Pediatric emergency medicine:

Optimizing risk assessment and safety netting in children with infectious diseases.

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Pediatric emergency medicine:

Optimizing risk assessment and safety netting in children with infectious diseases.

Spoedeisende Kindergeneeskunde:

Optimaliseren van risico inschatting en het vangnet rondom kinderen met koorts.

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Chapter 1

Introduction

Pediatric emergency medicine

Worldwide, a significant number of children need emergency care. In order to meet these needs, up-to-date trained health care professionals in pediatric emergency medicine (PEM) are needed. Subsequently, in many countries, PEM has developed into a subspecialty, focusing on maintaining high quality of care by 1) advocacy, 2) teaching, 3) composing guidelines and stimulate its implementation and hereby its use, as well as 4) encouraging evidence- based care performing research and collaborating in research networks.

In The Netherlands, awareness on the importance of high quality care for the acute ill child is increasing, however, currently without an acknowledged PEM subspecialty. Children in The Netherlands receive care primarily from their general practitioner (GP) or the GP out-of-office clinic and, if needed specialized pediatric care at the hospital. The GP will refer the patient to the ED if necessary, or the parents will turn directly with their child to the ED by themselves (self- referral) or by ambulance, in case of a life- threatening illness. After the ED visit, the patient is either admitted to the hospital, or discharged with or without a planned revisit to the outpatient clinic, to the GP's office or the ED.

For children with infectious diseases visiting the ED, pediatric emergency medicine research mainly aimed to improve the development of prediction rules and recognition of serious infections (SI). Further improvement can be achieved by focusing on 1) early recognition by parents, 2) integrate developed prediction rules into daily practice and 3) fine tune and standardize discharge plans.

Variability in acute illnesses in children at the ED

Worldwide, the leading causes of death among children 1 month to five years old were besides injuries, pneumonia and diarrhea, complicated malaria, measles and HIV/AIDS. [1] In 2010 in the US, more than 25,5 million children < 18 years (mean age 7.0 years, 52.8% boys) visited the ED.[2] Most common reasons were injury and poisoning, respiratory diseases, nervous system diseases and infectious disease. Admission rate overall was 4%.

In The Netherlands 1,8 million ED visits took place in 2013.[3] More than 15% of patients were under the age of 18 years old. Most frequent complaints were injury or poisoning, cardiovascular, respiratory and gastro-intestinal disorders.

At the ED of the Erasmus Medical Centre in Rotterdam, an inner-city university hospital, children comprise about one third of the population. In more detail, between 2010 and 2013, in total, 25108 children, 1-16 years (median age 4.1 years; 60% male) visited because of trauma (28%) or a medical complaint (69%) (Table 1). Over 40% of the population was self-referred and 20% of patients had some kind of co-morbidity, 11 % having complex co-morbidity. On admission to the ED, patients are assigned to a triage category according to the Manchester Triage System (MTS). In our population, 14557(58%) of children were assigned to the emergent, very urgent and urgent

Table 1 Patient characteristics Emergency Department ErasmusMC- Sophia Children's Hospital 2010—2013

	N (%)
Total number of patients	25108 (100)
Gender (male)	14800 (58.9)
Median age, median (IQR)	4.1 (1.4-9.5)
Age, subgroups	
≤3 months	1938 (7.7)
3 months – 1 year	3081 (12.3)
1 – 4 years	7223 (28.8)
4-8 years	5179 (20.6)
8-16 years	7687 (30.6)
Serious co-morbidity	
No chronic co-morbidity	7664 (30.5)
Non-complex chronic co-morbidity	1977 (7.9)
Complex chronic co-morbidity	2866 (11.4)
Missing	12601 (50.2)
Referral	
Self-referral	10368 (41.3)
General practitioner	4014 (16.0)
Emergency service	1882 (7.5)
Other	8844 (35.2)
MTS-urgency	
Emergent	488 (1.9)
Very urgent	2877 (11.5)
Urgent	11192 (44.6)
Standard	9082 (36.2)
Non urgent	683 (2.7)
Missing	786 (3.1)
Presenting problem	
Trauma	7134 (28.4)
Medical	17188 (68.5)
Other	786 (3.1)
Medical	17188 (100)
Non- infectious	9595 (55.8)
Dyspnea	2070 (12.0)
Vomiting/ diarrhea	1595 (9.3)
Fever other	3928 (22.9)
Diagnostic interventions	
No intervention	11457 (45.6)
Simple lab	4431 (17.6)
Simple radiology	5666 (22.6)
Extensive laboratory or extensive radiology	3554 (14.2)
Therapeutic interventions	
No intervention	10868 (43.3)
Self-care advice/medication on prescription	3058 (12.2)
Oral medication or chirurgic intervention on ED	6018 (24.0)
IV medication/extensive surgical intervention	5164 (20.6)

Table 1 Patient characteristics Emergency Department ErasmusMC- Sophia Children's Hospital 2010—2013 (*continued*)

	N (%)
Disposition	
Discharge, no follow- up	9031 (36.0)
Follow-up primary care	284 (1.1)
Follow-up outpatient clinic	10483 (41.8)
Hospital admission	4336 (17.3)
Intensive Care admission	555 (2.2)
Mortality	23 (0.1)
Other/ unknown	396 (1.6)

categories and 9765 (39%) were assigned to the standard and non-urgent categories. About 20% of all patients underwent simple lab tests and/or radiology and 14 % of the patients underwent extensive diagnostic tests. After the diagnostic process, almost half of all patients received no treatment or written discharge instructions, 12 % received a documented self-care advice or oral prescription, 24 % received treatment at the ED and 21% received IV medication or a surgical intervention. After the ED discharge, 36% of all patients were discharged without scheduled follow-up and 43 % received a scheduled follow-up appointment, mainly to the outpatient clinic. Of all patients admitted to the hospital, 17 % was admitted to the general pediatric ward and 2% was admitted to the pediatric intensive care unit. Twenty-three patients (0.1%) died at the ED.

Regarding our population, several topics can be addressed**. First,** mortality at the ED still exists. Pneumonia is a common serious infection. Because antibiotic treatment is available, mortality should be very low in countries in Western Europe, however, mortality rates are variable and differ from 0 till 76 per 100 000. [4] In our local population, 23 children died at the ED (median age 2.0 years (IQR 0.3-7.1), male 13 (56.5%)) (table2). Although detailed information is lacking, almost all children died because of acute respiratory failure or 'unresponsive child/ decreased consciousness'. One third of these children had comorbidity.

Second, infectious diseases and fever were present in 45% of all children with medical complaints. In febrile children in western/ developed countries, the most common cause of fever is a viral infection. However, serious bacterial infections do occur, mostly pneumonia, complicated urinary tract infections/ pyelonephritis and sepsis. Sepsis still has a hospital mortality rate of 3-10% and even higher in case of hypovolemic shock.[5] The incidence of serious bacterial infections (SBI) has decreased respectively with 90 % and 64 % after the introduction of Haemophilus B vaccination in 1993 and pneumococcus vaccination in 2006. [6,7] The decreased incidence of SBI as well as nonspecific signs and symptoms early in the disease course hamper early recognition of SBI. In the last decade, associations between patient characteristics and SBI have been evaluated in order to develop evidence- based guidelines. The frequency of SBI depends on the population

Table 2 Mortality at the ED

	N (%)
Total number of children	23 (0.1)
Median age (IQR)	2.0 (0.3-7.1)
Gender (male)	13 (56.5)
Medical problem	
Acute respiratory failure	10 (43.4)
Unresponsive child	8 (34.8)
Shock	2 (8.6)
Acute cardiac failure	1 (4.3)
Seizure	1 (4.3)
Unknown	1 (4.3)
Chronic comorbidity	
No chronic comorbidity	4 (17.4)
Non- complex chronic comorbidity	3 (13.0)
Complex chronic comorbidity	3 (13.0)
Missing	13 (56.5)

and the setting. In primary care, the incidence of SBI has decreased; less than 1% of children with fever will have a serious infection.[8] This makes early recognition even more difficult compared to the ED, where the incidence of SBI is 10-15%, depending on the population mix.[9,10].[11] This has to be taken into account by attending physicians, working in different settings, having to deal with the same patient group at risk with a different a priori risk.

Serious morbidity and mortality may not only arise from serious bacterial infections, but also from a complicated disease course of a common viral infection. Viral diseases with a complicated disease course together with all diagnoses covered by SBI define serious infections (SI). An important common viral illness with a risk of a complicated disease course is acute gastro-enteritis (AGE). Usually AGE is a self-limiting viral infection. However, if early recognition and treatment of extensive vomiting or diarrhea are delayed, and alarming signs and symptoms are not adequately interpreted, severe dehydration and eventually hypovolemic shock can occur. This is the main reason that AGE still is in the top 3 diagnosis related with childhood fatalities in malpractice, next to sepsis and meningitis.[12,13] In this thesis, we will focus on AGE in order to address early diagnosis and treatment as well as discharge instructions (safety netting). Consensus guidelines and systematic reviews have gained evidence for alarming signs in primary and hospital care. [14] (Table 3) In an extensive review on the evidence for alarming signs, the association between SI and 'cyanosis', 'tachypnea', 'decreased capillary refill', 'non-blanching rash', meningeal irritation' and 'decreased consciousness' was shown. [15] To our

knowledge, no single clinical sign or symptom, or guideline, captures in- or exclusion of a serious infection.[10] In addition, more general or subjective items were evaluated. Worried parent' and attending physicians or nurses' gut-feeling 'something is wrong' appeared of value in predicting a SI.[16,17]

Table 3 Alarming signs and symptoms mentioned in guidelines versus systematic review evidence. Adapted to "Alarm symptoms of meningitis in children with fever". Geurts DH, Moll HA. Ned Tijdschr Geneeskd. 2011;155:A2293.

Alarming Sign	**NHG- guideline 2016[20]**	**NVK guideline 2013[21]**	**Evidence review 2010[16]**
Ill appearance	X	X	Yes
Pale	X	X	No
Drowsy	X	X	No
Unresponsive	X	X	Yes
Irritable/ inconsolable	X	X	No
Tachypnea	X	X	Yes
Chest wall retractions	X	X	Yes
Cyanosis	X		Yes
Feeding difficulties			No
Dry mucous membranes			No
Decreased skin elasticity	X	X	No
Abnormal capillary refill	X	X	Yes
Decreased urine production			No
Persistent vomiting	X		No
Temperature > 38 ˚C age 0-3 months			No
Temperature > 38 ˚C age >3 months			No
Temperature > 38 ˚C age <1 month		X	
Non-blanching rash	X	X	Yes
Bulging fontanelle	X	X	NA
Meningeal irritation	X	X	Yes
Convulsion	X	X	Yes
Focal neurological symptoms	X	X	No
Bilious vomiting		X	NA
Worried parent			Yes
Clinician instinct that something wrong			Yes

NA= not applicable

= evidence- based sign present in both guidelines

A **third** learning point is that we observed 40% revisits in the entire ED population, which is a high number.[18] Revisits depend on patient mix and admission policy. Moreover, we could not identify a standardized discharge procedure. The main components of discharge instructions have been identified by the concept of safety netting, i.e. to include standardized information on expected disease course, when and how to seek help en instructions on alarming signs and symptoms. [19]

Gaps

We will discuss gaps in pediatric emergency medicine research in this thesis. In the post-vaccination era with a low-prevalence of SI, health care professionals, as well as parents and caretakers of (young) children need to be aware and educated on early recognition of alarming signs and symptoms. A number of good quality guidelines exist, however several of them are not appropriately validated or implemented. Last, evidence is lacking on how to arrange optimal safety netting after an ED visit.

Aims and outline

In this thesis we aimed to improve risk assessment and safety netting at the ED in children with infectious diseases. We focus on:

1. **Early recognition and treatment** of a vulnerable population of children at the ED
2. **Optimizing** the implementation and use of guidelines and clinical decision support
3. **Improving** the process of discharge from the ED

In order to answer these research questions, the importance of **early recognition** of serious infections in general is addressed (chapter 2 'Malpractice in paediatric emergency care in the Netherlands- what can we learn?'). In children with AGE, risk assessment and treatment as well as follow-up are discussed (chapter 3 'Do we need weight in the assessment of dehydration in children with acute gastro-enteritis at the emergency department?', chapter 4 'Implementation of clinical decision support in young children with gastroenteritis at the emergency department: a randomised controlled trial' and chapter 5 How to predict failure of rehydration in children with acute gastroenteritis').

After recognizing the patients at risk, the process of diagnosis and treatment can be improved by **optimizing** the implementation of up to date guidelines. (chapter 6 'Urinary tract infection in children: impact analysis of an evidence based guideline', and chapter 7 'Implementation of a written safety netting advice for parents of feverish children at risk for serious infection at the emergency department'). Last, in order sustain the use of guidelines and decision rules, we have to monitor and fine-tune implementation (chapter 8 ' Measuring acceptability of two clinical decision models in the emergency department using the Ottawa Acceptability of Decision Rules Instrument (OADRI)').

As uncertainty on diagnosis or disease course remain in a significant number of patients after an ED visit, patients at risk in need for a revisit need to be identified and

discharge instructions need to be **improved** in order to empower (parents of) patients in adequate at home management and initiate adequate return visits (chapter 9 'Tools for 'safety netting' in common paediatric illnesses: a systematic review in emergency care', and chapter 10 ' Characteristics of revisits of children at risk for serious infections in paediatric emergency care').

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Chapter 2

Malpractice in pediatric emergency medicine: what can be learned?

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INTRODUCTION

Pediatric malpractice lawsuits are rare in the Netherlands, and very traumatic for health care workers, as well as parents. Children are a vulnerable, in particular at the emergency department (ED), where patients are in need of acute assessment and immediate treatment. Moreover, we are increasingly faced with children with a (complex) underlying illness and involvement of several medical specialists. This patient group is even more at risk, due to multiple medication use and a higher risk of a complicated disease course.

In this chapter, we review 19 pediatric emergency care malpractice lawsuits dated from 2001 until 2010. A patient case of an infant who died of a meningococcal sepsis underlines the main messages (Box1). This is one of the most serious infections in children with fever, with non-specific symptoms early in the disease course, leading to a fulminant sepsis, with a high mortality rate. The child was presented at the GP office. The GP assessed the child as seriously ill and admitted the child to the ED. The different claims in this particular case, made by the parents and the decisions of the court are presented in Table 1. In this case, the claims were declared grounded by the disciplinary court. The disciplinary measure was based on the following aspects: diagnosis, starting of treatment, medical guidance, observation of the patient during admission, composing and management of the medical record and communication.

The aim of this chapter is to give insight in all malpractice lawsuits in pediatric emergency medicine in the Netherlands in the last decade and to evaluate which lessons can be learned. From these insights, interventions can be developed to improve pediatric emergency care.

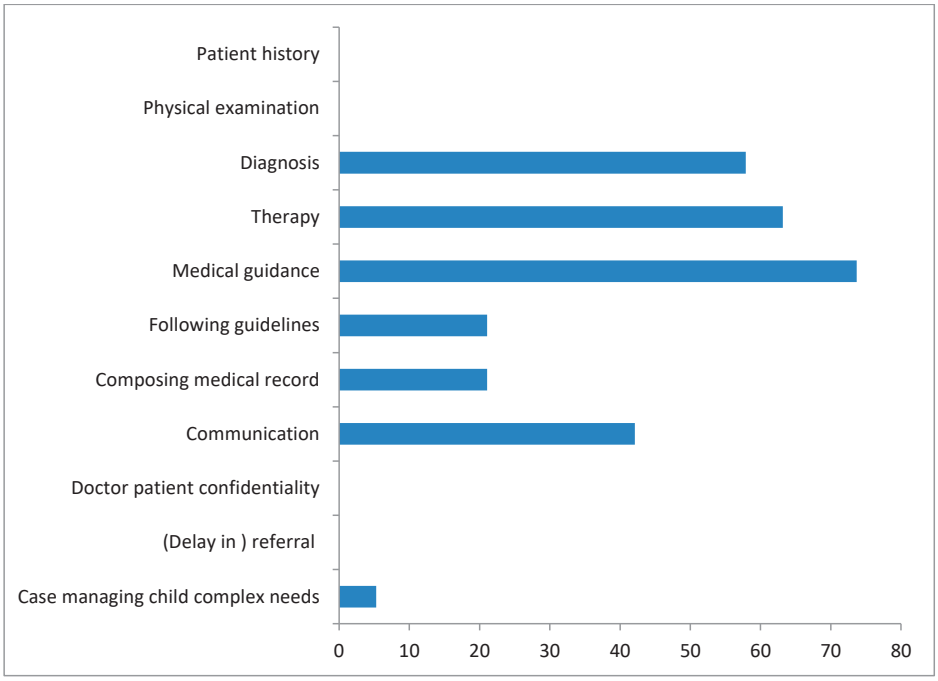
OVERVIEW

Nineteen malpractice lawsuits (2001 to 2010) were handled by the Regional Disciplinary Committee (RTG) and at the Central Disciplinary Committee (CTG) (appendix 1). Eleven complaint categories were identified (Figure 1).

In 16 cases the lawsuits were declared grounded. The five most frequent claims concerned the following categories 1) diagnosis, 2) treatment, 3) medical guidance, 4) providing insufficient information and 5) communication. Together, they make up 80% of all claims, with claims in multiple categories in 10 lawsuits. Most common diagnoses were serious (bacterial) infection and a (complicated disease course of) rare disease. Patients were of young age (50% was under the age of two years), 67% were male and 5 children died.

In England, 234 pediatric medical lawsuits (2004 until 2011) with a lethal outcome were described.[1] The most common causes of death were delay in diagnosis and/or

Figure 1 Complaint categories of all included law suits (N=19)



treatment, followed by complications from procedures or surgeries, poor quality of care, medication errors, inadequate medical advice leading to a delay in first presentation and communicational complaints. The most common diagnoses were sepsis/meningitis, cardiac disease, gastrointestinal disease, intracranial hemorrhage and malignancies. Medical law suits of 228 children in France (2003-2007) more often addressed children younger than 2 years (52%) and children with a more serious outcome. Meningitis and dehydration were the most common diagnoses.[2] In these lawsuits, mostly pediatric emergency physicians and general practitioners were involved. Claims addressed most often a delay in diagnosis and treatment, leading to severe morbidity and mortality.

Medical law suits provide insight into medical errors, although most medical errors do not lead to a medical law suit. It is important to not only report medical errors leading to a medical law suit, but to report all medical errors, in order to evaluate and to implement measures to prevent occurrence of the same errors in the future.

In the past few years, increasing attention is drawn to improve patient safety and safety management systems. It is important that there is an easy to use and available report system with a low threshold also for ' almost-errors'; that ' blame-free reporting

is possible and that all employees, at all levels, are involved. Conclusions and measures should be regularly evaluated and reported.[3]

WHAT CAN BE LEARNED ?

Diagnostics/diagnosis

The example patient A (Box 1) describes a patient with a serious bacterial infection with a fatal disease course. Dilemmas, decisions and considerations of the medical team are described, as well as the parental perspective. Serious bacterial infections in children with fever are rare, concerning around 1% of the patients in general practice, to 10-15% of the children at the emergency department. [4,5] The most common serious infections in young children are meningitis, sepsis, urinary tract infections, pneumonia and dehydration in acute gastroenteritis.

After the introduction of the Haemophilus influenzae b (HIB) vaccination in 1993 and the pneumococcal vaccine (PCV7) in 2006, serious infections such as meningitis, decreased by 90% and 64% respectively.[6,7] As a result, early recognition of a serious infection in children is an increasing diagnostic dilemma. Because it is rare, expertise in recognizing serious infection decreases. The time course can be an important diagnostic tool, with initially non-specific symptoms resulting in a serious infection with alarming symptoms. [8]

Box 1

A. is a one year old boy. At 17:45 complainants arrived at the GP. The doctor noted the following: "He had been vomiting all day." Parents described him having a fever, although they did had not measured it. He would not eat or drink. His breathing was heavy/laboured, he was not responding to his mother. On physical examination, the GP saw a pale, sick child with tachypnea, who was unresponsive. He had a temperature of 40.8 ˚C.. No petechiae, no meningeal irritation.

The GP concluded that the boy was unwell, with a probable diagnosis of meningitis, and referred the child directly/urgently to the emergency department.

Within fifteen minutes the parents arrived at the emergency department where the pediatrician was already present. The attending pediatrician took the history once more, noticing a minor difference: instead of "vomiting all day", "vomited twice" was noted in the patient file. Vital signs measured at the start of physical examination were: a temperature of 41 ˚C, a heart rate of 183/ min, a respiratory rate of 80/ min and the oxygen saturation of 96%. At that moment, the attending pediatrician noted minimal neck stiffness in a pale, but awake child, who did not respond adequately. Additional diagnostics were performed, namely hematology, chemistry, blood gas analysis, urine sediment, blood culture, lumbar puncture with CSF tests and chest X-ray. C-reactive protein was 26 mg/L, the number of leukocytes in full blood count were 2.1 x 109/1. The liquor/ CSF was clear and the CSF Gram stain showed no bacteria. The patient file/medical notes included the following differential diagnosis: 1.meningitis 2.viral infection 3.bacteraemia. At the ED, he received paracetamol 240 mg rectally, and he received an intravenous fluid bolus of 270 mL of NaCl 0.9% in 30 minutes, he was started on and continues intravenous fluid therapy of 5% glucose / NaCl 0.45% at 50 ml/hour was started. Meanwhile his clinical situation improved. The attending pediatrician concluded the patient was suffering from fever without origin due to a viral infection, sepsis/ meningitis as the differential diagnosis.

Next, the patient was admitted to the pediatric ward. The attending paediatrician (who was covering both wards and the ED) left after providing instructions for regular monitoring of vital signs to the nurse.

A few hours later, the attending nurse measured a temperature of 37 ˚C. There was some urinary output. When changing the diaper, two petechiae were observed. The attending pediatrician was informed immediately, arriving shortly after the call. Blood pressure had dropped from 91/43 mmHg to 61/31 mmHg, with a heart rate 168/min, respiratory rate of 30/ min and an oxygen saturation of 94%. Antibiotic treatment was started, changing the diagnosis to presumed meningococcal sepsis with shock and impending respiratory failure.

Two hours later, the attending pediatrician informed the PICU team by telephone with the pediatric intensive care (PICU) doctor, who concluded that the patient was hemodynamically unstable, and advised to give additional intravascular fluid, and to consider endotracheal intubation if intravenous boluses exceeded 60 mL / kg, and to start intravenous inotropic support with dopamine as peripheral infusion. Also, PICU advised to transfer the patient to the local intensive care unit in awaiting the of the pediatric intensive care transport retrieval team; the patient was transferred to the local ITU immediately and the retrieval team mobilized.

Half an hour later, the local on call anesthesiologist was notified. He observed a patient with a stable blood pressure and 100% oxygen saturation. The anesthesiologist was asked to intubate the patient, which was declined, stating that endotracheal intubation was not indicated at that time.

A second consultation with the off-site pediatric intensive care doctor took place, again advising endotracheal intubation alongside providing central venous access and an arterial line. The attending pediatrician did not have the skills/competencies to provide this type of care and requested the local anesthesiologist again for support. .

The attending pediatrician re-examined the patient and that moment in time, the PICU retrieval team arrived. They proceeded to nasal endotracheal intubation immediately, which was complicated by a massive nosebleed. Subsequently, the local anesthesiologist was called back in, who then intubated by oral ETT, with the insertion of a gastric tube.

Directly after this procedure, the patient deteriorated, with a drop in blood pressure accompanied by bradycardia. Compressions were started, dopamine dosage was raised twice. Also atropine and intravascular boluses were administered. Thirty minutes after intubation there was no return of spontaneous circulation and the patient had non- responsive, pinpoint pupils. At this point in time, the decision was made to cease resuscitation efforts.

Parents were sent outside the resuscitation room during the intubation and were not present during resuscitation. When the parents returned, a nurse informed them that the patient/their child had died. The attending pediatrician approached the parents, providing them with antibiotic prophylaxis (rifampicine). Parents were advised to send anyone to the hospital, who had been in contact with their child. The next morning, the parents gave permission for an autopsy. The syndrome of Waterhouse-fried Homer (double adrenal hemorrhage) was the designated cause of death.

Table 1 Complaints in patient case A (Box 1)

Complaint categories	Complaint- detailed description	Verdict
Patient history and physical examination Diagnosis thesis	Disregard of the probable diagnosis of the GP	Unfounded, differential diagnosis of fever without source was accurate
Therapy	Delayed administration of antibiotics	Unfounded, although peer collegues will probably start antibiotics earlier, one single protocol does not exist
Medical supervision during treatment (sufficient urgency, proper execution of procedures)	Insufficiently providing specific observation instructions to the pediatric nurses Administration of dosage rifampicin was incorrect.	Partially grounded, there was continuous monitoring surveillance, however, inadequate frequency of blood pressure checks. Given the stressful circumstances and self-reporting of the incorrect dosage by the attending pediatrician, no serious accusation is justified. This complaint is of insufficient weight to be of disciplinary relevance.
Compliance to guidelines	Not following resuscitation guidelines. Failure to follow up the advice from the pediatric intensive care doctor	Unfounded and not in conflict with resuscitation guidelines Endotracheal intubation and providing central venous acces id not a standard skill of a local pediatrician Advice of the local anesthesiologist was indeed followed up
Patient file management	Records of the intensive care admission were lacking	Grounded, regarded as negligent, should take place immediately after acute situation
Patient information is insufficient, inadequate communication	Communicating insufficiently with the parents during the resuscitation process Refusing parents access to their child in a resuscitation setting	Unfounded, at that time it was hospital policy to not let parents be present during resuscitation of their child
Professional confidentiality / sharing medical data	Violating the privacy of parents to provide third parties with information about the autopsy results	Grounded, except for the duty to warn relatives of the patient who had been in contact, the attending pediatrician was not allowed to communicate on the cause of death with others
Referral	Not applicable	
Leading pediatrician in team of multiple specialist.	Not applicable	

An important recent development in the appraisal of the complaint in medical law suits concerning children at the ED is that the penalty is largely based on the severity of the consequences. In civil, but also in criminal law, a trend exists towards assessing the penalty with regard to the severity of the consequences or the damage done. Next, backwards reasoning leads to legal responsibility. This is legally not accurate, but happens increasingly in daily practice.

In conclusion, in case of a hypothetically larger risk, the better the safeguarding must be. The downside is, that this leads to defensive medicine, which might be in conflict with best practice.

Therapy

Medical guidance includes diligence. Example case A describes a young child with fever with initially nonspecific signs and symptoms, resulting in a serious bacterial infection. Although other pediatricians in a comparable professional discipline probably would engage a less watchful waiting policy concerning the start of antibiotics, a consensus opinion does not exist and it was regarded as a non- imputable act. This indicates how difficult it can be to assess these children and make a decision. It is therefore advisable to weigh the cost of error and create a safety net, especially after discharge from the emergency room. This includes instructing parents (preferably in writing) on a number of aspects: the uncertainty of the diagnosis, with a severe bacterial infection as a possibility, the expected time course of the disease, alarming signs and symptoms and how to seek medical care if and when needed.[9] This concept can also be used during a clinical observation. Take the expected clinical course as a reference, determine the expected moment in time alarming signs and symptoms might occur and include appropriate monitoring and evaluations in order to register any deterioration in time.

In the example case, the Disciplinary Board determined that taking blood pressure measurements every three hours was of not frequent enough to notice any deterioration in time. This was concluded because of the seriousness of the disease and the rapid deterioration, although continuous monitoring of respiratory and heart rate had been carried out as agreed. The starting point in a disciplinary assessment will more and more the ' worst-case scenario'.

One could come to the conclusion that the pediatrician should use the most invasive diagnostic tools and treatment methods as early as possible. However, to put this in perspective, pediatricians actually can restrain in used management by taking reasonable cost-effectiveness into account. The reasonable cost-effectiveness is valued as usual and acceptable by professional peers.

Communication

In a number of cases parents indicated that the disease was different than their child's previous illness-episodes (i.e. parental concern).[5] Parents are quite capable of assessing the disease severity of their child. Parents can consult the general practioner (GP) for their child, but it happens quite often that a parent decides to go directly to the emergency room (self-referred), particularly in the large cities. Comparing disease severity of children with fever referred by the GP, to the disease severity of children whose parents came directly to the emergency room (self-referred), showed, although self-referred

children appeared less seriously ill, that 1 in 4 self-referred children received extensive diagnostics and/or treatment and/or admission.[10] Additionally, 'parental concern' appeared a significant predictor of a serious bacterial infection.[5]. It is important to literally ask parents this question.

Communication is an integral part of pediatric care. Communication takes place between the patient, the parents and the team of doctors, nurses and other health care providers. An emergency department visit or admission is a stressful event for patients and parents. Careful communication is even more sensitive under emotional conditions, since parents experience emotions of helplessness, insecurity and anxiety. These emotions influence non-verbal and verbal reactions. Communication between parents and healthcare providers contains aspects like negotiation, recognizing and careful consideration. The needs of parents should be met as much as possible. A health care professional should show interest in the parents ' perspective and adapt, in order to work together and involve the parents in their child's treatment.[11]

Following guidelines and expert opinion

The number of guidelines for diagnosis and treatment are increasing. In emergency care, not only disease-specific guidelines, but also problem-oriented guidelines are needed (for example 'fever in children'). Per individual patient the indication to follow a guideline or deviate from it will be decided by the physician. However, if a pediatrician deviates from a specific guideline without documenting arguments, this will be judged as inaccurate medical practice. In our case, the pediatric intensive care doctor advised, in anticipation of his arrival, to transfer the patient to the local intensive care unit, and to intubate and line-up the patient. The local attending anesthesiologist did not consider this as necessary. Which advice needs to be followed? The most correct answer is: the most safe advice. In the present case, the pediatric intensive care doctor's advice had to be followed, overruling the local anesthesiologist. Surely, a difficult task, especially if it concerns a pediatrician with little experience. We recommend to describe in your patients file whether or not guidelines were followed and why. In this case, if reasoning for treatment indications and patient file management were clearly addressed, there will be no room for a slap on the wrist.

Patient file management

Patient file management should be carried out immediately, or as soon as possible after patient assessment, diagnostics and treatment. In the current electronic file systems who entered which data at what time is registered automatically. Also file adjustments are traceable. Late patient file adjustments (for example, a day later), will often seem 'suspicious'. All aspects of assessment, monitoring, diagnostics and treatment should be adequately registered, including consultation of other professionals. This seems a

lot of effort, but it pays off when the incident must be evaluated in retrospect. The (disciplinary) law attaches more value to the actual content of the patient file, than to later statements of involved parties. The patient file is regarded as 'what really happened'.

Coordination of care

Case 7 (in appendix 2) describes a patient with a complex chronic illness of multiple organ systems, treated and monitored by several medical specialists. The complaint concerned 1) failure to inform the entire multidisciplinary treatment team through a complete medical file, 2) not using the appropriate pain protocol, 3) wrongly drawing the conclusion, the patient died a natural death and 4) the incorrect/incomplete request of an autopsy. Only remark number three was legitimate, especially because death took place within hours after surgery.

Managing and informing everyone in the multidisciplinary treatment team of patients with a complex chronic condition should be of high priority, in order to prevent calamities and unexpected complications. In this case, the patient was not seen by his pediatrician for over 14 months, because the patient had not shown up for his appointments and visited another hospital. Therefore, the complaint was regarded as unfounded.

The number of children with (complex) co-morbidity and multiple medication use increases, due to better survival rates. They form a very vulnerable patient group in the pediatric emergency department, because of 1) a higher risk of under- triage with a delayed evaluation as a consequence [12] , 2) often several medical specialists are involved (who coordinates care?), 3) the higher risk for a complicated disease course of an apparently common disease and 4) the multiple medication use with a higher risk of dosing and interaction errors.[13] All these aspect should be taken into account during the assessment at the emergency department. It is essential in these chronic complex patients that one physician is appointed as the case manager. In addition, each individual physician has to have an overview over the whole medical file and also provide his/her contribution, especially changes in medication regime. Information can be misunderstood or lacking during transfer and communication between stakeholders. Therefore, it remains important to keep the file complete and fully updated!

CONCLUSION

Pediatricians will encounter patients with a serious disease or serious complication , as well as patients with rare diseases. Furthermore, the number of patients with severe complex co-morbidities and use of multiple medication will increase. As the risk and the consequences will be more serious, the judgement afterwards will be stricter.

Be watchful, and include safety measures like consultations with colleagues, the use of guidelines, clear agreements on which physician plays what role in the diagnosis and treatment. Also, manage your patient file adequately. Last, in safe pediatric emergency care, parents play an important role; give them appropriate and re-useable information on alarming signs and symptoms, and inform them on when and how to seek help and to organize a secure safety net.

Appendix 1 All included malpractice cases

	Patient characteristics	Complaint category	Considerations	Verdict	Measure
1	Male, 2 months, operating room / hospital, burns after warm heat mattress, sequelae.	Therapy, compliance to guidelines, incomplete patient file	Attending physician should have thought of cooling. incomplete patient file	Partly grounded	Warning.
1a	Same as 1.	Same as 1.	Adequate therapy (cooling) was considered; expert advice was followed	Unfounded.	Rejected.
2	Male, 1 year, hospital, fatal intracranial hemorrhage	Diagnosis, incomplete patient file, medical guidance, communication.	Insufficient forceful medical handling, adequate differential diagnosis and initiated therapy, however missing essential blood values, adequate medical file, communication intangible	Partly grounded. Basic error in underestimating severity of illness, in which physician's attitude has played role.	Reprimand.
3	Female, 1 year, fatal medication error	Therapy, medical counseling.	Negligence denied on all complaints.	Rejected.	No.
3 a	Same as 3 .	Therapy, medical counseling.	Negligent on dosage control, worried parent dienied instead of interpreted as an alarming signal. Other unfounded.	Partly grounded	Reprimand.
3 b	Same as 3 , Focused on supervisor	Therapy.	Negligent on dosage control	Grounded.	Warning.
4	Male in hospital with fatal meningitis	Diagnosis, therapy, medical guidance	Incorrect treatment grounded	Partly grounded.	Warning.
5	Male, 14 years, hospital, fatal Addisons crisis	Diagnosis, therapy.	Situation underestimated, insufficient forceful medical handling,	Grounded.	Warning.
6	Female, 14, suspected sepsis / meningitis, no sequaelae	Diagnosis, therapy.	Out of hours with hospital-unfamiliar attending physician Situation underestimated sufficient up-to-date medical knowledge, insufficient forceful medical handling,, inadequate communication nurse.	Grounded.	Reprimand.

