support evacuation of bronchial secretion and increase gas exchange, thus also reducing the respiratory distress following an increased work of breathing. The aim of physiotherapy treatment has also been to reduce time to clinical stability or reduce the duration of a hospital stay (46,52).

In most described methods, infants lie supine in bed and the PT applies manual pressure on their chest in different ways. Examples of these methods are: percussions (46,47,49,54); vibrations (46-49,51); the forced expiration technique (44,52); the slow expiration technique (43,46,50); and thoracic compressions (46,48,49). Furthermore, inducing cough by briefly applying manual pressure on the child's trachea or tickling the suprasternal notch is also commonly described (12,44,50,52,53). Another frequently described method is postural drainage, which is performed by placing the infant in different positions in the bed, often with their head down (46,47,49,51). Additionally, using an inflatable vest to perform oscillating compressions of the chest wall has been suggested (53).

Physiotherapy treatment tradition in Sweden

In Sweden, physiotherapists work independently and normally choose treatment methods depending on their own professional judgement, which is based on relevant scientific evidence and personal experience (55). When this research project began, there were no descriptions to be found for physiotherapy treatment methods specific to infants with ALRI in Sweden. An outline of general treatment methods in respiratory care are displayed in a textbook about physiotherapy for children and adolescents (56). The physiotherapy treatment that is generally used for children with respiratory difficulties in Sweden appears to be influenced by physiotherapy treatment for children with CF. That treatment changed in the 1980s in Sweden, from drainage positions and percussions to physical activity in combination with the forced expiration technique (57), and it also includes alterations in body position (58). This treatment programme has excellent outcomes for this patient group, even on a long-term basis, and is used both in the acute phase of CF and as a maintenance treatment (49,59-61).

Minimal handling versus changes in body position and physical activity

Some guidelines recommend 'minimal handling' as part of supportive care for infants with ALRI, which may have impacted many clinicians (62-64). It is unclear, however, what rationale underlies this recommendation. In contrast, as opposed to merely lying supine, there is evidence pointing to increased oxygen saturation and reduced work of breathing for infants with ALRI when they are placed in a prone position, which has been mostly studied on mechanically ventilated and pre-term infants (65,66). Nursing pre-term infants with either the head of the bed elevated or prone with the head and thorax in an elevated position has also had a favourable effect on oxygenation (67,68). Additionally, mucus transportation is greater in the dependent lung compared to the non-dependent lung when side-lying in adults with CF, which Lannefors and Wollmer hypothesise is due to high air flow and mechanical squeeze (69). It is not clear if this is also valid for infants, although if mucus transportation is increased by mechanical pressure on the chest wall, infants might benefit even more from these changes in position since they have a more compliant chest. Ventilation distribution in infants is reported to be more similar to that of adults than was previously believed, with increased ventilation in the dependent lung (and not the reverse) (70,71). Moreover, general physiological evidence and observations support changes in body position and physical activity to increase lung volumes, enhance mucus transportation, and increase oxygenation (2,7,72,73).

Lack of evidence

As is described earlier, physiotherapy treatment is commonly used as an addition to general supportive care in treating infants with ALRI, although this is sometimes questioned or is not recommended in treatment guidelines. The general terms

‘physiotherapy’ or ‘chest physiotherapy’ are often used, and there are uncertainties about what specific physiotherapy treatment methods, if any, should be selected and, if so, to which patients they should be applied (44,74-78). The evaluations of the effects and adverse effects of these different methods vary and ascertaining the most efficient method is difficult. Confirmational studies are still needed in many cases. Some therapies have been rejected, although founded on an under-powered study and the judgement to reject them somewhat premature (52); and some studies have been carried out with only a small number of participants, which requires cautious interpretation of results (47,50). In a Cochrane review from 2005 (79) “chest physiotherapy” is not recommended for these infants. The review has been updated several times, and in the most recent version from 2016 (78), forced passive expiratory techniques in particular are not recommended, nor are vibration and percussion in combination with postural drainage, as no beneficial effects had been detected. On the other hand, adverse effects such as vomiting, bradycardia with desaturation, and transient respiratory destabilisation are reported, and these methods are associated with rib fractures. Slow passive expiratory techniques are questioned because there are only few studies covering their efficacy and there are questions regarding these studies’ designs. These views on slow passive expiratory techniques, moreover, have been debated (43,76).

In the light of the diversity of treatment methods and of study design, more evidence on treatment strategies is needed to increase understanding about how to manage the often severely affected infants and their families in hospitals.

Rationale

This doctoral project was initiated because of a perceived gap between evidence in the scientific literature, treatment guidelines, and the clinical management of infants with acute respiratory infections in hospitals.

At the time when this doctoral project began, ‘chest physiotherapy’ for infants with bronchiolitis was not generally recommended, for example, in a website that guides health care professionals (Internetmedicin.se). These recommendations were mainly based on a Cochrane review evaluating published studies on this subject (78). The generalisability of that review and of much published research on so-called ‘chest physiotherapy’ for these patients is problematic, however, because of the great diversity of available PT treatment methods. Treatment methods described in the literature, furthermore, do not resemble treatment methods used in Sweden, which is why Swedish physiotherapists experience difficulties in interpreting and relating to the prevailing international guidelines. The recommendation to refrain from treatment and to employ ‘minimal handling’ is also difficult to understand. The adverse effects such as vomiting, bradycardia, destabilisation, stress or even rib fractures (78) are not familiar to physiotherapists in Sweden when employing their treatment methods. The panorama of treatment methods used in Sweden for infants with respiratory difficulties was not yet fully understood, and a description of clinical practice in Sweden was lacking. Additionally, the effect of the current physiotherapy praxis in Sweden was not known.

Aims

The overall aim

The overall aim of this thesis was to increase knowledge about physiotherapy treatment in infants with breathing difficulties due to lower respiratory tract infections.

Specific aims

- Explore what physiotherapy treatment methods are being used in Sweden when treating hospitalised infants with acute breathing difficulties due to lower respiratory tract infections. The aim was also to investigate if there are any differences in choice of treatment/s related to background characteristics of the physiotherapists, such as professional experience, gender, type of hospital, and graduation country (Paper I).
- Thoroughly describe a randomised control trial that aimed to compare the effect of an individualised physiotherapy intervention, a non-individualised intervention, and a control group receiving standard care, in hospitalised infants 0–24 months of age (Paper II).
- Address uncertainties concerning the ongoing RCT and determine whether or not the trial was feasible, or what adjustments to the protocol were needed (Paper III).
- Evaluate the effect of a physiotherapy treatment method including frequent changes in body position and stimulation of physical activity compared to standard care for infants aged 0–24 months hospitalised with acute respiratory infections. These interventions were delivered by different health professionals and parents (Paper IV).

Methods

The research process

Complex interventions

The design of the different studies in this thesis has been inspired by the Medical Research Council's (MRC) guidelines on complex interventions (80), which are further explained by Craig et al. (81) and Richards and Hallberg (82). Complex interventions in health care have been described in different ways, and the MRC uses the following definition: "An intervention is conceived to be complex either (1) because of the characteristics of the intervention itself, for example multiple components or mechanisms of change, and/or (2) because how the intervention generates outcomes is dependent on exogenous factors, including the characteristics of recipients, and/or the context or system within which it is implemented" (83 p. xxi). Adhering to this definition, much clinical research in health care and in the social sciences can be described as complex in different ways, and the model has been extensively used by researchers in nursing (84). In the MRC framework, theory modelling and change is acknowledged throughout the process. Thus, it is also inspired by program theory, which includes building a theory or a model of how an intervention is expected to lead to likely effects and under what conditions (85).

The MRC emphasises that it is important to acknowledge and to structure the research process in different steps in order to produce valid results. Other sources stress the importance of reducing research waste (86, 87). See Figure 4 for an outline of the different steps of the MRC process.

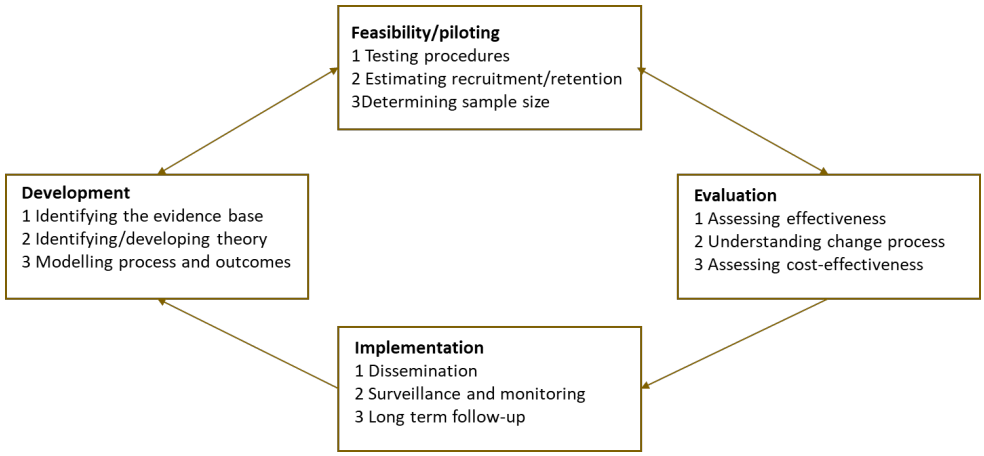


Figure 4. The research process in complex interventions as described by the MRC (80). Used by kind permission of the Medical Research Council, as part of UK Research and Innovation

In Figure 5, this thesis' research process has been merged into the figure from the MRC. This figure was created to visualise the process that is elaborated below.

Development

In the Development step, we reviewed scientific literature on different physiotherapy treatment and evaluation methods being used for infants hospitalised with acute respiratory infections. We also conducted a survey study to explore methods being used in Sweden. When designing the survey, I started by reviewing literature on survey design and interviewed the system administrator of the online survey tool Sunet Survey at Lund University. Using examples from the first literature review on treatment and evaluation methods combined with personal clinical experience, I drafted an initial survey. The questions with answer alternatives were then discussed by a panel of eight physiotherapists, some with expert knowledge and experience in the area and some with more general paediatric or respiratory knowledge. Using input from the panel, I constructed the final version of the survey that was used in the study.

Physiotherapy treatment methods that are used in Sweden for this patient group had not been previously described in scientific literature. These findings are reported in Paper I. Using the results from the literature review and the survey, we decided on what variables to assess in the RCT, and we collaborated with paediatric staff in order to make the assessment protocol valid and easy to use. At this stage we also developed printed information material for parents, which were translated to the languages most commonly used in the hospital—Arabic, Persian and English—based on figures from patient administrative records on the use of interpreters in the paediatric wards at that time.

In the research process, we returned to the Development step a few times when adjusting assessment protocols according to useful feedback from the staff. We enhanced the information we were providing to parents by producing short instruction videos as a complement to the printed material in order to make the material easier to understand and to follow. That is why the arrow between the Development and the Implementation boxes points both ways in Figure 5. The printed material and the videos also served as instructions to the staff who initially trained the parents.

Furthermore, in a study protocol (Paper II) we thoroughly described the process of participant enrolment, as well as interventions, outcomes, and analyses planned for the RCT. This is generally regarded as important to enhance research transparency and replicability (88).

Feasibility/piloting

Early in the Feasibility and Piloting step of the RCT, before starting the main trial, we made a small pilot evaluation (unpublished material) in order to assess the minimal clinically important difference and estimate the sample size. In continuing the feasibility and piloting work, we designed the feasibility study as an internal pilot (Paper III) with the aim of analysing and possibly optimising the study design. In this step, according to the MRC's guidelines and those of others (80, 89), the researchers test the procedures, the outcome measures, estimate recruitment and retention, and examine eligibility criteria. The feasibility study enabled us to make use of data which was already collected and continue to evaluate the effect of the physiotherapy treatment for this patient group.

Evaluation

Building on the previous steps in the research process of complex interventions, we continued to the Evaluation step. In Paper IV, we evaluated the physiotherapy treatment that was identified in Paper I, comparing this treatment to 'standard care'. The procedures and outcomes had been analysed and partly adjusted after Paper III, although they still mainly followed the originally design (thoroughly described in Paper II).