Appendix 1 All included malpractice cases (*continued*)

	Patient characteristics	Complaint category	Considerations	Verdict	Measure
7	Female, 8 years, spina bifida, hospital, fatal resuscitation hours after elective surgery	Incomplete medical file, medical support, compliance guidelines.	Incomplete medical file, incorrect protocol, unjustly 'natural death', issued incorrectly applied autopsy.	Grounded.	Warning.
8	Male, 7 years, outpatient clinic, mother drugging, no sequelae.	Therapy, medical guidance, communication.	Unusual medication dose, lack of medical guidance, insufficient information, GP not informed.	Grounded.	
9	Female, 2 months, failure to thrive, pallor, nutritional problems.	Diagnosis, medical guidance, communication		Partly grounded (pediatric cardiologist should have been consulted), other unfounded.	Warning.
10	Female, 16 years old, fatal cerebral herniation and cerebellar hemorrhage due to severe staphylococcal pneumonia following influenza infection	Diagnosis, therapy, medical guidance, communication	Negligence, inadequate observation, underestimate situation (after previous intensive care transfer), insufficient communication on the severity of illness	Initially unfounded; grounded after appeal.	Warning.
11	Male, 9 years, hospital, divorced parents, attending physician depends solely on history mother; father not heard, no sequelae.	Therapy, medical guidance, communication	Insufficient history taking, no expertise others invoked, prescribing of medication without first checking all caregivers	Grounded.	Measure.
11a	Same as 11	Therapy, medical guidance, communication	Same as 11.	Grounded for prescribing medication (dipiperon), not grounded on other complaints	

Appendix 1 All included malpractice cases (*continued*)

	Patient characteristics	Complaint category	Considerations	Verdict	Measure
12	Male, 1 year, hospital, fatal sepsis / meningitis	Diagnosis, therapy, compliance to guidelines, insufficient medical file, medical guidance, communication	Diagnosis, inadequate observation, not following up ICU consultation, not following resuscitation guidelines, insufficient medical file, inadequate communication during resuscitation, parental access denied during child CPR , incorrect dosage antibiotic prophylaxis, privacy violated by providing information to third parties .	Partly grounded for insufficient specific observation instructions, observation, insufficient medical file, violation of privacy. All others unfounded.	Warning.
12a	Same as 12	Diagnosis, therapy, compliance to guidelines, insufficient medical file, medical guidance, communications.	Same as 12	Grounded on not adequate differential diagnosis (sepsis); not immediately starting of antibiotics (but for shooting under observation); also to low dose prophylactic antibiotics.	Reprimand.
13	Female, 6 months, bullous congenital ichtyosiforme erythroderma, meningitis.	Diagnosis, medical guidance, communication	Diagnosis, inadequate attention to history and growth chart, parental concern	Unfounded.	No.
13a	Same as 13	Diagnosis, medical guidance, communication	Same as 13	Grounded, negligence.	Warning.
14	Male, 6 months, hospital, vesico-urethral reflux, contracted kidney	Therapy, medical monitoring, compliance to guidelines.	Insufficient monitoring patient out of hospital, possibly leading to kidney failure as a result, unregistered foreign doctor.	Founded on unregistered doctor, however because worked under supervision, no measure was taken. Other complaints unfounded.	No.

Appendix 1 All included malpractice cases (*continued*)

	Patient characteristics	Complaint category	Considerations	Verdict	Measure
15	Male, 13 years old, swelling jaw, diagnosis fibrous dysplasia, no sequealae	Diagnosis,, medical guidance, lack of leading physician.	Insufficient communication on diagnosis, lack of guidance and communication.	Grounded, doctor did not provide care that was needed.	Warning.
15 a	Same as 15	Diagnosis, insufficient / medical supervision, directing lining.	Diagnosis, insufficient incomplete parental information adequate ,referral to tertiary center, but also monitoring local hospital, poor communication, lack of guidance.	Grounded, doctor did not provide care that was needed.	Warning.
16	Male, 2 months, hospital, cow milk allergy, maternal diet, vomiting, rash, diarrhea, crying.	Medical guidance, communication.	Poor communication and failed diagnostic consultation. Inadequate medical history, social situation (post-natal depression mother in recent history) disregarded.	Grounded on communication, other unfounded.	No measure.
17	Male, metabolic disease and epilepsy, hospital, high dose of morphine administered No sequealae.	Therapy.	Inadequate treatment.	Grounded.	Warning.
18	Male, 3 years old, abdominal pain, infection / testicular torsion which removed testis as a result.	Diagnosis	Incorrect diagnosis, delay treatment.	Grounded.	Warning.
19	Male, 6 years, ADHD, PDD NOS, limited intelligence level, outpatient clinic.	Diagnosis, therapy, medical guidance.	Disagreement on medication treatment (starting Ritalin) between divorced parents, doubts on diagnosis by psychologist	Partly grounded (insufficient evaluation before starting medication)	Warning.

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Chapter 3

Do we need weight in the assessment of dehydration in children with acute gastro-enteritis at the emergency department?

Geurts DHF, Moll HA, Oostenbrink R.

Eur J Pediatr. 2018 Feb;177(2):273-274.

ABSTRACT

We respond to Falszewska et al. who concluded that the Clinical Dehydration Scale (CDS) is of limited diagnostic value only in ruling-in severe weight-change based dehydration in children with acute gastroenteritis (AGE), whereas the WHO and the Gorelick scale showed no association.

We performed a cross-sectional observational study on the association between weight change and the CDS in children, aged 1 month- 5 years with AGE at the ED of the Erasmus Medical Centre, Rotterdam, The Netherlands, between 2010- 2012.

In 222 included children, we achieved repeated weight measurements in only 58(26%; male 44.8%, median age 1.2 years). A mean weight difference(kg) of 0.06 kg(CI95% -0.02 - 0.14 kg) was observed. CDS showed absent to mild dehydration in 32 (55%) patients. CDS-based dehydration had a sensitivity of 0.80 (95%CI 0.30-0.99), specificity of 0.58 (95%CI 0.44-0.72), positive likelihood ratio 1.90 (95%CI 1.12-3.32) and negative likelihood ratio 0.34 (95% CI 0.06-2.00) to predict weight-change based dehydration.

Conclusion

In a pediatric ED population with AGE, repeated weight measurements appeared not feasible in clinical practice. Weight change was very limited given the mildly dehydrated population. The CDS showed moderate sensitivity and low specificity for weight-change based dehydration. Given the low feasibility of weight-change based dehydration, use of CDS may outperform weight change in the assessment of children with AGE in a setting with a low prevalence of moderate /severe dehydration.

CORRESPONDENCE LETTER

With great interest we read the paper of Falszewska et al.[1]on the diagnostic accuracy of clinical dehydration scales in children. They observed limited diagnostic value of the Clinical Dehydration Scale (CDS)[2] only in ruling-in severe weight-change based dehydration, whereas the WHO[3] and the Gorelick scale[4] showed no association.

Pre- and post- illness weight change is considered the gold standard in the assessment of dehydration in children with acute gastroenteritis(AGE). However, pre- illness weight rarely is available at presentation. Similar to Falszewska, we used weight change as a reference standard of dehydration during our Randomized Controlled Trial (NTR number2304) on ambulant rehydration in children aged 1 month- 5 years with AGE visiting the emergency department (ED) of the Erasmus Medical Centre, Rotterdam, The Netherlands,2010- 2012.[5]

Of 222 included children, we achieved repeated weight measurements after 24 hours (median 22 hours, IQR18-37 hours) in only 58 (26%; male 44.8%, median age1.2 years) due to lack of cooperation of parents. A mean weight difference(kg) of 0.06kg(CI95%0.02 - 0.14) was observed after rehydration. The CDS showed absent to mild dehydration(CDS-score≤4) in 32(55%) patients. CDS-based dehydration(score>4) showed a sensitivity of 0.80 (CI95%0.30-0.99) and a specificity 0.58(CI95%0.44-0.72) to predict weight-change based dehydration, with a positive likelihood ratio of 1.90 (CI95%1.12-3.32) and negative likelihood ratio 0.34 (CI95%0.06-2.00).

In conclusion, repeated weight measurements were not feasible, our cohort showed a very low prevalence of children with clinical dehydration and CDS-based dehydration showed low performance to predict weight-change based dehydration in a pediatric emergency population with AGE. Observing safe and feasible CDS-based nurse-led rehydration, with adequate rehydration in the few children with moderate dehydration[5], use of the CDS may outperform weight change in the assessment of children with AGE in a setting with a low prevalence of moderate /severe dehydration.

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Chapter 4

Implementation of clinical decision support in young children with acute gastroenteritis: a randomized controlled trial at the emergency department.

Geurts DHF, de Vos-Kerkhof E, Polinder S, Steyerberg E, van der Lei J,
Moll HA, Oostenbrink R.

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ABSTRACT

Acute gastroenteritis (AGE) is one of the most frequent reasons for young children to visit emergency departments (EDs).

We aimed to evaluate1) feasibility of a nurse- guided clinical decision support system for rehydration treatment in children with AGE and2) the impact on diagnostics, treatment and costs compared with usual care by attending physician.

A Randomized Controlled Trial was performed in222 children, aged 1 month-5 years at the ED of the Erasmus MC-Sophia Children's hospital in The Netherlands(2010- 2012).

Outcome included1) feasibility, measured by compliance of the nurses and2) length of stay (LOS) at the ED, the number of diagnostic tests, treatment, follow-up and costs. Due to failure of post- ED weight measurement, we could not evaluate weight difference as measure for dehydration.

Patient characteristics were comparable between the intervention (N=113) and the usual care group (N=109). Implementation of the clinical decision support system proved a high compliance rate. The standardised use of oral ORS (oral rehydration solution) significantly increased from52% to65%(RR2,2, 95%CI 1,09-4,31 p <0.05). We observed no differences in other outcome measures.

Conclusion

Implementation of nurse-guided clinical decision support system on rehydration treatment in children with AGE showed high compliance and increase standardised use of ORS, without differences in other outcome measures.

INTRODUCTION

Acute gastroenteritis (AGE) is one of the most frequent reasons for young children to visit the emergency department (ED). Clinical dehydration scores are often used to assess severity of dehydration. These scores attempt to differentiate children without signs of dehydration from those with moderate dehydration or those with severe dehydration with signs of hypovolemic shock. [1; 2] The most commonly used clinical dehydration scale (CDS) is a 4- point scale, which includes four clinical signs (ie. general appearance, eyes, mucous membranes and tears). [1] The CDS has been incorporated in several clinical guidelines for appropriately managing acute gastroenteritis or dehydration. [3-6] Although clinical guidelines aim to assist standardised assessment and treatment of dehydration, clinicians often don't adhere to the guidelines' recommendations. Incorporating a guideline in an electronic, easily accessible clinical decision support system can improve guideline- adherence and therefore quality of care. [7]

In this study, we aimed to evaluate the feasibility of an electronic, easily accessible, guideline-based clinical decision support system, as well as the impact of this nurse-guided clinical decision support system for managing children with AGE at the ED compared to usual care on diagnostics, treatment and costs.

METHODS

Design

We conducted a randomized controlled trial comparing management of children with AGE at risk for dehydration by clinical decision support recommendations with usual care (Nederlands Trial Register (NTR), http://www.trialregister.nl/trialreg/index.asp; NTR2304).

Patients and setting

We included children with acute vomiting and/ or diarrhoea, aged 1 month- 5 years, who visited the ED of the Erasmus MC –Sophia, Rotterdam between May 2010 and December 2012. The Erasmus MC-Sophia is an inner-city pediatric university hospital, with annually 9000 children presenting at the ED. [8] About 35 % of the ED population has chronic co-morbidity.[9] We excluded children with chronic diarrhoea (>7 days), severe dehydration with hypovolemic shock, children with vomiting/diarrhoea with a focus for another infectious disease (e.g.otitis media, urinary tract infection) and chronically ill children with complex needs.

Ethical approval for this study was obtained by the institutional review board (IRB) of the Erasmus MC. Informed consent was required and obtained from all parents (MEC-2008-071).

Standard of care: initial patient assessment and treatment

Following the standard of care, during the process of triage, trained nurses registered vital signs and weight, as well as signs and symptoms and risk-factors for dehydration for all patients. [10]

Patients randomized to usual care were evaluated by the attending physician who subsequently decided on further rehydration management based on the patients clinical assessment and estimated level of dehydration. Our current guidelines advised rehydration treatment of 10-20 ml/kg/ hour during the length of stay at ED, followed by parental guidance on fluid maintenance as well as treatment of ongoing losses was advised.[11] If oral rehydration did not succeed due to refusal of oral intake ór persistent vomiting, secondly, rehydration by a nasogastric tube was started. As rehydration therapy already was mostly based on oral rehydration using ORS, they received ORS ór any rehydration fluid as prescribed by the attending physician. Anti-emetics were not a part of our national guideline, as evidence on the use of ant-emetics, as well as on safety of ondansetron, was lacking. The guideline could be retrieved from the protocol server of the Erasmus MC website on initiative of the clinician.

The intervention

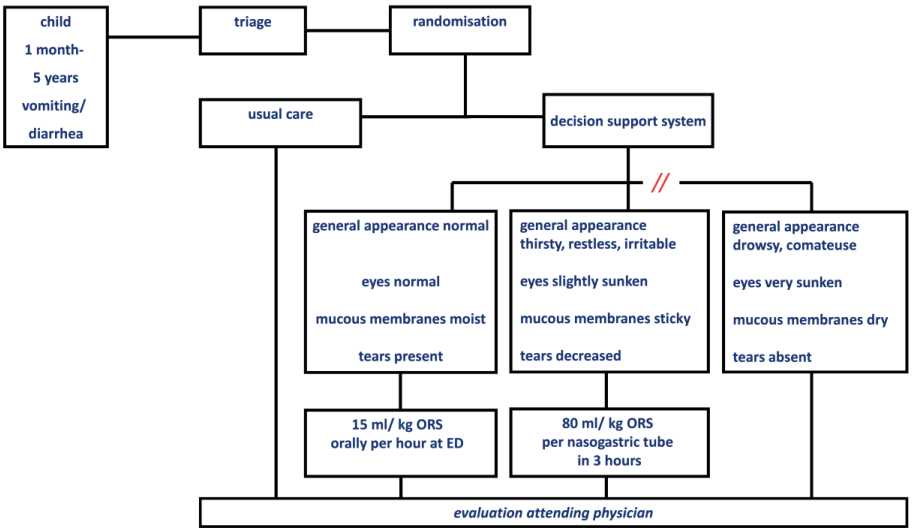
The clinical dehydration scale and current guidelines on treatment of AGE were incorporated in an electronic, easily accessible clinical decision support system, available at each desktop at the ED [1] (figure 1). [3-6] At the time, anti-emetics were not a part of our national guidelines, as evidence on the use of ant-emetics, as well as on safety of ondansetron, was lacking. Therefore, we did not incorporate it in our electronic clinical decision support system.

Through the clinical decision support system, structured data were collected by the nurses on clinical signs and symptoms of all included patients. As the actual intervention included a treatment advice, most important difference with the usual care concerned a standardised amount of ORS for every dehydration level.

If randomized to the intervention, the decision support system generated a guideline-based rehydration advice corresponding to the level of dehydration of the patient (fig 1). The nurse generated the rehydration advice by the clinical decision support system and started the rehydration. Children with mild or moderate dehydration received orally ORS 15 ml/kg/hour. Children with signs of moderate dehydration and/ or persistent vomiting received 80 ml/kg ORS per nasogastric tube in 3 hours. Children without clinical signs of

dehydration also started treatment to prevent dehydration and to assess tolerability of oral fluids, whilst assessing volume of on-going losses.

Figure 1 Clinical decision support system



The randomization was computer-generated and integrated in the clinical decision support system (randomly assigned to both groups depending on even and odd seconds of the digital computer clock). All patients, irrespective of randomization, were evaluated within the time frame generated by the triage system as well as discharged after rehydration by the attending physician. All the clinical dehydration score items had to be completed in order to get a rehydration advice in the CDS. Nurses were blinded for the contribution of predictors on the risk score. If nurse were in doubt on diagnosis and/ or starting treatment, they could, at any stage, overrule the advice of the intervention and consult the attending physician.

Creating an optimal environment for implementation of the decision support system, we created group lectures for nurses at the start of their shift, repeated individual briefings and reminders by posters, email and newsletters periodically. The implementation process was closely monitored and evaluated.[12]

Data collection

We prospectively collected patient characteristics, data on signs and symptoms, vital signs, diagnostic tests, presumed diagnoses, treatment, referral and discharge in a structured electronic hospital patient record system. [13] During the study period,

compliance of CDS recommendations was measured and checked with digital logbook information generated by the clinical decision support system.

To ensure correct diagnosis and ruling-out the possibility a complicated disease course, and be informed about revisits, telephonic follow-up was performed in all patients with standardised questionnaires three days after ED-discharge.

Outcome measures

Feasibility was measured by compliance of the nurses to the recommendations generated by the clinical decision support system. Outcome measures included length of stay (LOS, based on triage registration until the moment of ED- discharge) at the ED, the number of diagnostic tests (electrolytes, acid- base analysis), treatment and follow-up (telephonic consultation, outpatient clinic visit, ED revisit, hospitalisation); and costs. In order to determine the association between level of dehydration and weight change, the ED nurse measure the weight of all included patients at triage and intended weight measurement 24 hours after discharge.

Statistical analysis

Power analysis

Based on previous research at our ED, inclusion of 450 children with acute vomiting/ diarrhoea in 24 months was expected. [14] Initial power estimates were based on the number of correct diagnosed dehydrated children, based on weight change, and its associated false positives and false negatives as described in the trial register. Despite extensive efforts, we did not succeed in repetitive weight measurements in our population, due to lack of cooperation of parents to determine weight after 24 hours, neither at the ED, nor elsewhere. Therefore, we were forced to recalculate power on length of stay (LOS) at the ED. In order to detect a reduction of 10 minutes consultation time (30 minutes standard deviation), 99 patients had to be included in each group for reliable assessment of the actual impact on LOS with a power of 0.8 and an alpha of 0.05 (one-sided test).

Evaluation of the clinical decision system

Being an randomised controlled trial an intention-to-treat analysis was performed.

Feasibility was measured by comparing treatment advice generated by the clinical decision support system with the actual treatment using Chi square analysis. Outcome measures were evaluated using Chi square and Student's t test. Due to failure of measurement of post ED weight, we had to delete the outcome for correct diagnosis of dehydration. A p-value <0.05 was considered statistically significant. We used SPSS version 20.0 for Windows.

Cost analysis

Cost-analysis was performed from the hospital perspective (Appendix). [15] Medical costs were calculated by multiplying the volumes of health care use with unit prices. We used real unit prices when available; otherwise charges were used as a proxy for real costs. Salary schemes were used to calculate costs per hour for each health care worker. In-hospital medical costs included costs of initiated diagnostics and treatment, length of stay at the ED, hospitalization and revisits. Volumes of diagnostics and treatment were measured according to the computer-based hospital information system. Effects of the clinical decision support system were defined as the differences in the number of false positive and false negative errors. Because the clinical decision support system resulted in comparable patient outcomes, a cost-minimization study was required. In a sensitivity analysis we considered variation of doctor's time and variation in costs of diagnostic tests and therapy.

RESULTS

Of 915 eligible children visiting the ED with vomiting/diarrhoea, 693 (75%) children were not included due to early assessment of the physician before randomisation and lack of time for the nurses to obtain informed consent. We could include 222 children with informed consent in the randomised controlled trial. (Figure 2). Compared with the included population, the eligible population included more highly urgent patients according to the Manchester Triage System (indicating physicians' evaluation within 10 minutes) and more patients with increased heart rate.

The intervention (N=113) and the control group (N= 109) were comparable with respect to age (median age 1.5 years (IQR 0.9-2.4) versus 1.3 years (IQR 0.8-2.4) in the usual care group), gender, triage urgency, vital signs and CDS-items (table1).

Compliance to the clinical decision support system

In the intervention group 72/113 patients (64%) were mildly and 41/113 (36%) moderately dehydrated children, compared with 61/ 109 (56%) and 47/ 109 (43%) in the control group. In the intervention group, 4/ 88 (4.5%) children received oral rehydration solution (ORS) via a nasogastric tube. These four children refused to drink ORS (Table 2). Twelve of 25 (48.0 %) children assigned to nasogastric tube rehydration by the clinical decision support system, drank the ORS themselves instead. Compliance of the nurse to the treatment advice occurred in 97/113 patients (86%; CI 95% 0.78 -0.92)).

There were significant differences in rehydration treatment between the intervention group and the usual care group (p 0.01). In the intervention group 90/113 (80%) patients received ORS, compared with 66/109 (61 %) in the usual care group, fewer patients received other liquids instead of ORS (18/113(16 %) vs 30/109 (28 %) in the usual care

group) and no patients received intravenous rehydration compared with 2/109(1.8%) patients in the usual care group. In the intervention group 10/113 (8.8%) patients were hospitalized compared with 7/109 (6.4%) in the usual care group (p 0.47). After discharge from the ED, 30/113 (26.5 %) of the intervention group revisited the ED; one (0.9%) of these patients was hospitalized. In the usual care group, 30/109 (27.5%) revisited the ED; 4/109 (3.7%) patients were hospitalized.

Figure 2 Patient flow chart

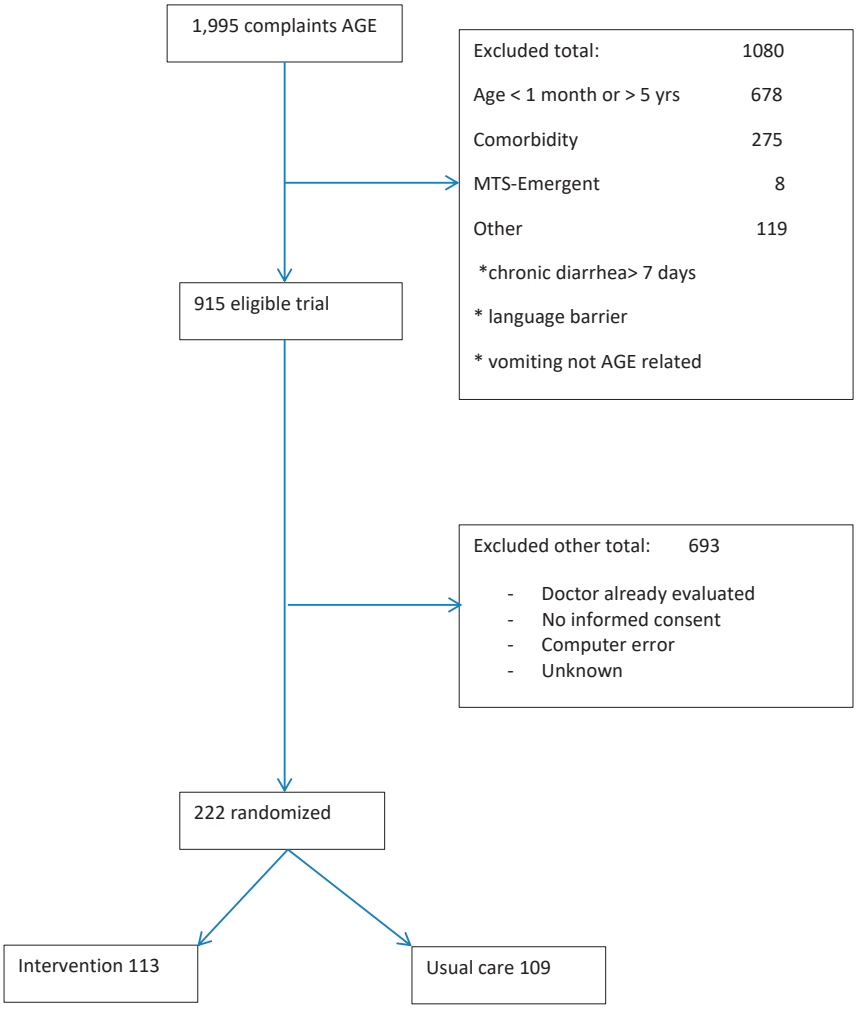


Table 1 Patient characteristics

		Intervention N= 113 (100%)	Usual care N= 109 (100%)
Age (years)[a]		1.5 (0.9-2.4)	1.3 (0.8-2.4)
Sex, male		61 (54.0)	57 (52.3)
Vital signs			
Temperature^ (degrees Celsius)		37.6 (1)	37.7 (1)
Heart rate ^ (beats per minute)		127 (24)	128 (21)
Respiratory rate^ (breaths per minute)		30 (8)	30 (8.4)
MTS urgency			
Emergent		0 (0)	1 (0.9)
Very urgent		13 (11.5)	11 (10.2)
Urgent		45 (39.8)	57 (52.8)
Standard		53 (46.9)	39 (36.1)
Non-urgent		2 (1.8)	0 (0)
Missing		0 (0.0)	1 (0.9)
Referral			
Own initiative		72 (63.7)	59 (54.1)
Primary care		31 (27.4)	35 (32.1)
Ambulance		4 (3.5)	1 (0.9)
Others[#]		6 (5.4)	14 (12.9)
Clinical dehydration score overall			
Mild		72 (63.7)	61 (56.0)
Moderate		41 (36.3)	47 (43.1)
Severe		0 (0)	1 (0.9)
Clinical dehydration score variables			
General appearance	Normal	101 (89.4)	96 (88.1)
	Thirsty/ restless/ irritable	11 (9.7)	13 (11.9)
	Drowsy/ comatose	1 (0.9)	0 (0)
Eyes	Normal	91 (80.5)	79 (72.5)
	Slightly sunken	22 (19.5)	27 (24.8)
	Very sunken	0 (0)	3 (2.8)
Mucous membranes	Moist	101 (89.4)	91 (83.5)
	Dry	12 (10.6)	18 (16.5)
	Very dry	0 (0)	0 (0)
Tears	Present	98 (86.7)	90 (82.6)
	Decreased	10 (8.8)	15 (13.8)
	Absent	5 (4.4)	4 (3.7)

[*] Absolute number (percentage)

[a] Median (IQR)

^ Mean (SD)

[#] Others' include secondary care and after telephone contact

Impact of the clinical decision support system

We did not find differences between the intervention and the control group for LOS at the ED (table 2). We observed a non- significant trend in reduction of laboratory tests, which were decreased with 50%. The number of revisits or hospitalisation did not differ. All parents of children were contacted for follow-up, with a median follow-up time of 72 hours. We did not observe adverse events.

Table 2 Outcome measures

	Intervention N= 113 (100%)*	**Usual care N= 109 (100%)***	**P- value**
Compliance			
Advice oral rehydration	88	Not applicable	
Compliance	84		
Non-compliance*	4		
Advice nasogastric tube rehydration	25		
Compliance	13		
Non- compliance**	12		
Patient consultation time			
Time spent at the ED (min)[a]	136 (98-206)	133 (92-184)	NS
Diagnostic procedures performed			NS
Electrolytes	15 (13.3)	23 (21.1)	
Acid base balance	13 (11.5)	16 (14.7)	
Treatment procedures performed			0.01
ORS oral	73 (64.6)	57 (52.3)	0.04
ORS nasogastric tube	17 (15.0)	9 (8.3)	NS
Intravenous rehydration	0 (0.0)	2 (1.8)	NS
Liquid other	18 (15.9)	30 (27.5)	0.02
Unknown	5 (4.4)	11 (10.1)	NS
Follow-up			NS
No	57 (50.4)	59 (54.1)	
Hospitalisation	10 (8.8)	7 (6.4)	
Outpatient clinic	25 (22.1)	26 (23.9)	
Telephonic consultation	21 (18.6)	15 (13.8)	
Other	0 (0.0)	2 (1.8)	
Revisits	30 (26.5)	20 (27.5)	
Hospitalisation after revisit	1 (0.9)	4 (3.7)	

* Absolute number (percentage)

[a] Median (IQR)

** nasogastric tube by nurse in patient with oral ORS advice*

*** oral rehydration in patient with nasogastric tube rehydration advice*

Costs

In the cost minimisation study no differences in costs in the intervention group compared with the usual care group were detected. (Table 3) The differences in patient outcome between the intervention group and the usual care group consisted of more rehydration by nasogastric tube, without adverse events, and were therefore not regarded as long-term effect. Because nasogastric tubes and diagnostic tests only account for a very small part of (health care) costs, differences did not significantly influence total costs. A cost

Table 3 Cost- analysis (Euro °)

		Intervention (N=113)		Usual Care (N=109)	
	Cost price	**Volume**	**Costs**	**Volume**	**Costs**
CDSS					
Development (hours)	36	144	5184	-	-
Implementation					
Researcher (hours)	54	4	216	-	-
Nurse* (number *hours)	40	20*2	1600	-	-
Total costs CDSS implementation			7000		
ED visit					
Physician (hours * visit number)	68	0,33*113	2535	0,33*109	2445
Nurse (hours * visit number)	40	0,5*113	2260	0,5*109	2180
Hospital costs	114	113	12882	109	12426
Diagnostics					
Electrolytes	3.8	15	57	23	87
Acid-base balance	5.10	13	66	16	82
Treatment					
Unknown		6		11	
ORS portion	0.3	73	22	57	17
Liquid other	NA	18	NA	30	NA
ORS nasogastric tube	28.2	17	479	9	254
IV rehydration	5.0	0	5	2	10
Follow-up/hospitalisation					
Hospitalisation patients * (LOS days)	575	10*2	11500	7*2	8050
Outpatient clinic	129	25	3225	26	3354
Telephonic follow-up	20	21	420	15	300
Costs of missed diagnoses/adverse events					
Revisit ED	144	30	4464	30	4320
Admission after revisit (LOS- days * patients)	575	2*1	1150	2*4	4600
Mean costs per patient (including CDSS)			408		350
Mean costs per patient (without CDSS)			346		350

LOS: length of stay

° Currency rate EUR/USD 1,11; Nov 8th 2016.

minimization study showed comparable costs for the intervention group and the usual care group: mean costs per patient were 346 euro in the intervention group and 350 euro in the usual care group. Total (once-only) costs for development and implementation of the clinical decision support system amounted to 7000 euro/ US dollar 7770 (EUR/USD 1,11; currency rate dated Nov 8th 2016).

Considering a reduction of 50% doctor's consultation time, sensitivity analysis showed a reduction of costs by 3% (12 euro/ 13,2 USD). Further sensitivity analysis were not performed due to relatively low impact of diagnostic and treatment costs compared with total costs.

DISCUSSION

We observed good compliance to the recommendations of the clinical decision support system for early rehydration in children with AGE by ED nurses and a significant increase in appropriate use of ORS compared to usual care. We did not observe adverse events. However, despite a stricter rehydration policy, we did not observe more successful rehydration in this mildly dehydrated study population, as expressed in (lack of) differences in revisits, hospitalisation rates or costs.

Adherence to the treatment advice generated by the intervention was good, however compliance to use the application of the clinical decision support system can be influenced by several factors, such as crowding hours and increased time needed to use a clinical decision support system. In our study we indeed observed that, during crowded ED hours, the nurses did not complete all clinical dehydration score items, a prerequisite for including patients. This may point out the limitations of the implementation process. Notably, we noticed reduced inclusion of children with more severe dehydration. The substantial loss of eligible patients, and in particular those with more severe dehydration, may reflect problems of performing research and obtaining informed consent in emergency care settings as was noted by others previously.[16] Given the randomized controlled character of our trial, we believe our results remain valid. Non-included patients, however, might affect generalization of our results to more severe dehydrated children. Therefore, extrapolating our results to all dehydrated children with signs of dehydration should be done with care. The high compliance to recommendations on treatment of the clinical decision support system in the included population is encouraging for further implementation. Factors contributing to this high compliance can be explained: first, our nursing staff consists of trained paediatric nurses, who who were skilled and experienced in the clinical assessment of dehydrated children. Second, an implementation program was used.[17] Third, treatment recommendations of the clinical decision support system were based on a pre-existing rehydration protocol, with

which the medical staff was already familiar. Last, the clinical decision support system was designed for easy use with readily available standardized clinical items, and was accessible from every computer at the ED. [18; 19]

According to the rehydration treatment guidelines underlying the decision support system, oral rehydration with ORS is recommended and biochemical testing is only indicated in severely dehydrated children. In the study population of mildly dehydrated children, the clinical decision support system showed a trend to fewer diagnostic tests and more frequent use of standardised amounts of ORS.

We did not find a beneficial effect on costs. A major reason is our low hospitalisation rate, as hospitalisation dominates the costs in AGE management. Nurse-guided patient assessment and treatment in the intervention group suggest that patient flow can be managed more efficiently. Sensitivity analysis on the reduction of doctor's consultation time by 50%, showed a reduction of costs by 3% (12 euro). Although this estimation is hypothetical, this might imply lower costs due to a reallocation of tasks as already described in emergency medicine, HIV-care and mental health care.[20; 21] [22; 23]

Strength and limitations

The main strength of this study is a randomised clinical trial on the impact of a clinical decision support system in paediatric emergency care. Impact analysis completes the final step in the translation process of clinical decision rules to routine practice.[24] We applied the decision support system in an electronic environment enabling easy access in routine practice and easy adaptation by other EDs.