Implementation

The Implementation step was initiated by sharing the printed information and the videos that describe the two different interventions that has been evaluated in Paper IV. This material was used for instruction in the Paediatric emergency departments at the study hospitals during the unexpected and high rate of hospital admittance for infants with ALRI during the autumn 2021. Skåne University Hospital's Department of Communication prompted distribution of the instructions and assisted in spreading them via the hospital's internal web pages. This was well-received by the management and staff as helping to manage the flow of infants

needing inhalation therapy or those who were being discharged but were still affected. Following discussions on social media, the printed material and the videos were also made available for physiotherapists in Sweden who work with infants with ALRI, serving as examples of interventions. They were also distributed by email to a network of physiotherapists in southern Sweden. The planned submission of Paper IV for publication, together with the printing of this thesis will further disseminate the findings.

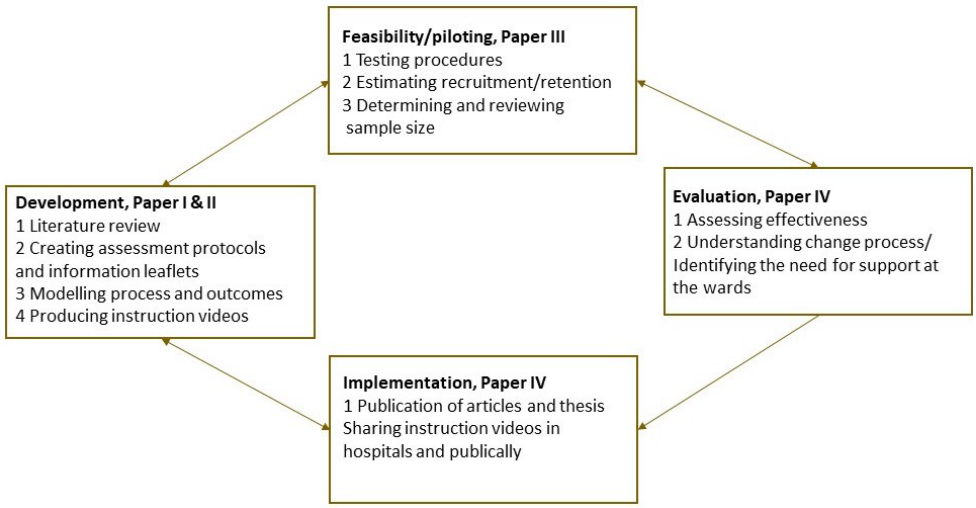


Figure 5. Adaptation of the MRC figure (80) for the reseach process of this thesis

Study design

Different study designs in this thesis are displayed in Table 1.

Table 1. The design of the studies in the thesis.

Study	Design
Paper I	Digital survey. Prospective explorative design
Paper II	Study protocol. Description of an RCT* (Paper IV)
Paper III	Feasibility study. An internal pilot study of an ongoing RCT*
Paper IV	Clinical RCT* with individual randomisation and parallel groups at two sites

*RCT, Randomised controlled trial

Data collection and study population

Paper I

In this study, we investigated what different treatment methods Swedish physiotherapists use when treating infants with respiratory infections in hospitals, and constructed a digital web-based survey, Survey&Report (Artisan Global Media). We asked informants about their use of different physiotherapy treatment methods and outcome measures concerning infants in hospitals with acute breathing difficulties due to, for example bronchiolitis, RSV, and pneumonia.

The survey was distributed in April and June 2017. A link to the survey was posted on two different closed Facebook groups for physiotherapists in Sweden and on the websites for the departments of respiration and paediatrics in the professional union "Fysioterapeuterna". We also distributed the link by email directly to physiotherapist working in paediatrics at hospitals in southern Sweden and to physiotherapists working with paediatric heart diseases, known from previous collaborations. Additionally, it was sent by email to 21 contact nurses at hospitals in Sweden where there are children's wards, with a request to forward the link with the survey to the relevant physiotherapists working in the hospital's children's ward. A reminder with the same link and information was posted two weeks after the first distribution.

After removing the blank submitted forms and the ones from physiotherapists not having treated infants in the age group of 0–24 months with respiratory infections in the last two years, 52 completed surveys remained to be analysed. The process of handling the submitted forms is demonstrated in Figure 6.

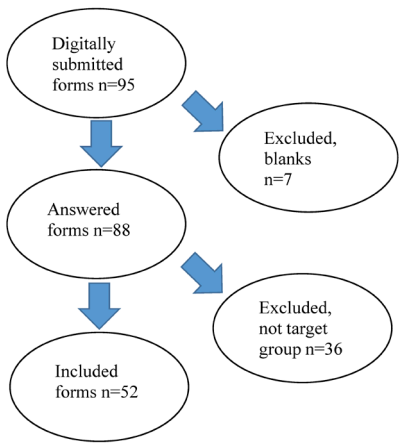


Figure 6. Flow chart of the submitted forms in the survey, Paper I.

An overview of informant characteristics is displayed in Table 2.

Table 2. Background information of the informants in Paper I, n=88

	n (%)
Gender	
Woman	84 (95.5)
Working place[a]	
Local hospital	42 (47.7)
County hospital	32 (36.4)
Treated target group last 2 years	
1-6 times	10 (11.3)
>6 times	42 (47.7)
Never	36 (40.9)
Graduation country	
Sweden	83 (94.3)
Other Scandinavian	1 (1.1)
Outside Scandinavia	4 (4.5)
Years graduated[b]	
Median (min-max) years	17 (1-49)

[a]n=74, [b]n=87

Paper II

Paper II is a study protocol describing the RCT, and no data was collected for this paper. To illustrate the procedure of the RCT, we used the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) flow chart, which is displayed in Figure 7.

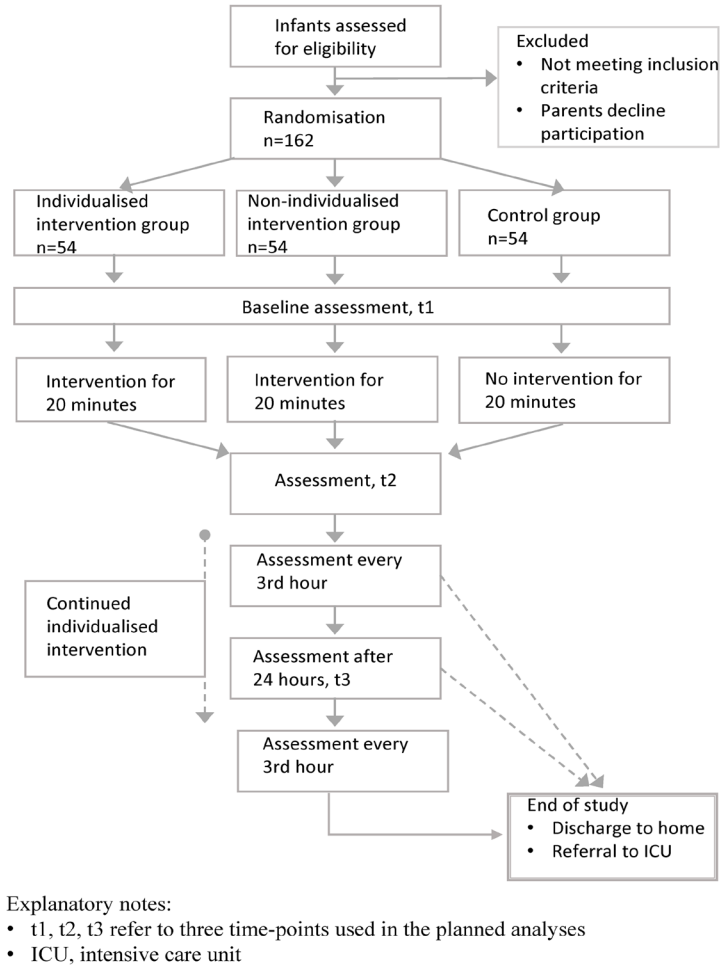


Figure 7. The SPIRIT flow chart of the RCT as described in Paper II.

Paper III

In Paper III, the feasibility study, analyses were conducted on data from 91 participants enrolled in the clinical RCT between November 2017 and April 2020 at a paediatric ward in Skåne University Hospital in Malmö, and between April 2018 and April 2020 at a paediatric ward in Centrallasarettet in Växjö. Both hospitals are situated in southern Sweden, approximately 200 km apart. The hospital in Malmö has a catchment area of about 500,000 inhabitants, and the one in Växjö has a catchment area of about 100,000 inhabitants. The participant flow is displayed in Figure 8.

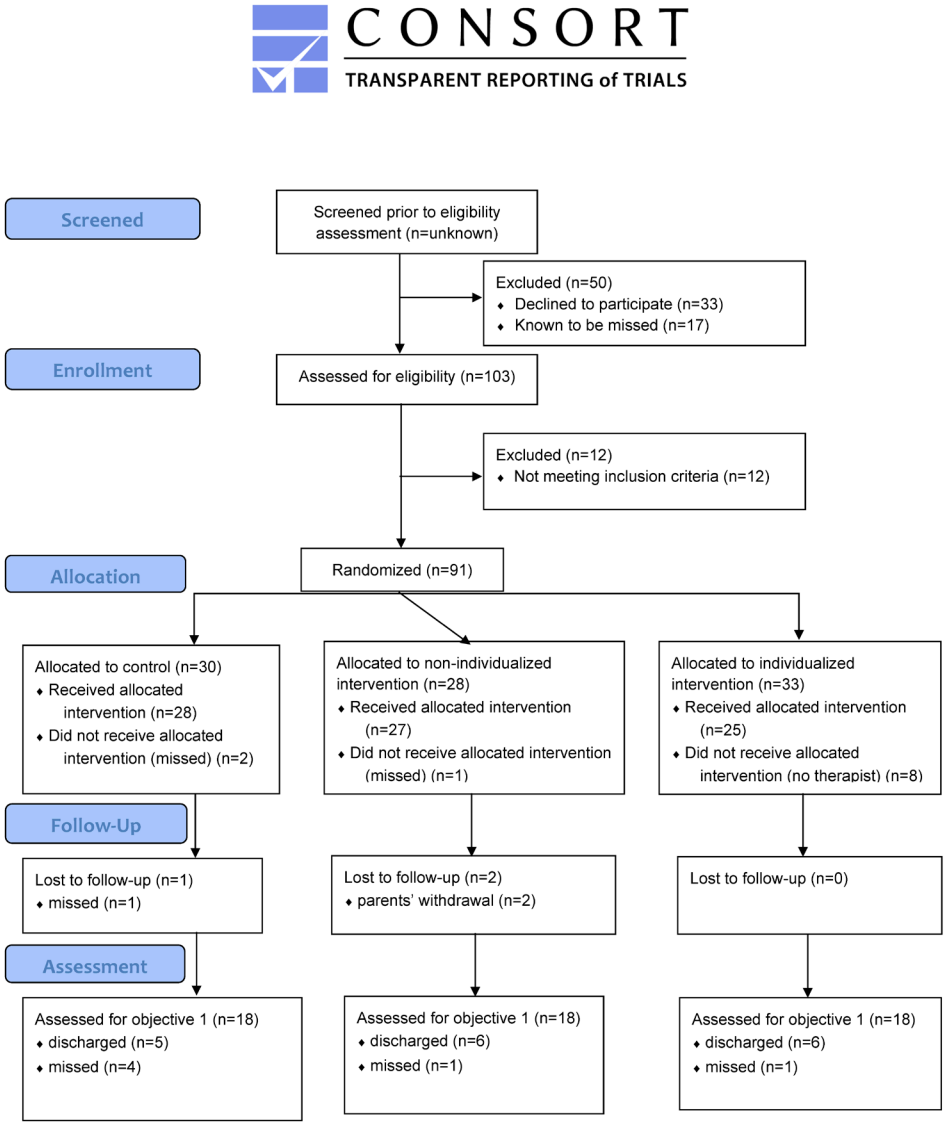


Figure 8. A flow chart of participant enrollement in Paper III.

The baseline characteristics of the participants in Paper III are displayed in Table 3.

Table 3. Baseline characteristics of the included participants, n=91

	Control group n=30	Non-individualized intervention n=28	Individualized intervention n=33	Total sample n=91
Gender n (%) male/female	21 (67.7) /9 (30.0)	15 (54.6) /13 (46.4)	23 (69.7) /10 (30.3)	59 (64.8) /32 (35.2)
Age median (min–max) months	3.3 (0.2–22.4)	2.9 (0.5–22.2)	2.1 (0.3–23.7)	2.5 (0.2–23.7) IQR* 1.2; 6.9
Infectious agent n (%)**				
RSV***	18 (60.0)	19 (67.9)	22 (66.7)	59 (64.8)
influenza	2 (6.7)	3 (10.7)	4 (12.1)	9 (9.9)
other	1 (3.3)	3 (10.7)	3 (9.1)	7 (7.7)
negative	5 (16.6)	1 (3.6)	1 (3.0)	7 (7.7)
missing	5 (16.6)	2 (7.1)	4 (12.1)	11 (12.1)
Heredity atopic disease n (%)				
asthma	10 (33.3)	10 (35.7)	12 (36.4)	32 (35.2)
other (allergies, eczema etc)	7 (23.3)	5 (17.9)	11 (33.3)	23 (25.3)
none	10 (33.3)	10 (35.7)	3 (9.1)	23 (25.3)
missing	3 (10.0)	3 (10.7)	7 (21.2)	13 (14.3)
Passive smoking exposure n (%)				
no	22 (73.3)	21 (75.0)	17 (51.6)	60 (65.9)
yes	5 (16.6)	3 (10.7)	8 (24.2)	16 (17.6)
missing	3 (10.0)	4 (14.3)	8 (24.2)	15 (16.5)

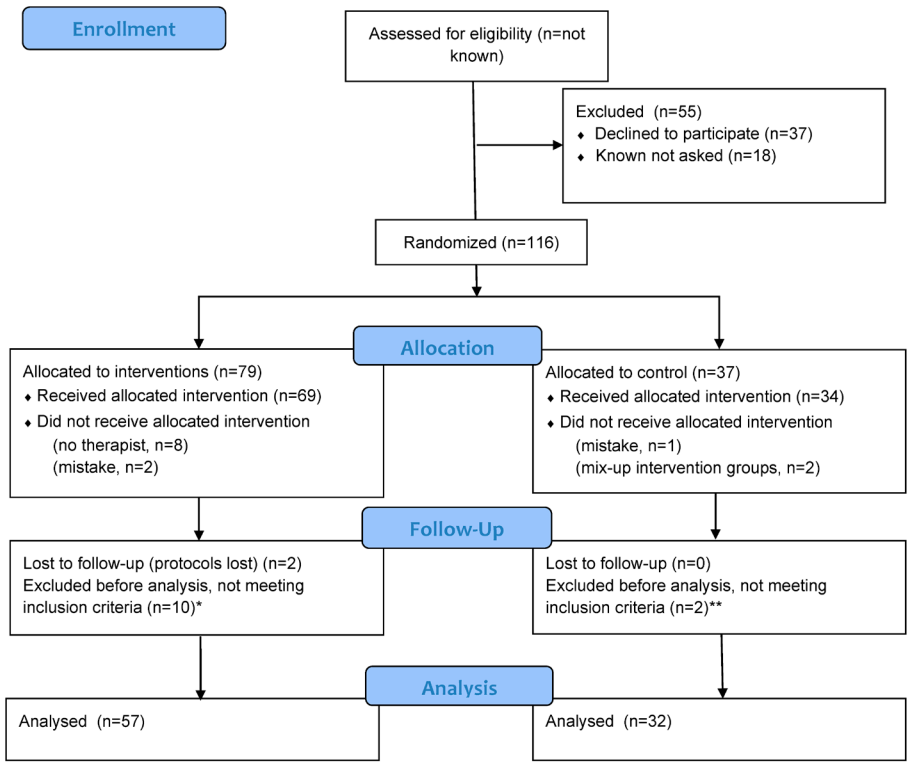
*IQR=Interquartile range, **two individuals had positive tests for both RVS and influenza, ***RSV=respiratory syncytial virus

Paper IV

For Paper IV, the report from the clinical RCT, a total of 116 participants were enrolled. The data collection continued after the time allotted for the feasibility study (Paper III), and data for Paper IV was collected from either November 2017 (Skåne University Hospital in Malmö) or from April 2018 (Centrallasarettet in Växjö) to November 2021. Not all enrolled infants met the inclusion criteria, and 104 participants remained after excluding those who had been enrolled by mistake. Final analyses were conducted on 89 participants who met the inclusion criteria, who received the correct interventions according to randomisation, and for whom the correct protocols were collected. Participant flow is displayed in Figure 9.

CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram



* n=9 included after more than 24 hours at the ward; n=1 premature
** n=2 included after more than 24 hours at the ward

Figure 9. Flow chart of participants in Paper IV.

Demographics and characteristics of the 104 participants who were enrolled correctly are displayed in Table 4. The dropouts are individuals who were included correctly but were omitted after randomisation (for different reasons; see Figure 9).

Table 4. Demographics and characteristics of the participants, n=104

	Control n=32	Intervention n=57	Dropouts n=15
Age in months			
-median (min–max)	3.55 (0.56–22.37)	2.53 (0.26–23.65)	1.02 (0.20–5.10)
Girls n (%)	10 (31.3)	24 (42.1)	5 (33.3)
Boys n (%)	22 (68.8)	33 (57.9)	10 (66.7)
Heredity asthma/atop disease n (%)	18 (56.3)	37 (64.9)	6 (40.0)
Tobacco smoke exposure n (%)	5 (15.6)	11 (19.3)	1 (6.7)
RSV* n (%)	21 (65.6)	40 (70.2)	10 (66.7)
Early RSV if RSV**	14 (43.8)	30 (52.6)	1 (6.7)
Oxygen saturation[a]			
-median (min–max)	96 (85–100)	96 (85–100)	94 (88–100)
Heart rate[a]			
-median (min–max)	151.5 (72–210)	151.0 (42–194)	153 (68–190)
Respiratory rate[a]			
-median (min–max)	50.0 (29–218)	52.0 (27–147)	51 (32–170)
Wang total score [b]			
-median (min–max)	6 (2–11)	6 (0–10)	
-mean (SD)	5.79 (2.56)	5.70 (2.46)	
Supplemented oxygen[b] n (%)	9 (28.1)	29 (50.9)	
HFNC*[b] **n (%)**	5 (15.6)	20 (35.1)	
Gastric tube feeding first 24 hours n (%)	10 (31.3)	20 (35.1)	
Days hospitalised			
-median (min–max)	2.76 (0.47–10.44)	3.00 (0.52–6.86)	2.03 (0.48–5.60)

*RSV, infected with the Respiratory syncytial virus

**Defined as less than 7 days since the start of coughing or severe infection for those infected with the RSV, at admission to the ward

[a] At admission to the ward

[b] At baseline

***HFNC, High flow nasal cannula

Interventions

Interventions in the randomised controlled trial are described in detail in the study protocol (Paper II). They were selected based on the results in the survey study (Paper I), as the most common physiotherapy interventions used by physiotherapists treating infants with respiratory infections in Sweden. All parents in the intervention groups in the RCT were encouraged to perform interventions regularly throughout the day, after instructions from physiotherapists or the nursing staff. This is also routine praxis in Swedish hospitals.

The individualised intervention

The individualised intervention was performed by a physiotherapist at least once daily. The physiotherapist lifted the infant up in their arms and placed the infant in different body positions in their arms with firm support while bouncing on a large ball for approximately 20 seconds in each position. The physiotherapist also stimulated physical activity by placing the infant in a prone position and in other ways encouraging active movements of the arms and legs. They also passively moved the infant's arms and legs and supplied thoracic compressions. Furthermore, they could administer inhalations and manual cough support to the infant's belly and chest. The physiotherapist may additionally have suggested other treatments, such as different inhalations or CPAP. Examples of body positions and movements in the intervention are demonstrated in Figure 10. The written information given to the parents is supplemented in Appendix 1 together with links to a video demonstrating the individualised intervention.

The video is also available through the following link:
https://players.brightcove.net/3193745440001/b859b2ab-6e32-4a70-a0dd-ee8b2ca7bb94_default/index.html?videoId=6278327570001

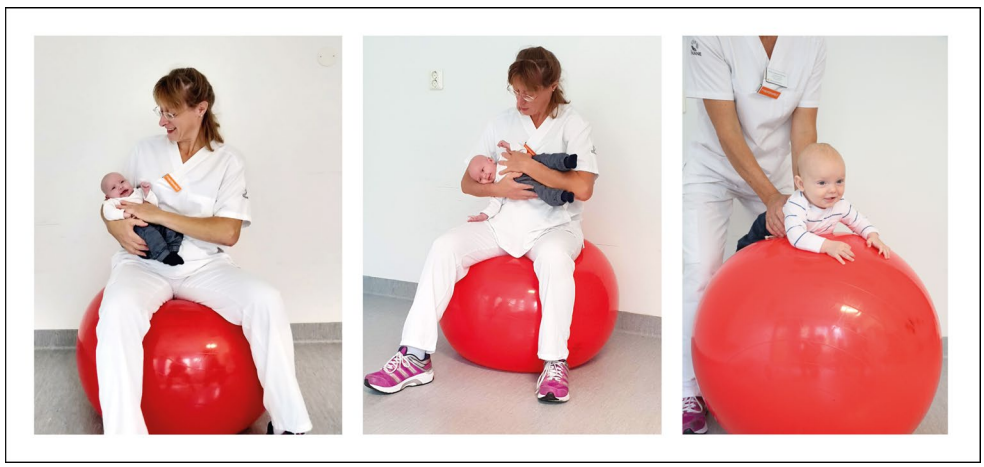


Figure 10. Examples of movements in the individualised intervention. Photos of the infants are displayed with written consent from guardians. The infants pictured were not part of the study population.

The non-individualised intervention

The non-individualised intervention was performed by the nursing staff at the ward at least once—shortly after inclusion. They lifted the infant up in their arms and made frequent changes to body position, mainly out bed, moved the infant's arms and legs, and administered manual cough support on the belly and chest. This standardised intervention can be described as a reduced version of the individualised

intervention, where the large ball was not used, and possible inhalation therapy was administered only in the upright position and not during frequent position changes while being held. The intensity of the treatment was also typically reduced, as staff only had to perform the intervention once, but they could choose to repeat it. The written information made available to parents is supplemented in Appendix 2 with links to a video demonstrating the non-individualised intervention.

The video is also available through the following link:
https://players.brightcove.net/3193745440001/b859b2ab-6e32-4a70-a0dd-ee8b2ca7bb94_default/index.html?videoId=6276714556001

The standard care

All participants received basic standard care at the wards without limitation. The participants in the intervention groups were given extra treatment in addition to standard care, which the control group was not. The standard care at the wards consisted of information to parents about the importance of fluid intake for their infant, oxygen supplementation, nose drops and suctioning, HFNC, inhalations, fluid supplementation, and analgesics, according to patient need.

Outcome measures

Answer options and free text

In the survey (Paper I), informants reported on their choice of treatment and evaluation methods. Closed questions with listed answer options were mainly used, but it was also possible to answer in free text. Some additional questions on details were displayed if informants chose certain answers. Background characteristics of the informants were also collected to evaluate the relationship between their choice of treatment and their graduation country, years since graduation, frequency of treating the patient group, gender, and type of hospital. The entire survey is displayed in Swedish in Appendix 3.

The original outcome measures in the RCT

For a clear description of the outcomes and the procedures in the RCT we used The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) check list (90) in the study protocol (Paper II), as well as the SPIRIT figure (see Figure 11). These documents are recommended to enhance the transparency and completeness of trial protocols (91), which is in line with our intent to clearly describe and openly display all procedures in the RCT.