One of our limitations is the absence of inclusion criteria based on strict signs and symptoms. Rather, we aimed for a pragmatic approach, including children with vomiting and/or diarrhea in the absence of another clear infectious focus, instead of using a strict definition based on signs and symptoms[3]. Secondly, despite our best efforts, we could not recruit the calculated number of patients. During the study period we observed no epidemic of acute gastroenteritis. Also, we were confronted with higher than anticipated exclusion rates for serious co-morbidity as well as a high number of not- included eligible patients. Hence, we abandoned our envisioned primary endpoint and recalculated power for length of stay at the ED (LOS). One could argue that our main outcome measure LOS is subject to influence of other factors, such as admission method, discharge destination, provider (hospital) type and speciality (acute vs non-acute). Especially discharge destination and admission methods appeared important influencing factors.[25] As we observed hospitalization in only resp. 10 (8.8%) and 7 (6.4%) of all patients and all other patients are discharged for further treatment at home directly after finishing rehydration treatment, we think LOS was a valid outcome in our study. We expect that the presence of dedicated research personnel at the ED would have improved the whole research process, but especially the inclusion of eligible

patients during crowding at the ED. Third, we could not evaluate impact on diagnosis due to failure of measurement of post ED weight. Fourth, the limited impact on (secondary) process outcome measures may be caused by the population of rather mildly dehydrated children, evaluated at a relative low volume university hospital, and the high experienced medical and nursing staff in evaluating children. Although we proved a significant increase in appropriate use of ORS in our study, we expect larger impact also on process outcome measures in more severely dehydrated patients, or in settings with high volume or less experienced personnel.

Finally, 12 out of 25 children (48%) assigned to nasogastric route in the intervention group drank their ORS and therefore did not receive nasogastric tube. The decision support system may induce excessive use of nasogastric route. This result highlights the moderate validity of the clinical decision support system and the risks associated with the indiscriminate use of the system. The clinical decision support system must therefore be considered only as an additional tool and should not replace common sense.

CONCLUSION

Implementation of a nurse-guided clinical decision support system on rehydration treatment in children with AGE showed high compliance and an increase standardised use of ORS, without differences the number of diagnostic tests, LOS, revisits and hospitalisation or costs.

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Chapter 5

How to predict failure of rehydration in children with acute gastroenteritis.

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ABSTRACT

Oral rehydration is the standard in most current guidelines for young children with acute gastroenteritis (AGE). Failure of oral rehydration can complicate the disease course, leading to morbidity due to severe dehydration. We aimed to identify prognostic factors of oral rehydration failure in children with AGE.

Design A prospective, observational study.

Setting Emergency department (ED), Erasmus Medical Centre, Rotterdam, The Netherlands, 2010- 2012.

Patients 802 previously healthy children, aged 1 month-5 years with AGE.

Outcome Failure of oral rehydration was defined by secondary rehydration by a nasogastric tube, or hospitalisation or revisit for dehydration within 72 hours after initial ED visit.

We observed 167 (21%) failures of oral rehydration in a population of 802 children with AGE (median 1.03 years old, IQR 0.4-2.1; 60% male). In multivariate logistic regression analysis, independent predictors for failure of oral rehydration were a higher Manchester Triage Urgency (MTS) level, abnormal capillary refill time (CRT) and a higher clinical dehydration scale (CDS) score.

Conclusion

Early recognition of young children with AGE at risk of failure of oral rehydration therapy is important, as emphasized by the 21% therapy failure in our population. Associated with oral rehydration failure are higher MTS urgency level, abnormal CRT and a higher CDS score.

INTRODUCTION

Acute gastroenteritis (AGE) frequently occurs in young children. The highest incidence occurs in children 1-4 years of age, with norovirus and rotavirus as the most common causes. Every year in Europe, among 23.6 million children under the age of five years, approximately 3.6 million rotavirus-related AGE episodes occur, leading to more than 87,000 children being hospitalized and almost 700,000 children visiting the outpatient clinic.(1) Oral rehydration using oral rehydration solution (ORS) is the standard therapy in the current European guidelines for young children with AGE. (2-4) In developed countries most patients have mild dehydration and the disease course is usually uncomplicated. However, even in mildly dehydrated children, treatment failure due to frequent vomiting and diarrhea, lack of sufficient intake or a combination of both, can complicate the disease course, with potential severe dehydration or even hypovolemic shock. Although rare, severe dehydration due to treatment failure explains why AGE is in the top 10 of diagnoses of malpractice claims in children.(5, 6) Early identification of children at risk for severe dehydration may reduce morbidity.

We aimed to identify prognostic factors of failure of oral rehydration in patients younger than 5 years of age with mild or moderate dehydration due to AGE, after attending the emergency department (ED).

METHODS

Design

We conducted a prospective, observational study on AGE in children attending the ED. (7, 8) Ethical approval for this study was obtained by the institutional review board (IRB) of the Erasmus MC. Informed consent was required and obtained from all parents (MEC-2008-071; MEC- 2005-314).

Outcomes and definitions

The primary outcome was failure of oral rehydration, defined as: secondary nasogastric tube rehydration in children with mild or moderate dehydration (after persistent refusal of ORS or persistent vomiting during oral rehydration), a revisit with an intervention within 72 hours after the initial ED visit or (secondary) hospitalisation. According to our previous study, a revisit with intervention was defined as secondary oral or nasogastric rehydration treatment at ED, performance of diagnostic laboratory tests and/ or hospitalisation. (8)

As viral AGE is the most common cause of acute vomiting or diarrhea in healthy children under the age of 5 years, AGE was defined as acute infectious related vomit-

ing and/or diarrhea in paediatric patients admitted to the ED, lasting less than 7 days, with a symptom-free period of two weeks before.(9, 10) Our definition was previously used (7) and only differs from ESPGHAN guideline (3) not including vomit and/ or stool frequency. Although frequency of evacuations was not part of the definition we think this selection reflects the ED population of children at risk for dehydration at the ED. Moreover, change in stool consistency is more indicative of diarrhea than stool number, particularly in the first months of life. (3)

The clinical dehydration scale (CDS) is based on the items general appearance, mucous membranes, eyes and tears.(11) As these items were recorded in a dichotomised way, every item showed a normal (0 points) or an abnormal (2 points) value, added up to a total CDS (max 8 points).

A capillary refill time (CRT) of three seconds or more was defined as prolonged.(12)

Patients and setting

Previously healthy children 1 month- 5 years of age with acute vomiting and/ or diarrhea were consecutively included at the ED of the Sophia Children's Hospital. This is an inner-city paediatric university hospital, with 7000 children attending the ED annually. About 35 % of the children presenting with infectious causes at the ED suffer from chronic co-morbidity.(13)

We included children, suspected of AGE based on the complaint of vomiting and/or diarrhea at presentation at the ED. (3) We excluded children with chronic diarrhea (> 7 days), children suspected of a paediatric surgical disease or trauma and children with vomiting due to another infectious disease, such as urinary tract infection or pneumonia. Also excluded were children with complex chronic conditions, such as congenital heart disease, renal failure, metabolic disease and chronically ill children with complex needs.

Data collection

We collected data on age, gender, MTS urgency level, vital signs, data on vomiting and diarrhea, as well as data on referral, discharge and follow-up. Data were prospectively collected from a structured electronic patient record system from May 1st 2010 till Dec 1st 2012. (14)

In practice, the nurse assigned the child to a triage urgency level according to the Manchester Triage system (MTS)(15), indicating the patients appropriate maximum waiting time of respectively 120 minutes (level: non urgent), 90 minutes (level: standard), 30 minutes (level: urgent), 10 minutes (level: very urgent) or 0 minutes (level: emergent, indicating immediate treatment). Then, the nurse assessed the clinical condition of the child and registered signs and symptoms for dehydration.

All patients were evaluated and treated by the attending physician within the time frame allocated by the MTS. As the study was performed in a tertiary teaching hospital,

the attending physician was a member of staff supervising a paediatric resident in all patients. In general, patients received ORS appropriate for the level of dehydration, according to the current protocol.(16) Children without clinical signs of dehydration were provided with ORS in order to inform parents on signs and symptoms of dehydration as well as at home-management, including on the preparation of ORS. In these patients other liquids (for example apple juice) were provided if ORS was refused. Patients with mild dehydration received 50 ml/kg during ED stay of about 120 minutes (median 133 minutes; IQR 94-179), patients with moderate to severe dehydration (without signs or symptoms indicating hypovolemic shock) ór persistent vomiting received (primarily) nasogastric tube rehydration 80 ml/kg ORS during 3-4 hours at the ED. Children with clinical signs of hypovolemic shock received appropriate treatment immediately, including intravenous fluid resuscitation. In these children nasogastric tube rehydration and intravenous rehydration were considered appropriate treatment, they were not identified as treatment failure.

Telephonic follow-up after discharge was performed with standardised questionnaires three days after ED discharge and then every 24 hours until the patient was symptom-free.(8)

Statistical analysis

Based on international guidelines and reviews we focused our analyses on age, gender, MTS urgency, items of the CDS, heart rate, respiratory rate, CRT, frequent vomiting and diarrhea (Table 1) (3, 4, 18, 19). We used Chi square, Student's t test and logistic regression analysis as appropriate. Receiver operating characteristic (ROC) curves with 95% confidence interval (95%CI) were calculated for failure- associated variables. A p-value <0.05 was considered statistically significant.

Observing missing data in mainly the CDS- related variables and data on frequency of vomiting and diarrhea (Table 2), we decided to impute these missing data in order to increase methodological validity, assuming they were missing at random. Missing data were imputed using a multiple imputation model including age, gender, MTS urgency level, vital signs, data on vomiting and diarrhea, and referral, discharge and information during follow-up. This imputation process resulted in ten databases, that were used for pooled analyses.(17) Imputation was performed by using the Design and Hmisc packages (AregImpute function) in R version 2.15.2. For the comparative analysis the statistical Packages for the Social Sciences (SPSS) version 20.0 (Chicago, IL) was used.

Table 1 Risk factors according to guidelines.

	ESPGHAN 2014(3)	NICE 2009(4)	Bruel Lancet 2010(25)	NVK 2012(16)
Age	< 6 months <2 months hospital visit	<12 months (in particular <6)		< 6 months
Gender				
MTS Urgency level				
Vital signs				
Tachycardia		X		X
Abnormal breathing	X	X	X	X
Prolonged capillairy refill time	X	X	X	X
Pale/ mottled skin		X		X
Clinical signs and symptoms				
Clinical Dehydration Scale (11)	X			
General appearance/ altered mental state	X	X	X	X
Mucous membranes				
Tears				
Eyes				
Urine output	X	X		
Turgor	X			
Weight loss	X			
Vomiting during rehydration		X		X
Persistent vomiting	X	X >2/ 24 hours		X >4/ 24 hours
Diarrhea frequency	X	X >5/ 24 hours		X >8/24 hours
Other				
Etiology (ROTA/NORO +)	X			
Feeding/ stop breastfeeding		X		
Children with signs of malnutrition		X		
Co-morbidity	X	X		
Parents not able	X	X		

RESULTS

Of 7,061 paediatric patients visiting the ED, 1,995 had complaints of AGE. We excluded 1,080 children, predominantly because of age and co-morbidity. An additional 113 children who participated in an intervention study on standardised assessment and treatment of AGE were excluded as the intervention could influence our outcome parameter. (7)

The study population consisted of 802 children with vomiting/ diarrhea (age 1.03 years, IQR 0.4-2.1; 60% male) (Table 2). Oral rehydration therapy failed in 167 patients (21%). Twenty-nine percent of the patients with treatment failure were allocated to the MTS urgency level 'emergent-very urgent', compared with 12% in the non-failure category. Three quarter of children with complaints of AGE in our population were classified by 9 out of 50 MTS discriminators: fever discriminator in 25%, discriminator vomiting and diarrhea in 26%, level of pain discriminator in 10% and the discriminator 'recent' problem in 13%. In the children with oral therapy failure, we observed age adjusted heart rate and respiratory rate above percentile 99% (18) in 342 (43%) respectively, compared with and 317 (40%) in the children in the non-failure group (non-significant difference). CRT

Table 2 Patient characteristics

	Available data ° N (%)	**Failure ° N=167 (100)**	**Non- failure ° N= 635**	**P<0.05**
Age (years)[a]	802 (100)	1.03 (0.4-2.1)	1.23 (0.5-2.5)	
Sex, male	802 (100)	100 (59.9)	352 (55.4)	
Referral	802 (100)			*
Self- referral		45 (26.8)	336 (53.0)	
Referred [#]		122 (73.1)	299 (47.0)	
MTS urgency	798 (99.5)			*
Emergent/ Very urgent		48 (28.6)	77 (12.1)	
Urgent		83 (49.7)	305 (48.0)	
Standard/ Non-urgent		36 (21.4)	249 (39.3)	
Clinical characteristics				
Heart rate (/ min) [^]	639 (79.7)	141(26)	132 (24)	*
Respiratory rate (/min) [^]	484 (60.3)	39(12)	34 (11)	*
Temperature (°C) [a]	763 (95.1)	37.5 (37.0-38.6)	37.8 (35.4-41.0)	
Capillary refill time	609 (75.9)			*
Normal		97 (58.1)	434 (68.5)	
Prolonged		33 (19.8)	45(7.1)	
Missing		37 (22.2)	156 (24.6)	
Symptoms				
Vomiting frequency	478 (59.6)			
None		11 (6.6)	53 (8.3)	
≤4 times/ day		66 (39.5)	229 (36.1)	
> 4 times/ day		30 (18.0)	89 (14.0)	
Diarrhea frequency	406 (50.6)			
None		36 (59.9)	124 (19.5)	
≤ 8 times per day		45 (26.9)	186 (29.3)	
>8 times per day		3 (1.8)	12 (1.9)	

Table 2 Patient characteristics *(continued)*

	Available data ° N (%)	Failure °	Non- failure °	
		N=167 (100)	N= 635	P<0.05
Clinical Dehydration Scale				
Consciousness	376 (46.9)			
Well		79 (47.3)	572 (90.2)	
Abnormal		2 (1.2)	1 (0.2)	
Mucous membranes	468 (58.4)			*
Moist		77 (46.1)	363 (57.2)	
Dry		13 (7.8)	15 (2.4)	
Eyes	294 (36.7)			
Normal		40 (24.0)	248 (39.1)	
Sunken		3 (1.8)	3 (0.5)	
Tears	420 (52.4)			*
Normal		61 (36.5)	337 (53.1)	
Decreased		10 (6.0)	12 (1.9)	
Dehydration scale total [a]	271 (33.8)	0.0 (0-0)	0.0 (0-0)	*
Score 0 (0 abnormal items)		148 (88.6)	609 (95.9)	
Score 2 (1 abnormal item)		13 (7.8)	22 (3.5)	
Score 4 (2 abnormal items)		5 (3.0)	4 (0.6)	
Score 6 (3 abnormal items)		1 (0.6)	0	
Score 8 (4 abnormal items)		0	0	
Failure of oral rehydration	802 (100)			
Nasogastric tube		2 (1.2)	NA	
Revisits		46 (27.5)	NA	
Hospitalisation		120 (71.9)	NA	

Absolute number (percentage)
[a] Median (IQR)
^ Mean (SD)
[#] Others' include secondary care and after telephone contact

was prolonged in resp. 78 (9.7%) patients compared with 45 (7.1%) patients in the non-failure group. Highest scores of the CDS were more frequently observed in the failure group compared to the non-failures, with 1 or more abnormal dehydration score item in 21/168 patients (12.5%) in the failure group, compared with 27 /635 (4.3%) in the non-failure group. In order to be able to predict failure of oral rehydration, we calculated

ROC values for these items, showing an ROC (95%CI) of resp. 0.63 (0.58-0.68) for MTS urgency, 0.58 (0.52-0.64) for CRT and 0.54 (0.49-0.59) for the CDS.

In multivariable analysis higher MTS urgency level, prolonged CRT and the total CDS score remained significantly associated with failure of oral rehydration. (Table 3). The ROC (95%CI) for the final model, including MTS, CRT and CDS score combined was 0.68 (0.63-0.74).

Table 3 Characteristics of patients with failure of oral rehydration treatment.

Variables	Univariable OR(95%CI)	P	Multivariable OR(95%CI)	P	ROC (95%CI)
Age (per year)	0.89 (0.78-1.02)	NS			
Gender (male)	1.20 (0.85-1.70)	NS			
MTS urgency					0.63 (0.58-0.68)
MTS Standard/ Non urgent	Ref				
MTS Urgent	1.89 (1.23- 2.89)	<0.05	1.83 (1.15-2.92)	<0.05	
MTS Emergent/ very urgent	4.32 (2.62- 7.14)	<0.05	3.97 (2.21-7.12)	<0.05	
Age- adjusted vital signs (18)					
Heart rate≤ p25	Ref	NS			
p25	0.64 (0.13-3.26)				
p50	0.38 (0.06-2.22)				
p75	1.29 (0.35-4.84)				
p90	1.17 (0.37-3.69)				
≥ p99	1.88 (0.61-5.78)				
Respiratory rate≤ p25	Ref	NS			
p25	4.2 (0.88-20.45)				
p50	2.45 (0.74-8.0)				
p75	2.66 (0.40-17.50)				
p90	2.36 (0.71-7.88)				
≥ p99	3.60 (1.24-10.39)				
Capillary refill time (CRT)					0.58 (0.52-0.64)
Normal	Ref				
Abnormal	3.21 (2.02- 5.09)	<0.05	2.26 (1.35- 3.78)	<0.05	
Vomiting					
None	Ref				
≤ 4 /day	1.3 (0.82- 2.07)	NS			
>4 / day	NA				
Diarrhea					
None	Ref				
≤ 8 /day	1.02 (0.45- 2.32)	NS			
>8 / day	NA				
Dehydration scale total	1.14(1.04-1.27)	<0.05	2.54 (1.30-4.98)	<0.05	0.54 (0.49-0.59)
Model MTS CRT CDS-total					0.68 (0.63-0.74)

The statistical analysis was performed on the imputed dataset, as well as on the original dataset, showing associations in the same direction.

DISCUSSION

Therapy failure was observed in 167 (21%) of all patients. This emphasizes the importance of early recognition of failure of oral rehydration therapy also in western populations of children. According to several guidelines, important signs and symptoms in assessment and treatment of children with AGE are (young) age, (abnormal) vital signs, the CDS, urine output, frequency of vomiting and diarrhea and 'parents not able' (to manage rehydration therapy at home). Complementary to former studies mostly addressing assessment and treatment of AGE, we focused on prognostic factors of oral rehydration. The strongest independent effects for rehydration failure were found for MTS, CRT and the total CDS score. The prognostic value of this final model (ROC area) was moderate, but substantially higher than the ROC areas of these separate items.

The MTS assigns patients to 5 urgency categories based on specific signs and symptoms (discriminators) in one of the 50 flowcharts representing complaints. Although the primary aim of the triage system is to differentiate the patients in need of (direct) care from those who can safely wait, in our study, the MTS triage system also identified the patients at risk of a complicated disease course.

Next, a prolonged CRT was observed in children with rehydration failure. In initial patient assessment, a prolonged CRT increases the risk of a serious illness. (19) Interpreted within the clinical context of temperature, CRT is also useful in the assessment of children with dehydration. (20) (21) In a recent meta-analysis, a prolonged CRT showed a high specificity of 89-94 % for identifying 5 % dehydration, with a wide range in sensitivity (0-94%). (12) ESPGHAN guideline 2014 described 3 best individual signs of assessment of dehydration being: CRT, abnormal skin turgor and abnormal respiratory pattern.(3) In our study, CRT showed a high specificity of 90% in particular (with substantial positive LR of 2.69 (CI95 % 2.43-2.99)), but low sensitivity of 27.2 % for failure of oral rehydration, with a negative likelihood ratio of 0.81 (CI95% 0.79-0.83). In contrast, MTS classification was characterized by a relative high sensitivity, but at the cost of a low specificity.

Last, oral children with rehydration failure showed a higher total CDS score in univariate and multivariate analysis, with an ROC curve 0.54 (CI95% 0.49-0.59). Former research on the CDS in children with AGE at their initial ED visit, showed a ROC curve 0.65 (CI95% 0.57-0.73) for hospitalization(22) compared with 0.54 (CI95% 0.49-0.59) for our

definition of failure (secondary nasogastric rehydration, revisits with an intervention, hospitalization).

Strength and limitations

The strength of our study is that we performed a prospective study in a large group of previously healthy young children with AGE. We showed MTS urgency level, CRT and the CDS to be associated with oral rehydration failure. The number of children with failure of rehydration (n= 167) was sufficient for reliable evaluation of the set of potential prognostic factors for failure of rehydration. (Table 1).

Several limitations need to be addressed. We note that the CDS is a four-item, three- dimensional scale. Unfortunately, in our study, the four items were coded as dichotomous variables. Only 48 (6%) children had one or more abnormal items 38 (4.7%) patients only had one abnormal item, 9 (1.1%) patients had two abnormal items and only one patient (0.1%) had three abnormal items Although we collected dichotomised variables instead of the original 3 categories and using a different outcome definition, we showed comparable findings. Given the low number of abnormal classifications on the variables in the CDS we do not expect that dichotomization has affected our conclusions on prognostic value.

Next, we had to deal with missing values. We consider our data of sufficient quantity and quality after imputation of missing data according to a sophisticated imputation method, and outcome variables showed no missing data and were not imputed.

Clinical implications

In developed countries, severe dehydration due to AGE is rare. Although rehydration with ORS is common practice, we still observed a 21% rehydration failure in our mildly dehydrated study population. Recent studies support a more feasible approach with oral rehydration using diluted apple juice and other preferred fluids, added with ondansetron if indicated. (23) Furthermore, adequate parental instruction can make (home) oral rehydration therapy more successful, reducing oral therapy failure. (24)

Our findings should raise awareness that dehydration after ED visit still occurs, also in the developed countries. This necessitates the identification of a vulnerable patient group. Our model may contribute to this aim, as we saw that a child with a high MTS urgency level, an abnormal CRT and an abnormal CDS score at initial assessment, is more prone for therapy failure. These characteristics are available at initial presentation. If we are sure to inform parents adequate and make adequate appointments for revision (based on e.g. our observations) we may safely refrain from invasive interventions at the ED in low risk patients.

CONCLUSION

In our study on predominantly mildly dehydrated children, we observed a 21% failure of oral rehydration therapy. Associated with oral rehydration failure are high MTS urgency level, prolonged capillary refill time and an abnormal CDS score.

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Chapter 6

Impact analysis of an evidence-based guideline on diagnosis of urinary tract infection in infants and young children with unexplained fever.

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ABSTRACT

Several guidelines exists on urinary tract infection (UTI) in children. The objectives of this study were to 1) implement an evidence- based diagnostic guideline on UTI and evaluate determinants of successful implementation, and 2) determine compliance to and impact of the guideline in febrile, non- toilet trained children at the emergency department (ED).

We performed a prospective cross-sectional observational study, with observations before and after implementation. Children aged 1 month to 2 years, presenting at the ED with unexplained fever (temperature above 38.5 degrees Celsius) were included. We excluded children with a chronic underlying disease. Primary outcome measure was compliance to the standardized diagnostic strategy and determinants influencing compliance. Secondary outcome parameters included: number of used dipsticks, contaminated cultures, number of genuine UTI, frequency of prescribed antibiotic treatment and hospitalization.

The pre-intervention group (169 children (male 60.4%, median age 1.0 (range 0.1 -2.0) was compared with the post- intervention group (150 children (male 54.7%, median age 1.0 (range 0.1-1.9). In 42 patients (24.9%) there was compliance to local guidelines before implementation, compared with 70 (46.7%) after implementation (*p*-value < 0.001). Improvement in compliance after implementation was higher in patients 3-24 months and outside the office hours (p<0.001).

Conclusion

Implementation of a guideline for diagnosing UTI in febrile children at the ED has led to a significantly better compliance, especially in children aged 3 - 24 months. However, this study also underlines the need for a well-defined implementation strategy after launching an (inter)national guideline, taking determinants influencing implementation into account.

INTRODUCTION

Fever is one of the most common presenting problems at a paediatric emergency department (ED), especially in young children. Most of these children have a viral infection and an uncomplicated disease course, however in five-to-ten percent of children with fever at the ED a serious bacterial infection (SBI) is described, such as meningitis, sepsis, pneumonia or urinary tract infection (UTI).[3, 6, 25] UTI is one of the most common serious bacterial infections with an overall prevalence of 7.0 % in all children, depending on age, gender and circumcision status.[23]

It is important , but difficult to make a reliable diagnosis of UTI, as signs and symptoms are often unspecific in (young) children, and controversies exist on preferred collection method and reliability of culture result in non- toilet trained children. Within this debate, guidelines have been published to answer the diagnostic dilemmas concerning urinary tract infection in non- toilet trained children. [1, 15, 17]

In 2007 the NICE (National Institute of Clinical Health and Excellence) guideline on urinary tract infection in children was published. [15] According to this evidence- based guideline infants and children with unexplained fever or who are suspected of having a UTI should have a urine specimen tested, preferably by way of midstream urine sample by clean catch. If this is not possible a urine specimen must be collected using bladder catheterization or suprapubic aspiration. Microscopy and culture will confirm the diagnosis. Dipstick testing can be used if microscopy is not available.

The clinical practice guideline released by the American Academy of Pediatrics in 1999 was revised in 2011 and is generally in accordance with the NICE guideline. [1]

Before 2010, local protocols on diagnosis and management of paediatric UTI existed, in general similar to AAP- and NICE- guidelines, but a uniform guideline was lacking, as was an implementation program.

In 2010, the evidence- based guideline 'Urinary tract infection in children' was published and implemented nationwide in The Netherlands. This guideline, generally based on the NICE guideline, recommends urine collection by clean catch, and if not possible, bladder catheterization or suprapubic aspiration. [17]

Moreover, compared with the AAP and the NICE guideline, this guideline clearly states that urine bags may be used to exclude UTI by dipstick slide (negative result on both leukocyte esterase and nitrite) in non-toilet trained children. In case leucocyte esterase or nitrite, or both are positive, urine culture must be obtained by midstream (clean-catch), bladder catheterization or suprapubic aspiration.

One of the diagnostic dilemmas in diagnosing UTI in young children concerns (young) children with fever with mild to moderate signs of upper airway infection, which can vary from a slightly runny nose to an acute otitis media. There is debate in literature about

co- existing serious bacterial infection in this population and whether urine screening, should take place. [5, 10, 19]

In principle, clinical guidelines developed for children with acute infection aim to alter clinical management. Only a few, however, have been validated. [13] Also implementation strategy is seldom described and impact of implementation on routine care is rarely measured. [7]

Aim

Our aim was to determine the compliance to and the impact of the guideline in young, non- toilet trained children with unexplained fever at the ED after implementation and to evaluate determinants of successful implementation.

METHODS

Design

We conducted a cross-sectional observational study, with observations before and after the introduction of the diagnostic guideline in children with fever without source at the ED of the Erasmus Medical Centre- Sophia Children's Hospital, pre- intervention from January 2008- January 2009 and post-intervention April 2010- April 2011.

Data collection

Patient characteristics, Manchester Triage System (MTS) urgency level at admission at the ED, diagnostic tests, diagnoses and treatment, were prospectively collected from a structured electronic patient record system at the emergency department (ED) of the Erasmus University Medical Centre – Sophia Children's Hospital, Rotterdam. According to the Manchester Triage System the patient is allocated to one of five urgency levels (immediate, very urgent, urgent, standard and non-urgent), indicating the maximum waiting time for medical evaluation for each patient. [22] We used the MTS urgency level as a proxy of patients' severity of illness.

Data from the pre-intervention group were collected within an ongoing diagnostic study assessing characteristics of all children with fever using a standardized patient record. [21]

The Sophia Children's hospital is an inner- city university hospital, with annually 9000 children visiting the emergency department, and 90% basic paediatric care. [16] About 40 % of the ED population has chronic co-morbidity.

This study was approved by the institutional medical ethics committee and the requirement for informed consent was waived.

Patients

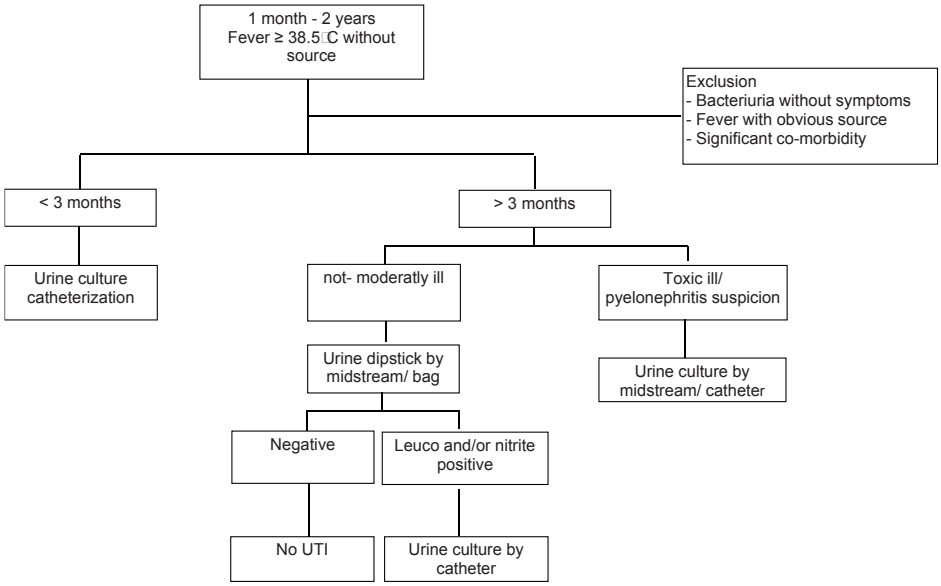
Children, 1 month- 2 years old, presenting at the emergency department with unexplained fever, defined as a temperature above 38.5 degrees Celsius, were eligible. We excluded children with a chronic underlying disease.

Guideline implementation

Our intervention was the national diagnostic guideline (**figure 1)** [17].

To optimize implementation in clinical practice we applied a targeted and multifaceted implementation strategy including instructions concerning the guideline on group and individual level adopted from implementation theories. [2] Before and during the course of the study we gave several group lectures in medical staff meetings to the paediatric staff and residents. Also, this was done at the ED to the attending medical and nursing staff at every shift for the period of one month. Laminated pamphlets of the guideline were available at the ED. Finally, written instructions were sent three times to all health care professionals working at the ED during the implementation period by email as a reminder.

Figure 1 Diagnostic guideline.



Definitions

Guideline compliance was defined as taking a urine culture using midstream, bladder catheterization or suprapubic aspiration in all children with unexplained fever when the dipstick showed a positive result for leucocyte esterase and/ or nitrite.

According to the guideline a UTI was defined by a combination of clinical features and the presence of positive bacterial culture in a reliably obtained urine sample.[17]

Outcome

Primary outcome measure was compliance to the standardized diagnostic strategy, as formulated in the guideline. In addition, potential determinants of guideline compliance after implementation were evaluated. These included patient characteristics as age, gender and triage urgency level; and ED characteristics such as time of presentation (inside or outside office hours) and doctor's experience. Secondary outcome parameters to determine clinical consequences of guideline compliance included: number of used dipsticks, contaminated cultures, number of UTI, frequency of prescribed antibiotic treatment and hospitalization.

At last, we evaluated screening for UTI in young children with fever with mild to moderate signs and or symptoms of (upper) airway infection.

Statistics

A pre (2008) - and post (2010-2011)-intervention comparison was performed on primary and secondary outcome parameters. For statistical testing the Chi-squared test and Fisher Exact test were used. A *p*-value <0.05 was considered statistically significant. Effects of determinants for successful implementation were evaluated using logistic regression analysis. We used SPSS version 20.0 for Windows.

RESULTS

In 2008 6814 patients visited the ED. The pre-intervention cohort included 169 eligible patients out of 427 children aged 1 month-2 years old with fever without source (male 60.4%, median age 1.0 (range 0.1-2.0; **table 1)** . The post-intervention cohort consisted of a total of 150 included patients (male 54.7%, median age 1.0 (range 0.1-1.9) out of 337 children 1 month- 2 years with unexplained fever of a total of 7274 patients visiting the ED. No significant differences existed in patient characteristics and MTS urgency level between the pre- and post-intervention groups.

Table 1: General characteristics

	Pre- intervention N= 169 (100 %)	Post- intervention N= 150 (100%)	P
Male gender	102 (60.4)	82 (54.7)	.31
Age (median, range)	0.96 (0.09-1.99)	1.03 (0.08- 1.93)	
1-3 months	10 (5.9)	12 (8.0)	
3-24 months	159 (94.0)	138 (92.0)	.51
Temperature (median, range)	39.4 (38.5- 41.3)	39.4 (38.5-41.2)	
MTS Urgency			
Emergent	6 (3.6)	6 (4.0)	.06
Very Urgent	64 (37.8)	39 (26.0)	
Urgent	72 (42.6)	85 (56.7)	
Standard	23 (13.6)	16 (10.6)	
Non urgent	0 (0)	0 (0)	
Missing	4 (2.4)	4 (2.6)	

Primary outcome: compliance to the guideline

Before implementation, compliance to the diagnostic strategy according to local protocols was correct in 42 patients (24.9%), compared with 70 (46.7%) after implementation of the guideline (*p*-value < 0.001; **table 2)**. This improvement was in particular observed in children aged 3-24 months (p < 0.001).

Besides patient age, compliance improved further outside the office hours (p<0.001). Patient gender, doctor's experience or triage urgency level did not influence compliance (data not shown).

Secondary outcome: clinical consequences of guideline compliance

A reflection of guideline compliance is the number of used dipstick tests. In the post-intervention group dipstick tests were significantly more used (28.4% vs 50.7%, *p*-value < 0.001; **table 2**). The increase of dipstick use was in particular observed in children 3- 24 months.

Although non- significant, the urine culture collection method improved in the post-implementation group. Midstream collection in young, non- toilet trained children included those with a clean- catch urine sample during preparation for catheterization.

The number of contaminated cultures (defined as multiple micro-organisms or < 10e5 CFU [17]) was low and did not differ in the pre- and post-intervention group.

In the pre-intervention group we observed a prevalence of UTI of 3.6% compared with 7.3% in the post-intervention group, all based on E. coli > 10e5. Median age in children

with UTI was higher in the post-intervention group (0.39 vs 0.58), due to an increased detection rate of UTI among children 3-24 months.

There was no significant difference in the number of patients with UTI who received antibiotics in the pre- and post-intervention group. In both groups most patients with UTI were initially hospitalized, 4.1 % before implementation compared with 6.0 % after, which is a non-significant difference (P 0.61).

Table 2 Outcome

	Pre- intervention N= 169 (100%)	Post- intervention N= 150 (100%)	P
Adherence to standardized diagnostic strategy	42 (24.9)	70 (46.7)	<0.01
Age			
Age 1-3 months	6	11	
Age 3-24 months	36	59	<0.01
Male	26	43	1.0
Total number of dipsticks	48 (28.4)	76 (50.7)	<0.01
Number of positive dipsticks*	9 (5.3)	17 (11.3)	<0.01
Urine culture collection method			.13
According to guideline (bladder catheterization, SPA, midstream)	5	11	
Not according to guideline (urine bag)	5	1	
Unknown	4	3	
Culture			
Total	14 (9.3)	15 (8.8)	.70
Positive culture (UTI, all E. coli)	6 (3.6)	11 (7.3)	.14
Contaminated culture (Defined as < 10e5 CFU or multiple micro-organisms)	2 (1.2)	2 (1.3)	1.0

Screening for UTI/ SBI in children with mild to moderate (upper) airway infection

Signs of (upper) airway infection were present in half of all children (60 % boys and 98% of these children were > 3 months of age in both groups**)**. Due to non-standardized report of medical examination with a large variation, we were not able to categorize these patients.

In the post- intervention group dipstick test was significantly more frequently performed in this subgroup (40.4% vs 59.6%, p 0.024), with two abnormal results. In these two children, according to the guideline urine culture was collected, showed a negative result in both patients, and therefore did not reveal any UTI.

DISCUSSION

By implementing a standardised diagnostic guideline on UTI in young non- toilet trained children with unexplained fever at the ED, we observed a significant increase in compliance.

Better compliance to the standardized diagnostic strategy in the guideline resulted in a significant higher use of dipstick urinalysis in the post-implementation group.

Although compliance improved substantially, assessment was still not accurate in almost half of all children. It was unfortunate that in depth information of reasons for non-compliance was lacking in our study. This information could further improve implementation strategies. We did identify some determinants of (non-) successful implementation, i.e. patient age, time of presentation at ED (inside or outside office hours) and signs/ symptoms of other infections, as best results were achieved in patients 3- 24 months of age and outside office hours.

Last, further awareness of the guideline may be improved by reminders integrated in a computerised medical file and showing the guidelines exact content.

Our findings were consistent with a recent study by Simon et al, USA, on the evaluation of children 3-36 months with fever without source (FWS) at the ED, in which urinalysis using dipstick was only performed in 43 % of all girls 3-24 months with FWS in whom it was recommended.[24]

Earlier literature showed higher compliance of clinicians to guidelines if they are involved in the development with regard to medical content and feasibility [18]. Our results support the difficulty of changing physician practice by implementing evidence based guidelines, which intend to assist and improve daily clinical practice.[4, 20] In our targeted implementation strategy we covered most important barriers and facilitators of implementation: [20] [8, 11]

1) the implemented guideline was developed in collaboration with health professionals, 2) the guideline included empowerment of nurses, who were instructed to initiate urine collection and urine dipstick test in eligible patients, [2, 7, 9, 12] 3) we applied an intensive instruction period, especially at the ED, 4) the guideline was easy accessible to the ED personnel by pamphlets and laminated copies.

Although proven in a small number, our study shows that children with signs of an upper respiratory tract infection did not have UTI. With this information we may more precisely define those children in whom urinalysis is recommended in an updated version of the guideline and hereby improve compliance.

In order to appreciate our results, we should address some strengths and limitations. Our study is one of few that describe implementation of a nationwide launched guideline

and measures the compliance to and the impact of this guideline on clinical practice. As our study sample constitutes a case mix selected from a multicultural, inner city ED population we think the results are generalizable to other ED populations of developed countries. This is supported by the prevalence of UTI in our study, which was 3.6-7.3%, which is reported in other studies on UTI in febrile children [6, 23].

As our guideline is conceptually similar to the NICE and AAP guidelines, our results support impact of these guidelines on routine care in United Kingdom [15] and USA after successful implementation [1]. The choice of the before-after design follows the fact that the guideline was published nationwide, and agrees with growing insights in studies on routine implementation and their appropriate design. [14] One may argue that the before-after design might be susceptible to changes in time on clinical management and epidemiology. However, we were neither aware of substantial changes in clinical approach of a child with fever, nor of epidemiological changes. Both the pre- and post-implementation cohort completed a whole year of children with fever without source presenting at the ED, with similar seasonal influences.

An important limitation was the collection of data in the pre- intervention period. We tested the research question retrospectively, on prospectively collected data in an ongoing diagnostic study.

CONCLUSION

Implementation of a standardized diagnostic strategy for diagnosing UTI in febrile children at the ED, according to a literature based implementation plan, has led to a significantly better compliance to the guideline, especially in children 3- 24 months. Increase in compliance was influenced by patient age and time of presentation at ED (shift) (children 3-24 months of age and outside office hours). This study also underlines the need for a well-defined implementation strategy after launching an (inter)national guideline, taking determinants of implementation into account.

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Chapter 7

Lessons learned from implementation of a written safety netting advice for parents of febrile children at the emergency department.

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Submitted

ABSTRACT

To evaluate the implementation of a written safety netting advice for parents of febrile children, presenting at the emergency department (ED) on revisits and hospitalisation.

In a before – after design, we performed a prospective study on the impact of a written safety netting advice on revisits and hospitalisation.

We included 256 children in the pre-intervention university hospital cohort (male147 (57.4%); median age 2.42 (IQR1.09-4.65). Post-intervention, 235 (25%) patients were included in the university hospital cohort (male 56.6%, median age 1.94 (IQR 0.97-4.65) and 115 (14%) patients in the teaching hospital cohort (male 60.9%, median age 1.53 (IQR 0.75-3.50). No significant differences existed between the pre- and post-intervention university cohort in patient characteristics and MTS- urgency level, as well as follow-up data (revisits, hospitalisation). Patients in the teaching hospital cohort were significantly more often self-referred, at younger age and had a higher MTS urgency category. The number of total revisits in both post- intervention cohorts was similar to the pre-intervention cohort. The number of unscheduled revisits decreased non-significantly from 21% (54/256) to 15.8% (37/235) and 14.8%(17/115) in both post-intervention cohorts. The number of hospitalisations did not differ. There was no association between the written intervention and having a revisit when corrected for age, vital signs or MTS urgency level.

Conclusion

In this prospective study on the impact of implementation of a written safety netting advice in children with fever at the ED, we observed no differences in the number of revisits or hospitalisation. Part of this negative effect may be due to setting- related implementation issues, such as identifying the patients the intervention was meant for, those patients in need of the intervention, and to actually handling the safety netting advice. In the future, health care workers have to be empowered to provide structured and concise health information, involving parents in the development.

INTRODUCTION

In early childhood, all children experience several febrile illnesses, that are mostly self-limiting viral infections with an uncomplicated disease course. Despite initial assessment, diagnostics at the ED, and a presumed diagnosis at discharge, the prediction of the course of the disease will remain uncertain in a number of febrile children. Safety netting can provide structured information to parents/carers on how to deal with uncertainty.[1]

The term safety netting applies to follow up-instructions after ED discharge and aims to educate parents/ carers in appropriate at home management. This safety netting advice should include structured information on the expected time course of the disease, alarming signs and symptoms and when and how to seek medical care. [1,2]

Debate remains on how patient information should be provided and conflicting evidence on the effect of safety netting reducing revisits exists.[3,45] As an ED visit is often stressful, written information in addition to verbal information has a positive effect on the uptake of the information. [6]

We aimed to evaluate the effect of providing a standardised safety netting advice to parents of febrile children on revisits and hospitalisation after first assessment at the ED.

METHODS

Design

We performed a prospective pre-and post-implementation study on the impact of providing a standardised safety netting advice to parents/carers. Ethical approval for this multi-centre study was obtained from the institutional review board (IRB) of the Erasmus MC (MEC- 2005-314). Informed consent was required and obtained from all parents.

Population and setting

We included parents/ carers of febrile children, 1 month to 16 years of age presenting at the Emergency Department of Erasmus MC-Sophia Children's Hospital. This is a university hospital with a paediatric emergency department and 7000 child visits per year, 35% of all patients have serious comorbidity. [7] Fever was defined as a rectal measured body temperature >38.5 ºC at the ED or measured at home in the last 24 hours or if a history of fever was the main reason for encounter. [5,8]

In Erasmus MC-Sophia Children's Hospital, patients and parents in the pre-intervention group were included from October 2011 till April 2012, patients in the post-intervention group were included from October 2012 till April 2013.

We also performed the implementation in the Maasstad Hospital, a general, non-academic teaching hospital with a mixed paediatric and adult ED, receiving about 38,000 patients a year.[9] Patients were included in the Maasstad Hospital from Dec 1st 2012 till July 31st 2013.

Children under the age of 1 month and chronically ill children with complex needs were excluded, because of the higher risk on a complicated disease course.

Outcome

The primary outcome measure was the number of revisits and hospitalisation after the ED visit. Revisits were defined as a second visit related to the same complaint to a health care service within 72 hours. Health care services could be a visit to a hospital or to a general practitioner (GP). Among revisits we distinguished unscheduled revisits. Unscheduled revisits were defined as revisits, initiated by the parents, without a scheduled appointment.

The secondary outcome measure was the satisfaction score of the parents. In a convenience sample of parents and caregivers in the university hospital cohort, we evaluated the effect of the educational intervention on the satisfaction level of parents. The core questionnaire for the assessment of patient satisfaction in university hospitals' (COPS) was applied. [10] We used questions with 5- point-scale answers on handling by and competence of the ED-nurses and physicians, on diagnosis and treatment, and on giving discharge instructions. These questions were integrated in the research protocol during a two- month period (December 2012 until January 2013) in the Erasmus MC Sophia Children's Hospital.

Intervention

The intervention, a standardised safety netting advice, consisted of a standardised oral advice, in addition to a written safety netting advice, as part of a children's picture book about a little piglet visiting the ED with fever ('Piglet has a fever'; translated in Dutch 'Varkentje heeft koorts') (Appendix 1).[11] The last two pages provided written information for parents/carers about fever, alarming signs and symptoms (drinking less than minimal intake, reduced urine output, reduced consciousness, confusion, irritability, non-blanching rash, neck stiffness, pain when changing diaper, difficult breathing and flaring), as well as instructions on when and how to seek help are described in accordance with recent literature and guidelines.[12,13]

The training of the ED-nurses to implement the intervention included a training to provide standardised oral information, in addition to the written information, as well as educational group lectures on children with fever, alarming symptoms and the concept of safety netting. Also, repeated individual briefings were applied to the ED personnel and reminders by newsletters were sent regularly.

In the university hospital cohort, the nurses handed out the intervention with a standardised oral explanation to parents or other caretakers before discharge of their febrile child from the ED. Because the nurses in the teaching hospital were unfamiliar with performing research and we were unable to integrate the intervention into their daily practice, adaptations to the delivery of the safety netting to the parents/carers was necessary. The paediatric residents/paediatricians handed out the intervention and received a similar implementation training in order to perform the exact same intervention.

In both hospitals, seventy-two hours after the initial visit, one of the members from our research team contacted the parents of the febrile child by telephone and conducted a structured telephone questionnaire. If parents could not be reached by telephone after three attempts (72 hours, 96 hours and 120 hours after the initial visit), a written questionnaire was sent to their home address. If the patient was still not well at the time of the initial telephone contact, a follow up call was made every 24 hours until the patient was well or had to be admitted for further management.

Data collection

Patient characteristics, diagnostic tests, diagnoses and treatment, were prospectively documented in a structured electronic patient record system. Data were collected for the on-going study in all children with fever, vomiting/ diarrhoea or dyspnoea, assessing patient characteristics using a standardized patient record.[5]

Data analyses

Outcome measures from pre- and post- implementation phase were evaluated using Chi square, parametric and non-parametric tests as appropriate and logistic regression analysis. A p-value <0.05 was considered statistically significant. We used SPSS version 20.0 for Windows.

RESULTS

Twenty percent of the eligible population were non-responders, i.e. participants who did not return the written questionnaires and could not be reached by telephone. They were excluded from the study. [5]

We included 256 (50%) of 535 eligible patients aged 1 month- 16 years with fever in the university hospital pre-intervention cohort (male 57.4%, median age 2.42 (IQR 1.09-4.65) (Table1). Post-intervention, 235 (90%) of 263 eligible patients were included in the university hospital cohort, (male 56.6%, median age 1.94 (IQR 0.97-4.65), 57 patients (24.2%) actually received the intervention. These 57 patients had a higher temperature

Table 1 Patient characteristics

	Pre-intervention	Post- intervention	Post-intervention
	university hospital N= 256 (100%)[*]	*university hospital N=235 (100%)*	*Teaching hospital N=115 (100)*
Age (years)[a]	2.42 (1.09-4.65)	1.94 (0.97-4.65)	1.53 (0.75-3.50)
Sex, male	147 (57.4)	133 (56.6)	70 (60.9)
MTS urgency			
Emergent	1 (0.4)	2 (0.9)	0
Very urgent	43 (16.8)	42 (17.9)	79 (68.7) °
Urgent	161 (62.9)	140 (59.6)	28 (24.8) °
Non-urgent	44 (17.2)	47 (20.0)	6 (5.2) °
Standard	1 (0.4)	1 (0.4)	0
Missing	6 (2.3)	3 (1.3)	2 (1.7)
Vital signs			
Temperature (°C) ^	38.7 (37.8-39.4)	38.6 (36.2-41.1)	38.5 (35.7-40.5)
Missing	6 (2.3)	7 (3.0)	1
Heart rate (bpm)^	136 (73-210)	136 (40-220)	136 (70-205)
Missing	27 (10.5)	53 (22.6)	9
Respiratory rate(bpm)^	33 (16-80)	31 (12-60)	27 (18-80)
Missing	57 (22.3)	102 (39.8)	22
Referral			
Own initiative	126 (49.2)	117 (49.8)	85 (73.9) °
Primary care	63 (24.6)	59 (25.1)	25 (21.7)
Ambulance	30 (11.7)	26 (11.1)	1 (0.9)
Others[#]	34 (13.3)	53 (20.7)	2 (1.8)
Missing	3 (1.2)	1 (0.4)	2 (1.8)

[*] Absolute number (percentage)

[a] Median (IQR)

^ Mean (SD)

[#] Others' include secondary care and after telephone contact

° $p<0.05$

at presentation, but age, gender and heart- and respiratory rate did not differ from those not receiving the intervention. The number of total revisits in the university hospital post- intervention cohort did not differ from the pre-intervention cohort if corrected for age, gender and MTS urgency(Table 2). The number of unscheduled revisits decreased non-significantly from 54 (21.0%) to 37 (15.8%).

In the teaching hospital cohort, 115 of 348 (33%) eligible patients were included in (male 60.9%, median age 1.53 (IQR 0.75-3.50). 103 of 115 patients (89.6) children received the intervention by the attending physician. Patients were more often self-referred, had a higher MTS urgency and younger age compared with the pre- intervention university hospital cohort. The number of revisits after introducing the intervention was 23

Table 2 Outcome

	Pre-intervention	Post-intervention		
	university hospital N= 256 (100%)	*university hospital N= 235 (100%)*	*teaching hospital N= 115(100%)*	
Intervention received				
Yes	NA	57 (24.3)	103 (89.6)	p <0.05
Revisit				
Yes	96 (37.5)	84 (35.4)	23 (20.0)	p<0.05
Unscheduled	54 (21.0)	37 (15.8)	17 (14.8)	
Hospitalisation (after revisit)	4 (1.6)	4 (1.7)	3 (2.6)	

(20.0%), which was lower compared with both the pre- and post- intervention cohort in the university hospital. The number of hospitalisations and unscheduled revisits did not differ.

The satisfaction survey was realised in a convenience sample of 36 parents and carers in the university post-intervention cohort (male 12 (33.3%); age 20-39 years in 32/36 (89%) of these parents. We observed a satisfaction level 4 and 5 (on a 5- point- scale) of 80- 96% on all of the four domains. No association existed between gender, age and highest form of education.

DISCUSSION

Main findings

Introduction of a standardised safety netting advice did not reduce the number of revisits or hospitalisation for both a university hospital as well as a teaching hospital. The number of unscheduled revisits slightly decreased from 54 (21.0%) to 37 (15.8%) (non-significant) in the university hospital setting. We did not observe an association between the intervention and the number of revisits when corrected for age, vital signs or MTS urgency level. In the university cohort barriers for the implementation raised from indeed providing the booklet, whereas in the teaching cohort barriers existed on identifying those patients the intervention was meant for. In a convenience sample of parents in the post-intervention university hospital cohort, we observed a good satisfaction level of the provided information.

Discussion of literature

Differences exist between patient education in an emergency department setting versus in a primary care or other non-emergency health care settings. From the general

practitioner's point of view, parents need to know about at home management and when to seek medical care.[14] At the ED, the information is more often focussed on alarming signs and symptoms and when to seek medical care without delay. As we provided the intervention during the ED visit, parents/carers are under the influence of stress and comprehension of information is more difficult. Therefore, to further improve effectiveness of education, information on when and how to seek medical care and information on the management of minor illness at home, needs to be clear and standardised. [15,16]

Empowerment may not only reduce revisits, but also improve parent satisfaction. We found a high satisfaction level in parents who were provided with oral and written information, regardless of gender, age and highest form of education. [17,18] This is in accordance with a recent study in children with breathing difficulties at the ED, showing increased satisfaction 1-2 weeks after the ED visit in parents who received multimedia based health information in addition to oral information, compared to parents receiving oral information alone. The decrease in anxiety level of parents did not differ between both groups. [19]

Strengths and limitations

In order to interpret the results we have to address some limitations. The before-after design may be influenced by changes in time in clinical management and follow-up. However, to the best of our knowledge, we were neither aware of changes in clinical management and follow-up, nor changes in epidemiology. Also, we included the pre- and post-intervention cohort in the same seasons, controlling for seasonal influences.

A major observed drawback was limited feasibility of the study, exposed by 1) the low application of the intervention in the university hospital cohort and 2) the low inclusion rate in the teaching hospital cohort, despite an extensive educational and implementation program in both settings.

Although nurses were familiar with health education within their work at the ED, this was the first standardised research-initiated patient education program in the university hospital. At nursing- level, the lack of administration assistance and lack of time are considered major barriers in performing research at the ED.[20] Both can improve by the availability of dedicated research nurses, who can include patients and assist in applying the intervention. Furthermore, the application of the intervention by the nurses on call can be improved by its incorporation into their routine practice[21] and by increasing nurses' awareness and confidence by providing a structured approach or tool in order to provide concise and structured health education.[21] The attending paediatric physicians may consider structured health education and parent empowerment already as a part of their consultation, which could explain the high application of the intervention tool in the teaching hospital. Despite this major drawback, we performed intention- to-treat- analysis, assuming that although not all parents received the information mate-

rial, parents were at least verbally informed about safety netting advice. Moreover, the characteristics of the included patients were comparable with the total population of febrile children visiting the ED.[22]

Unfortunately, our study does not prove a reduction of all revisits, as the decrease of unscheduled revisits in our study was 'compensated' by an increase of scheduled revisits. One may argue that the implementation process increased awareness among health care professionals on alarming signs and symptoms and the risk of a serious infection, although this is not supported by only 6 of 23 scheduled revisits in the teaching hospital.

In order to optimize generalisability, we also implemented the intervention at the ED of a teaching hospital. Although we aimed for an identical implementation, attending physicians performed the study, handed out the intervention and performed the parental education in the teaching hospital setting. As we used the same implementation program, however, we think the influence on outcome would be small.

Last, special attention should be paid to parents with low health literacy level or language barriers. Older children of parents with low literacy level may have higher risk to a non-urgent visit, probably of a multifactorial origin, but this was not confirmed for children under the age of two years.[23] This may indicate that parents of young children seek help for their febrile child regardless of health literacy level. Moreover, parents with low literacy level search the internet for health information less frequently, implying the need for written information.[24]

Therefore, in empowering patients and their caretakers, it is important to realise that even when the information is health literacy level- and culturally tailored, still almost 50% of parents may not comprehend the intended information.[25]

Future perspectives

Although providing information at the ED seems very simple, it apparently needs to be considered as a complex intervention. From this study implementing a standardized safety netting advice as a tool to inform parents on how to manage their child after ED visit, we learned that standardized oral information by health care professionals in addition to providing a written instruction is important, but also challenging. We experienced the importance of a targeted training of health care professionals on how to provide this information and to whom. In this study, we used the outcome measure revisits and hospitalization, but this may not cover the whole aspect of illness management by parents. Empowerment of parents includes information on the illness, but also developing skills and confidence on handling the child's illness at home and how to act upon. Last, the ED may not be the best place itself to provide information on contents of safety netting given the stressful situation.

In the future, development of provided information needs an integrated approach with parents (with low literacy level) involved to include their perspective and preferences on the content, the medium and the location to receive the information..[24]

CONCLUSION

In this prospective study on the impact of implementation of a written safety netting advice in parents of children with fever at the ED, we observed no differences in the number of revisits or hospitalisation. Part of this negative effect may be due to setting-related implementation issues. In the future, health care workers have to be empowered to provide structured and concise health information, involving parents in the development.

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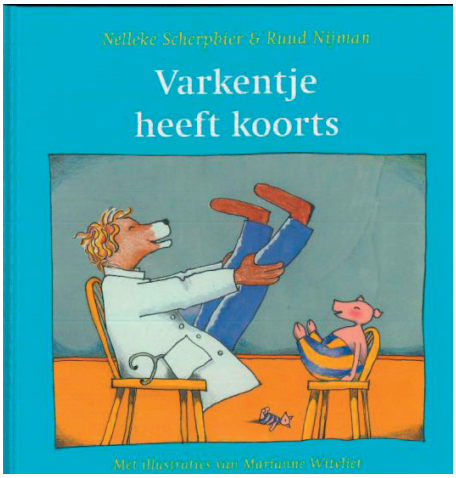
Appendix 1: Safety netting intervention "Piglet has a fever".



Varkentje ziet een groot gebouw. Er staan ziekenauto's voor de deur. Als ze binnenkomen, ziet Varkentje dat het heel druk is. Bijna alle stoelen zijn bezet.

Chapter 8

Measuring acceptability of two clinical decision models in the emergency department using the Ottawa Acceptability of Decision Rules Instrument (OADRI)

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ABSTRACT

For successful practical implementation of clinical decision rules, measuring their acceptability is essential. The Ottawa Acceptability of Decision Rules Instrument (OADRI) was developed to serve this need.

To make OADRI available in the Netherlands by translating the instrument into Dutch, to use this instrument to identify nurses' acceptability of two clinical decision rules in pediatric emergency care and to perform applicable validation analyses.

We performed a prospective questionnaire evaluation among pediatric emergency department (ED) nurses in the period September 2010-Oktober 2012.

The OADRI was translated into Dutch according to international guidelines. Decision rule acceptability was measured during three different moments of two impact trials. We described OADRI mean item scores and diversity of answer possibilities, where >50% "No opinion/ Don't know" where defined as non-informative OADRI items.

Implementation activities of the clinical decision rules were positively associated with acceptability scores, especially for the OADRI items of the subscales "aspects of innovation" and "environment". Validation activities showed ceiling effects for each OADRI item, indicating limited content validity of the instrument. The decision rules appeared to be clear, with only 2 out of 12 items being considered less informative.

Conclusions

The Dutch translated OADRI showed well dissemination in a non-English country to measure acceptability of clinical decision rules. Responses to individual OADRI items guided possible improvement of decision rule implementation. However, limitations in our validity analyses necessitate more broad-spectrum validation before OADRI implementation.

INTRODUCTION

Application of clinical decision rules may improve efficiency and quality of care by recommendations on, for example, performing additional diagnostic tests or initiating treatment [1,2]. They have been developed to aid physicians and nursing staff to make a diagnosis or predict an outcome [1,3,4]. After external validation, the next methodological step is to perform an impact analysis to test whether or not the decision rule actually improves clinical decisions and will benefit patient care or reduce costs [1,5,6]. During this last implementation phase compliance to rule advices is mostly one of the main outcome measures [7]. However, measuring its acceptability is essential for successful implementation.

The Acceptability of Decision Rules Instrument (OADRI), aimed to measure the acceptability of clinical decision rules, was developed by a research group who was informed by the Ottawa Model of Research Use [8-10]. They grouped various barriers and facilitators related to whether a research innovation was adopted into practice into three large categories: 1) aspects of the innovation; 2) decision making, and 3) environment. After pilot testing in a single tertiary care hospital, the 12-item instrument OADRI was validated via postal surveys amongst emergency physicians from Australia, Canada, United Kingdom and United States in the context of the Canadian C-Spine Rule and the Canadian CT head rule [11,12].

In previous research we performed two impact trials of clinical decision rules [13,14]. The first rule was based on a diagnostic decision model for children with fever at risk for serious bacterial infections (SBI) [13]. The second rule was a therapeutic decision model for children with vomiting and diarrhea, who were at risk for dehydration [14]. In the present study we used the OADRI instrument to measure the acceptability of these two clinical decision rules among nurses during their impact trials at the pediatric ED. We aimed to disseminate the OADRI to a non-English speaking country by translating the instrument into Dutch and we undertook applicable validation activities of the instrument.

METHODS

Study design and setting

We performed a prospective questionnaire evaluation among our 19 pediatric emergency department (ED) nurses at the Erasmus MC-Sophia Children's Hospital, Rotterdam, the Netherlands. A fixed sample of paediatric ED nurses anonymously completed the instrument at three evaluation moments during two impact trials as performed at our department in the period September 2010-Oktober 2012 [13,14]. We continuously updated the implementation process by reminders by mail, posters and group instruc-

tion. The first evaluation moment took place at the beginning of the impact trials (2010), the second moment was halfway the impact trials (2011) and the last moment was at the end of the impact trials (2012).

Study intervention and participants

The original OADRI was translated from English into Dutch according to international guidelines with written permission of Jamie C. Brehaut, one of its developers [10]. We translated OADRI according to international guidelines [15] with two including two forward and two backward translations by independent native speakers without knowledge of the questionnaire. The Dutch version of the OADRI was used to test the acceptability and measure potential facilitators and barriers during the impact trials of the two clinical decision rules. Data were assured to be analysed confidentially. Since no patients were involved in this acceptability study and all questionnaire data were anonymised, informed consent was IRB exempt.

The clinical decision rules used in the impact trials provided high- or low-risk estimates for SBI (trial I) [13] and dehydration (trial II) [14], respectively. These impact trials were running parallel to our OADRI evaluation study. In the intervention group nurses were guided, after initial triage, to initiate additional tests (trial I) or rehydration intervention (trial II) for high-risk children [13,14]. Both control groups were evaluated according to the usual emergency care.

Data collection

Respondents were asked to indicate their level of agreement with each of the 12 statements on a 6-point scale ranging from 1 (strongly disagree) to 6 (strongly agree), or indicating "no opinion/ don't know" (supplemental file 1). The first 7 items were phrased such that a higher number indicated greater acceptability and for the last 5 the opposite was true. This strategy was chosen by the developers to avoid yes-saying bias [16].

The final total score consisted of the mean of all 12 items (recoded where necessary) and thus ranged from 0 to 6. Non-completed items were excluded from the final total scores. The mean of the remaining items served as the instrument score. Respondents who completed less than 8 of the 12 items were considered as not having completed the instrument and were excluded from the final analyses.[10] Items for which "No opinion/ Don't know" was selected were coded as the middle of the scale in line with the original validation paper [10].

OADRI validation activities and decision rule acceptability

Taking our small study size into account we only performed applicable validation activities. First, we evaluated the rates of missing items, and the mean and range of item scores. Next, we evaluated ceiling and floor effects (i.e. >15% of responders reporting the highest or lowest response category [17].

We interpreted incomplete questionnaires, added free text parts (explanation of answers) and majority answers of "No opinion/ Don't know" as proxy statements for rule un-clarity. We evaluated the diversity of the different answer possibilities, items for which >50% "No opinion/ Don't know" was selected were defined as non-informative. We measured mean item scores, indicating greater acceptability when higher numbers were selected [10].

To test differences between the item scores of the OADRI during the three moments of the impact trials we used linear regression analyses. Moreover, we tested changes in mean item scores within the suggested original categories of OADRI items [10]: 1) Aspects of innovation: items 1-4; 2) Decision maker: items 6-9, 11 and 3) Environment: items 5 10, 12.

Finally, we visualized implementation strategies during the trial period (e.g. feedback and periodic teaching sessions) [13,14], which might influence rule acceptability. Outcome measures were compared between the two evaluated clinical decision rules. All analyses were performed using SPSS 20.0 for Windows.

RESULTS

Based on two forward translations of the OADRI one final Dutch OADRI questionnaire was defined. Two-fold backward translations, by independent native speakers without knowledge of the questionnaire, resulted in similar questionnaires to the original OADRI questionnaire. Of the 19 eligible pediatric ED nurses, 74-89% (14-17 nurses) completed the survey at the three different assessments during trial I (fever). For trial II (gastroenteritis) the response rate varied between 56-84% (11-16 nurses) during the different moments of the trial. Demographics of the participating nurses are presented in Table 1**.** The median age was 54 years (IQR 53-59), 89% were women (n=17), and the median years of working experience was 35 years (IQR 34-42).

Table 1: demographics participants

	Nurses (n=19)
demographics	
Age (years)[a]	54 (53-59)
Sex, female[*]	17 (89%)
Working experience (total in years)[a]	35 (34-42)
Working experience in our hospital (in years)[a]	34 (30-35)

[a] Median (25 – 75 percentiles)
[*]Absolute number (percentage)

OADRI validation activities and decision rule acceptability

Table 2 describes the mean item scores for each moment of the impact trials. A ceiling effect was observed for all 12 OADRI questions in both trials, where 67% (8/12) was caused by reporting the highest category. Floor effects were not observed in OADRI responses during both trials. There were no incomplete submissions (i.e. less than 8 of the 12 items completed). For OADRI responses during both trials we only had one missing answer in the total of all questionnaires. None of the participants added free text to their questionnaire. Overall percentage of items coded as "No opinion/ Don't know" was 16% for trial I and 18% for trial II, and mostly due to OADRI item 9 ("evidence supporting the rule is flawed") and 11 ("does not account for important clinical cue"). OADRI item 9 was consequently defined as non-informative (>50% "No opinion/ Don't know") for all moments in both trials in contrast to OADRI item 11 which was only partly non-informative (first two moments trial I, second moment trial II).

Mean item scores tended to be above 3, indicating overall acceptability of the rule (i.e. higher numbers indicate greater acceptability) (Table 2). Overall, the mean item scores increased over time, especially from moment 1 to moment 2. For trial I the mean item score improvement was significant (p=0.026), in contrast to trial II (p=0.260). When we categorized OADRI items into the original item classification we observed significant increases in mean item score in category I (aspects of the innovation) (p=0.020) and category III (environment) (p=0.048) for trial I (Table 2).

We observed improved acceptability in relation to implementation activities per study moment, measured by increased mean item scores (Figure 1).

DISCUSSION

Main findings

We completed the Dutch translation of the OADRI according to international guidelines and the disseminated use of OADRI to measure acceptability of clinical decision rules seems usable in this non-English country. Validation activities showed ceiling effects for each OADRI item indicating limited content validity of the instrument. However, we observed good acceptability of the introduction of two clinical decision rules among ED nurses as the rules appeared to be clear, with only 2 items being less informative ("evidence supporting the rule is flawed" (item 9) and "does not account for an important clinical cue" (item 11)). Responses to individual OADRI items guided possible improvement of decision rule implementation.