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT	$-t_1$	0	t_1 before intervention	t_2 after 20 min	t_3 at hour 24	t_x end of study
ENROLMENT:	X					
Eligibility screen	X					
Informed consent	X					
Naso-pharynx test		X				
Allocation						
INTERVENTIONS:						
Individualized intervention			→	→	→	→
Non-individualized intervention			→	→	→	→
Controls (no intervention						
ASSESSMENTS:			→	→	→	→
	X					
Demographics*			X	X	X	
Primary outcome:						
Clinical index			X	X	X	
Secondary outcomes:						
Wang respiratory score						
Other vital signs**						
Parents' report***			X	X	X	
Length of hospital stay			X	X	X	
Lung complications****						X
						X

age, gender, type of viral agent, heredity for atopic diseases, passive smoking habits, duration of the infection
****heart rate, body weight***
*****General condition, food intake***
******possible referral to an intensive care unit***

Figure 11. The SPIRIT figure of enrolment, interventions, and RCT outcomes as described in Paper II.

Outcome measures in the feasibility study

In the feasibility study (Paper III) we performed descriptive analyses of recruitment, retention, data supply for the primary end point (24 hours), and usability of the primary outcome measure. Furthermore, a safety analysis was conducted by an independent analysis group assessing the risk of harm. The variables in the safety analysis were oxygen saturation, supplemented high flow oxygen, oral fluid intake (% of daily need), supplemented HFNC in relation to body weight, the respiratory rate (in relation to age in months), time from inclusion to hospital discharge, ICU referrals, and deaths.

The final outcome measures in the RCT

Primary outcome

The primary outcome in the RCT as reported in Paper IV is 'time to improvement'. Improvement was defined as any of the following events: reduced total Wang respiratory score (92), ceased use of supplemental oxygen, ceased use of HFNC, ceased use of gastric tube for feeding, or discharge to the home. This item was reported in hours from baseline.

Secondary outcomes

The secondary outcomes in Paper IV are displayed in Table 5.

Table 5. Description of secondary outcome measures in Paper IV.

Item	Mode of measuring	Definition (time)
Oxygen saturation	Pulse oximetry*, probe on the foot, %	Change between baseline and assessment 2 (after 20 minutes)[a]
Heart rate	Pulse oximetry*, probe on the foot, beats per minute	Change between baseline and assessment 2 (after 20 minutes)
Respiratory rate	Manual count during one minute	Change between baseline and assessment 2 (after 20 minutes)
General condition, parents' assessment	NRS[b] 0-10 (10 is worst)	Time to first reduction in scores from baseline (assessed after 20 minutes and every subsequent 3rd hour[c])
Lung complications	yes/no	Referrals to an ICU[d] (at discharge)

*Carescape Monitor B650 (General Electric Company)

[a] For the intervention groups, this item was recorded in an upright position in the arms on assessment 2

[b] NRS, Numeric Rating Scale

[c]except during the night when the parents were asleep, typically between 10 pm and 7 am

[d]ICU, Intensive Care Unit

Assessments in the clinical study

In the RCT, participant characteristics were collected from (i) the nursing staff's interviews with parents (duration of the infection, heredity for atopic diseases, passive smoking habits) and (ii) medical records (gender, age, possible viral agent). To collect the main data, nursing staff made clinical assessments at baseline, after 20 minutes (directly following the first intervention/interval), and every subsequent third hour for the rest of the infant's hospital stay. Assessments were performed by the clinical staff available at that time. In the intervention groups, different members of the staff performed the interventions and made the first two assessments, to reduce the risk of bias.

The protocols for interviews with parents and for clinical assessments were constructed in collaboration with nursing staff, so that they would find them easy to use. Most variables collected were similar to what the nursing staff usually records

at wards, but some items were new, for example, the Wang respiratory score and the parents' scores. All members of the staff were regularly trained in how to perform the assessments, and written instructions were supplied in the study binder at the wards. Moreover, some staff with additional training—'contact staff'—had regular meetings with me and were designated to help their colleagues with the protocol, as well as remind their colleagues about the study. The contact staff also transferred opinions and observations from the wards back to the research group, which was very useful when adapting the protocols and the procedure. See Appendix 4 for the assessment protocols in Swedish.

Additional information was collected from the patient administrative system (time for admittance to and discharge from the ward) and from medical records (saturation, heart rate, and respiratory rate at the time of admittance to the ward, and details about inhalation therapy). Information from paper protocols were manually transferred to a database in the IBM SPSS Statistics 27 Windows (IBM Corporation, Armonk, NY, USA). Protocols from 10 randomly selected participants were double-checked by two of the researchers (ALJ and CH) to validate manual transference quality and correct any possible mistakes.

Statistical methods

Sample size calculations

For the survey study (Paper I) no sample size calculation was performed, due to the explorative nature of the study. In this study, I wanted to collect a wide range of methods and describe the current clinical use as broadly as possible.

In Paper II, the study protocol for the RCT, an initial sample size calculation is displayed. It was performed with the mean detectable difference in the primary outcome, clinical index at 24 hours, to be 2 score points. A previous pilot study (unpublished material) had shown that the standard deviation was approximately 2.8. The power probability for the test was 0.80, and to be able to correct for the three primary tests, comparing the individualised physiotherapy treatment, the non-individualised intervention programme and a control group receiving standard care, the type I error probability in the calculation was 0.016. The sample size calculation showed that 43 evaluable patients were needed in each group. The calculation was performed in SAS Enterprise Guide 6.1 for Windows (SAS Institute Inc., Cary, NC, USA). We expected incomplete observations and drop-outs to amount to about 20%, and accordingly decided to include 162 participants in the study.

For the feasibility study (Paper III) no sample size calculation was performed. Nevertheless, the study was executed when 50 % of the estimated participants in the

RCT had been included. This procedure was decided upon for the safety analysis and described in the study protocol (Paper II).

For Paper IV (the report from the RCT), we made two separate sample size calculations based on the median time to improvement in the data collected during the feasibility study to be 6 hours in the control group and 3 hours in the intervention groups. The minimal clinical difference to be detected was 3 hours, and the planned follow-up time was 48 hours. The power probability was determined to 80%. Sample size calculations were performed in PS Power and Sample Size Program (http://biostat.mc.vanderbilt.edu/wiki/Main/PowerSampleSize). For three groups of equal size, 40 participants in each group were needed for the two intervention groups to be compared to the control group with a significance level of 0.025, resulting in a total of 120 participants. This sample size calculation was displayed in the feasibility study (Paper III). For two groups (with the control group being half the size), and with a significance level of 0.05, 49 participants in the intervention group and 25 participants in the control group were needed. Due to limited participant inclusion, and because the interventions are similar, we decided to analyse the two interventions groups together when reporting the RCT in Paper IV, which means using the latter sample size calculation.

Statistical analyses

In Paper I, we mainly used descriptive statistics such as numbers and percentages. We also used Chi^2 tests at 0.05 level of significance when analysing the use of treatment modalities in relation to years since graduation, type of hospital, and frequency treating the patient group.

In Paper III, the feasibility study, analyses were descriptive, and we used numbers with percentages and medians with min–max and interquartile range (IQR) when reporting the results.

In Paper IV, the report from the RCT, an unadjusted Kaplan-Meier analysis followed by a log-rank test was used for the primary outcome, analysing time to the first improvement from baseline. We then used a Cox regression model, adjusted for age in months, sex, tobacco smoke exposure, heredity for asthma or atopic disease, and early stage of the infection (for those with RSV), to estimate differences between groups and the hazard ratio (HR). Assumptions about independent events and proportional hazards were met. For an overall goodness-of-fit, the Kaplan-Meier and the Cox regression were compared, showing overall similarities.

The analyses of the secondary outcomes in the RCT (Paper IV) were as follows: Independent sample T-tests were used to analyse differences between groups in mean change from baseline to the second assessment in oxygen saturation, respiratory rate, and heart rate. Effect sizes were reported using Cohen's d. The interpretation of effect sizes has been suggested to be: "effect sizes of (a) .20, (b)

.50, and (c) .80 are considered small, medium, or large, respectively" (93 p. 68). The time to improved general condition as assessed by parents was analysed with a Kaplan-Meier analysis, followed by a log-rank test. The incidence of lung complications, defined as referrals to an ICU, in the different arms was recorded. We had planned to use Fischer's exact test to analyse differences between groups, but due to lack of incidences no such analysis was performed.

IBM SPSS Statistics 27 Windows (IBM Corporation, Armonk, NY, USA) was used for the analyses.

Ethics

Ethical considerations

In the survey study, Paper I, there was no personal contact between informants and researchers. Answers were marked and collected electronically. Moreover, the study concerned the choice of professional treatment and evaluation methods, and not sensitive information. It was clearly stated in the adjacent text that it was anonymous, and that no individuals could be identified in the report. Had it not been anonymous, some colleagues may have felt exposed in answering. That is one reason informants were not asked to specify which hospital employed them. Due to the non-personalised link to the survey, there might possibly have been some physiotherapists who filled in the form more than once, deliberately wanting to skew the result. Looking at the spread of answers and the overall adequate number of submitted forms, however, I do not think that is a likely scenario. Overall, I do not see many ethical problems with the survey study.

For the clinical RCT, reported in Paper IV, there were more ethical questions to consider. Most importantly, the study involved small children, under two years of age, who were dependent on their parents and health care providers. They had limited possibilities to express opinions about treatments, and even less so regarding participation in research, which is why special ethical considerations are needed, according to Swedish law (94). Because of this, detailed written information was given to parents, and parents were informed that participation in the study was voluntary and that they could withdraw at any time without the withdrawal affecting the standard care of their child in any way. However, the trial did not involve collecting biological specimens for storage. Furthermore, the interventions were not expected to cause any pain or suffering to the infant. All position changes and movements were performed using close bodily contact with the infant, which is usually experienced as safe and positive for small children. They were regularly observed by nursing staff and parents. Thus, potential negative reactions were documented in the study. The interventions that were evaluated in the study are commonly in use in hospitals in Sweden. There was no anticipated harm or compensation for trial participation. The safety analysis was performed with the intent of examining whether there was any risk of harm in participating in the study. If the analysis group had reported any safety risks, our plan was to have either

changed the protocol or terminated the study. The safety analysis in Paper III found no risk of harm, thus supporting continuation of the full RCT.

Before inclusion, the parent/s received written and oral information about the study and had the opportunity to ask questions about taking part in the study. To approve participation of their child they signed a written consent form. On the consent form, they were also informed that no unauthorised person can access their personal data, and that the data was un-personalised and coded with a trial ID number before analysis.

All data from the studies are archived according to the Swedish Act concerning the Ethical Review of Research Involving Humans to maintain confidentiality.

Ethical approval

The Swedish Ethical Review Authority approved the studies in April 2017 (2017/190). We wrote an addition to this application when the study was expanded to another hospital site. That addition was approved in March 2018.

Throughout the different studies in this thesis, we have been following the principals of Good Clinical Practice, according to the Declaration of Helsinki.

Results

Results of the survey study

The results from the survey study showed that Swedish PTs use a wide variety of treatment methods for infants in hospital due to respiratory problems. In fact, all listed treatment options were selected at least twice. Moreover, the most commonly used methods can be described as active methods and involving the parents. See Table 6 for a display of the informants' choice of answer options.

Table 6. Treatment methods used by Swedish physiotherapists for infants hospitalised with breathing difficulties, listed in frequency order. Informants n =52.

Treatment	Most preferred[a] method, n (%)	Listed[b] method, n (%)	Type[c]
Bouncing on a big ball	25 (48.1)	49 (94.2)	a
Change of positions in arms	22 (42.3)	48 (92.3)	a
Physical activity	21 (40.4)	45 (86.5)	a
Passive arm movements	18 (34.6)	50 (96.2)	a
Passive leg movements	18 (34.6)	37 (71.2)	a
Information to parents	18 (34.6)	52 (100.0)	–
Change of positions in bed	14 (26.9)	46 (88.5)	a
Alternating inhalations with other methods	14 (26.9)	32 (61.5)	–
PEP	7 (13.5)	29 (55.8)	p
Resting position	5 (9.6)	28 (53.8)	p
Light chest compressions	4 (7.7)	26 (50.0)	p
Improving inhalation technique	3 (5.8)	23 (44.2)	p
Cough support, chest or abdomen	2 (3.8)	28 (53.8)	p
CPAP	1 (1.9)	16 (30.8)	p
Manual vibrations	1 (1.9)	11 (21.2)	p
Postural drainage	1 (1.9)	7 (13.5)	p
Prolonged slow expiration technique, PSET	0 (0)	2 (3.8)	p
Advice to health care providers	0 (0)	33 (63.5)	–
BilevelPAP	0 (0)	8 (15.4)	p
Hi Nasal Flow	0 (0)	11 (21.2)	p
Mechanical insufflation-exsufflation	0 (0)	11 (21.2)	p
Percussions on the chest	0 (0)	5 (9.6)	p
Induced/Provoked cough	0 (0)	2 (3.8)	p
Other treatment	0 (0)	2 (3.8)	–

[a] each respondent reported their three most commonly used methods
[b] each respondent selected treatment options, without limitations in numbers
[c] a, active treatment; p, passive treatment; –, neither active or passive

All PTs offered information to the parents, and a great majority used frequent changes in infant body position. The changes in body positions were often performed in combination with bouncing on a big ball with the infant either placed in various positions directly on the ball or held in the arms of an adult sitting on the ball. Several informants also commented that they selected treatment methods depending on the situation and the severity of the symptoms. No differences between PTs' background characteristics and choice of treatment methods were detected.

Results of the feasibility study

The results of the feasibility study were reported in Paper III using the CONSORT extended guideline for pilot and feasibility trials (95).

The aim was to address uncertainties concerning the ongoing RCT and to determine whether or not the trial was feasible, and whether adjustments to the protocol were needed. We made a critical analysis of the feasibility of the protocol concerning recruitment, retention, the chosen point of the primary analysis, and the primary outcome measure, and performed a safety analysis, following the intention of the study protocol.

The recruitment rate was 19%. The infants who were assessed and participated in interventions were included for a median of 13 hours (min–max: 0–24 hours, IQR: 6, 18) after admission to the hospital wards. Six of 91 infants in the study and 6 of 11 who were included after the admitted 24 hours had improved significantly before inclusion. The 80 participating infants remained in the study for a median of 46 hours (min-max: 2-159 hours, IQR: 22,71. The data supply for the primary end point and for the primary outcome measure was lower than anticipated in the original sample size calculation. See Table 7 for information on participant retention and data supply.

Table 7. Participant retention and data supply at different times for follow-up, n=91

	24 hours n (%)	36 hours n (%)	48 hours n (%)
Saturation			
valid	57 (62.6)	42 (46.2)	35 (38.5)
discharged	16 (17.6)	25 (27.5)	32 (35.2)
drop-outs*	13 (14.3)	13 (14.3)	13 (14.3)
missed**	5 (5.5)	11 (12.1)	11 (12.1)
still in the study***	62 (68.1)	52 (57.1)	46 (50.5)
Heart rate			
valid	57 (62.6)	43 (47.3)	34 (37.4)
discharged	16 (17.6)	25 (27.5)	32 (35.2)
drop-outs*	13 (14.3)	13 (14.3)	13 (14.3)
missed**	5 (5.5)	10 (11.0)	12 (13.2)
still in the study***	62 (68.1)	52 (57.1)	46 (50.5)

*'Drop-outs' indicates infants who either did not start the interventions at all (n=11), or infants for whom the parents withdrew their participation after some time (n=2)

** 'Missed' indicates that the score was not filled out at this specific time, but the patient was still at the ward and there are values that can be imputed from assessments before and/or after this timepoint

*** 'Still in the study' comprises the combined values for 'valid' and 'missed', i.e. recorded data or values possible to impute

Difficulties in utilising the primary outcome measure were identified. The proportion of complete recorded data for the primary outcome was lower than we anticipated when the sample size for the RCT was calculated. Registration of the participants' oxygen saturation either with or without supplementary oxygen, as well as the use of high and low flow oxygen supplementation at the wards, further complicated the use of the composite index.

The safety analysis group reported no adverse events or values indicating any safety risks associated with participation in the study when analysing the entire study population. Thus, they did not continue to analyse data divided into respective allocation groups.

Adjustments for the full RCT

Based on the analyses and data from the feasibility study, we decided to change the primary outcome measure in the RCT to 'time to improvement', which is defined as the time before one of the following events occurs: reduced total Wang respiratory score, ceased use of supplemental oxygen, ceased use of supplemented HFNC, ceased use of gastric tube for feeding, or discharge to the home. We also decided to change the statistical analysis method to a survival analysis (time-to-event).

Results from the RCT

The analyses of the effect of the interventions compared with the control group receiving standard care showed no statistically significant differences in outcomes between the groups.

In the unadjusted Kaplan-Meier analysis, the median time to improvement was 3.00 hours (CI 95% 1.01–4.99) in the intervention group and 6.00 hours (CI 95%; 2.62–9.38) in the control group. The difference between the groups was not statistically significant (p =0.36). See graph in Figure 12.

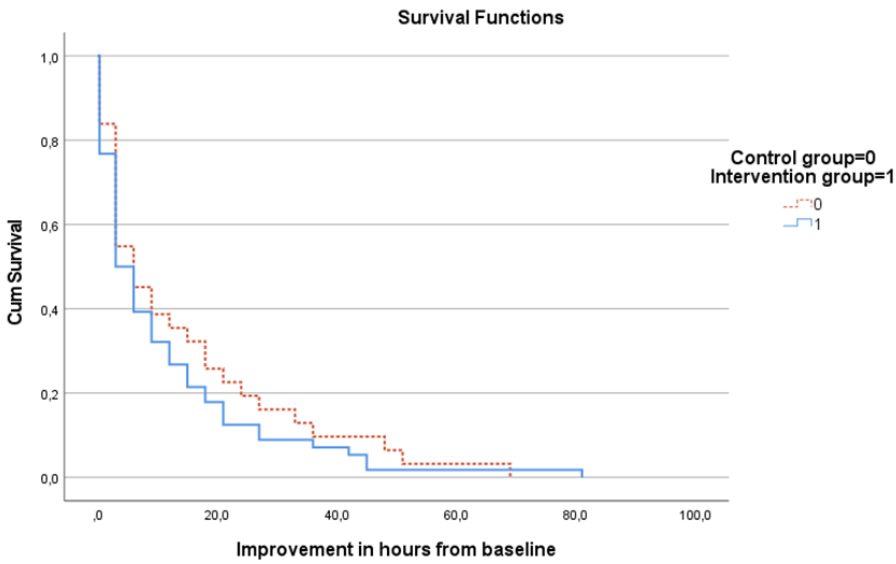


Figure 12. Survival curve from the un-adjusted Kaplan-Meier analysis of the primary outcome, time to improvement, n =89

The Cox regression model, adjusted for age in months, sex, tobacco smoking exposure, heredity for asthma/atopic disease, and early day-of-infection for those with RSV, showed no significant difference between the two groups, p =0.46. HR: 1.21; 95% CI: 0.73–1.99.

A description of the mean values in oxygen saturation, heart rate, and respiratory rate are displayed in Table 8.

Table 8. Descriptions of mean values of oxygen saturation, heart rate, and respiratory rate at baseline and after 20 minutes.

	Control group Mean (SD)	Intervention group Mean (SD)
Oxygen saturation baseline	95.97 (2.48)	96.44 (2.98)
Oxygen saturation 20 minutes	96.30 (2.40)	96.75 (2.98)
Heart rate baseline	146.22 (12.99)	146.82 (16.65)
Heart rate 20 minutes	149.67 (18.19)	152.82 (16.99)
Respiratory rate baseline	48.43 (12.01)	47.76 (12.83)
Respiratory rate 20 minutes	48.63 (11.42)	50.19 (11.03)

The mean changes from baseline to assessment 2, analysed with Independent samples T-tests for group differences, are displayed in Table 9.

Table 9. Group differences in changes from baseline in oxygen saturation, respiratory rate, and heart rate after 20 minutes.

	Control group		Intervention group		Mean difference (CI 95%)	p	Cohen's d (CI 95%)
	n	Mean change (SD)	n	Mean change (SD)			
Oxygen saturation	30	0.30 (2.80)	55	0.24 (3.06)	0.06 (-1.27–1.40)	0.93	0.02 (-0.42–0.47)
RR*	28	0.64 (8.02)	51	1.67 (9.51)	-1.02 (-5.24–3.20)	0.63	-0.11 (-0.58–0.35)
HR**	30	2.73 (13.33)	54	6.46 (17.40)	-3.73 (-10.49–3.04)	0.28	-0.23 (-0.68–0.22)

*RR=respiratory rate

**HR=heart rate

The intervention group increased somewhat more in respiratory rate and heart rate than the control group did, and less in oxygen saturation. There were no significant differences, however (p =0.28–0.92), and effect sizes were small. For an interpretation of effect sizes see Campo et al. (93).

The median time to improved general condition as reported by parents was 3.00 hours in the intervention group (CI 0.94–5.06) and 6.00 hours in the control group (CI 95% 0.00–14.97). The log-rank test revealed no significant differences between the groups (p =0.69).

No infants in either group were transferred to an ICU.

Before the clinical studies (Paper III and IV), it was not known how long infants with respiratory diagnoses stayed hospitalised, what viral agents were detected, or details of their treatment. The additional descriptive information below is valid for the entire study sample, n =104, unless otherwise is noted.

Participants were hospitalised for a median of 2.75 days (min 0.47–max 10.44) IQR: 1.76;4.12. During their hospital stay, 63 infants (60.6%) received inhalation therapy of any kind, and 24 (23.1%) did not. In 17 cases (16.3%) this data was missing. The time to the first improvement (primary outcome) for the whole sample was a median

(min–max) of 3.0 hours (0.3–81.0). Participants (n =89) remained in the study a median (min–max) of 1.95 days (0.2–6.63) IQR: 0.89;2.98. The distribution of viral agents in the study population are illustrated in Figure 13.

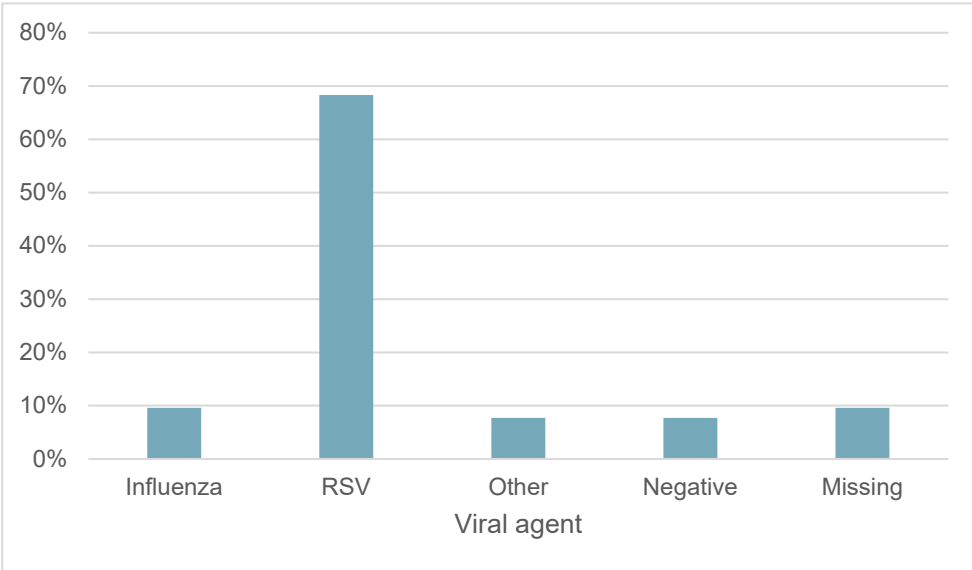


Figure 13. The distrubution of viral agents in nasopharynx tests in the participants in Paper IV, n=104.

The proportions of participants included at the different sites, as well as the distribution of boys and girls in the RCT (Paper IV) are displayed in Figure 14.