Table 2: OADRI internal consistency and item means during three consecutive moments of two impact trials

	Clinical decision rule: Fever				**Clinical decision rule: Gastro-enteritis**			
	Moment 1	Moment 2	Moment 3	*all moments*	Moment 1	Moment 2	Moment 3	*all moments*
n participants	15	17	14		15	16	11	
OADRI items 1-12	Mean (SD)	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	Mean (SD)	
1. Easy to use	4.70 (1.60)	5.35 (1.17)	5.64 (0.74)		5.43 (0.90)	5.56 (0.73)	5.82 (0.40)	
2. Easy to remember	4.57 (1.52)	5.29 (0.99)	5.54 (0.66)		4.63 (1.42)	5.38 (0.72)	5.27 (1.19)	
3. Useful in my practice	4.50 (1.48)	5.12 (0.93)	5.57 (0.76)		5.00 (0.91)	5.38 (0.62)	5.36 (0.81)	
4. Wording is clear and unambiguous	5.43 (1.18)	5.41 (0.80)	5.79 (0.43)		5.37 (0.97)	5.56 (0.81)	5.73 (0.65)	
5. My colleagues supports use of the rule	4.63 (1.41)	4.97 (1.40)	4.89 (0.88)		4.60 (1.49)	5.22 (0.66)	4.55 (1.11)	
6. Patients benefit from use of the rule	3.70 (1.52)	5.03 (0.94)	5.14 (0.77)		4.27 (1.19)	4.84 (0.98)	5.00 (0.77)	
7. Results in improved use of resources	3.80 (2.17)	5.03 (0.72)	5.04 (1.05)		4.03 (1.65)	4.53 (1.10)	5.00 (1.00)	
8. Would increase the chance of lawsuits (reversed)	4.53 (1.38)	4.62 (1.26)	4.64 (1.17)		4.23 (1.47)	4.44 (1.26)	4.64 (1.07)	
9. Evidence supporting the rule is flawed (reversed)	3.90 (1.04)	4.29 (1.20)	3.64 (1.13)		3.33 (1.10)	4.06 (1.17)	3.36 (0.81)	
10. Using another rule or similar strategy (reversed)	5.30 (1.39)	5.50 (1.00)	5.57 (0.85)		5.17 (1.36)	5.63 (0.89)	4.50 (1.43)	
11. Does not account for important clinical cue (reversed)	4.67 (1.52)	3.97 (1.22)	3.75 (1.42)		4.80 (1.50)	4.06 (1.22)	3.32 (1.45)	
12. Environment I work in makes it difficult to use (reversed)	3.07 (1.49)	4.71 (1.36)	4.50 (1.45)		3.80 (1.73)	4.50 (1.46)	5.00 (1.18)	
	Mean (SD)	Mean (SD)	Mean (SD)	*p-value*[*]	Mean (SD)	Mean (SD)	Mean (SD)	*p-value*[*]
Category I: aspects of the innovation[^]	4.80 (0.98)	5.29 (0.83)	5.54 (0.63)	0.020	5.11 (0.79)	5.47 (0.64)	5.55 (0.71)	0.113
Category II: decision maker[^]	4.12 (1.19)	4.59 (0.77)	4.44 (0.59)	0.324	4.13 (1.09)	4.39 (0.88)	4.26 (0.53)	0.665
Category III: environment[^]	4.33 (1.04)	5.06 (0.85)	4.99 (0.66)	0.048	4.52 (1.06)	5.11 (0.63)	4.55 (0.86)	0.796
Total mean (SD) per moment	4.40 (0.86)	4.94 (0.67)	4.97 (0.39)	0.026	4.56 (0.92)	4.93 (0.62)	4.84 (0.31)	0.260

Higher mean item scores indicate greater acceptability

[^] Category I: mean of OADRI items 1-4; Category II: mean of OADRI items 6-9, 11; Category III: mean of OADRI items 5 10, 12

[*] Linear regression analysis

Figure 1: mean OADRI item scores related to implementation activities

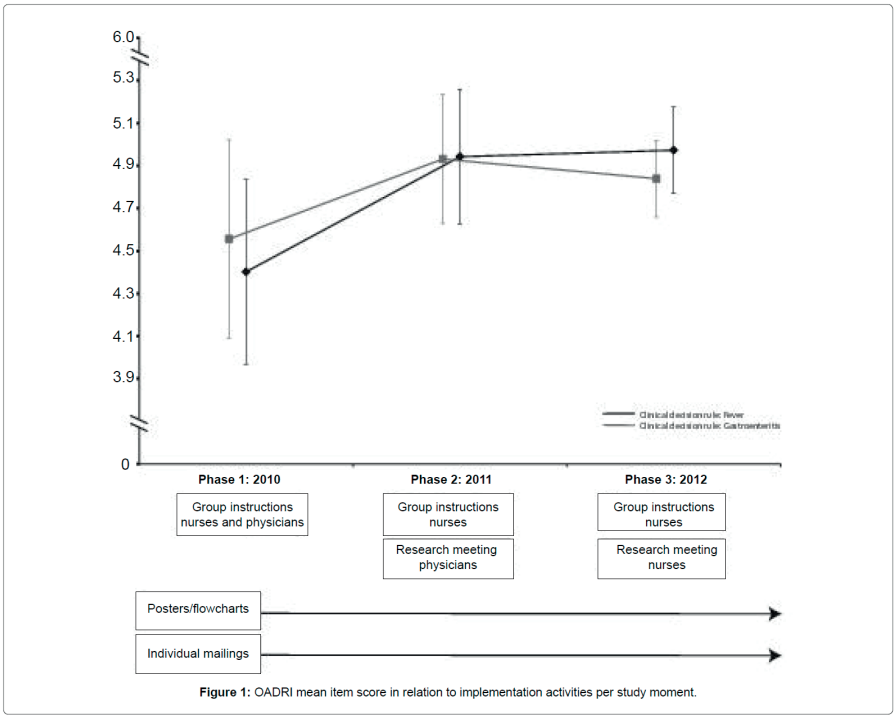

Figure 1: OADRI mean item score in relation to implementation activities per study moment.

Comparison with other studies

In this study, we evaluated the OADRI among ED nurses ass in our impact trials the clinical decision models were integrated in the nurses' regular work-flow to evaluate the possibility of standardization and/or reallocation of their diagnostic tasks. To our knowledge this is the first study measuring nurses' acceptability of two clinical decision rules in different moments of their implementation at the pediatric ED. Different strategies for successful implementation of clinical decision support systems in practice are reported in literature [1,18]. In line with their recommendations our decision rules were computer based and they were part of the clinical workflow containing recommendations, rather than just assessments [18]. Moreover, as recommended by Reilly et al., our ED nurses were checked for accurate use of the rules to provide feedback, but also to assess whether clinical judgment improves on decision rule based judgment [1]. Other studies have been written about the translation of clinical research into practice and the role of behavioural changes among health care professionals on this topic [1,7,19-21]. According to a systematic review effective interventions should include reminders; multifaceted interventions including e.g. auditing, feedback and interactive educational meetings [21].

Overall, all these different implementation strategies are supposed to increase rule acceptability in clinical practice. However, measuring acceptability of newly introduced clinical decision rules is not routinely done. A systematic review describing clinical prediction rules for children included 137 studies and reported in only 8 studies broad validation of the results. None of the included studies had undergone impact analysis and subsequently measured rule acceptability [22].

Clinical and research implications

From literature we learned that before we can improve clinical practice using clinical decision rules we should interact with all the barriers and incentives that are already known. But in clinical practice it is sometimes difficult to predict which barriers need more attention to support optimal implementation. At our ED, we used the OADRI for interactive periodic teaching sessions to increase the acceptability of using both decision rules. We discussed for example OADRI questions related to the importance of the rules, including the underlying evidence of rule development. Moreover, we discussed the difficulties of using the rules in clinical practice where the answers on OADRI questions related to environment were essential sources of information. Overall, we experienced the OADRI covered enough tools to support these teaching sessions. We observed that especially OADRI mean item scores considering aspects of the innovation (e.g. the rule is easy to use; the rule is useful in my practice) and aspects of environment (e.g. colleagues support, working environment) increased over time. Hence the OADRI can support this important study moment by interact on specific items scored on this questionnaire and this Dutch translated version is just the first step of OADRI dissemination through non-English speaking countries.

In our study we observed a better acceptability of trial I (fever) compared with trial II (gastroenteritis) as measured by the OADRI. One of the possible reasons for this result includes the limited response rate to OADRI by the nurses in trial II. Results may be underpowered and therefore no effect could be identified. Second, the rehydration advices of trial II might be less innovatory than guidance on initiating additional diagnostic tests regarding fever in trial I, taking the large study numbers into account evaluating rehydration therapy in children with gastroenteritis [23,24]. Moreover, responses to OADRI during trial II started with higher mean item scores than trial I, which may indicate higher acceptability from the beginning, but also might have resulted in fewer differences in mean OADRI item scores between the different study moments.

As previously mentioned, we focused on implementation of the clinical decision model on nurses' level, i.e. nurses were guided to initiate additional tests/interventions for high-risk children. However, OADRI is not specifically developed for nurses and future studies could focus on acceptability of physicians or other medical staff either.

Strengths and Limitations

The main strength of this study is our translation of the OADRI into Dutch to create more possibilities using this instrument more internationally including other populations and settings. As we measured the acceptability of rule implementation in time we could describe the process of implementation as a dynamic process and identify with the OADRI specific barriers and facilitators along this implementation period which gave the opportunity to intervene directly.

This study has also some limitations. First, as our study was covering one tertiary pediatric ED we could include only a limited number of ED nurses. Moreover, as our ED is a high research setting, nurses are very used to participate in different studies which might have resulted in a relative overestimation of our validation results of OADRI [25,26]. Second, our study size did not justify a full validation study. Reproducibility of OADRI, which is the degree to which repeated measurements in the test-retest period provide similar answers, was not measured in this study due to the anonymous questionnaire reply. Moreover, future research should focus on extended validation measures as internal consistency and construct validity. Third, the original categorization of OADRI items as suggested by the developers was based on their post-hoc thoughts, rather than based on reliable methods of item selection and reduction analyses [10,17]. Additional broader evaluation of studies with greater sample sizes could provide more complete validation information, including evaluation of possible reduction or changes in categorization of OADRI items. Moreover, the small sample size of our study prevents good generalizability to other ED nurses. Last, it would have been preferred to analyse individual changes in time rather than mean item scores differences in time. This would have corrected for variability between subjects [27]. However, due to the anonymously character of the study design we could not relate the questionnaires responses within the different study moments to persons.

CONCLUSION

Disseminated use of the OADRI seems usable in the acceptability measurement of newly implemented clinical decision rules in practice, as shown by an application of its Dutch version. Although broad-spectrum validation should be incorporated in future application of OADRI, we observed good acceptability of the introduction of two clinical decision rules among ED nurses at our emergency department. Improvement of clinical decision rules acceptability could be achieved by responses to individual guided interaction based on OADRI items.

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'THE OTTAWA ACCEPTABILITY OF DECISION RULES INSTRUMENT' *NEDERLANDSE VERTALING*

Geef aan in welke mate u het eens bent met de volgende stellingen over de 'koortsregel' door het hokje aan te vinken dat het dichtst bij uw eigen mening ligt. Als u op dit moment tijdens uw werkzaamheden geen gebruik maakt van deze regel, beantwoord de stellingen dan alsof u overweegt de regel te gaan gebruiken (de regel *zou* eenvoudig te gebruiken zijn, etc.).

Geef aan in welke mate u het eens bent met de volgende stellingen over de beslisregel.	**Volledig mee oneens**	**Gedeeltelijk mee oneens**	**Enigszins mee oneens**	**Enigszins mee eens**	**Gedeeltelijk mee eens**	**Volledig mee eens**	**Geen mening / weet ik niet**
De regel is eenvoudig in gebruik.							
De regel is eenvoudig te onthouden.							
De regel is bruikbaar in de praktijk.							
Het woordgebruik van de regel is helder en eenduidig.							
Mijn collega's ondersteunen het gebruik van de regel.							
Patiënten zijn gebaat bij het gebruik van de regel.							
Gebruik van de regel resulteert in een beter verloop van het zorgproces.							
Gebruik van de regel zal leiden tot een verhoogde kans op rechtszaken.							
Er bestaat onvoldoende wetenschappelijk bewijs om de regel te ondersteunen.							
Ik gebruik al een andere regel of vergelijkbare methode.							
In de regel ontbreekt een essentiële klinisch relevante variabele.							
Mijn werkomgeving belemmert het gebruik van de regel.							

Chapter 9

Tools for 'safety netting' in common paediatric illnesses: a systematic review in emergency care.

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ABSTRACT

Context Safety netting strategies after emergency department (ED) discharge is often based on the gut-feeling of the attending physician.

The objective was to systematically identify evaluated safety netting strategies after ED discharge and to describe determinants of paediatric ED revisits.

Data sources: Medline, Embase, CINAHL, Cochrane-central, OvidSP, Web-of-Science, Google-Scholar, PubMed.

Studies of any design reporting on safety netting/follow-up after ED discharge and/or determinants of ED revisits for the total paediatric population or specifically for children with fever, dyspnea and/or gastroenteritis. Outcomes included complicated course of disease after initial ED visit (e.g. revisits, hospitalization).

Two reviewers independently assessed studies for eligibility and study quality. As meta-analysis was not possible due to heterogeneity of studies, we performed a narrative synthesis of study results. A best-evidence synthesis was used to identify the level of evidence.

We summarised 58 studies, 36%(21/58) were assessed as having low-risk of bias. Limited evidence was observed for different strategies of safety netting, with educational interventions being mostly studied. Young children, a relevant medical history, infectious/respiratory symptoms or seizures and progression/persistence of symptoms were strongly associated with ED revisits. Gender, emergency crowding, physicians' characteristics and diagnostic tests and/or therapeutic interventions at the index visit were not associated with revisits.

Conclusion

Within the heterogenous available evidence we indentified a set of strong determinants of revisits that identify high-risk groups in need for safety netting in paediatric emergency care, being related to age and clinical symptoms. Gaps remain on intervention studies concerning specific application of a uniform safety netting strategy and its included time frame.

INTRODUCTION

When patients are discharged from the emergency department (ED) without definite diagnosis, monitoring children's course of disease to rule-out SI is mandatory.(1) This theme is covered by the term 'safety netting', introduced to general practice in 2004 by Roger Neighbour who considered it a core component of general practice consultation.(2) Safety netting can be described as a set of procedures or guidelines which should be followed when a patient is discharged from the ED. This strategy is required in situations with increased risk for serious complications, either in the diagnosis itself (e.g. dehydration in patients with gastroenteritis) or if individual patient characteristics are associated with a high risk of complications (e.g. significant co-morbidity or immunosuppressive therapy).(1) Patients who revisit the ED may be regarded as the high-risk population of possible failure of this safety netting strategy.

The importance of safety netting is increasingly recognised in emergency care and literature.(3) Healthcare physicians lack standardised safety netting methods since strategies are often based on the gut-feeling of the ED physician (4) and key gaps are described in need of studies on methods and effects of safety netting.(3, 5) Therefore, we planned to systematically review the literature on this important topic.

Our first aim was to systematically summarise evaluated safety netting strategies after ED discharge. Secondly, we identified children at risk for revisits to improve the identification of children prone to deteriorate after emergency discharge, by studying determinants of ED revisits. Both aims were studied in the total ED population or specifically for children with common illnesses as fever, dyspnea and gastroenteritis.

METHODS

Inclusion criteria

We considered all types of studies eligible if they reported about safety netting after ED discharge and extended our search for determinants of ED revisits as a proxy of failing safety netting strategies. We included studies on the total ED population or specific for children with fever, dyspnea and gastroenteritis. Studies reporting data on adult and children together, as well as studies in low-income countries, were excluded. Two reviewers independently assessed inclusion (EK, MW); discrepancies were resolved by a third reviewer (RO).

Outcome measures

Outcomes included complicated course of disease after initial ED visit, mainly dominated by revisits and hospitalisation.

Search strategy

We searched the following electronic databases: Medline OvidSP, Embase (Excerpta Medica dataBASE), CINAHL (Cumulative Index to Nursing and Allied Health Literature), Cochrane central register of controlled trials, Web-of-Science, Google-Scholar and PubMed as publisher (searches updated in January 2014) (supplemental information 1). We checked the reference list of these papers for additional articles not included in the initial computerised search.

Data extraction

We retrieved the full text copies of all articles identified as potentially relevant by reviewing the abstracts of search results. Two reviewers' extracted data on the following: study design, disease/working diagnosis, study population, number of revisits, follow-up period and type of revisit. The determinants were grouped into: child characteristics; social/demographics; disease characteristics; physician and process characteristics. Finally, data on follow-up after ED discharge were extracted.

Risk of bias assessment and best-evidence synthesis

Two authors (EK/DHFG) independently assessed the potential assessed risk of bias of the studies included using the *MINORS*, a methodological index for non-randomised studies,(6) together with the presence of revisits as primary outcome measure and the number of events (supplementary file 2). Consensus was reached by the two reviewers (EK/DFHG), otherwise the independent opinion of a third reviewer was decisive (RO).

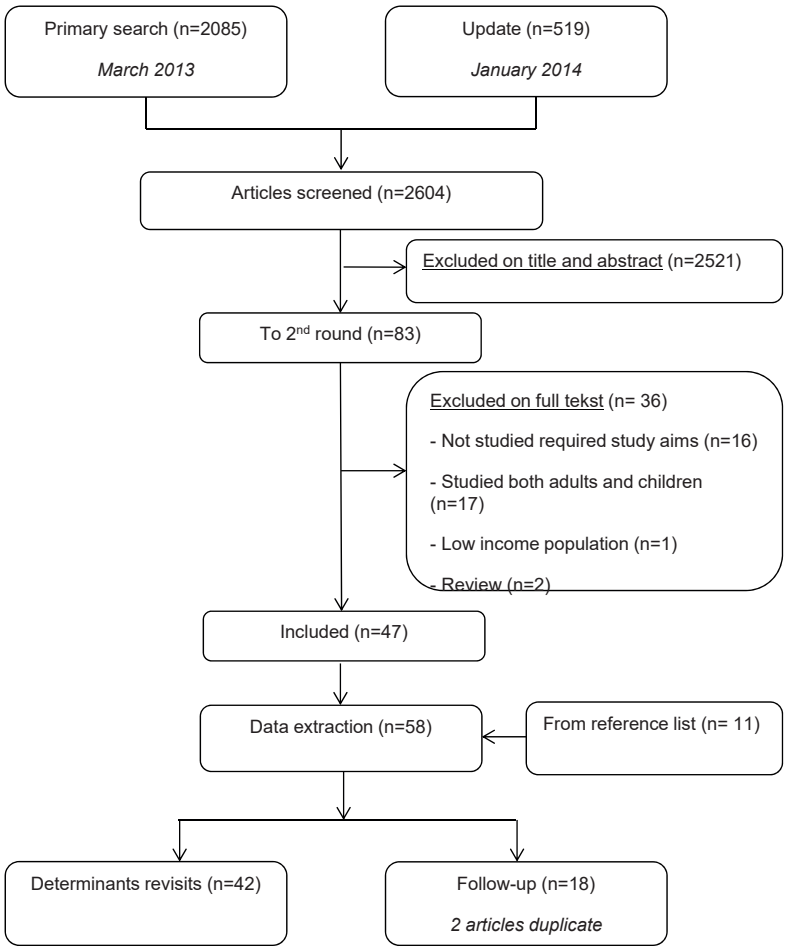
We performed two separate 'best-evidence' syntheses based on the study of Tulder et al.(7); one according to safety netting strategies and one according to determinants of revisits as meta-analysis of results was not possible owing to heterogeneity in participants, interventions, outcome measures and methodological quality(7) (supplementary file 2).

RESULTS

Identification and selection of the literature

The literature search identified 2604 references (figure 1). Overall 36 of 83 full text articles screened for eligibility were excluded on the basis of incorrect study aims, data on adult patients, reviews or low-income populations. Data extraction was performed for 58 articles including 11 articles added from reference lists. 42 articles described determinants of revisits and 18 articles *(2 articles duplicate)* reported on follow-up after ED discharge (figure 1).

Figure 1: Flowchart of the study selection and exclusion stages during the systematic review process



Description of included studies

Study characteristics are presented in tables 1 and table 2. Included studies were mostly cohort studies (72%; n=42). Fifty-two percent (n=30) of the studies originated from the United States of America and 19% (n=11) from the United Kingdom. Year of publication varied between 1995 and 2013, with 33% (n=19) published in the last two years. Most studies (n=34) included all children presented to the ED or the most common paediatric illnesses; 14 studied febrile children and 10 studies reported specific diseases only (e.g. gastroenteritis, influenza, respiratory tract infections). Study populations varied

between 13 and 568,845 children (median: n=1,371) and number of events (revisits or hospitalisation after revisit) varied between 9 and 36,734 (median: n=189). Follow-up period after ED discharge varied between 1 and 656 days (median: 3 days). Most studies (n=29; 50%) described scheduled and unscheduled revisits together; 19 (33%) only measured unscheduled revisits (tables 1 and 2).

Risk of bias assessment

Supplemental information 2 shows the potential risk of bias with 36% (n=21) of the studies having low-risk of bias. For all studies the reviewers achieved uniform bias assessment. Ten studies (17%) were scored as high-risk of bias because only abstracts were available (9 congress abstracts and 1 Spanish abstract). Initial disagreement on 55 out of 880 assessed items (6%) for opportunity of bias was solved by consensus reached by the two reviewers (EK/DG) or by decision of a third reviewer (RO).

Safety Netting after discharge

Figure 2 presents an overview of the different safety netting strategies evaluated in the included studies (n=18) and the corresponding level of evidence according to the best-evidence synthesis (details in supplemental information 3a and 3c).

Figure 2: Level of evidence safety netting strategies according to the best-evidence synthesis

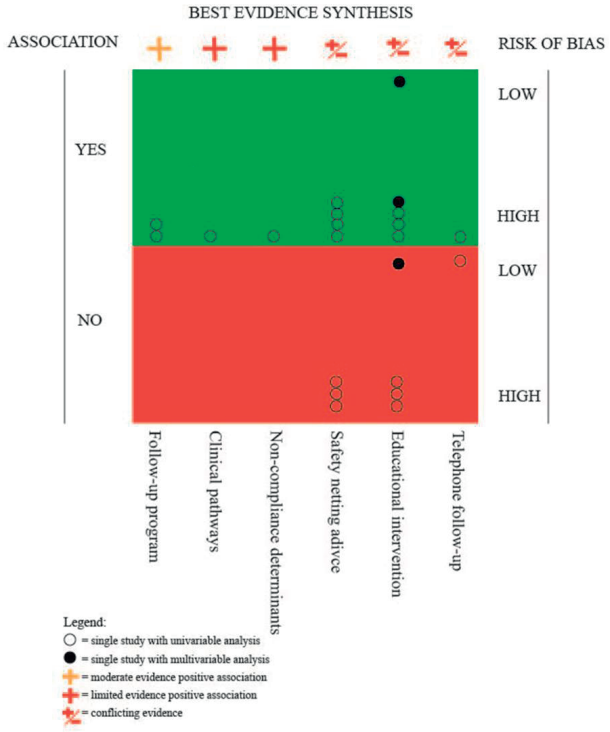


Table 1: characteristics of included studies regarding the first study aim: safety netting strategies after ED discharge

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male %	N outcome, male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up** (days)	Type of revisit	Risk of bias (high/low)
Baker 2009 USA	CP	Article	Fever	Yes	280 NR	105 NR	3-36 m NR	319 -656~	suR	Low
Bloch 2013 USA	RCT	Article	All=	No	436 54%	216 58%	1m-18y NR	2-5	NA	Low
Browne 2001 Australia	BA	Article	GE, asthma, croup	Yes	5534 NR	240 NR	NR	NR	suR	High
Considine 2007 Australia	BA	Article	Fever	No	40 NR	15 NR	<16y 3.1y ±2.5*before* 1.8y ±1.3 *after*	2	NA	High
Chande 1996 USA	RCT	Article	All	Yes	130 59%	37 NR	All 39m^ ±36 63m^^ ±58	30, 90 and 180	suR	High
Fagbuyi 2011 USA	CP	Article	Influenza-like	No	38,646 53%	1,091 NR	6m-21y 82.3m ±84.6	7	uR	High
Horne 1995 USA	CP	Article	All	No	250 NR	171 NR	All NR	3	NA	Low
Ismail 2013 USA	RCT	Abstract	Fever	No	63 16%	NR	NR	14	NR	High

Table 1: characteristics of included studies regarding the first study aim: safety netting strategies after ED discharge (*continued*)

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male %	N outcome, male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up** (days)	Type of revisit	Risk of bias (high/low)
Lawrence 2009 USA	CR	Article	All	Yes	40,418 NR	979 NR	NR 2y (0.5-7.0)	3	suR	High
Maguire 2011 UK	CP	Article	Fever	No	220 56%	29/56 NR	<5y 27% ≤1y	NS	suR	High
Moineau 2004 Canada	CR	Abstract	GE	Yes	1,862 NR	108 NR	NR 2.6y ±2.8	7	uR	High
O'Neill-Murphy 2001 USA	BA	Article	Fever	No	87 NR	NR	3m-5y NR	14, 56	suR	High
O'Neill 2001 USA	CR	Article	All	No	NR	NR	NR	NR	NA	High
Patel 2009 USA	nRCT	Article	GE	No	291 NS	NA	3m-18y 60% <1y	1, 2	NA	High
Porter 2000 USA	CP	Article	Fever	No	92 NR	NA	≤36m 27,4y ±9,2	NA	NA	High
Roland 2011 UK	CP	Abstract	Fever	No	457 NR	NR	NR	NR	uR	High

Table 1: characteristics of included studies regarding the first study aim: safety netting strategies after ED discharge (*continued*)

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male %	N outcome, male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up** (days)	Type of revisit	Risk of bias (high/low)
Scarfone 1996 USA	CP	Article	All	No	179 55%	91 NR	NR 31m*	1	NA	Low
Yang 2012 Taiwan	BA	Article	All	Yes	1,285 54%	9 56%	NR 34m* (0-207)	3	suR	High

Table 2: characteristics of included studies regarding the second study aim: determinants of revisits

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male % of total population	N outcome (revisits), male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up** (days)	Type of revisit	Risk of bias~ (high/low)
Alessandrini 2004 USA	CR	Article	All	Yes	54,784 NR	1,893 NR	All 4.6y ±4.9#	2	suR	Low
Ali 2012 USA	CP	Article	All	Yes	8,742 NR	124 52%	All 3.0y (1.1-12)#	3	suR	High
Angoulvant 2012 France	CP	Article	All=	Yes	501 NR	206 51%	<6y 18m (7-39)	7	suR	High
Augustine 2013 USA	CS	Abstract	All	Yes	13 NR	13 NR	All 4.2y*	2	uR	High
Berry 2013 USA	CR	Article	All	Yes	568,845 NR	36,734^ NR	≤18y 3y (0-10)	30	uR	Low
Black 2010 UK	CR	Abstract	All	Yes	2,345 NR	91 NR	<17y 76% <5y	3	uR	High
Callery 2010 UK	CR	Article	All	Yes	43,372 NR	2,433 NR	<15y NR	7	suR	Low
Chang 2008 Taiwan	CR	Article	All	No	3,216 58%	188 NR	<18y 5.y ±0.1	3	suR	Low

Table 2: characteristics of included studies regarding the second study aim: determinants of revisits (*continued*)

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male % of total population	N outcome (revisits), male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up[**] (days)	Type of revisit	Risk of bias[~] (high/low)
DePiero 2002 USA	CR	Article	All	Yes	51,195 NR	261[^] NR	All NR	3	suR	Low
Dunlop 2005 Australia	CR	Article	Fever	No	260 52%	35 NR	6m-6y 25.7m[+]	1	suR	High
Easter 2012 USA	CR	Article	All	Yes	97,374 NR	1,091[^] 52%	0-21y 52% <5y[#]	4	suR	Low
Florin 2013 USA	CR	Article	Pneumonia	Yes	100,615 54%	6,439 NR	2m-18y 3y (1-6)	3	suR	Low
Freedman 2013 Canada	CR	Article	GE	Yes	3,346 55%	526 57%	<18y 3.4y ±3.5	7	uR	Low
Gallagher 2013 USA	CR	Article	All	Yes	119,792 53%	1,499[^] NR	All 7.6y[*]	3	uR	Low
Gaucher 2012 Canada	CR	Article	All	No	49,146 51%	2,534 NR	<19y 62% <5y	2	uR	Low
Goldman 2006 Canada	CR	Article	All	Yes	37,725 NR	1,990 NR	<19y 18% <1y	3	uR	Low
Goldman 2011 Canada	CR	Article	All	Yes	2,062 55%	353[^] 59%	<19y 57m (0-215)	3	suR	High

Table 2: characteristics of included studies regarding the second study aim: determinants of revisits (*continued*)

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male % of total population	N outcome (revisits), male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up[**] (days)	Type of revisit	Risk of bias[~] (high/low)
Gregor 2009 USA	CP	Article	RTI/ GE	No	455 59%	49 NR	6w-8y 1.9y ±1.9	60	suR	High
Hacking 2012 UK	CR	Abstract	All	Yes	2,453 NR	130 NR	NR 4y[+]	NR	uR	High
Jacobstein 2005 USA	CC	Article	Fever	Yes	15,384 54%	165 54%	All 38m ±43	3	uR	Low
Jain 2010 USA	CR	Article	All	No	452,868 54%	17,335 NR	<19y 22% <1y	3	suR	Low
Klein-Kremer 2011 Canada	CR	Article	Fever	Yes	397 NR	92 67%	3-36m 17m ±8 [#]	3	suR	High
Lal et al. 1999 UK	CP	Article	All	Yes	7,328 NR	65 NR	NR	3	uR	High
LeDuc 2006 USA	CP	Article	All	Yes	932 NR	237 49%	All 4y[*]	2, 90	suR	High
Liberman 2012 USA	CR	Article	RTI	No	467 59%	189 NR	<19y NR	7, 30	suR	Low
Logue 2013 Canada	CR	Article	All	Yes	1,173 NR	261 61%	All 4.4y[*]	3	suR	High

Table 2: characteristics of included studies regarding the second study aim: determinants of revisits (*continued*)

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male % of total population	N outcome (revisits), male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up** (days)	Type of revisit	Risk of bias~ (high/low)
Maguire[<] 2011 UK	CP	Article	Fever	No	220 56%	127 NR	<5y 27% ≤1y	NS	suR	High
Mansbach 2008 USA	CP	Article	Bronchiolitis	No	1,456 58%	837 58%	<2y 6.9(4.2-11.3)[$]	14	NS	Low
Michelson 2012 USA	CR	Article	All	No	198,778 NR	7281 NR	All 10% <1y	2	suR	High
Mintegui 2000 Spain	CR	Abstract	All	Yes	3,667 NR	495 NR	All NR	7	uR	High
Mistry 2007 USA	CP	Article	Fever	Yes	322 57%	76 NR	28d-17y 31.5m[*]	10	uR	High
Mistry 2009 USA	CP	Article	Fever	No	97 56%	18 NR	2-18 y 58,7m ±40.1	7-10	uR	High
Moineau[<] 2004 Canada	CR	Abstract	GE	Yes	1,862 NR	108 NR	NR 2.6y ±2.8	7	uR	High
O'Loughlin 2012 UK	CR	Article	All	Yes	10,573 NR	532 NR	<16y 34% <2y	7	uR	High
Roback 1997 USA	CC	Article	Bronchiolitis	Yes	181 NR	57 NR	<1year NR	4	NS	High

Table 2: characteristics of included studies regarding the second study aim: determinants of revisits (*continued*)

Author Year Country	Study design	Article/ abstract	Disease/ working diagnosis	Primary outcome: revisits	N total, male % of total population	N outcome (revisits), male %	Age inclusion Median (IQR)/ mean age (SD)	Follow-up[**] (days)	Type of revisit	Risk of bias[~] (high/low)
Roggen 2012 Belgium	CR	Abstract	All[=]	Yes	46,386 NR	1,864 NR	<16y NR	3	suR	High
Samuels-Kalow 2013 Canada	CR	Abstract	Fever	Yes	202 NR	14 NR	2-24m NR	3	suR	High
Sartain 2002 UK	RCT	Article	All	No	399	31 NS	All 25.7m[*]	90	suR	High
Seow 2007 Taiwan	CR	Article	Fever	No	345 47%	115 NR	3-36m NR	3	uR	Low
Simmons 2012 UK	CR	Abstract	All	Yes	NR	51 NR	All 59% <2y	7	uR	High
Small 2005 UK	CP	Article	GE	No	112 NR	56 NR	1-6 y 1.9 (1.3)^	7, 30	suR	Low
Zimmerman 1996 USA	CR	Article	All	Yes	5,228 58%	242 NR	<18y 13% <1 y	14	suR	Low

Legend table 1 & 2
* Mean (CI)
[+] Median (IQR)
** Time until revisit
[~] See supplemental information 3
^ revisits requiring admission
# of the number of children with revisits
[$] of the number of children sent home
[~] minimum and maximum
[ˆ] in the intervention group; [ˆˆ]in the control group
[=] common illnesses, without children with traumatic complaints
[<] Studies included for both study aims (Maguire et al. 2011 and Moineau et al. 2004)
y= years; m = months; w= weeks
CC= case control study; CR= cohort study, retrospective; CP= cohort study, prospective ; CS=cross-sectional study; RCT= randomised controlled trial; nRCT non-randomised controlled trial; BA=before after trial; GE= gastroenteritis; All= all ED diagnoses; RTI= respiratory tract illnesses
NA= not applicable; NR= not recorded
sR= scheduled revisit; uR= unscheduled revisit; suR= scheduled and unscheduled revisit

Moderate/ limited evidence

There was moderate evidence for the positive influence of a standardised follow-up program (including e.g. a venue for handling calls after ED visits) (8) on patient care and patient satisfaction.(8, 9) Limited evidence was found that clinical pathways at the ED resulted in a reduced admission rate, shortened length of stay and fewer revisits after discharge.(10) We found limited evidence for risk factors associated with noncompliance of scheduled revisits; for example parents' perception that their child is not severely ill; parents' age (<21y) and ED physicians uncertainty about patients' return.(11)

Conflicting evidence

We found conflicting evidence for the association between safety- netting advice and the reduction of revisits. According to four studies(9, 12-14) , revisits could be reduced by providing consistent verbal and written discharge information regarding the natural history of disease(13) and temperature measurement/treatment.(14) In contrast, other studies concluded that the provision of safety- net advice did not affect the number of revisits.(15, 16) We found conflicting evidence for the association between educational interventions at the ED and parental recall of discharge instructions or revisits.(16-24) One study reported that video home-management of fever improved caregiver knowledge of fever, but did not decrease ED use.(18)

There was conflicting evidence about the role of telephone follow-up as safety netting strategy. One study reported this was an effective way of providing for example health information, managing remaining symptoms and recognising complications.(25) In contrast, another study advocated caution in the implementation of telephone follow-up, because of moderate success rate in reaching patients.(26)

Determinants of revisits

Figure 3 presents an overview of all determinants of revisits described in the included studies (n=42), their association with revisits and the corresponding level of evidence according to the best-evidence synthesis (details in supplemental information 4b and 4c).