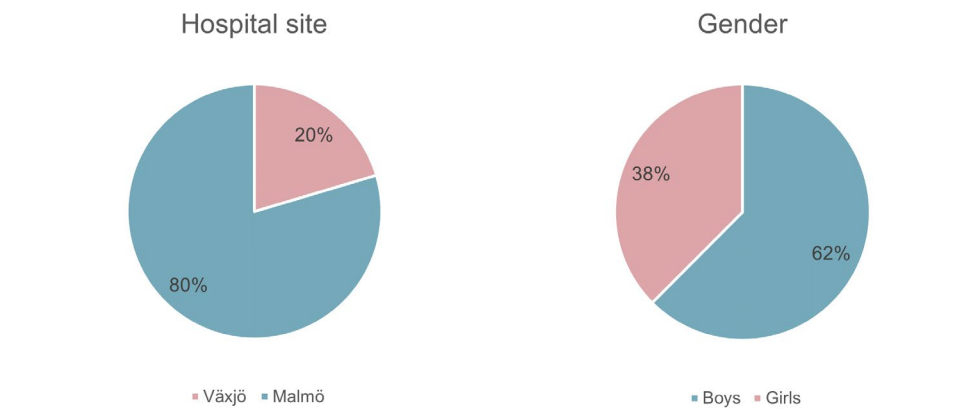


Figure 14. Distribution of participants included at the different study sites and distribution of boys and girls respectively.

Discussion

Methodological considerations

Constructing and evaluating the survey study

The survey was purpose-built for this study (Paper I) and, as is recommended in different sources (96,97), we chose different actions to ensure its validity: careful reading up on survey design, giving answering options based on scientific literature and professional experience, and using a reference group. This procedure ensured a functional survey, that we believe was easy to understand and fill out and subsequently to interpret. Informants could also add methods that were not listed, or write out comments, in free text. This design permitted a broad representation of opinions. However, it would have been interesting if we had also used 'no treatment' or 'minimal handling' as options, as this might have added information about decisions to refrain from treatment.

There are some limitations to a survey study regarding how informants remember and retrospectively report. Moreover, to secure the anonymity of the informants we could not track individuals in the responses. For that reason, we cannot rule out the risk that individuals other than the intended population have answered the survey, but we used professional channels to direct the survey to the intended group. The aim of the study was to get as wide a view of the methods as possible, and for that purpose, a survey was chosen, in spite of the possible risks above. We wanted answers from many individuals with a great variation in experience, from different types of hospitals, and with a broad geographic representation. The digital format enabled easy distribution of the survey to many physiotherapists throughout Sweden. Although this does not guarantee that all eligible PTs got the opportunity to answer the survey, we are of the opinion that enough information was collected.

Publication of a study protocol

Because of the great diversity in interventions and outcomes in studies about physiotherapy treatment for infants with ALRI, we found it increasingly important to clarify how our research was carried out. Notably, the interventions differ from the treatment methods that are most commonly used in Sweden, which made it

difficult for us to understand exactly what these interventions comprised or how they were carried out. We accordingly deduced that the interventions used in this project might not be familiar to clinicians outside of Sweden, which was one reason behind writing the study protocol (Paper II). We also wanted to give detailed descriptions of the outcomes and analyses, thus increasing the ability for others to interpret the findings. Here, we agree with Chan et al. (88) who argue: "complete documentation of key trial elements can facilitate transparency and protocol review for the benefit of all stakeholders" (p. 1).

The feasibility of completing the RCT

Data collection

We agree with Chalmers et al. (87) in that for scientific and ethical reasons it is important that clinical research is well-designed, as it is performed using public funds and involves many people, in this case infants with respiratory infections, their parents, and busy nursing staff. The analyses and decisions in Paper III contributed to increasing the feasibility of the ongoing trial. The feasibility study showed that hospital stays were short, which, together with dropouts and missed registrations, resulted in a low data supply. These findings were important for us when considering continuation of the full RCT and may also be interesting for other researchers planning to undertake similar clinical studies.

Recruitment of participants

We expected many infants to be pre-terms or to have comorbidities, and thus meet exclusion criteria. Data in the feasibility study partly support this theory, but the recruitment rate was even lower than we expected, based on clinical reasoning about the high prevalence of infants with ALRI in hospitals. Some parents rejected the offer to participate in the study, the reasons for which remain unknown. However, the most likely contributory factor to the low recruitment rate was that many parents were not asked to participate. Many infants with respiratory diagnoses are hospitalised at night, and we have received informal information from the staff that they were reluctant to ask for participation in the study at those late hours, so as not to disturb the families or because of working routines. On the other hand, many families were also not asked to participate during the day. During the peaks of the RSV infection, staff also expressed that they were sometimes too busy to enrol participants. Some of the infants that were included in the study within the stipulated time showed a clinically significant improvement before the interventions started, and of the infants included after 24 hours a larger proportion improved before inclusion. This supports our view that it would have been preferable if all participants had been included immediately after admittance to the ward, which unfortunately may prove difficult in clinical reality as demonstrated by the feasibility study.

Outcome measures of the feasibility study

Due to paucity of previous data, progression criteria or cut-off points for the different outcomes were difficult to determine, which is otherwise desirable for feasibility studies (86). However, we tried to compensate for the lack of external guidance through informed clinical reasoning. Adding interviews with staff might have provided further information about difficulties concerning recruitment and data recording, and possibly also pointed towards solutions for these issues. However, the first author regularly received informal information—although not scientifically structured—from meetings with contact staff, the management, and with all staff together while running the trial.

The feasibility to perform clinical research at the wards

Paper III and Paper IV have revealed deficits relating to the fundamental prerequisites of performing clinical research in the acute paediatric wards and have identified areas which need to be improved if future research is to be carried out successfully. The support for performing research on complex clinical interventions in acute hospital settings needs to be enforced in several ways, not least regarding attitudes towards clinical research and participant recruitment.

In the RCT, although we also worked through contact staff with extra training, different staff members all had the responsibility of recruiting participants and making assessments every third hour around the clock, which possibly masked each person's individual responsibility. At times, the workload at the wards was heavy, and we also witnessed a big staff turnover during the study period. On the other hand, we received informal reports from staff saying that they welcome studies on clinical health care interventions in addition to research on medical therapies. Moreover, the studies received financial support from Skåne University Hospital as well as Skåne County council and were formally approved by the management of the paediatric departments of the two study hospitals. Although this constituted strong support for this research project at certain levels, affirmation would also have been needed at other levels, clearly indicating in what way the staff was to prioritise research alongside with the ordinary work of the day. As a part of an increased support from different levels of the hospital organisation, it would probably have been useful to have extra staff present on the sites with the responsibility of recruiting participants and supporting data collection.

The interventions in the RCT

Even though the interventions in the clinical study are extensively described in the study protocol (Paper II) as well as in videos, there are aspects of the interventions that are not captured there. The interventions consist not only of different movements of the infant's body, but also individually adapted advice to the parents

and communication with both the infants and the parents by health care staff of different professions. The extent and exact ingredient of this extra relationship may be difficult to describe in a study protocol, and thus difficult to replicate in other studies. This may, furthermore, affect our understanding of the results. Persson et al (98) argue that, in some nursing research, interventions may work on both "informational and motivational levels", and that an "entire […] vehicle of communication is lacking in the control group" (p. 550). This description could also apply to the interventional study in this thesis (Paper IV).

Inhalations of 3 % hypertonic saline were not generally administered in the intervention group before the interventions as they are suggested in some sources to reduce bronchial wall oedema and thus reduce airway obstruction (76,77,99). Such inhalations may possibly have added an effect resulting in increased evacuation of mucus.

Staff was used to deliver the study interventions in their ordinary work, which, together with limited experience in clinical research, complicated the use of a control group. We were notified that some infants had mistakenly received the intervention of changing body positions despite being randomised to the control group. In these known cases, the infants were excluded from the study, but we cannot rule out that this may have also occurred without having been recorded. This risk might have been reduced if we had chosen one hospital site for the controls and another for the interventions. In Sweden that would have been difficult to undertake, however, as several hospitals had already declined to join the study—having high faith in the interventions and not wanting any of their infants to be randomised to controls. Additionally, in the control group, parents were not actively prevented from lifting their infants up in the arms if they chose to do so. These aspects may have influenced the results somewhat, contributing to the low difference between the groups.

Adaptations of analyses and outcome measures in the RCT

The decision to analyse the two intervention groups together was necessitated by the COVID-19 pandemic that severely reduced the already low recruitment rate. Between April 2020 and August 2021 no participant was enrolled in the study. During this time, the number of infants with RSV infections in Sweden was dramatically reduced, thus minimizing eligible participants (100). Staff resources were also at times needed elsewhere, and one of the paediatric wards was temporarily dedicated to adult patients with COVID-19. Later, the staff—fatigued after challenging working conditions—had difficulties in recruiting enough participants, despite a large number of infants admitted to hospitals at times. The two interventions differ somewhat, mainly in intensity and in the professions delivering the interventions, which may have influenced the outcome to some

extent. On the other hand, as the interventions are essentially similar, we find that merging the groups made the study more relevant and clinically adapted.

Because of low data supply and difficulties in utilising the composite index, we changed the primary outcome measure for the full RCT. The change of primary outcome measure and analysis method had the advantage of capturing improvement through the entire hospital stay and was thus not restricted to one pre-set time (previous 24 hours), which was supported by study data. Moreover, the new sample size calculation, assuming less participants than originally planned, was favourable considering the low recruitment rate.

When changing the originally intended primary outcome measure after the feasibility study to a dichotomised use of supplemental oxygen, HFNC, and gastric tube feeding, we possibly chose a less discriminating outcome. We also abandoned the detailed record of oral food intake due to difficulties in collecting that data. For infants who were breastfed, we learned that the mothers themselves often were encouraged to put the infant on the scales before and after feeding and make a note of the different weights. This is understandably difficult to undertake at all hours, not least of which during the night, and might have contributed to the low data level. The reason for including this outcome measure was because of its clinical relevance, as reduced food intake is associated with low oxygen saturation in bronchiolitis and has been suggested to represent the severity of the illness, although it excludes breastfed infants from measurements (31).

It is possible that some effects went undetected because of the outcome measures chosen for the final analysis. It is not obvious what outcomes to choose for studies with this patient group, however, and we agree with Castro-Roderiguez et al. (36) about the need to discuss and determine relevant outcome measures and the minimal clinically important difference. Outcomes and evaluation methods in different studies vary, and there is a need to find outcome measures that may capture any relevant effect of physiotherapy treatment. In the RCT (Paper IV) we found it appropriate to treat the Wang respiratory score as an ordinal scale, not using parametric tests, whereas in other studies this score has sometimes been used as a continuous, normally distributed scale in parametric tests (50,53). The different approaches complicate comparisons between studies.

Assumptions about effects

It has been suggested that the explanatory value of interventional studies depends on the strength of the hypothesis driving the research (98). Based on earlier direct and indirect evidence, we deduced a rather high probability that frequent changes in body position and stimulation of physical activity would be beneficial for infants with ALRI. Moreover, personal clinical experience and experience reported by colleagues suggested clinical benefits for infants. We encountered further examples

of a widespread positive view of this PT treatment when we contacted different hospitals in southern Sweden for participation in the study. Even when the physiotherapists and management were mostly positive about joining the research project, the nursing staff in several hospitals refused to participate—not wanting even a third of their infants to be randomised to controls, having high faith in the interventions that were being tested. One hospital did not want to participate in the study because they had recently implemented this treatment method formally in paediatric wards, and the physiotherapists had carried out an educational programme for staff about this treatment to be used for all infants with ALRI. Thus, they did not want to change their routines. In summary, when this doctoral project started, there was an overall positive view of this treatment including changes in body position in Swedish hospitals. These clinical views on benefits are supported by previous evidence of a beneficial effect of nursing infants with ALRI in different body positions as opposed to nursing them lying flat on their back (65-68).

The positive experiences of changing body positions for patients with acute respiratory infections was further recognised during the COVID-19 pandemic. Physiotherapists in ICUs placed critically ill patients in a prone position and thus dramatically increased oxygen saturation and subsequent survival (101-103). Very early mobilisation has also recently been recognised as beneficial to oxygen saturation in patients who have undergone abdominal surgery (104). These experiences, together with earlier evidence of generally increased lung volumes in upright positions (105) has further increased the indirect evidence of the treatment to have some positive components, even though no statistically significant effect was found in Paper IV.