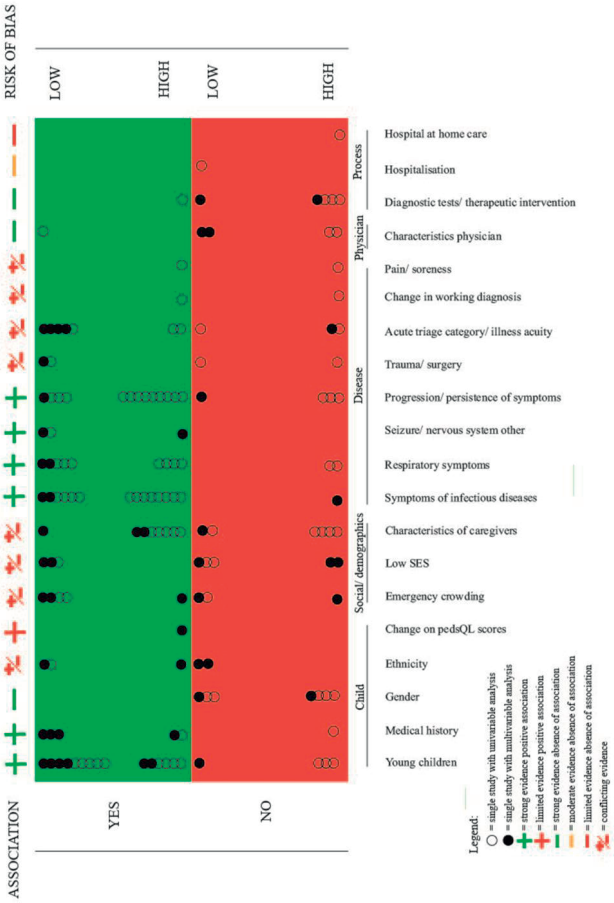


Figure 3: Level of evidence determinants of revisits according to the best-evidence synthesis

Strong evidence

Child characteristics

We found strong evidence for the association of ED revisits with younger children, ranging from ≤12 months until <6 years.(12, 27-40) Moreover, for the association of medical history and revisits, although including heterogeneous definitions, we found strong evidence.(12, 28, 35, 37, 41, 42) Maquire et al. concluded that history of illness in febrile children was one of the reasons for parental advice seeking behavior.(12) However, for children with bronchiolitis this association was conflicting.(35) (41) With strong evidence, no association was found between gender and revisits to the ED(27, 30) (43) or revisits to the primary care provider.(33) Gender was neither discriminating in the comparison of admitted children to discharged ones after revisiting the ED, nor a prognostic factor in safe discharge of children with bronchiolitis.(35, 41, 44)

Social and demographic characteristics

There was conflicting evidence that ED revisits were associated with ED crowding. (27, 29, 42) Two studies were positively associated with revisits(39, 45), and three other studies were even associated with lower ED crowding during late evening or night shifts.(32, 40, 46)

Disease characteristics

Strong evidence was found for the association with revisits of children with symptoms of infectious diseases(9, 29, 31, 33, 35-37, 39, 43, 46-50) or respiratory symptoms,(29, 30, 35, 37, 41, 46-49, 51) compared with all ED revisits. Strong evidence was found for the association of revisits and seizures or other nervous system diseases.(27, 37, 39) Last, strong association was found for progression/persistence of symptoms and revisits.(9, 13, 36, 38, 39, 44, 48, 51-56)

Physician characteristics

We found no association between physicians' characteristics, such as being paediatrician or resident(42, 57) or physician's years of experience(41, 58) and revisits.(41, 42, 57, 58)

Process characteristics

We observed strong evidence for the absence of the association between revisits and the performance of diagnostic tests or therapeutic interventions at the index visit.(43, 48, 55, 59, 60)

Limited/ moderate evidence

Child characteristics

Mistry et al. studied a health-related quality-of-life instrument (PedsQL). There was limited evidence for the association of lower changes in PedsQL scores and ED revisits, which implied less improved quality of life for the revisiting child.(61)

Process characteristics

No association was found for revisits and paediatric hospital at home service compared with conventional hospital care for children suffering from breathing difficulty; diarrhoea and vomiting or fever.(62) We found no association between revisits and children with acute gastro-enteritis admitted to hospital compared with a comparable group of children managed at home.(63)

Conflicting evidence

Child characteristics

There was conflicting evidence for the association of ethnicity and revisits. In disease specific studies (bronchiolitis and fever) ethnicity was not associated with revisits,(42) (35) in contrast to studies including the total ED population.(27, 30, 37)

Social and demographic characteristics

There was conflicting evidence for the association of revisits and characteristics of caregivers. For example, caregiver's age, marital status and presence/age of other children were not associated with revisits in five studies.(33, 42-44, 55) In contrast, other studies concluded that e.g. language spoken at home or single caregivers were associated with revisits.(9, 12, 28, 36, 40, 50, 51, 64) Next, we found conflicting evidence for the association of lower socio-economic status and revisits.(27, 28, 30, 33, 37, 40, 42, 46)

Disease characteristics

Associations between trauma, surgical problems or pain (43, 48) and revisits were conflicting.(29, 30, 37, 48) Conflicting evidence was found for the association with revisits in change of working diagnosis, (44, 47) and ED triage acuity. (13, 28, 29, 32, 33, 36, 38, 40, 42)

DISCUSSION

Follow-up after discharge and determinants of revisits: main outcomes

Limited evidence was observed for different strategies of safety netting, with educational interventions being mostly studied. Identified determinants of children at risk for revisits included young children, relevant medical history, infectious/respiratory symptoms or seizures and progression/persistence of symptoms. No association with revisits was found for gender, emergency crowding, physicians' characteristics and diagnostic tests and/or therapeutic interventions at the index ED. For other described determinants no statement was possible due to conflicting evidence.

Strengths and weaknesses of this review

The development of evidence based strategies of safety netting is a challenging new topic. Available studies describing revisits of the ED population and their characteristics vary in populations, study aims and methodology. The main strength of this systematic review is combining all information on determinants of revisits using a best-evidence synthesis. Most studies about safety netting are rather descriptive and did not study their effectiveness.(1, 5) In our review we summarised the literature that evaluated the clinical consequences of their safety netting intervention.

This review has some limitations. Because of the heterogeneity of the studies we could not perform a meta-analysis. This systematic review is limited to the provision of whether there is evidence for a significant association or not. This approach limits the interpretation and clinical relevance of the reported associations, but is a consequence of the large heterogeneity of present studies on this topic. Second, there is no standardised risk of bias assessment method for the variation of study designs and outcomes included in this systematic review. To overcome lack of general accepted thresholds determining study's risk of bias and to include relevance to the research question on the risk of bias criteria(65) we used the *MINORS* risk of bias criteria.(6) We added two important items, which would be the most appropriate for our included studies. With this approach we aimed to perform best available systematic risk- of- bias analysis. We classified determinants to 'strong evidence' on the presence of low-risk bias studies, although high risk-of-bias studies may also have studied the same determinants (see online supplementary file 2). Furthermore, there are limitations embedded in the study design of the included studies itself. The majority of studies are analysed with univariable statistical approaches, with only 35% (20/58) of the studies using multivariable statistical analysis. It remains unknown to what extent the determinants are independently associated with revisits. Second, although we followed the focus of most studies by defining 'revisits' as proxy for high-risk populations of failed safety netting strategies, hospitalisation after revisiting the ED is probably the most effective outcome to evaluate this topic.

However, this outcome is limited studied due to its low prevalence. Third, some study characteristics increased heterogeneity between our different determinant-categories. For example, determinants were not always specified, for example,. 'history of illnesses' was not further described in the study of Maguire et al. Furthermore, outcome measures were not homogenous and included, for example, revisits or admission after revisit. Finally, study comparisons varied between revisits vs. total ED population or subgroups of revisits (discharged vs. admitted children).

IMPLICATIONS FOR CLINICAL PRACTICE AND FUTURE RESEARCH

A content of safety- net advice, as included in the NICE guideline,(66) has been published in relation to general practice where consensus was reached among general practitioners and paediatric ED consultants using a modified Delphi approach(1, 4). Safety netting advice should include 1) the existence of uncertainty; 2) what exactly to look out for; 3) how exactly to seek further help; 4) what to expect about time course. Our systematic review shows that a variety of safety netting techniques are used but the effective components or the best way to perform remains unknown, as has been identified by others(1, 5). Secondly, we generated answers on what determinants are associated with revisits and, those who are not. Moreover, the conclusions of our review can improve homogeneity in study design on follow-up strategies, and can add to progress in this research area. In essence, the importance of this

knowledge should be combined with parent-related factors as their ability to understand and to comply with the designed safety-netting strategy. (11) Lastly, one notable gap in safety-netting literature is its time frame strategy. The NICE fever guideline claims 'to arrange a follow-up appointment at a certain time and place'.(6, 7) In future research, we need to study the (efficacy of) safety-netting strategies in which the aspect of time is taken into account.(5, 67)

CONCLUSION

Determination of a high-risk group in need for safety-netting strategies in paediatric emergency care remains difficult. We identified a set of strongly associated determinants of revisits that could be used for this identification; being young children, relevant medical history, infectious/respiratory symptoms or seizures and progression/persistence of symptoms. Gaps remain on intervention studies concerning specific application of a uniform safety-netting strategy and its included time frame.

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SUPPLEMENTAL INFORMATION 1A: SYSTEMATIC REVIEW SEARCH STRATEGY

Embase

(('hospital readmission'/de OR (readmiss* OR reattend* OR rehospital* OR revisit* OR ((re OR second OR return* OR repeat* OR recur*) NEAR/3 (admiss* OR attend* OR visit* OR hospital* OR emergenc* OR present*)) OR (safe* NEAR/3 net*)):ab,ti) OR (('hospital discharge'/de OR (discharge* OR postdischarge*):ab,ti) AND ('evaluation and follow up'/de OR 'health care quality'/exp OR evaluation/de OR 'follow up'/de OR (evaluat* OR (follow* NEXT/1 up) OR followup):ab,ti))) AND ('emergency ward'/de OR 'emergency patient'/de OR 'emergency treatment'/de OR 'first aid'/de OR 'emergency care'/de OR 'emergency health service'/de OR 'emergency medicine'/de OR (emergen* OR 'first aid'):ab,ti) AND (child/exp OR newborn/exp OR adolescent/exp OR adolescence/exp OR 'child behavior'/de OR 'child parent relation'/de OR (adolescen* OR infan* OR newborn* OR (new NEXT/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under NEXT/1 ag*) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR paediatric* OR paediatric* OR school* OR preschool* OR highschool*):ab,ti) AND (infection/exp OR fever/de OR dyspnea/exp OR gastroenteritis/de OR vomiting/de OR diarrhea/exp OR (infecti* OR virus* OR viral OR bacterial OR fever OR febril* OR dyspne* OR dyspnoe* OR gastroenterit* OR vomit* OR diarrh*):ab,ti)

Medline OvidSP

(("Patient Readmission"/ OR (readmiss* OR reattend* OR rehospital* OR revisit* OR ((re OR second OR return* OR repeat* OR recur*) ADJ3 (admiss* OR attend* OR visit* OR hospital* OR emergenc* OR present*)) OR (safe* ADJ3 net*)).ab,ti.) OR (("Patient Discharge"/ OR (discharge* OR postdischarge*).ab,ti.) AND ("Program Evaluation"/ OR Evaluation Studies.pt. OR exp "Quality of Health Care"/ OR "Follow-Up Studies"/ OR (evaluat* OR (follow* ADJ up) OR followup).ab,ti.))) AND ("Emergency Service, Hospital"/ OR "Emergency Medical Services"/ OR "emergency treatment"/ OR "emergency medicine"/ OR "first aid"/ OR (emergen* OR "first aid").ab,ti.) AND (exp child/ OR exp infant/ OR adolescent/ OR exp "child behavior"/ OR exp "Parent-Child Relations"/ OR (adolescen* OR infan* OR newborn* OR (new ADJ born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under ADJ ag*) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR paediatric* OR paediatric* OR school* OR preschool* OR highschool*).ab,ti.) AND (exp infection/ OR exp fever/ OR exp dyspnea/ OR gastroenteritis/ OR vomiting/ OR exp diarrhea/ OR (infecti* OR virus* OR viral OR bacterial OR fever OR febril* OR dyspne* OR dyspnoe* OR gastroenterit* OR vomit* OR diarrh*).ab,ti.)

Cochrane central

(((readmiss* OR reattend* OR rehospital* OR revisit* OR ((re OR second OR return* OR repeat* OR recur*) NEAR/3 (admiss* OR attend* OR visit* OR hospital* OR emergenc* OR present*)) OR (safe* NEAR/3 net*)):ab,ti) OR (((discharge* OR postdischarge*):ab,ti) AND ((evaluat* OR (follow* NEXT/1 up) OR followup):ab,ti))) AND ((emergen* OR 'first aid'):ab,ti) AND ((adolescen* OR infan* OR newborn* OR (new NEXT/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under NEXT/1 ag*) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR paediatric* OR paediatric* OR school* OR preschool* OR highschool*):ab,ti) AND ((infecti* OR virus* OR viral OR bacterial OR fever OR febril* OR dyspne* OR dyspnoe* OR gastroenterit* OR vomit* OR diarrh*):ab,ti)

Web-of-Science

TS=((((readmiss* OR reattend* OR rehospital* OR revisit* OR ((re OR second OR return* OR repeat* OR recur*) NEAR/3 (admiss* OR attend* OR visit* OR hospital* OR emergenc* OR present*)) OR (safe* NEAR/3 net*))) OR (((discharge* OR postdischarge*)) AND ((evaluat* OR (follow* NEXT/1 up) OR followup)))) AND ((emergen* OR "first aid")) AND ((adolescen* OR infan* OR newborn* OR (new NEXT/1 born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR under age* OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR paediatric* OR paediatric* OR school* OR preschool* OR highschool*)) AND ((infecti* OR virus* OR viral OR bacterial OR fever OR febril* OR dyspne* OR dyspnoe* OR gastroenterit* OR vomit* OR diarrh*)))

PubMed as publisher

(((readmiss*[tiab] OR reattend*[tiab] OR rehospital*[tiab] OR revisit*[tiab] OR ((re[tiab] OR second[tiab] OR return*[tiab] OR repeat*[tiab] OR recur*[tiab]) AND (admiss*[tiab] OR attend*[tiab] OR visit*[tiab] OR hospital*[tiab] OR emergenc*[tiab] OR present*[tiab])) OR safety net*[tiab])) OR (((discharge*[tiab] OR postdischarge*[tiab])) AND ((evaluat*[tiab] OR follow up[tiab] OR followup[tiab])))) AND ((emergen*[tiab] OR first aid[tiab])) AND ((adolescen*[tiab] OR infan*[tiab] OR newborn*[tiab] OR new born*[tiab] OR baby[tiab] OR babies[tiab] OR neonat*[tiab] OR child*[tiab] OR kid[tiab] OR kids[tiab] OR toddler*[tiab] OR teen*[tiab] OR boy*[tiab] OR girl*[tiab] OR minors[tiab] OR underag*[tiab] OR under ag*[tiab] OR juvenil*[tiab] OR youth*[tiab] OR kindergar*[tiab]

OR puber*[tiab] OR pubescen*[tiab] OR prepubescen*[tiab] OR prepubert*[tiab] OR paediatric*[tiab] OR paediatric*[tiab] OR school*[tiab] OR preschool*[tiab] OR highschool*[tiab])) AND ((infection*[tiab] OR infectious*[tiab] OR virus*[tiab] OR viral OR bacterial OR fever OR febril*[tiab] OR dyspne*[tiab] OR dyspnoe*[tiab] OR gastroenterit*[tiab] OR vomit*[tiab] OR diarrh*[tiab])) AND publisher[sb]

CINAHL

((MH "Readmission"+ OR (readmiss* OR reattend* OR rehospital* OR revisit* OR ((re OR second OR return* OR repeat* OR recur*) N3 (admiss* OR attend* OR visit* OR hospital* OR emergenc* OR present*)) OR (safe* N3 net*))) OR ((MH "Patient Discharge"+ OR (discharge* OR postdischarge*)) AND (MH "Program Evaluation"+ OR MH "Quality of Health Care"+ OR MH "Prospective Studies"+ OR (evaluat* OR (follow* N up) OR followup)))) AND (MH "Emergency Service "+ OR MH "Emergency Treatment (Non-Cinahl)"+ OR MH "emergency medicine"+ OR (emergen* OR "first aid")) AND (MH child+ OR MH infant+ OR adolescent+ OR MH "child behavior"+ OR MH "Parent-Child Relations"+ OR (adolescen* OR infan* OR newborn* OR (new N born*) OR baby OR babies OR neonat* OR child* OR kid OR kids OR toddler* OR teen* OR boy* OR girl* OR minors OR underag* OR (under N ag*) OR juvenil* OR youth* OR kindergar* OR puber* OR pubescen* OR prepubescen* OR prepubert* OR paediatric* OR paediatric* OR school* OR preschool* OR highschool*)) AND (MH infection+ OR MH fever+ OR MH dyspnea+ OR MH gastroenteritis OR MH vomiting+ OR MH diarrhea+ OR (infecti* OR virus* OR viral OR bacterial OR fever OR febril* OR dyspne* OR dyspnoe* OR gastroenterit* OR vomit* OR diarrh*))

Google Scholar

(readmission|reattendance|rehospitalization|"safety (netting|net)") (emergency|"first aid")

(child|newborn|adolescent|adolescence|baby|babies|neonates|children)

(infection|fever|dyspnea|gastroenteritis|vomiting|diarrhea|virus|virussus|viral|bacterial)

SUPPLEMENTAL INFORMATION 1B: NUMBER OF ARTICLES PER DATABASE

Database	Number of articles	Number of articles after deleting duplicates
Embase	1842	1835
Medline OvidSP	1268	425
Web-of-Science	538	131
CINAHL	199	25
Cochrane central	54	3
PubMed as publisher	28	23
Google Scholar	200	162
	4129	**2604**

SUPPLEMENTAL INFORMATION 2

Risk of bias assessment

Two authors (EK/DG) independently assessed the potential assessed risk of bias of the studies included using the *MINORS*, a methodological index for non-randomised studies.[1] The items were scored 0 if not reported; 1 when reported but inadequate; and 2 when reported and adequate. The global ideal score was 16 for non-comparative studies and 24 for comparative studies (supplemental information 2). As a higher event rate allows to give a more precise estimate of the influence of studied determinants we chose to select the number of events to include in our risk of bias assessment (score 2: A for >500 events, B for 100-500 events and C if less events occurred) , and together with the presence of revisits as primary outcome measure (score 1: A for revisits as primary outcome and B if not) the total risk of bias was assessed (supplemental information 3). We considered low risk of bias when studies fulfilling all *MINORS* criteria; or studies scored a minimum of two A's in score 1 and 2; or studies scored a minimum of B in score 1, 2 and *MINORS*. We considered high risk of bias in all other studies (supplemental information 3). If only aabstracts were available they were automatically judged to be at high risk of bias. Consensus was reached by the two reviewers (EK/DG) when there was difference in opinion on an item. If no consensus was reached, the independent opinion of a third reviewer was decisive (RO).

Data analysis - best-evidence synthesis

A narrative 'best-evidence' synthesis based on the study of Tulder et al.(11) was carried out, as meta-analysis of results was not possible owing to heterogeneity in participants, interventions, outcome measures and methodological quality.(11) We performed separate syntheses for the two separated study aims. Strong evidence was defined as

two or more studies with low risk of bias and generally consistent findings in all studies (≥75% of the studies reported consistent findings). Moderate evidence was defined as one study with low risk of bias and/or two or more studies with high risk of bias and generally consistent results. Limited evidence was defined as generally consistent findings were found in one study with high risk of bias. Conflicting evidence was defined as less than 75% of the studies reported consistent findings.

Table 2.1: Risk of bias assessment

Table 1: individual MINORS score

	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Unbiased assessment of study endpoint	Follow-up period appropriate to study aim	<5% lost to follow-up	Prospective calculation of study size	Adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	Total
Alessandrini 2004[2]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	13/16
Ali 2012[3]	2	1	2	2	2	2	1	0	NA	NA	NA	NA	12/16
Angoulvant 2013[4]	2	1	2	2	1	2	1	0	NA	NA	NA	NA	11/16
Augustine 2013[5]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Baker 2009[6]	2	1	2	2	2	1	2	2	2	2	2	2	22/24
Berry 2013[7]	2	1	1	2	2	1	2	0	NA	NA	NA	NA	11/16
Black 2010[8]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Bloch 2013[9]	2	2	2	2	2	2	1	0	2	2	2	2	21/24
Browne 2001[10]	2	2	2	2	2	1	2	0	2	1	2	2	20/24
Callery 2010[11]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	13/16
Chang 2008[12]	2	1	1	2	2	2	0	0	2	2	2	2	18/24
Considine 2007[13]	2	1	2	2	2	2	2	0	2	2	2	2	21/24
DePiero 2002[14]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	13/16
Dunlop 2005[15]	2	2	1	2	2	0	2	0	NA	NA	NA	NA	11/16
Easter 2012[16]	2	2	1	2	2	2	1	0	NA	NA	NA	NA	12/16
Fagbuyi 2011[17]	2	2	2	2	2	2	2	0	2	1	2	2	21/24
Florin 2013[18]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	13/16
Freedman 2013[19]	2	2	1	2	2	2	1	1	NA	NA	NA	NA	13/16
Gallagher 2013[20]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	13/16
Gaucher 2012[21]	2	2	1	2	2	2	2	1	NA	NA	NA	NA	14/16
Goldman 2006[22]	2	2	1	2	2	2	2	0	2	2	2	2	21/24
Goldman 2011[23]	2	2	1	2	2	2	2	0	2	2	2	1	20/24
Gregor 2009[24]	2	2	2	2	2	2	1	2	NA	NA	NA	NA	15/16
Horne 1995[25]	2	2	2	2	2	2	1	0	NA	NA	NA	NA	13/16

Table 1: individual MINORS score (*continued*)

	Clearly stated aim	Inclusion of consecutive patients	Prospective data collection	Endpoints appropriate to study aim	Unbiased assessment of study endpoint	Follow-up period appropriate to study aim	<5% lost to follow-up	Prospective calculation of study size	Adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	Total
Hacking 2012[26]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ismail 2013[27]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Jacobstein 2005[28]	2	2	1	2	2	2	1	2	2	2	2	2	22/24
Jain 2010[29]	2	2	1	2	2	2	2	0	2	2	2	2	21/24
Klein-Kremer 2011[30]	2	2	1	2	2	2	1	0	2	2	2	2	20/24
Lal et al. 1999[31]	1	2	2	2	2	2	2	0	NA	NA	NA	NA	13/16
Lawrence 2009[32]	2	2	1	2	2	2	2	0	2	1	2	2	20/24
LeDuc 2006[33]	2	1	1	2	2	2	1	0	NA	NA	NA	NA	11/16
Liberman 2012[34]	2	1	1	2	2	2	1	2	NA	NA	NA	NA	13/16
Logue 2013[35]	2	1	1	2	2	2	1	0	NA	NA	NA	NA	11/16
Maguire 2011[36]	2	2	2	2	1	0	1	0	NA	NA	NA	NA	10/16
Mansbach 2008[37]	2	2	2	2	2	2	1	0	2	2	2	2	21/24
Michelson 2012[38]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	11/16
Mintegui 2000[39]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Mistry 2007[40]	2	1	2	2	2	2	1	2	NA	NA	NA	NA	14/16
Mistry 2009[41]	2	2	2	2	2	2	1	2	NA	NA	NA	NA	15/16
Moineau 2004[42]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Roback 1997[43]	2	2	1	2	2	2	2	1	2	2	2	2	22/24
O'Loughlin 2012[44]	2	1	1	2	1	2	1	0	NA	NA	NA	NA	10/16
O'Neill 2001[45]	2	0	1	1	1	1	0	0	NA	NA	NA	NA	6/16
Patel 2009[46]	2	1	2	2	2	2	1	2	1	2	2	2	21/24
Porter 2000[47]	2	1	2	2	2	0	1	0	NA	NA	NA	NA	10/16
Roland 2011[48]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Roggen 2012[49]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Samuels-Kalow 2013[50]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sartain 2002[51]	2	1	2	2	2	1	2	2	2	2	2	2	22/24
Scarfone 1996[52]	2	1	2	2	2	2	2	0	NA	NA	NA	NA	13/16
Seow 2007[53]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	13/16
Simmons 2012[54]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Small 2005[55]	2	2	2	2	2	2	2	2	2	2	2	2	24/24
Yang 2012[56]	2	2	2	2	2	2	1	0	2	1	2	2	20/24
Zimmerman 1996[57]	2	2	1	2	2	2	2	0	NA	NA	NA	NA	13/16

Score 1: Revisit primary outcome		**Score 2:** Number of events (revisits)		**Score 3:** MINORS score	
Yes	A	>500	A	16 or 24	A
No	B	100-500	B	>12 - <16 or >20 - <24	B
		<100	C	≤12 or ≤20	C

Risk of bias (low/ high)

Low risk of bias:

1. Studies fulfilling all MINORS criteria (A)
2. Full article with a minimum of 2 A's in score 1 and 2
3. Minimum of B in score 1, 2 and MINORS

High risk of bias:

1. all other studies

Table 2.2: Risk of bias assessment

Author Year Country	**Revisits primary outcome**	**Score 1**	**N outcome (revisits)**	**Score 2**	**MINORS quality score***	**Score 3**	**Risk of bias (low/ high)**
Alessandrini 2004 USA	Yes	A	1,893	A	13/16	B	Low risk of bias
Ali 2012 USA	Yes	A	124	B	12/16	C	High risk of bias
Angoulvant 2012 France	Yes	A	206	B	11/16	C	High risk of bias
Augustine 2013 USA	Yes	A	13	B	NA	NA	High risk of bias
Baker 2009 USA	Yes	A	105	B	22/24	B	Low risk of bias
Berry 2013 USA	Yes	A	36,734	A	11/16	C	Low risk of bias
Black 2010 UK	Yes	A	91	C	NA	NA	High risk of bias
Bloch 2013 USA	No	B	216	B	21/24	B	Low risk of bias

Table 2.2: Risk of bias assessment (*continued*)

Author Year Country	Revisits primary outcome	Score 1	N outcome (revisits)	Score 2	MINORS quality score*	Score 3	Risk of bias (low/ high)
Browne 2001 Australia	Yes	A	240	B	20/24	C	High risk of bias
Callery 2010 UK	Yes	A	2,433	A	13/16	B	Low risk of bias
Chang 2008 Taiwan	No	B	188	B	18/24	B	Low risk of bias
Considine 2007 Australia	No	B	15	C	21/24	B	High risk of bias
DePiero 2002 USA	Yes	A	261	B	13/16	B	Low risk of bias
Dunlop 2005 Australia	No	B	35	C	11/16	C	High risk of bias
Easter 2012 USA	Yes	A	1,091	A	12/16	C	Low risk of bias
Fagbuyi 2011 USA	No	B	620	A	21/24	C	High risk of bias
Florin 2013 USA	Yes	A	6,439	A	13/16	B	Low risk of bias
Freedman 2013 Canada	Yes	A	543	A	13/16	B	Low risk of bias
Gallagher 2013 USA	Yes	A	1,499	A	13/16	B	Low risk of bias
Gaucher 2012 Canada	No	B	2,534	A	14/16	B	Low risk of bias
Goldman 2006 Canada	Yes	A	1,990	A	21/24	B	Low risk of bias
Goldman 2011 Canada	Yes	A	353	B	20/24	C	High risk of bias
Hacking 2012 UK	Yes	A	130	B	NA	NA	High risk of bias

Table 2.2: Risk of bias assessment (*continued*)

Author Year Country	Revisits primary outcome	Score 1	N outcome (revisits)	Score 2	MINORS quality score*	Score 3	Risk of bias (low/ high)
Gregor 2009 USA	No	B	49	C	15/16	B	High risk of bias
Horne 1995 USA	No	B	171	B	14/16	B	Low risk of bias
Ismail 2013 USA	No	B	63	C	NA	NA	High risk of bias
Jacobstein 2005 USA	Yes	A	165	B	22/24	B	Low risk of bias
Jain 2010 USA	No	B	17,335	A	21/24	B	Low risk of bias
Klein-Kremer 2011 Canada	Yes	A	92	C	20/24	C	High risk of bias
Lal et al. 1999 UK	Yes	A	65	C	13/16	B	High risk of bias
Lawrence 2009 USA	Yes	A	979	A	20/24	C	High risk of bias
LeDuc 2006 USA	Yes	A	237	B	11/16	C	High risk of bias
Liberman 2012 USA	No	B	189	B	13/16	B	Low risk of bias
Logue 2013 Canada	Yes	A	261	B	11/16	C	High risk of bias
Maguire 2011 UK	No	B	29	C	10/16	C	High risk of bias
Mansbach 2008 USA	No	B	837	A	22/24	B	Low risk of bias
Michelson 2012 USA	No	B	7,281	A	12/16	C	High risk of bias
Mintegui 2000 Spain	Yes	A	495	B	NA	NA	High risk of bias

Table 2.2: Risk of bias assessment (*continued*)

Author Year Country	Revisits primary outcome	Score 1	N outcome (revisits)	Score 2	MINORS quality score*	Score 3	Risk of bias (low/ high)
Mistry 2007 USA	Yes	A	76	C	14/16	B	High risk of bias
Mistry 2009 USA	No	B	18	C	15/16	B	High risk of bias
Moineau 2004 Canada	Yes	A	108	B	NA	NA	High risk of bias
Roback 1997 USA	Yes	A	57	C	22/24	B	High risk of bias
O'Loughlin 2012 UK	Yes	A	532	A	10/16	C	High risk of bias
O'Neill 2001 USA	No	B	NS	C	6/16	C	High risk of bias
Patel 2009 USA	No	B	NA	C	21/24	B	High risk of bias
Porter 2000 USA	No	B	NA	C	10/16	C	High risk of bias
Roggen 2012 Belgium	Yes	A	1,864	A	NA	NA	High risk of bias
Roland 2011 UK	No	B	NR	NA	NA	NA	High risk of bias
Samuels-Kalow 2013 USA	Yes	A	14	C	NA	NA	High risk of bias
Sartain 2002 UK	No	B	31	C	22/24	B	High risk of bias
Scarfone 1996 USA	No	B	91	C	13/16	B	High risk of bias
Seow 2007 Taiwan	No	B	115	B	13/16	B	Low risk of bias
Simmons 2012 UK	Yes	A	51	C	NA	NA	High risk of bias

Table 2.2: Risk of bias assessment (*continued*)

Author Year Country	Revisits primary outcome	Score 1	N outcome (revisits)	Score 2	MINORS quality score*	Score 3	Risk of bias (low/ high)
Small 2005 UK	No	B	56	C	24/24	A	Low risk of bias
Yang 2012 Taiwan	Yes	A	9	C	20/24	C	High risk of bias
Zimmerman 1996 USA	Yes	A	242	B	13/16	B	Low risk of bias

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LEGEND SUPPLEMENTAL INFORMATION 3:

[*] Minors: 1. clearly stated aim; 2. inclusion of consecutive patients; 3. prospective data collection; 4. end-points appropriate to study aim; 5. unbiased assessment of study endpoint; 7. <5% lost to follow-up; 8. prospective calculation of study size; *Additional criteria in the case of comparative study:* 9. adequate control group; 10. contemporary groups; 11. baseline equivalence; 12. adequate statistical analyses

Supplemental information 3a: Detailed study information about safety netting after ED discharge

	Univariable		Multivariable		Best evidence synthesis	
	Low risk of bias	High risk of bias	Low risk of bias	High risk of bias	Association	Level of evidence
Approach of safety netting management						
Follow-up program		yes (2) Augustine 2013 (all) O'Neill 2001 (all)			Yes	Moderate
Clinical pathways at initial ED visit		yes (1) Browne 2001 (spec)			Yes	Limited
Non-compliance to scheduled revisit		yes (1) Scarfone 1996 (all)			Yes	Limited
Explicit and consistent safety netting advice[^]		yes (4) Augustine 2013 (all) Maguire 2011 (fever) Moineau 2004 (spec) Porter 1999 (all) no (3) Fagbuyi. 2011 (spec) Liberman 2012 (spec) Roland 2011 (fever)			unclear	Conflicting
Educational intervention[*]		yes (3) Considine 2007 (fever) Ismail 2013 (fever) O'Neill 2001 (fever) no (3) Chande 1996 (all) Fagbuyi. 2011 (spec) Lawrence 2009 (all)	yes (1) Bloch 2013 (all) no (1) Baker 2009 (fever)	yes (1) Patel 2009 (spec)	unclear	Conflicting
Telephone follow-up	no (1) Horne 1995 (all)	yes (1) Yang 2011 (all)			unclear	Conflicting

Supplemental information 3b: Detailed study information about determinants of revisits

	Univariable		Multivariable		Best evidence synthesis	
	Low risk of bias	High risk of bias	Low risk of bias	High risk of bias	Association	Level of evidence
DETERMINANTS OF REVISITS						
CHILD CHARACTERISTICS						
Younger children	yes (5) Alessandrini 2004 (all) Easter 2012 (all) Goldman 2006 (all) Liberman 2012 (spec) Zimmerman 1996 (all)	yes (4) Black 2010 (all) Logue 2013 (all) Maguire 2011 (fever) O'Loughlin 2012 (all) no (3) Angoulvant 2013 (all) Goldman 2011 (all) Roback 1997 (spec)	yes (4) Berry 2013 (all) Gallagher 2013 (all) Freedman (spec) Mansbach 2008 (spec) no (1) Jacobstein 2002 (fever)	yes (2) Gregor 2009 (spec) LeDuc2006 (all)	**Yes**	**Strong**
Medical history[j]		yes (1) Maguire 2011 (fever) no (1) Roback 1997 (spec)	yes (3) Berry 2013 (all) Mansbach 2008 (spec) Jacobstein 2002 (fever)	yes (1) Gregor 2009 (spec)	**Yes**	**Strong**
Gender	no (2) Liberman 2012 (spec) Zimmerman 1996 (all)	no (3) Angoulvant 2013 (all) Goldman 2011 (all) Roback 1997 (spec)	no (1) Mansbach 2008 (spec)	no (1) LeDuc2006 (all)	**No**	**Strong**
Ethnicity[=]	yes (1) Zimmerman 1996 (all)		yes (1) Berry 2013 (all) no (2) Jacobstein 2002 (fever) Mansbach 2008 (spec)	yes (1) LeDuc2006 (all)	unclear	Conflicting

Supplemental information 3b: Detailed study information about determinants of revisits (*continued*)

	Univariable		Multivariable		Best evidence synthesis	
Change on pedsQL scores				yes (1) Mistry 2009 (fever)	Yes	Limited
SOCIAL/ DEMOGRAPHIC CHARACTERISTICS						
Emergency crowding[+]	no (1) Alessandrini 2004 (all) yes (2) Callery 2010 (all) Easter 2012 (all)		yes (1) Goldman 2006 (all) Gallagher 2013 (all) no (2) Jacobstein 2002 (fever)	yes (1) Michelson 2012 (all) no (1) LeDuc2006 (all)	unclear	Conflicting
Low SES[##]	no (2) Callery 2010 (all) Liberman 2012 (spec) yes (1) Zimmerman 1996 (all)		no (1) Gallagher 2013 (all) yes (2) Berry 2013 (all) Jacobstein 2002 (fever)	no (2) Gregor 2009 (spec) LeDuc 2006 (all)	unclear	Conflicting
Characteristics care givers[#]	no (1) Liberman 2012 (spec)	yes (5) Augustine 2013 (all) Logue 2013 (all) Lal 1999 (all) Maguire 2011 (fever) Simmons 2012 (all) no (4) Angoulvant 2013 (all) Goldman 2011 (all) Mistry 2007 (fever) Roback 1997 (spec)	yes (1) Gallagher 2013 (all) no (1) Jacobstein 2002 (fever)	yes (2) Gregor 2009 (spec) Samuels-Kalow 2013 (fever)	unclear	Conflicting

Supplemental information 3b: Detailed study information about determinants of revisits (*continued*)

	Univariable		Multivariable		Best evidence synthesis	
DISEASE CHARACTERISTICS						
Symptoms of infectious diseases*	yes (4) Alessandrini 2004 (all) Callery 2010 (all) Easter 2012 (all) Liberman 2012 (spec)	yes (8) Angoulvant 2013 (all) Augustine 2013 (all) Black 2010 (all) Hacking 2012 (all) Klein-Kremer 2011 (fever) Logue 2013 (all) Mintegui 2000 (all) Simmons 2012 (all)	yes (2) Berry 2013 (all) Mansbach 2008 (spec)	no (1) LeDuc2006 (all)	**Yes**	**Strong**
Respiratory symptoms**	yes (3) Alessandrini 2004 (all) Callery 2010 (all) Zimmerman 1996 (all)	yes (4) Hacking (2012) Klein-Kremer 2011 Lal 1999 (all) Mintegui 2000 (all) no (2) Angoulvant 2013 (all) Roback 1997 (spec)	yes (2) Berry 2013 (all) Mansbach 2008 (spec)		**Yes**	**Strong**
Seizure and other nervous system	yes (1) Easter 2012 (all)		yes (1) Berry 2013 (all)	yes (1) LeDuc2006 (all)	**Yes**	**Strong**

Supplemental information 3b: Detailed study information about determinants of revisits (*continued*)

	Univariable		Multivariable		Best evidence synthesis	
Progression/ persistence of symptoms[^]	yes (3) Ali 2012 (all) DePiero 2002 (all) Easter 2012 (all)	yes (9) Augustine 2013 (all) Dunlop 2005 (fever) Klein-Kremer.2011 (fever) Lal 1999 (all) Logue 2013 (all) Maguire 2011 (fever) Mistry 2007 (fever) Moineau 2004 (spec) Roggen 2012 (all) no (3) Hacking 2012 (all) Roback 1997 (spec) Goldman 2011 (all)	yes (1) Freedman (spec) no (1) Mansbach 2008 (spec)		**Yes**	**Strong**
Trauma/ surgery	yes (1) Alessandrini 2004 (all) no (1) Zimmerman 1996 (all)	no (1) Klein-Kremer 2011 (fever)	yes (1) Berry 2013 (all)		unclear	Conflicting
Acute triage category/ Illness acuity[$]	yes (1) Alessandrini 2004 (all) no (1) Liberman 2012 (spec)	yes (2) Goldman 2011 (all) Logue 2013 (all) no (1) Moineau 2004 (spec)	yes (4) Freedman 2013 (spec) Gallagher 2013 (all) Goldman 2006 (all) Jacobstein 2002 (fever)	no (1) Gregor 2009 (spec)	unclear	Conflicting
Change in working diagnosis		yes (1) Mintegui 2000 (all) no (1) Goldman 2011 (all)			unclear	Conflicting

Supplemental information 3b: Detailed study information about determinants of revisits (*continued*)

	Univariable		Multivariable		Best evidence synthesis	
Pain/ soreness		yes (1) Klein-Kremer 2011 (fever) no (1) Angoulvant 2013 (all)			unclear	Conflicting
PHYSICIAN CHARACTERISTICS						
Characteristics physician~~	yes (1) Seow 2007 (fever)	no (2) Chang 2008 (all) Roback 1997 (spec)	no (2) Gaucher 2012 (all) Jacobstein 2002 (fever)		**No**	**Strong**
PROCESS CHARACTERISTICS						
Diagnostic tests/ therapeutic intervention^^		no (3) Angoulvant 2013 (all) Klein-Kremer 2011 (fever) Mistry 2007 (fever) yes (1) Angoulvant 2013 (all)	no (1) Jain 2010 (all)	no (1) Florin 2013 (spec)	**No**	**Strong**
Hospitalisation	no (1) Small 2005 (spec)				No	Moderate
Hospital at home care		no (1) Sartain 2002 (all)			No	Limited

SUPPLEMENTAL INFORMATION 3C

- explaining determinant-differences of all included studies-

All: all disease studied;
Fever: febrile patients studied;
Spec: disease specific studies, e.g. respiratory tract infections, gastroenteritis, bronchiolitis, influenza-like illness

^ *Explicit and consistent safety netting advice, including:*
- Generic discharge instructions (Augustine 2013)
- Pre-printed discharge prescription and instructions (Fagbuyi 2011)
- Discharge information sheets (Moineau 2004)

* *Educational intervention, including:*
- Classroom-style parent discharge education (Fagbuyi 2011)
- Evidence-based education of emergency nurses on parental advice regarding fever management (Considine 2007)
- Video discharge instructions (Bloch 2013; Ismail 2013)
- Computer-generated diagnosis-specific discharge instructions (Lawrence 2009)
- Verbal reinforcement of written discharge instructions by a bilingual discharge facilitator (Patel 2009)

= *Ethnicity, including:*
- Hispanic vs white (LeDuc 2006; Zimmerman 1996)
- Black vs other (Jacobstein 2002)
- Non-white vs white (Mansbach 2008)
- Black and Latino vs white (Berry 2013)

} *Medical history, including:*
- History of intubation and/or eczema (Mansbach 2008)
- No ED visit during past week (Mansbach 2008)
- History of wheezing and family history of asthma (Roback 1997)
- Chronic condition indicator (CCI) group and CCI count (Berry 2013)
- Prior ED use (Gregor 2009)
- Chronic disease (Jacobstein 2002)
- Anemia or neutropenia (Berry 2013)
- Sickle cell anemia crisis (Berry 2013)

Characteristics care givers, including:

- Caregivers age; education status; employment status (Jacobstein 2002)
- Living near hospital/ primary care physician (Jacobstein 2002; Liberman et al. 2012)
- Family demographics: age primary caregiver; marital status; presence and age of other children; presence of other caregivers (Mistry 2007)
- Language spoken at home (Gallagher 2013; Goldman 2011; Samuels 2013)
- Parental perception of illness (Maguire 2011; Lal 1999)
- Single caregivers (Gregor et al. 2009)
- Consultation with sibling (Angoulvant 2013)
- Dissatisfaction with initial visit (Augustine 2013)
- Anxious/ stressed carer (Logue 2013; Simmons 2012)
- Demographical data (Roback 1997)

[##] *Low social economic status (SES), including:*
- Living in low SES area (Callery et al. 2010)
- Insurance type (Jacobstein 2002; Liberman 2012)
- Public insurance (Zimmerman 1996)
- Insurance type (Berry 2013; Gregor 2009; LeDuc 2006)
- Carers' highest level of education (Gallagher 2013)

[+] *Emergency crowding, including:*
- Timing of revisit (Alessandrini 2004)
- Same day discharges (Callery 2010)
- Weekend/ weekday (Jacobstein 2002)
- Arriving 3pm-11pm via private transportation (Easter.2012)
- Arrival in evening/ weekend hours (Goldman 2006; leDuc 2006)
- Arrival during overnight shift (Gallagher 2013)

**Symptoms of infectious diseases, including:*
- Feverish illnesses (Angoulvant 2013; Augustine 2013; Callery 2010; Easter 2012; Mintegui 2000)
- Initial diagnosis of URTI (Black 2010; Easter 2012; Hacking 2012)
- Gastroenteritis//diarrhoea/ dehydration/ vomiting (Berry 2013; Black 2010; Callery 2010; Easter 2012; Hacking 2012; Klein-Kremer 2011; LeDuc 2006; Simmons 2012)
- No adequate oral intake (Mansbach 2008)
- Temperature in triage (Klein-Kremer2011)

[**] *Respiratory symptoms, including:*
- Respiratory related illnesses (Alessandrini 2004)
- Breathing difficulty (Callery 2010)

- Cough (Klein-Kremer 2011)
- Respiratory symptoms (Angoulvant 2013; Mintegui 2000)
- Respiratory diagnoses (Berry 2013; Hacking 2012; Zimmerman 1996)
- Specific respiratory symptoms, including:
 - Age-specific respiratory rates (Mansbach 2008; Roback 1997)
 - Severe retractions (Mansbach 2008; Roback 1997)
 - Initial oxygen saturation <94% (Mansbach 2008; Roback 1997)
 - More albuterol/epinephrine in first hour (Mansbach 2008; Roback 1997)
 - No adequate oral intake (Mansbach 2008)

[=] *Trauma/ surgery*
- Limping (Klein-Kremer 2011)
- Trauma (Allessandrini 2004)
- Minor trauma (Zimmerman 1996)
- Ventricular shunt procedures (Berry 2013)

[$] *Illness acuity, including:*
- Mild disease severity at ED index visit (Gregor 2009)
- Higher acuity in 2nd visit (Goldman 2011)

[^] *Progression/ persistence of symptoms, including:*
- Prolonged fever (Klein-Kremer 2011)
- Impairment in child activities (Mistry 2007)
- Parental perception of illness (Lal 1999; Maguire 2011)
- Time elapsing from 1st visit – revisit (Goldman 2011)

[~~] *Characteristics physician, including:*
- Treatment by physician versus intern (Jacobstein 2005)
- Physicians' year of experience/ training level (Gaucher 2012; Roback 1997)
- Attending physician versus resident (Chang 2008)
- Pediatrician vs Emergency physician (Seow 2007)

[^^] *Diagnostic tests/ therapeutic intervention, including:*
- Obtaining blood cultures/ tests (Angoulvant 2013; Klein-Kremer 2011)
- Radiological assessment (Angoulvant 2013)

Chapter 10

Characteristics of revisits of children at risk for serious infections in paediatric emergency care.

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Eur J Pediatr, Feb 3, 2018

ABSTRACT

In this study, we aimed to identify characteristics of (unscheduled) revisits and its optimal time frame after Emergency Department (ED) discharge.

Children with fever, dyspnea or vomiting/diarrhea(1 month-16 years) who attended the ED of Erasmus MC-Sophia, Rotterdam(2010-2013), the Netherlands were prospectively included. Three days after ED-discharge we applied standardised telephonic questionnaires on disease course and revisits. Multivariable logistic regression analysis was used to identify independent characteristics of revisits.

Young age, parental concern and alarming signs and symptoms (chest wall retractions, ill appearance, clinical signs of dehydration and tachypnea) were associated with revisits (n=527) in children at risk for serious infections discharged from the ED (n=1765). Children revisited the ED within a median of 2 days (IQR 1.0-3.0), but this was proven to be shorter in children with vomiting/diarrhea (1.0 day (IQR 1.0-2.0)) compared to children with fever or dyspnea (2.0 (IQR 1.0-3.0)).

Conclusion

Young age, parental concern and alarming signs and symptoms (chest wall retractions, ill appearance, clinical signs of dehydration and tachypnea) were associated with emergency health care revisits in children with fever, dyspnea and vomiting/diarrhea. These characteristics could help to define targeted review of children during post discharge period. We observed a disease specific and differential timing of control revisits after ED discharge.

INTRODUCTION

Fever, dyspnea and vomiting/diarrhea are major causes of emergency care attendance in childhood. Serious infections (SI) could be the underlying cause of these symptoms. Morbidity and mortality after ED visit due to serious infections or a complicated disease course of a self-limiting viral illness should not be underestimated. Infections account for 20% of childhood deaths in England, Wales, and Northern Ireland, with the greatest number in children aged 1–4 years. [1; 2]In the Netherlands, between 1969 en 2006, mortality due to infectious diseases compared to total childhood mortality was around 3.0 %. [3]

Serious infections are mostly defined as sepsis (including bacteraemia), meningitis, pneumonia, osteomyelitis, cellulitis, gastroenteritis with severe dehydration, complicated urinary tract infection (positive urine culture and systemic effects such as fever), and viral respiratory tract infections complicated by hypoxia (eg. bronchiolitis). [4] At the ED, serious infections can be hard to recognize, as they can present similar to a self-limiting (viral) disease during early presentation, eventually leading to a diagnostic or treatment delay.

Dealing with this uncertainty on diagnosis or disease course after ED discharge, clinicians usually schedule revisits in a substantial number of cases. In addition they provide parents with instructions on expected disease course, alarming signs and symptoms and when to revisit, a well- known concept called 'safety netting'. [5; 6]

A recent systematic review concluded that studies concerning effects of safety netting interventions were mostly conflicting or with limited evidence.[7] They described strong associated characteristics of revisits as young children, infectious/respiratory symptoms and progression of symptoms. However, evidence on follow-up management and its time frame as a part of the whole process of safety netting in children at risk for serious infections is lacking.[8]

To improve the process of safety netting, we aimed to identify characteristics of (unscheduled) revisits and the timing of these revisits in a prospectively collected cohort of children with fever, vomiting/ diarrhea or dyspnea, discharged from the ED.

METHODS

Study design and setting

We conducted a prospective follow-up study at the ED of the Erasmus MC-Sophia Children's Hospital in Rotterdam. This large inner-city university hospital is visited annually by nearly 7000 children with a mixed ethnic population of which 35% have chronic co-morbidity.

Participants

We prospectively enrolled all consecutive children (≥1 month - <16 years) attending the ED with fever, vomiting/diarrhea or dyspnea from March 2010 until October 2013. Febrile children were defined as eligible if fever had been noted at home in the 24 hours prior to presentation, when body temperature measured at the ED was ≥38.5°C or fever was used as a positive discriminator of the Manchester Triage System (MTS). [9]Children with vomiting/diarrhea needed to be suspected of a recent infectious cause. To be included, the illness episode had to be preceded by a minimum symptom free period of two weeks and the illness episode needed to be related to an infectious disease. Children were assigned to dyspnea when respiratory complaints, with or without bronchoconstriction, were the main reason of visiting the ED. Children with dyspnea who also suffered from fever where assigned to dyspnea if these symptoms took precedence over fever-related complaints. Given the aim of the study, i.e. improving discharge advice, we excluded children who were admitted to the hospital ward after initial ED visit. Next, as children with a known medical history or medical diagnosis get specific safety netting advice for their chronic condition in their outpatient follow-up (by paediatrician and specialist nurse), they are another population compared to the children with common acute illnesses at the ED. As children with a known medical history or medical diagnosis may be managed differently at ED or by (experienced) parents, we excluded children with complex needs as well as children with predefined asthma. [10]

Data collection

All children who attended the ED were routinely triaged with the Manchester triage system (MTS). This digital recorded triage system is used to prioritize patients according to acuity. [11] In the analysis, MTS categories were reformatted into three categories: 1) emergent/very urgent, 2) urgent, and 3) non-urgent/ standard to guarantee sufficient numbers per category. We collected patient characteristics from a structured electronic patient record system (gender, age, reason of ED visit, visit date, triage information), referral profile, duration of the complaints, clinical signs and symptoms, observations and measures from physical examination (e.g., vital signs, temperature, breathing difficulty, clinical appearance. [12] [10] [13])

During the process of discharge, patients received information on alarming signs and symptoms, expected disease course and on when and how to return. Part of the children received a scheduled revisit, by judgement icat of the attending physician, based on either the clinical signs and symptoms or expected complications, or on parental concern. In addition to these scheduled revisit (i.e. initiated/appointed by the physician at discharge), patients could revisit unscheduled (i.e. patient- initiated). These data were collected using a standardized telephonic questionnaire on the disease course which parents were asked to answer three days after ED discharge., The questionnaire included

specifically data on duration or reoccurrence of symptoms as well as on complications, and on revisits to the hospital ED, to primary care, or to other health care settings. When the child was not yet fully recovered we continued our follow-up by telephone until complete remission of their symptoms.

Outcome measures and definitions

Our primary outcome measures were 1) revisits, defined as all revisits occurring for the same health care problem at either the GP (primary care) and the emergency department (secondary care) after the first ED visit and 2) the time until this revisit, measured as the time gap between discharge and revisit. Secondary outcome measures included unscheduled revisits (defined as an unplanned control visits after the initial visit) and hospitalisation following a revisit.

To evaluate parental concern, parents were asked if they considered their child's illness at initial ED revisit to be different from earlier episodes. This is in accordance with previous studies in primary care, showing that parental concern is an important determinant of serious infections [4; 14].

Ethics

Ethical approval was obtained from the institutional review board (IRB) of the Erasmus MC (MEC- 2005-314). Informed consent was required and obtained from all parents.

Statistical analysis

Variable selection

Variable selection for studying potential characteristics of revisits were based on previously published decision models or risk scores[15-17] and a recent systematic review on characteristics of paediatric health care revisits (**table 1**).[8]

Characteristics of revisits

Since patients with fever, vomiting/diarrhea or dyspnea may differ in their disease course and time frame , we performed analysis separately for each of these patient groups. Time until ED revisit was evaluated by Kaplan-Meier survival analysis. Previous research in our setting showed that 12% of all discharged children underwent revisits of which 4% included interventions.[18] To analyse 10-15 characteristics of revisits it was decided that we should have at least 10 times as many events (100-150 revisits).[18; 19] With these distributions we estimated to include at least around 830 (100/0.12) to 1250 (150/0.12) children.

Table 1: variable selection according to decision model, risk scores and systematic review

	Feverkidstool[1]	Friedman dehydration score[2]	Indicators of dyspnea[3]	Systematic review[4]
Child characteristics				
Age	X			X
Gender	X			
Ill appearance	X	X		
Characteristics general				
Tachycardia	X			
Prolonged cap. refill time	X			
Relevant medical history				X
Infectious/ respiratory symptoms				X
Seizures				X
Progression/persistence of symptoms				X
CRP bedside (ln)	X			
Characteristics fever				
Duration of fever	X			
Temperature (°C)	X			
Characteristics dehydration				
Eyes		X		
Dry mucosa		X		
Tears		X		
Vomiting				
Characteristics dyspnoea				
Dyspnea			X	
Chestwall retractions	X		X	
Decreased oxygen saturation	X		X	
Tachypnea	X		X	
Auscultation			X	

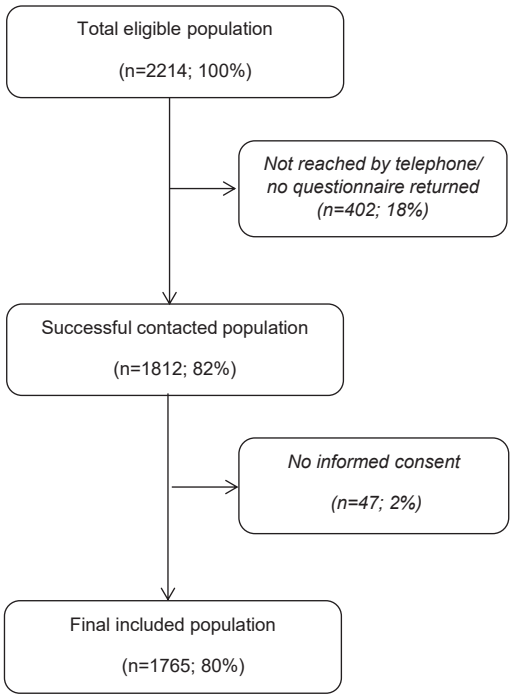
Missing values

To allow optimal use of available data in multivariate models, missing data were imputed 10 times using a multiple imputation process with the mice algorithm in R software (version 3.0) under the assumption to be missing at random.[20] The imputation model included all variables which were considered in the multivariable logistic regression analysis, the outcome variable (revisits), and several relevant variables describing case mix of the patients (e.g. gender and MTS urgency). (Supplementary files) All analyses, except for multiple imputation, were performed with SPSS software (version 20.0, SPSS Inc, Chicago).

RESULTS

Successful follow-up by telephone was achieved for 1765 children, encompassing 80% of the total eligible population (n=2214) (**figure 1**). Overall patients' median age was 22 months (IQR 11-48), with 57% boys (n=1000). The revisit rate was 30% (n=527) and 3%

Figure 1 Patient flow chart



(n=54) of the children were hospitalised after revisiting the ED (**table 2**). Most children were triaged as urgent patients (54%; n=944) and 51% were referred by physicians.

Febrile children constituted 64% (n=1136) of included children, with 346 (n=31%) revisits. Twenty-one percent (n=372) children suffered from vomiting/diarrhea with 108 (29%) revisits. Fifteen percent (n=257) of all children had dyspnea, with 73 (n=28%) revisits.

Table 2: demographics total population

	PRESENTING PROBLEM, n (%)			
	TOTAL	FEVER	VOMITING/ DIARRHEA	DYSPNEA
	n=1765 (100)	n=1136 (64.4)	n=372 (21.1)	n=257 (14.5)
Sex, male[*]	1000 (56.7)[^]	635 (55.9)	194 (52.2)	171 (66.5)
Age (months)[a]	22.0 (11.0-48.0)[^]	23.0 (12.0-51.0)	18.0 (9.0-41.0)	21.0 (8.0-41.0)
All revisits[*]	527 (29.9)	346 (30.5)	108 (29.0)	73 (28.4)
Unscheduled revisit[*]	352 (19.9)[^]	240 (21.1)	57 (15.3)	55 (21.4)
Secondary hospitalisation	54 (3.1)	28 (2.5)	17 (4.6)	9 (3.5)
Parental concern	1410 (79.9)[^]	952 (83.8)	285 (76.6)	173 (67.3)
MTS urgency initial ED visit				
Emergent/Very urgent	331 (18.7)[^]	203 (17.9)	34 (9.1)	94 (36.6)
Urgent	944 (53.5)[^]	700 (61.6)	161(43.3)	83 (32.3)
Standard/Non-urgent	490 (27.8)[^]	233 (20.5)	177 (47.6)	80 (31.1)
Type of refer initial ED visit				
Self-referral	865 (49.0)[^]	547 (48.2)	216 (58.1)	102 (39.7)
Physician[$]	900 (51.0)[^]	589 (51.8)	156 (41.9)	155 (60.3)

[*] Absolute number (percentage)
[a] Median (IQR)
[$] Including primary, secondary and ambulance care
[^] P-value <0.05

Characteristics of revisits overall

Out of 527 revisits, 352 (67%) revisits were unscheduled (**table 3**). The number of unscheduled revisits was the lowest for children with vomiting/diarrhea (n=57, 15.3%) and the highest for children with dyspnea (n=55; 21.4%) (**table 3**).

Children revisited the ED after a median of 2 days (IQR 1.0-3.0). Children with vomiting/diarrhea revisited the ED significantly at a shorter interval (1.0 day (IQR 1.0-2.0)) than children with fever or dyspnea (2.0 (IQR 1.0-3.0)) (log rank p<0.0001).

Table 3: characteristics of revisits

	PRESENTING PROBLEM, n (%)			
	TOTAL	Fever	Vomiting/ diarrhea	Dyspnea
	n= 527/1765 (29.9)	n=346/1136 (30.5)	n=108/372 (29.0)	n=73/257 (28.4)
Revisits with intervention [*]	293 (55.6)[^]	199 (57.5)	47 (43.5)	47 (64.4)
Unscheduled[*]	352 (66.8)[^]	240 (69.4)	57 (52.8)	55 (75.3)
Time until revisit (days)[a]	2.0 (1.0-3.0)	2.0 (1.0-3.0)	1.0 (1.0-2.0)	2.0 (1.0-4.0)[**]
Time until unscheduled revisit	3.0 (2.8-3.2)	2.0 (1.7-2.3)	2.0 (1.4-2.6)	3.0 (2.4-3.6)
Setting of revisit				
Primary care	249 (47.2)	180 (52.0)	35 (32.4)	34 (46.6)
Emergency care	278 (52.8)	166 (48.0)	73 (67.6)	39 (53.4)

[*] Absolute number (percentage)
[a] Median (IQR)
[**] Log-rank<0.000
[^] P-value <0.05:
- More revisits with intervention in febrile children versus children with vomiting/diarrhea (Chi-square)
- More unscheduled revisits in febrile children versus children with vomiting/diarrhea (Chi-square)
- More prescribed antibiotics in febrile children versus children with vomiting/diarrhea and children with dyspnea (Chi-square)
- More prescribed airway medicine in children with dyspnea versus febrile children and children with vomiting/diarrhea (Chi-square)
- More prescribed gastro-intestinal medicine in children with vomiting/diarrhea versus febrile children and children with dyspnea (Chi-square)

Characteristics of revisits of febrile children

Age, parental concern and chest wall retractions were associated with revisits in febrile children (multivariable ORs between 1.30-1.98) (p-value <0.1) (**table 4**). Young age and parental concern, in particular, were associated with unscheduled revisits (resp. OR (CI 95%) 1.42 (1.04-1.95 and OR (CI 95%) 1.81 (1.13-2.90) **(table 4)**.

Characteristics of revisits of children with vomiting/diarrhea

The characteristics age<1year, ill appearance, clinical signs of dehydration at initial assessment and tachypnea were associated with revisits (p-value <0.10) **(table 4)**. Age and tachypnea remained strongly independent associated with unscheduled revisits **(table 4)**.

Characteristics of revisits of children with dyspnea

In children with dyspnea, we could only identify the determinant ' age <3 years' to be significantly associated with revisits (p-value <0.10) **(table 4)**.

Table 4: determinants of revisits in children with fever, vomiting/diarrhea and dyspnea

Determinants	REVISITS *n=346*	UNSCHEDULED REVISITS *n=240*
Fever	*OR (95% CI)*	*OR (95% CI)*
Age <1y	1.30 (0.98-1.72)*	1.42 (1.04-1.95)**
Parental concern	1.71 (1.15-2.55)**	1.81 (1.13-2.90)**
Chestwall retractions	1.98 (1.02-3.82) **	1.68 (0.82-3.44)
vomiting/ diarrhea	*n=108*	*n=57*
Age <1y	1.87 (1.14-3.07)**	2.09 (1.15-3.80)**
Ill appearance	1.91 (1.03-3.53)**	1.29 (0.58-2.85)
Clinical signs of dehydration	2.26 (1.12-4.53)**	1.96 (0.85-4.54)
Tachypnea	5.08 (2.30-11.25)**	4.12 (1.59-10.69)**
any sign of dyspnea	*n=73*	*n=55*
Age <3y	0.58 (0.31-1.09)*	0.58 (0.28-1.17)

** significant predictors (p<0.10)*
*** significant predictors (p<0.05)*

DISCUSSION

Main findings

In a prospectively study on clinical symptoms and signs that are associated with health care revisits in children with fever, dyspnea and vomiting/diarrhea, we observed young age, parental concern and alarming signs and symptoms (chest wall retractions, ill appearance, clinical signs of dehydration and tachypnea) to be the most important. Children with vomiting/diarrhea revisited the ED at a shorter interval (median 1 day; IQR 1.0-2.0) compared with children with fever or dyspnea (median 2 days; IQR 1.0-4.0).

Clinical implications and comparison with other studies

In order to optimize the process of safety netting, we prospectively evaluated characteristics of revisits in children at risk for serious infections discharged from the ED, originating from the question on which children need revisits and in what time frame. Although we identified various characteristics, they do not select a definite population that will not (need to) revisit the ED.

In summary, there is a need for safety netting in all children after discharge from the ED, however, with special attention for a subgroup of children at risk with young age, parental concern and specific symptoms and signs. Our results support specific time frames for specific presenting conditions.

Strengths and limitations

The major strength of this prospective study is the large number of children with complete follow-up, as we included up to 80% of the eligible children successfully in our study. Second, our study did not only include revisits to our hospital ED, but also to other EDs in the area as well as revisits to primary care or other emergency care settings.

Last, we studied the role of parental concern in the emergency care setting. [4; 14] We found an association between parental concern and revisits only in the group of febrile children. In the majority of affirmative answers parental concern was caused by a longer duration or a more severe illness. It is important to remark this indicator of a probable complicated clinical course, as it emphasizes the meaningful role of parents in the assessment of their child's illness in secondary care settings in addition to the known role in primary care. [4]

This study has some limitations. In our study we chose revisits as our primary outcome measure and we separately analyzed unscheduled revisits. As former research showed the following risk factors for pediatric ED revisits: arrival in the evening, respiratory diagnosis and acute triage category[21], one might argue that our secondary outcome, i.e. unscheduled revisit and hospitalisation would be of more clinical relevance. However, unscheduled revisits can be influenced by the clinical setting and by the timeframe the scheduled revisit was originally planned in, and also would be related to parental background and concepts of disease and their uncertainty or comprehension ability to understand provided information.

There are several factors, influencing the attending physician's decision to schedule a follow-up appointment or to admit a patient, besides having to perform further diagnostic tests or treatment. We observed 293/527 (55.6%) visits with an intervention (defined as diagnostics, treatment or admission).(Table3). Admission occurred in 54 (10.2%) patients.

In all other revisits (234/ 527; 44,4%) patients did not receive any diagnostics or treatment, nor were they admitted to the hospital. However, to regard them just as a 'reassurance'-revisit for parents would be too simplistic, as other factors like alarming signs, gut feeling and experience of the attending physician can influence this decision. We can only speculate about the reasons as detailed information is missing and this topic was beyond the scope of our study.

Selection bias and recall bias are well-known problems of questionnaire studies.[22; 23] However our study reached a high response rate of 80%, in contrast to most response rates of telephonic or postal questionnaire studies of less than 60%.[24] Recall bias may especially have influenced the subjective determinant parental concern. However, as parents were called only three days after ED discharge this should be less of a problem in our study.

CONCLUSION

In this prospective cohort study on ED patients we observed young age, parental concern and alarming signs and symptoms (chest wall retractions, ill appearance, clinical signs of dehydration and tachypnea) being associated with emergency health care revisits in children with fever, dyspnea and vomiting/diarrhea. In addition to the general need for safety netting procedures in children at risk for serious infections, these characteristics could help to define targeted review of children during post discharge period. A control visit after ED discharge is disease-specific and the post- discharge interval seems to be shorter for children with vomiting/diarrhea than others in particular.