Research on complex interventions

Complex interventions consist of diverse components, and it has been proposed that it might be difficult, and, interestingly, not always desirable, to isolate the 'active ingredient' and find a causal relation between the interventions and the outcomes, and moreover, not rely solely on quantitative outcomes (106). As complexity is recognised as an essential component of this kind of research it may not be avoided: "complex interventions may work best if tailored to local circumstances rather than completely standardised" (81 p. 587). The intensity of the interventions in the clinical study (Paper III and IV) was not monitored, and we did not monitor what possible interventions the control group was given. This approach also follows the design of the so-called pragmatic RCT, which places the research close to clinical praxis, and is described as aiming to help choose between treatment options and to enhance implementation of the findings to usual care settings (107). We chose this design to evaluate a treatment that already exists in hospitals, but that has not been scientifically evaluated before, as our aim was to guide future care for this large and vulnerable patient group. These aspects of performing research on complex

interventions in health care may partially explain the lack of difference between the different groups in the RCT. Additionally, Craig et al. argue that a lack of effect of complex interventions may be caused by limitations in the implementation, and, moreover, that sample sizes may need to be larger because of extra individual variability, which may be applicable to this study. Thorough process evaluations are suggested to identify areas to be improved (81). Although not strictly following this strategy, the studies in this thesis have added knowledge to the area of research about infants in acute hospital settings with a potentially significant contribution to future research.

Results

Treatment methods for ALRI in Sweden

The survey study (Paper I) showed that physiotherapists in Sweden use a wide range of treatment methods for infants with respiratory infections, and commonly lift the infant up from bed to perform frequent changes in body position and stimulate physical activity. This treatment strategy had not previously been described for infants with ALRI in hospitals, and the study thus added knowledge about the use of physiotherapy methods for this patient group.

The widespread use of this treatment strategy in Sweden, even though it was not evaluated for this patient group, may be explained by the fact that physiotherapists mainly treat symptoms of the infants and not diagnoses (76). It is likely that physiotherapists in other countries also use similar methods. In fact, one source suggests: "…vigorous activity such as skipping and jumping can precede postural drainage in order to loosen the secretions, provided such activity is not contraindicated" (108 p. 563). Further studies are needed to explore the treatment methods physiotherapists use for this patient group in other parts of the world.

Almost all informants used the method of bouncing on a big ball at some time, and it is described by Van Ginderdeuren et al (109) and Lannefors et al (61) in the treatment of infants with CF, and by Lagerkvist (110) when treating children with neuromuscular disorders in Sweden. The aim of using the big ball for children with neuromuscular disorders and secondary respiratory impairments seems to be the same as the desired effect for infants with ALRI: to increase deep breathing and mucus transportation, and thus increase oxygen saturation (56,110). The fact that all informants marked that they gave information to parents suggests that the parents are commonly involved in treatment sessions. In clinical practice, the physiotherapist often starts the treatment session, and the parents continue to do the same activities with their child throughout the hospital stay, with support by the physiotherapist.

Effect of the treatment

To our knowledge, no previous studies had evaluated the effect of this treatment for infants with acute lower respiratory tract infections in hospital, and that was the rationale for performing the RCT (Paper IV). The most important finding was the overall similarity of outcomes for the different groups. This study did not detect any effects of the intervention, but on the other hand, it also detected no disadvantages.

Although not statistically significant, and thus not possible to generalise beyond this study, the median difference in improvement rate—three hours shorter in the intervention group—is clinically relevant, especially considering the overall short hospital stay. The same median difference (three hours) was found in the secondary outcome 'time to improved general condition' (parental assessment). The hazard ratio of the Cox regression indicates that the probability for participants in the intervention group to have improved was 1.21 times higher than for the controls at each time. In the analyses of short-term effects, both groups increased somewhat in oxygen saturation, respiratory rate, and heart rate. The intervention group increased somewhat more in respiratory rate and heart rate than the control group did and less so in oxygen saturation. There were no significant differences, however, and effect sizes were small. An increased respiratory rate and heart rate might have been explained by the fact that the infants in the intervention groups were being physically active, because physical activity would increase heart rate and respiratory rate. The small difference in changes in oxygen saturation is most likely explained by the fact that all infants had a rather high level of oxygen saturation at baseline, either on room air or with supplemental oxygen, and they were thus not likely to improve much further. Importantly, the intervention group did not deteriorate in oxygen saturation immediately after the intervention, which might have been the case if the intervention would have been stressful or had involved too much exertion.

The standard care in the study was intended to mimic the basic care recommended in guidelines without the use of physiotherapy treatment, comparable to the previously mentioned 'minimal handling'. We understand that the recommendation of minimal handling with its implication of constituting supportive care for the infants with ALRI (44, 52, 62-64) may very well have been suggested from a general concern about severely affected infants and a wish not to cause them any further distress. Nevertheless, the findings in the RCT (Paper IV) do not support that recommendation, as there was no evidence of a favourable effect of minimal handling (control group) compared to stimulation of physical activity and frequent changes in body position for infants. These different approaches merit further evaluation.

In summary, the most common PT treatment methods include frequent body position changes and stimulation of physical activity. No statistically significant effects of this treatment compared to 'standard care' were detected in this thesis, and neither were any adverse effects. Through analyses in the feasibility study and

the full RCT, knowledge has also been gained about the feasibility of performing clinical research on infants in acute hospital settings. Moreover, we have gained information about the length of hospital stay and details about treatment with oxygen supplementation, HFNC, gastric tube, and inhalation therapy, which was not known before. The proportion of viral agents and the distribution of boys and girls in these studies correspond to figures in other/previous studies (23,24). Knowledge about the effects of standard care has also been obtained.

Clinical implications

As there were no significant differences between the groups in the RCT (Paper IV), our interpretation of the findings is that there is no reason to abandon the praxis that is widespread in Sweden, especially if therapists see clinical benefits from these interventions, also including other possible effects that have not been studied in this trial. Previous studies recognise a beneficial effect of nursing infants with ALRI in different body positions as opposed to lying flat on their back (65-68). No adverse effects were detected in this evaluation (Paper IV) or in the previous safety analysis (Paper III). In fact, as other benefits for managing infants in the arms with close bodily contact are widely recognised in the literature, we can safely recommend these treatments to be continued if desired. For instance, close bodily contact is generally regarded as positive for infants, as it "conveys feelings of security [and] transmits interactional warmth" (111 p. 418) and supports the psychological maturation (112). Parenting 'skin-to-skin' is recommended by the WHO, especially for pre-term infants, because of its link to increased survival (113,114). Positive effects of close bodily contact have also been demonstrated on breast feeding, weight gain, prevention of hospital referrals, and increased well-being (115,116). Furthermore, holding infants in the arms while bouncing on a large ball has, in another study, been used to help infants relax during treatment (117).

Comparisons can be made between the physiotherapy treatment for infants with ALRI and the treatment for children with CF. The praxis in Sweden for children with CF changed in the 1980s, following a study which demonstrated preserved lung functions when the more traditional 'passive' treatment was replaced with an intervention that comprised physical activity (57). In analogy with those conclusions, findings suggest that the interventions described and evaluated in this thesis can be safely continued, if desired, which is in line with previous evidence demonstrating positive effects for infants nursed with close bodily contact and changing positions in bed.

Future perspectives

The work of this thesis has identified areas where further research or development is needed. Some of these areas are listed below.

- Possible long-term effects of the current interventions on hospital re-admissions, visits to emergency departments, or calls or searches for medical advice.
- Parents' experiences of physiotherapy interventions. Do they experience support of their ability to help their child, or possibly further strain being placed on them? What possible effects do they identify?
- Further analyses of the interventions in this thesis: exploration of possible PT differentiation of interventions depending on age or severity of illness.
- Exploration of what physiotherapy treatment methods are used in other countries for infants with ALRI.
- Development of support for clinical research in acute hospital settings, including further analyses of what areas mainly need to be enforced.
- Review of methods for evaluating the severity of illness/effect of treatments in infants with ALRI and the usability of these methods, for example by interviews with PTs or nursing staff. Evaluation of validity and sensitivity of different methods in relationship to minimal clinically important difference.
- Evaluation of isolated effects of changes in body position on lung volumes, low oxygen saturation (without supplemental oxygen), vital signs, respiratory pattern, or mucus transportation.

Conclusions

The studies in this thesis have added new knowledge to the area of physiotherapy treatment for infants in hospital with acute respiratory infections. The conclusions are, firstly, about what treatment methods are being used in Sweden (Paper I), secondly about the feasibility of continuing the RCT (Paper III), and finally about the clinical evaluation of the effects of specific physiotherapy treatments (Paper IV):

A variety of treatment methods are used by the Swedish physiotherapists. The most common methods involve frequent changes in body position and stimulation of physical activity. Thus, the praxis in Sweden seem to differ from methods described in the literature. Methods are chosen depending on the symptoms of the patients. No differences in the choice of treatment methods were found regarding physiotherapists' background characteristics.

It was feasible to continue the full RCT with modifications to the analysis plan. As the study concerned treatment for a large and vulnerable group of patients, it was considered valuable for clinical as well as ethical reasons to make use of the collected data, continue the ongoing RCT, and evaluate the effect of the physiotherapy interventions. Participation in the study was not associated with any safety risks.

No significant differences were detected between the intervention group and the control group in the rate of improvement or in the immediate changes in oxygen saturation, heart rate, or respiratory rate. Both strategies were found to be equally effective and safe, indicating that the current recommendation of minimal handling for these infants should be reconsidered.

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Appendix 1

Skånes universitetssjukhus
En del av Region Skåne

Leg fysioterapeut 2021-10-26
Sonja Andersson Marforio

ANDNINGSBEHANDLING FÖR SMÅ BARN

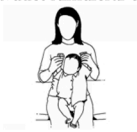
- **Inhalera** gärna med barnet i sittande eller så upprätt som möjligt. Barnet ska inte ha napp i munnen och masken ska helst vara tätt in till ansiktet.

- Ändra läge/ställning regelbundet. Lungorna luftas olika beroende på kroppen position.

- Gunga barnet på en stor boll eller i knäet i olika positioner (sidliggande, magliggande, sittande). Tryck lätt på barnets bröstkorg för att stimulera extra vid utandning.



- Hjälp barnet/locka barnet till att röra på armar och ben. Benaktivitet samt armrörelser över huvudet stimulerar till djupa andetag.




- Ge gärna barnet hoststöd genom att stödja över barnets mage eller genom att ta upp barnet i famnen och ”krama om”

QR-kod och länk till instruktionsfilm:

https://players.brightcove.net/3193745440001/b859b2ab-6e32-4a70-a0dd-ee8b2ca7bb94_default/index.html?videoId=6278327570001

Upprepa ofta, minst var annan vaken timme!

Appendix 2

Skånes universitetssjukhus
En del av Region Skåne

2022-03-28

Leg fysioterapeut
Sonja Andersson Marforio
Barnsjukvården, SUS

LÄGESÄNDRINGAR FÖR SMÅ BARN - FÖRÄLDRAINFORMATION

Så här kan du hjälpa barnet att ta djupa andetag och hosta bort slem.

- Ge gärna barnet hoststöd genom att ta upp barnet över axeln och ”krama om”.

- Ändra läge/ställning regelbundet. Lungorna luftas olika beroende på kroppens position. Låt gärna barnet ligga på sidorna i sängen också.

- Hjälp barnet att röra på armar och ben. Benaktivitet och armrörelser över huvudet stimulerar till djupa andetag.
  Man kan stimulera barnet till djupandning och spontan hosta genom ökad aktivitet som t ex att busa, kittla, sjunga.

- Gunga barnet i knäet eller uppe i famnen.

Länk till instruktionsfilm:

https://players.brightcove.net/3193745440001/b859b2ab-6e32-4a70-a0dd-ee8b2ca7bb94_default/index.html?videoId=6276714556001

Upprepa ofta, minst var annan vaken timme.

Appendix 3

Studie om fysioterapi för spädbarn med andningssvårigheter.

Enkäten syftar till att ge ökad kunskap om hur fysioterapeuter/sjukgymnaster i Sverige arbetar med små barn med andningssvårigheter, och vilka metoder som används.

Varje svar är av stort intresse - så stort **tack** för att du väljer att medverka med ditt svar!

När du är färdig med svaren skickar du in genom att klicka på knappen "Skicka nu".

Sonja Andersson Marforio,

Leg sjukgymnast, specialist i pediatrik,

Doktorand vid Lunds universitet

1. Vilken region/landsting är du huvudsakligen verksam i? Välj ett alternativ som visas när pilen markeras.

- ☐ Landstinget Blekinge
- ☐ Landstinget Dalarna
- ☐ Region Gotland
- ☐ Region Gävleborg
- ☐ Västra Götalandsregionen
- ☐ Region Halland
- ☐ Region Jämtland Härjedalen
- ☐ Region Jönköpings län
- ☐ Landstinget i Kalmar län
- ☐ Region Kronoberg
- ☐ Norrbottens läns landsting
- ☐ Region Skåne
- ☐ Stockholms läns landsting
- ☐ Landstinget Sörmland
- ☐ Landstinget i Värmland
- ☐ Västerbottens läns landsting
- ☐ Landstinget Västernorrland
- ☐ Landstinget Västmanland
- ☐ Landstinget i Uppsala län
- ☐ Region Örebro län
- ☐ Region Östergötland

2. Vilken typ av sjukhus arbetar du huvudsakligen vid?

- ☐ Länssjukhus
- ☐ Regionsjukhus

3. Vilket år tog du sjukgymnast- eller fysioterapeutexamen?

4. Är din grundexamen

- ☐ svensk
- ☐ utländsk, från ett skandinaviskt land
- ☐ utländsk, från ett land utanför Skandinavien

5. Är du

☐ Kvinna

☐ Man

☐ Definierar mig varken som kvinna eller man

6. Hur många gånger har du behandlat spädbarn (0-2 år) för andningssvårigheter de senaste 2 åren?

☐ Aldrig

☐ 1-2 ggr

☐ 3-6 ggr

☐ mer än 6 ggr

7. Vilka behandlingsmetoder har du använt vid behandling av spädbarn (0-2 år) med andningssvårigheter, exempelvis bronkiolit? Flera alternativ kan väljas.

☐ PEP

☐ CPAP

☐ BilevelPAP

☐ Högflödesgrimma (High nasal flow)

☐ Hostmaskin (Mechanical insufflation-exsufflation)

☐ Bankningar/Tapotement/Percussion

☐ Manuella bröstkorgsvibrationer

☐ Dränagebehandling

☐ Assisterad/Inducerad hosta genom kompression av trachea strax över sternum

☐ Förlängd långsam expirationsteknik (PSET), hålla kvar maximal thoraxkompression 2-3 andningscykler

☐ Lättare thorax/sternumkompressioner för ökad expiration, som följer barnets egen andning

☐ Manuellt hoststöd

☐ Viloställning för att underlätta andningen

☐ Lägesändringar i sängen

☐ Lägesändringar i famn (egen eller föräldrars)

☐ Gungningar på stor boll

☐ Passiva armrörelser

☐ Passiva benrörelser

☐ Fysisk aktivitet/ aktiva rörelser

☐ Inhalationer varvat med annan behandling.

☐ Träna/förbättra inhalationsteknik ev tillsammans med föräldrar/vårdnadshavare

☐ Information/rådgivning till förälder/vårdnadshavare

☐ Rådgivning till annan personal

☐ Andra åtgärder (beskriv gärna i sista frågan)

Du som svarat Aldrig kan nu skicka in enkäten genom att klicka på Skicka nu nere till höger.

När du använde viloställning, hur positionerades barnet? Skriv svaret i textfältet.

När du använde lägesändringar i sängen, vilka positioner placerades barnet i?

- ☐ Sidliggande
- ☐ Rulla från sida till sida
- ☐ Magläge
- ☐ Rygläge
- ☐ Annat (beskriv gärna i sista frågan)

När du använde lägesändringar i famn, i vilken position placerades barnet?

- ☐ Upprätt mot vuxens axel
- ☐ Sidliggande i vuxens famn
- ☐ Magliggande i vuxens famn
- ☐ Ryggliggande i vuxens famn
- ☐ Magliggande mot vuxens bröstkorg (som halvligger)
- ☐ Sittande i vuxens knä
- ☐ Annat (beskriv gärna i sista frågan)

När du använde gungningar/studs på stor boll, hur var barnet placerat?

- ☐ På rygg på bollen
- ☐ På sidorna på bollen
- ☐ På mage på bollen
- ☐ Sittande på bollen
- ☐ Upprätt mot axel på vuxen som sitter på bollen
- ☐ Sittande i vuxens knä på bollen
- ☐ Sidliggande i vuxens famn på bollen
- ☐ Magliggande i vuxens famn på bollen
- ☐ Ryggliggande i vuxens famn på bollen.
- ☐ Annat (beskriv gärna i sista frågan)

Du som angett rådgivning till annan personal, vad handlade rådgivningen om?

- ☐ Aktuella inhalationsmediciner
- ☐ Aktuell inhalationsapparat
- ☐ Aktuell inhalationsteknik
- ☐ Vidare utredning
- ☐ Annan åtgärd (exempelvis medicinska åtgärder/lekterapi etc)
- ☐ Användandet av högflödesgrimma, CPAP eller BilvelPAP
- ☐ Annat (beskriv gärna i sista frågan)

8. Vilka är dina vanligaste åtgärder? Vänligen markera de 3 vanligaste åtgärderna i listan nedan.

- ☐ PEP
- ☐ CPAP
- ☐ BilevelPAP
- ☐ Högflödesgrimma (High nasal flow)
- ☐ Hostmaskin (Mechanical insufflation-exsufflation)
- ☐ Bankningar/Tapotement/Percussion
- ☐ Manuella bröstkorgsvibrationer
- ☐ Dränagebehandling
- ☐ Assisterad/Inducerad hosta genom kompression av trachea strax över sternum
- ☐ Förlängd långsam expirationsteknik (PSET), hålla kvar maximal thoraxkompression 2-3 andningscykler
- ☐ Lättare thorax/sternumkompressioner för ökad expiration, som följer barnets egen andning
- ☐ Manuellt hoststöd
- ☐ Viloställning för att underlätta andningen
- ☐ Lägesändringar i sängen
- ☐ Lägesändringar i famn (egen eller föräldrars)
- ☐ Gungningar på stor boll
- ☐ Passiva arm- och benrörelser
- ☐ Fysisk aktivitet/ aktiva rörelser
- ☐ Inhalationer varvat med annan behandling.
- ☐ Träna/förbättra inhalationsteknik ev tillsammans med föräldrar/vårdnadshavare
- ☐ Information/rådgivning till förälder/vårdnadshavare
- ☐ Rådgivning till annan personal
- ☐ Andra åtgärder (beskriv gärna i sista frågan)

9. Vilken effekt märker du omedelbart/direkt vid behandling?

- ☐ Märker ingen effekt
- ☐ Ökad kapillär återfyllnad
- ☐ Förbättrade blodgaser
- ☐ Bättre röntgenbild
- ☐ Ökad saturation
- ☐ Minskad andningsfrekvens
- ☐ Mindre ansträngd andning
- ☐ Minskade indragningar
- ☐ Minskad puls
- ☐ Piggare allmäntillstånd
- ☐ Förbättrat matintag
- ☐ Bättre sömn
- ☐ Mer produktiv/ökad eller minskad hosta
- ☐ Ändrade slemljud
- ☐ Mindre väsande andningsljud
- ☐ Föräldrarna uppger att barnet mår bättre
- ☐ Annat (beskriv gärna i sista frågan)

Du som bedömer slem- eller annat andningsljud, hur gör du det?

- ☐ Lyssnar med blotta örat
- ☐ Lyssnar med stetoskop
- ☐ Känner kring bröstkorgen

10. Vilken effekt märker du på något längre tid?

- ☐ Märker ingen effekt
- ☐ Ökad kapillär återfyllnad
- ☐ Förbättrade blodgaser
- ☐ Bättre röntgenbild
- ☐ Ökad saturation
- ☐ Minskad andningsfrekvens
- ☐ Mindre ansträngd andning
- ☐ Minskade indragningar
- ☐ Minskad puls
- ☐ Piggare allmäntillstånd
- ☐ Förbättrat matintag
- ☐ Bättre sömn
- ☐ Mer produktiv/ökad eller minskad hosta
- ☐ Ändrade slemljud
- ☐ Mindre väsande andningsljud
- ☐ Föräldrarna uppger att barnet mår bättre
- ☐ Annat (beskriv gärna i sista frågan)

11. Har du kompletterande svar på frågorna eller ytterligare synpunkter på denna undersökning så skriv dem gärna här.

Appendix 4

Observationsprotokoll andningsstudien.

Grupp Fysioterapi dag 1.

Patientens namn:	Dagens datum:
Personnummer:	

Daglig vikt (kl…….):_____ Dagligt vätskebehov:_____

Har **inhalerat:** Ja / Nej (ringa in det som gäller för dygnet)

Barnet är **aktivt** (ex kryper, sätter sig/ställer sig, går)? Ja / Nej (ringa in det som gäller)

Vätskelista:

Klockan:													
Amning/flaska (g/ml)													
Sond (ml)													

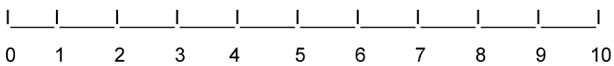
Behandling med fysioterapeut/sjukgymnast 20 minuter

Tidpunkt/ klockan: 2: a obs efter 20 min sedan var 3:e (2:a) timme	1:a obs	2:a obs											
Saturation i upprätt ställning vid 2:a obs													
Puls													
Andn frekvens													
Tillsatt syrgas (**%** eller **l/min**)													
Högflöde i näsgrimma (l/min)													
Väsande ljud (0-3) **0**:Inga **1**: Slut-utandning **2**: Hela utandning **3**: In och utandning													
Allmäntillstånd (0-3 **0**: Vanligt **3**: Irriterad/slö/nedsatt matintag													
Indragningar (**0**=inga/ **B**uk/**H**als)													
Näsvingespel **Ja/Nej**													
Föräldraskattning (**0-10**) mående ej på natten													
Föräldr skattn mat **0-3**													

Föräldrars skattning: Var god vänd på pappret för skalorna!

Utskrivning till: hemmet eller intensivvårdsavdelning (ringa in aktuellt), klockan_____

Förälders skattning: **Mående** (peka på siffra)**:**



Som vanligt

Mycket påverkad/sjuk

Förälders skattning: **Mat** (ange hur ditt barn äter)

0 = äter som vanligt

1 = äter mindre än vanligt

2 = äter ingenting själv

Kontaktperson för forskningsstudien:

Sonja Andersson Marforio, leg sjukgymnast, doktorand Tel:
mail: sonja.andersson_marforio@med.lu.se

Bakgrundsinformation om patienten.

Dagens datum:
Patientens namn:
Personnummer:

Ringa in eller skriv aktuellt svar:

Är det någon i barnets närhet hemma som är rökare?	Ja Nej
Finns ärftlighet för …?	Astma .....(vem?) Hösnuva .....(vem?) Allergier .....(vem?) Eksem .....(vem?)
”Hostdebutsdag” (var i infektionen befinner sig patienten)	
Multiplex luftvägspanel (PCR)	Taget datum: tid:

Signatur: _____

(den person som noterade uppgifterna)

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About the author

This doctoral thesis is founded on clinical queries and comprises clinical as well as methodological studies. Sonja Andersson Marforio is a registered physiotherapist, specialised in paediatrics. She has a wide clinical experience from both Primary Health Care and acute hospital care, and for many years she has worked with patients with diverse health conditions of all different ages. In the last 20 years, she has mostly focused on patients below 18 years of age, at paediatric hospital departments in Trollhättan and Lund, and more specifically children with either respiratory disorders or infants with congenital muscular torticollis or developmental issues. Since 1995, she has been teaching physiotherapy students at the Faculty of Medicine at Lund university, and she regularly gives courses to physiotherapists and other health professionals in Primary Health Care. The work on this thesis was conducted parallel to her clinical work in Skåne University Hospital.

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