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Supplementary file 1: missing data per patient category

DETERMINANTS	FEVER n=1136 (100%)	VOMITING/DIARRHOEA n=372 (100%)	DYSPNOEA n=257 (100%)
Patient characteristics			
Age	0	0	0
Gender (male)	0	0	0
Disease characteristics			
Parental concern	18 (1.6)	34 (9.1)	8 (3.1)
Duration of fever/ illness	175 (15.4)	40 (10.8)	22 (8.6)
Ill appaerance	48 (4.2)	28 (7.5)	25 (9.7)
Temperature (°C)	7 (0.6)	6 (1.6)	19 (7.4)
Tachypnoea	140 (12.3)	79 (21.2)	19 (7.4)
Tachycardia	106 (9.3)	34 (9.1)	18 (7.0)
Decreased oxygen saturation	286 (25.2)	237 (63.7)	8 (3.1)
Prolonged cap. refill time (peripheral)	41 (3.6)	48 (12.9)	37 (14.4)
Chestwall retractions	217 (19.1)		20 (7.8)
Diagnostics			
CRP bedside (ln)	419 (36.9)	277 (74.5)	210 (81.7)
Less eating	-	49 (13.2)	-
Decreased urine output	-	90 (24.2)	-
Dry mucous membranes	-	40 (10.8)	-
Sunken fontanel	-	86 (23.1)	-
Decreased turgor	-	66 (17.7)	-
Decreased tears	-	115 (30.9)	-
Thirsty	-	200 (53.8)	-
Sunken eyes	-	78 (21.0)	-
Vomiting	-	52 (14.0)	-
Coughing	-	-	33 (12.8)
Stridor	-	-	20 (7.8)
Nasal flairing	-	-	49 (19.1)
Groaning	-	-	62 (24.1)
Auscultation	-	-	16 (6.2)

0 no missing data

- no relevant determinant regarding the presenting problem

Supplementary file 2: variable selection

Table 2.1: multivariable regression analysis in children with fever

DETERMINANTS	REVISITS *n=346*	
Patient characteristics *n=1136*	*OR* *(95% CI)*	*n/total (%)*
Age		
0-3m	1.23 (0.56-2.69)	12 (3.5)
3-6m	1.02 (0.57-1.84)	23 (6.6)
6-12m	1.35 (0.88-2.07)*	74 (21.3)
1-5y	0.96 (0.67-1.36)	175 (50.6)
>5y (REF)	*ref*	62 (17.9)
Age <1y	1.31 (0.96-1.77)*	109 (31.5)
Age <3y		
Age <5y	1.05 (0.74-1.49)	284 (82.1)
Gender (male)	1.24 (0.95-1.62)*	208 (60.1)
Disease characteristics		
Parental concern	1.73 (1.15-2.60)*	310 (89.6)
Duration of fever	1.00 (0.92-1.09)	*continuous*
Ill appearance	1.05 (0.74-1.48)	79 (22.8)
Temperature (°C)	1.07 (0.93-1.24)	*continuous*
Tachypnoea	1.19 (0.86-1.64)	105 (30.3)
Tachycardia	1.17 (0.85-1.61)	114 (32.9)
Decreased oxygen saturation	0.57 (0.08-4.28)	6 (1.7)
Prolonged cap. refill time (peripheral)	1.30 (0.77-2.19)	28 (8.1)
Chestwall retractions	1.82 (0.94-3.54)*	32 (9.2)
Diagnostics		
CRP bedside (ln)	1.00 (1.00-1.00)	*continuous*

**significant determinants (p<0.20)*

Table 2.2: multivariable regression analysis in children with vomiting and diarrhoea

DETERMINANTS	REVISITS *n=108*	
Patient characteristics *n=372*	*OR (95% CI)*	*n/total (%)*
Age		
0-3m	2.54 (0.72-9.00)*	6 (5.6)
3-6m	2.10 (0.70-6.31)*	13 (12.0)
6-12m	3.03 (1.15-7.99)*	33 (30.6)
1-5y	1.61 (0.68-3.84)	44 (40.7)
>5y (REF)	*Ref*	12 (11.1)
Age <1y	1.59 (0.89-2.83)*	52 (48.1)
Age <3y	1.29 (0.47-3.51)	88 (81.5)
Age <5y	1.32 (0.43-4.12)	96 (88.9)
Gender (male)	1.08 (0.63-1.87)	60 (55.5)
Disease characteristics		
Parental concern	1.46 (0.65-3.30)	97 (89.8)
Duration of fever	1.06 (0.92-1.23)	*continuous*
Ill appaerance	1.89 (0.96-3.72)*	32 (29.6)
Temperature (°C)	1.28 (0.91-1.78)*	*continuous*
Tachypnoea	4.85 (2.19-10.72)*	35 (32.4)
Tachycardia	0.52 (0.20-1.38)*	12 (11.1)
Prolonged cap. refill time (peripheral)	0.83 (0.36-1.94)	17 (15.7)
Signs of dehydration	2.21 (1.08-4.52)*	
Diagnostics		
CRP bedside (ln)	1.01 (0.99-1.02)	*continuous*

**significant determinants (p<0.20)*

Table 2.3: multivariable regression analysis in children with dyspnea

DETERMINANTS	REVISITS *n=73*	
Patient characteristics *n=257*	*OR* *(95% CI)*	*n/total (%)*
Age		
0-3m	2.59 (0.64-10.53)*	7 (9.6)
3-6m	1.40 (0.40-4.88)	9 (12.3)
6-12m	1.85 (0.56-6.07)	13 (17.8)
1-5y	1.64 (0.61-4.40)	36 (49.3)
>5y (ref)	*ref*	8 (11.0)
Gender (male)	1.55 (0.80-3.00)*	54 (74.0)
Disease characteristics		
Parental concern	1.08 (0.54-2.17)	52 (71.2)
Ill appearance	0.79 (0.28-2.19)	10 (13.7)
Tachypnoea	1.52 (0.78-2.96)	42 (57.5)
Tachycardia	1.19 (0.55-2.55)	18 (24.7)
Decreased oxygen saturation	0.81 (0.11-5.79)	3 (4.1)
Chestwall retractions	0.81 (0.37-1.76)	34 (46.6)
Coughing	1.06 (0.44-2.52)	60 (82.2)
Stridor	1.18 (0.48-2.90)	20 (27.4)
Nasal flairing	0.85 (0.26-2.82)	10 (13.7)
Groaning	0.80 (0.22-2.88)	10 (13.7)
Auscultation	0.67 (0.34-1.32)	38 (52.1)
Diagnostics		
CRP bedside (ln)	1.16 (0.66-2.03)	*continuous*

** significant determinants (p<0.20)*

Chapter 11

General discussion

CHALLENGES IN RESEARCH AT THE ED: LESSONS LEARNED

Research in pediatric emergency medicine is challenging. Every step in the process from performing research to implementation of new insights and evaluation of the impact has its own profits in practice, as well as its barriers and limitations. A few of the difficulties related to the ED studies of this thesis will be discussed.

How to (early) recognize and treat patients at risk for serious infections or a complicated disease course (in developed low-prevalence) countries- decision making at the ED (aim 1)

The importance of early recognition of serious infections is well recognized by studies on the consequences of delayed diagnosis, mortality studies and malpractice cases.[1,2] The latter was in accordance with 16 acknowledged malpractice cases in pediatric emergency medicine of a total of 19 in the Netherlands. [3] The greater part of lawsuits concerned: (delayed) diagnostics and/ or therapy, medical guidance and/or communication. Patients were of young age, with fifty percent of children under the age of 2 years, and most common illnesses were serious bacterial infections or a complicated disease course in a child with complex needs.

In The Netherlands, 0.5-1 % of all pediatricians encounters a malpractice case at some point in their career. In **chapter 2**, several learning points were highlighted. First, serious bacterial infections and a complicated disease course occur infrequently and can be hard to recognize in an early stage. Second, the most frequent given advice in lawsuits is to evaluate and monitor your patient as if it is a worst case scenario. A child with non-specific signs and symptoms can develop a serious infection within a short period of time and therefore it is important to assign vital signs measurements within appropriate time intervals.

In this thesis we focused on diagnosis and treatment in children with acute gastroenteritis (AGE) at the ED, in order to discuss early recognition of dehydration, early standardized oral rehydration by nurses and early recognition of therapy failure.

As in our population of 800 children with AGE, only 9 patients (1,1%) showed two abnormal items on the Clinical Dehydration Score, indicating moderate dehydration, and only one (0.1%) of these patients had three abnormal items. So, severe dehydration is rare in a western healthy population of children.[4]

In the clinical assessment of children with AGE, we evaluated the value of weight change in relation to the Clinical Dehydration Score (CDS). [4] We observed parents were not willing to revisit or cooperate in weight measurements after rehydration, and in the absence of severe dehydrated children, we did not find a weight difference in de

children in whom consecutively weight measurements succeeded. We concluded that weight change in the assessment of children with dehydration is not useful **(chapter 3).**

To assess dehydration in children, technical devices and point-of-care diagnostic tests can be used, besides clinical assessment. Recently, novel methods for assessment of dehydration were tested, however in a pre-clinical phase.[5,6] In the era of point of care testing the use of laboratory tests have been investigated, also in children with acute gastroenteritis. Bicarbonate showed to be consistently decreased in children with moderate and severe dehydration.[7] Recent developments in pediatric emergency medicine include point-of-care ultrasound. Dehydrated children showed significant differences in the cross-sectional IVC/Aorta (Ao) ratio, with an improvement after rehydration therapy.[8] As in our population moderate and severe dehydration is rare, routine performing of diagnostic tests is not useful.

In our western population of children with mild or moderate dehydration, a clinical assessment is sufficient and oral rehydration therapy can be safely started **(chapter 4).** However, although rare, we should be aware of and keep on recognizing in an early phase, the few children with moderate to severe dehydration and the children with AGE at risk for a complicated disease course. These patients may be identified based on a combination of abnormal signs and symptoms and an abnormal CDS, a physicians' gut feeling something's wrong, and/or a mismatch in history and clinical examination.

Next, we implemented a nurse-guided clinical decision support system on early rehydration treatment in children with AGE, showing high compliance rates and increase standardized use of ORS, without differences in the outcome measures diagnostic tests, length of stay at the ED and hospital admission **(chapter 4).**

Incorporation in routine care appeared essential. We showed that oral rehydration by the nurses according to a strict protocol was safe. We also showed that moderate to severe dehydration only occurred in less than 5% of all patients. All these patients were adequately assessed and acted up on by the nurses. Moreover, recently, diluted apple juice or other preferred liquids appeared an appropriate alternative for children with no or mild dehydration in AGE who refuse to drink ORS.[9] Knowing all this, the next step is to bring oral rehydration into the office of the general practitioner. This will result in a decrease of the number of patients referred to the ED. We believe, oral rehydration can safely take place in the GP's office, whereas only children who are not able to drink or have extreme (predicted) loss of vomit or stool, have to be referred.

It would be helpful if we could predict in whom oral rehydration has a high chance of failing. These children need to be frequently monitored with the opportunity for early intervention. We observed 21% failure of oral rehydration therapy in predominantly mildly dehydrated children, showing that dehydration after the first ED visit still occurs **(chapter 5).** Determinants associated with oral rehydration failure are high MTS urgency

level, prolonged capillary refill time and an abnormal CDS, all available at initial presentation, making early recognition possible.

In conclusion, AGE is a common problem in children at the ED (9.3 % of all visits). and severe dehydration is rare. Nurse lead oral rehydration is effective and safe. We conclude therefore that assessment and rehydration treatment can primarily take place at the GP's office, reducing referrals to the ED. As we identified patient characteristics associated with rehydration failure, patients with these characteristics should be referred in an early stage.

Optimize: implementation of guidelines and interventions at the ED (aim2)

Barriers as well as facilitators were experienced in the implementation process of a guideline on the diagnosis of urinary tract infection **(chapter 6),** a nurse-lead clinical decision support system in rehydration of young children with AGE **(chapter 4)** and a written safety netting advice for parents of febrile children **(chapter 7).** Recently an increase in implementation papers was described, however, many of these publications describe gaps in evidence based practice, instead of the implementation and impact of interventions at the ED in order to fill in the gap.[10] Important in the implementation process is the acceptability by professionals. How to measure the acceptability in order to improve adherence is discussed in **chapter 8**, showing good feasibility for acceptability measurement of the OADRI in order to identify specific barriers in different areas and to make targeted improvements.

After the implementation of a guideline on the diagnosis of urinary tract infection for attending physicians, an improved but still limited compliance was observed. Best compliance occurred outside the office hours and in young children (3-24 months of age). The implementation process included important facilitators such as: 1) the development of the guideline in collaboration with peer health care professionals, 2) the implementation was performed according to a structured implementation plan, and 3) included empowerment of the nurses and 4) the guideline was easy accessible on paper, as well as electronic incorporated in daily practice. However, the limited increase of adherence to 50%, indicates room for improvement, starting with creating awareness among attending physicians to improve guideline adherence in older children and during the daytime.

In the implementation of a clinical decision support system for nurse-led early rehydration of children with AGE, three important observations were noted:1) although nurses perform the first patient assessment, it was difficult to get the nurses to do a clinical assessment of dehydration and start the rehydration treatment, as it made them feel uncomfortable; empowerment was needed in order to achieve a behavioral change; 2) when applied, adherence to the treatment advice generated by the decision tool was good and 3) especially during crowding hours, nurses did not complete filling in all

clinical dehydration signs, which was required in order to use the decision tool, hereby increasing the exclusion of patients. So, nurses agreed with the intervention with respect to the content, but they feel that they lacked the time to finish the whole intervention.

Also on nurses-level, we implemented a written safety netting advice for parents of children with fever to inform about alarming signs for serious illness or complicated disease course. The written safety netting advice was a leaflet, containing standardized discharge information. However according to the research protocol, the nurse was obliged to provide standardized oral information when handing over the leaflet. Furthermore, the implementation took place in two settings. One, a university hospital and the second, a teaching hospital. The difference between the two settings was that the leaflet at the university was handed over by the nurse. At the teaching hospital, the leaflet was provided by the attending physician due to local feasibility issues. We observed correct identification of eligible patients with low application of the intervention in the university hospital So, inclusion was hampered because a number of patients did not actually get the leaflet. In the teaching hospital we observed a low inclusion number. So here, identification of eligible patients was hampered. We hypothesized the availability of dedicated research nurses, as well as incorporating the intervention in daily practice and increasing awareness among parents (for example by advertising posters), could have improved adherence.

Effective implementation of interventions in health care, aiming behavioral change of health care professionals, has proved to be a major challenge. Most interventions now are complex interventions, where health care workers with different backgrounds, have to cooperate. [11] Awareness of evidence based practice (EBP) differs among these groups. In order to successfully implement EBP, there has to be a positive perception on EBP in all health care workers involved, all health care workers have to feel competent and skilled in order to use EBP, and targeted educational training is necessary. [12] So, a multifaceted intervention strategy, facilitated by a local opinion leader seemed most effective.[13] Effectiveness increased when potential barriers were identified in advance.

On nurse- level, we observed improvement of clinical decision rules acceptability could be achieved by responses to individual guided interaction based on OADRI items.

A current study on the implementation of a clinical pathway on oral rehydration in children with AGE showed sustained change over a 10-year period. [14] The evidence based clinical pathway was developed in a multidisciplinary team of health care workers, including ED physicians and nurses, as well as pharmacists and others. Implementation was led by dedicated ED physicians and nurses, and included multiple strategies, leading to a successful long-term change.

In this thesis, we presented the implementation of guidelines and decision rules at the ED. The ED is a complicated environment with many decisions to be made under a high level of time pressure, concerning patients with a large diversity of problems, parents

and patients experienced a stressful situation, often with a uncertainty of diagnosis at presentation, and many disruptions and distractions.

Evidence based guidelines and clinical decision tools can be added tools in clinical assessment or treatment. We now have to implement new diagnostic or therapeutic interventions and evaluate its impact. At the ED, research embedded in patient care, performed by dedicated research personnel, would improve the implementation process at the ED.

In conclusion, in order to implement successfully at the ED, one needs not only an evidence based intervention, developed in collaboration with health care workers, but also an ED-tailor made thorough implementation strategy with pre-identification of barriers, such as easy to use under pressure, and a dedicated implementation team which include the ED staff.

Improve discharge instructions- safety netting (aim3)

The systematic review in c**hapter 9** identifies several determinants of revisits that could be used for the identification of risk groups, like young age, relevant medical history, infectious/respiratory symptoms or seizures and progression or persistence of symptoms.

Although we could not design a 'safety netting protocol' for all patients, we did learn that young age, parental concern and alarming signs and symptoms (chest wall retractions, ill appearance, clinical signs of dehydration and tachypnea) were associated with emergency health care revisits in children with fever, dyspnea and vomiting/diarrhea. The post- ED discharge interval for a control visit was disease-specific and appeared to be shorter for children with vomiting/diarrhea than others in particular **(chapter 10).**

Last, due to ineffective communication, parents can feel that they were not taken seriously and lose trust. This can influences their decision-making and help-seeking behavior.[15] The advice is to listen carefully to parents, acknowledge their gut feeling, involve them and then explain their child's further treatment.

Gaps remain the application of a uniform safety-netting strategy and its time frame. The empowerment of parents by parental health care education remains a keystone in a safe and adequate discharge plan.[15]

METHODOLOGICAL CHALLENGES IN CLINICAL STUDIES AT THE ED

The process of inclusion of patients, how to clearly define outcome measures, and how to deal with missing value in routine data collection are important methodological problems at the ED.

The inclusion of patients at the ED

Including pediatric patients at the ED requires a written informed consent. Informed consent can be hampered in an acute care setting, as it is a stressful moment in time, usually concerning a first contact between the patient and the physician or nurse, with parents that are usually very anxious. Furthermore, before obtaining informed consent, one should always check literacy level and comprehension of information. And last under stress, it is known that more than half of provided medical information is lost and possibly half of memorized information is incorrect. [16] A written document on preoperative information in addition to oral information showed significant improvement of the comprehension- memorization score and parental satisfaction, while decreasing level of anxiety.

Recently was shown in a small sample that deferred consent, a delayed informed consent, can be an acceptable alternative if the study meets strict criteria.[17] Deferred consent may lead to higher inclusion rates, as health care professionals can chose the appropriate moment in time to discuss the informed consent and parents or other legal guardians are more able to adequately consider whether or not to participate.

Besides a hampered informed consent process in children with AGE, we observed lack of inclusion of patients as we were confronted with higher than anticipated exclusion rates for serious co-morbidity (setting related) **(chapter 4).**

Outcome measures at ED disease and process outcome

Over the past years great progress has been made in performing research with international partners due to electronic patient records and data files. However, in an international multicenter study significant differences can exist between countries (such as disease incidence, immunization schedules and differences in definitions), settings (academic versus teaching hospitals) as well as local differences (guideline use, task shifting).[18] These differences may lead to significant differences in the patient population and management.

Furthermore, outcome measures in itself can be defined differently. For example, the outcome measure length of stay (LOS) can be influenced by setting (academic versus teaching hospitals and its own facilities), resource use, crowding and time quality criteria.

Use of routine datasets and dealing with missing values

One has to strike a balance between a large routine collected dataset and a small in-depth study specific dataset. A small in-depth dataset with a limited number of patients with standardized detailed information, can be more suitable for answering one specific research question. The analysis of analyzing routine collected data may show higher variability. [19]

Routine datasets are increasingly used in medical research. And they all have missing data to some extent. In this thesis **(chapter 5)** , a routinely collected dataset was analyzed, containing missing data. Several methods have been proposed in handling missing data. [20] All individuals with missing data can be excluded (complete case analysis), single imputation methods exists and multiple imputation (MI). In our study **(chapter 5)** we chose to use MI, as it is a flexible and accepted method to handle missing data. In MI has to be determined whether data are assumed to be missing at random (crowding) or missing not at random (blood pressure is not measured, as heart rate and capillary refill are normal). Multiple imputation usually assumes data are missing at random. Second, important in the process of multiple imputation is which variables should be included in the model, the method of imputation, and the number of imputations. Last, recent literature recommends performing a sensitivity analysis, in order to test the explanation for missing of the data, as this cannot be determined with certainty.[20]

We discussed several challenges in research in pediatric emergency medicine research. First, including pediatric patients at a crowded ED is a complex process, requiring identification of all eligible patients, taking setting characteristics into account, approaching anxious parents in order to obtain informed consent, and fulfill all requirements, such as an intervention. This process can be hampered when dedicated research personnel is lacking and research is not embedded in routine patient care **(chapter 7).** At the ED of an academic hospital, a high number of patients has complex comorbidity, which may be an exclusion criteria for a number of studies. At teaching hospitals, larger volumes of eligible patients present at the ED, however research experience is often lacking at the ED. Therefore, consider combining the research experience in the academic center with the high eligible patient load in the teaching hospital.

Second, generalizing or pooling of results should be done with care, as data and outcome measures can be influenced by differences in country and setting.

Third, multiple imputation is a good option when dealing with missing data, however, providing detailed information on the missing data and the multiple imputation process in itself, as well as information on the impact of the missing data on the results, have to be taken into account.

FUTURE DIRECTIONS

The clinical practice of the ED is the 'laboratory' where most research questions develop and can be answered. As evidence- based guidelines often are international, it is important to collaborate in international research networks with the opportunity of using

routine collected datasets, leading to broad generalizability of the results. Furthermore, collaboration is needed, as some topics and outcome measures are important but rare.

Predictive value of alarming signs and symptoms has been investigated in previously healthy children. Now, it is important to focus on improvement and standardization of discharge instructions, empowering parents to take care of their ill child at home.

Next, as survival in children with chronic conditions has improved, these children with complex needs increasingly visit the ED having a higher risk on a complicated disease course. However, little is known about the evidence for alarming signs and symptoms in children with complex needs, nor on the combination of signs and symptoms with point of care tests. Decision tools supporting clinical decision making for diagnostic tests, antibiotic treatment or hospital admission are lacking.

When children with complex needs visit the ED with fever, they are at risk (due to under-triage, complicated disease course, multiple (interactive) drug use, multiple medical specialists). Chapter 2 showed that this patient group comprises a relative important number of malpractice cases. Because at the ED, children with complex needs are regarded more vulnerable, they undergo more diagnostic tests, receive more treatment and their admission rate is higher.[21] This is only partially due to their underlying disease. Because they often have extensive treatment modalities and medication at their home, as well as trained parents, they present later on in the disease course. Furthermore, triage according to the MTS appeared less accurate in complex ill children with fever compared with the triage of previously healthy children. Last, parents are experienced to compose a tailored discharge plan, as well as the communication and the comprehension of it. However, as complexity of discharge plans is increasing with the increase of the number of children with complex needs, composing a feasible discharge plan after discharge remains a challenge for the multidisciplinary health care team. [22-24]

In conclusion, after decades of research mainly focused on diagnosis and treatment of previously healthy children presenting at the ED, it is now time to re-focus to early recognition by parental empowerment and optimizing discharge plans.

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Chapter 12

Summary/ samenvatting

ENGLISH SUMMARY

INTRODUCTION

In the introduction, the importance of good quality pediatric emergency care is explained. Acute illnesses in children differ among countries and settings. Regarding our population of the ED at the Erasmus MC in Rotterdam, The Netherlands, 1) we still observe mortality, although rare, 2) 45% of children with medical (non-trauma) complaints suffer from infectious diseases and 3) the number of revisits is high. As the main focus in research in pediatric emergency medicine has been on the development of good quality guidelines, we aimed to improve early recognition and treatment (aim 1), the implementation and use of guidelines (aim 2) and the discharge process after the ED visit (aim 3).

How to (early) recognize and treat patients at risk for serious infections or a complicated disease course (in developed low-prevalence) countries- decision making at the ED (aim 1)

In order to answer these research questions, the importance of early recognition of serious infections in general is addressed in chapter 2: 'Malpractice in pediatric emergency care in the Netherlands- what can we learn?' Nineteen malpractice lawsuits are described, of which 16 were acknowledged. Important lessons learned are: 1) Pediatricians need to be aware that, although rare, serious illnesses and serious complications do exist, as well as patients with rare diseases. 2) The number of patients with severe complex co-morbidities and use of multiple medication will increase. 3) In general, if the risk and the consequences will be more serious, the judgement afterwards will be stricter. The advice is to be watchful, and include safety measures. 4) Manage your patient file adequately and up to date. 5) After discharge, optimize the empowerment of the parents and organize a secure safety net.

Children with AGE are an important patient group at the ED. Early assessment and treatment and adequate follow-up are needed in order to prevent a complicated disease course, still leading to serious morbidity and mortality in children. Weight change was used as an important marker in the early assessment of children with AGE, however, an accurate recent (pre-dehydration) weight is lacking in most children. This is the subject of chapter 3 'Do we need weight in the assessment of dehydration in children with acute gastro-enteritis at the emergency department?'. In conclusion, repeated weight measurements appeared to be not feasible, our cohort showed a very low prevalence of children with clinical dehydration and CDS-based dehydration showed low perfor-

mance to predict weight-change based dehydration in a pediatric emergency population with AGE. As we observed safe and feasible Clinical Decision Score (CDS)-based nurse-led rehydration in chapter 4 'Impact of clinical decision support in young children with gastroenteritis at the emergency department: a randomized controlled trial', with adequate rehydration in the few children with moderate dehydration, we conclude that the use of the CDS may outperform weight change in the assessment of children with AGE in a setting with a low prevalence of moderate /severe dehydration. Furthermore, the implementation of nurse-guided clinical decision support system on rehydration treatment in children with AGE showed high compliance and increase standardized use of ORS, without differences in other outcome measures. Because adequate follow-up and safety netting can prevent a complicated disease course in most children, but not in all, it would be helpful to be able to predict which children are at risk to fail oral rehydration therapy. This was described in chapter 5 'How to predict failure of rehydration in children with acute gastroenteritis'. We observed failure of oral rehydration therapy in 21% predominantly mildly dehydrated patients. Associated with oral rehydration failure were high MTS urgency level, prolonged capillary refill time and an abnormal CDS score.

Optimize implementation of guidelines and interventions at the ED (aim2)

After recognizing the patients at risk, the process of diagnosis and treatment can be improved by optimizing the implementation and the use of up to date guidelines after implementation. This is described in chapter 6 'Urinary tract infection in children: impact analysis of an evidence based guideline', and chapter 7 'Implementation of a written safety netting advice for parents of feverish children at risk for serious infection at the emergency department'. How to further improve and monitor implementation is described in chapter 8 'Measuring acceptability of two clinical decision models in the emergency department using the Ottawa Acceptability of Decision Rules Instrument (OADRI)'.

The implementation of a standardized diagnostic strategy for diagnosing UTI in febrile children at the ED, according to a literature based implementation plan, showed a significantly better compliance to the guideline, especially in children 3- 24 months. Increase in compliance was influenced by patient age and time of presentation at ED (shift) (children 3-24 months of age and outside office hours). This study also underlines the need for a well-defined implementation strategy after launching an (inter)national guideline.

Next, we implemented a standardized safety netting tool for parents after discharge from their ill child from the ED. A decrease in the number of revisits or hospitalization was not observed, with part of this negative effect due to setting- related implementation issues, extensively described in chapter 7. Also, in the future, health care workers

have to be empowered to provide structured and concise health information for parents, involving them in the development.

In order to optimize a implementation strategy and making health care professionals actually use the intervention, barriers and facilitators have to be identified, preferably upfront. During the implementation process, barriers and facilitators can be monitored in order to make adjustments, if and when needed. This is shown in chapter 8 'Measuring acceptability of two clinical decision models in the emergency department using the Ottawa Acceptability of Decision Rules Instrument (OADRI)'. Although further validation is needed, we received adequate responses to individual items, usable to make further improvements in the implementation process.

Improve discharge instructions- safety net building (aim3)

As uncertainty on diagnosis or disease course remain in a significant number of patients after an ED visit, patients at risk in need for a revisit need to be identified and discharge instructions need to be improved in order to empower (parents of) patients in adequate at home management and initiate adequate return visits. This is described in chapter 9 'Tools for 'safety netting' in common pediatric illnesses: a systematic review in emergency care'. We assessed available evidence as heterogeneous. Strong determinants for revisits were identified, indicating patients with these signs and symptoms as high risk patients. Next, we aimed for a safety netting protocol in children with fever, vomiting/diarrhea and dyspnea in chapter 10 'Characteristics of revisits of children at risk for serious infections in paediatric emergency care'. Though we were not able to form a standardized usable protocol, we observed young age, parental concern and alarming signs and symptoms (chest wall retractions, ill appearance, clinical signs of dehydration and tachypnea) being associated with emergency health care revisits. We also observed that a control visit after ED discharge is indeed disease-specific and the post- discharge interval seems to be shorter for children with vomiting/diarrhea than others in particular.

DISCUSSION

Research in pediatric emergency medicine is challenging. Every step in the process from performing research to implementation of new insights and evaluation of the impact has its own profits in practice, as well as its barriers and limitations. We next discuss a few of the difficulties related to the ED studies of this thesis.

Next, we discuss methodological difficulties in research in pediatric emergency medicine. First, including pediatric patients at a crowded ED is a complex process, requiring identification of all eligible patients, taking setting characteristics into account, approaching anxious parents in order to obtain informed consent, and fulfill all require-

ments, such as an intervention. This process can be hampered when dedicated research personnel is lacking and research is not embedded in routine patient care (chapter 7). At the ED of an academic hospital, a high number of patients has complex comorbidity, which may be an exclusion criteria for a number of studies. At teaching hospitals, larger volumes of eligible patients present at the ED, however research experience is often lacking at the ED. Therefore, consider combining the research experience in the academic center with the high eligible patient load in the teaching hospital. Second, generalizing or pooling of results should be done with care, as data and outcome measures can be influenced by differences in country and setting. Third, multiple imputation is a good option when dealing with missing data, however, providing detailed information on the missing data and the multiple imputation process in itself, as well as information on the impact of the missing data on the results, have to be taken into account.

In conclusion, after decades of research mainly focused on diagnosis and treatment of previously healthy children presenting at the ED, it is now time to re-focus to early recognition by parental empowerment and optimizing discharge plans.

NEDERLANDSE SAMENVATTING

Inleiding

In de inleiding wordt het belang van goede kindergeneeskundige spoedzorg nader toegelicht. Acute ziektebeelden bij kinderen verschillen per land en behandelingsniveau (eerste, tweede en derde lijn). Binnen onze populatie van de spoedeisende hulp (SEH) van het Erasmus MC in Rotterdam 1) bestaat mortaliteit nog steeds, hoewel zeldzaam, 2) lijdt 45% van de kinderen met medische (niet-traumatische) klachten aan infectieziekten en 3) is het aantal controlebezoeken hoog. Aangezien de nadruk in wetenschappelijk onderzoek op het gebied van kindergeneeskundige spoedzorg ligt op het ontwikkelen van ziekte- en probleem-georiënteerde richtlijnen, hebben wij ons juist gericht op verbeteren van vroege herkenning van ernstige ziekte en behandeling hiervan (doelstelling 1), de implementatie en het gebruik van de ontwikkelde richtlijnen (doelstelling 2) en verbeteren van het ontslagproces vanuit de spoedeisende hulp (doel 3).

Verbeteren van herkenning en behandeling van patiënten met een risico op ernstige infecties of een gecompliceerd ziekteverloop- besluitvorming op de spoedeisende hulp (doel 1)

Om deze onderzoeksvragen te beantwoorden, wordt het belang van vroege herkenning van ernstige infecties in het algemeen behandeld in hoofdstuk 2: 'Tuchtrecht in de spoedeisende kindergeneeskunde: wat kunnen we leren?' Negentien tuchtzaken worden beschreven, waarvan er 16 werden erkend. Belangrijke lessen hieruit zijn: 1) Kinderartsen moeten zich ervan bewust zijn dat, hoewel zeldzaam, ernstige ziekten en ernstige complicaties bestaan, evenals patiënten met zeldzame ziekten. 2) het aantal patiënten met ernstige complexe co-morbiditeit en het gebruik van meerdere geneesmiddelen zal toenemen. Men dient hier alert op te zijn. 3) In het algemeen, als het risico en de gevolgen ernstiger zijn, zal het oordeel naderhand strenger zijn. Het advies is om waakzaam te zijn en veiligheidsmaatregelen in te bouwen. 4) Het patiëntendossier dient adequaat en up-to-date beheert te worden. 5) Kennis en vaardigheden van de ouders/verzorgers dienen geoptimaliseerd te worden en een veilig vangnet na ontslag georganiseerd.

Kinderen met acute gastro-enteritis (AGE) zijn een belangrijke patiëntengroep op de SEH. Vroegtijdige beoordeling en behandeling en adequate follow-up zijn nodig om een gecompliceerd ziekteverloop te voorkomen. Gewichtsverandering werd gebruikt als een belangrijke marker in de vroege beoordeling van kinderen met AGE , maar bij de meeste kinderen ontbreekt een nauwkeurig recent (pre-dehydratatie-) gewicht. Dit is het onderwerp van hoofdstuk 3 'Hebben we gewicht nodig bij de beoordeling van dehydratie van kinderen met acute gastro-enteritis op de spoedeisende hulp?'. Her-

haalde gewicht-metingen bleken niet haalbaar, het patiënten cohort toonde een zeer lage prevalentie van kinderen met klinische dehydratie en Clinical Dehydration Score (CDS)-gebaseerde uitdroging bleek een slechte maat om gewichtsverandering op basis van uitdroging te voorspellen. Bij beoordeling en behandeling van kinderen met AGE in een omgeving met een lage prevalentie van matige / ernstige uitdroging, kan het gebruik van de CDS daarom beter zijn dan gewichtsverandering. Dit mede gezien dat (CDS) -gebaseerde rehydratie door verpleegkundigen veilig en goed uitvoerbaar bleek met ook adequate rehydratie in de weinige matig gedehydreerde kinderen in hoofdstuk 4 'Impact van de ondersteuning van klinische besluitvorming bij jonge kinderen met gastro-enteritis bij de afdeling spoedeisende hulp: een gerandomiseerde gecontroleerde trial'. Bovendien bleek therapietrouw hoog en nam het gestandaardiseerde gebruik van ORS toe, zonder verschillen in andere uitkomstmaten. Omdat adequate follow-up en een veiligheidsnet een gecompliceerd ziekteverloop niet in alle kinderen kan voorkomen zou het nuttig zijn om te kunnen voorspellen bij welke kinderen orale rehydratietherapie faalt. Dit is beschreven in hoofdstuk 5 ' Is het falen van rehydratie bij kinderen met acute gastro-enteritis te voorspellen?'. We hebben het falen van orale rehydratie-therapie waargenomen bij 21% van de, voornamelijk mild uitgedroogde patiënten. Geassocieerd met falen van orale rehydratatietherapie waren een hoog MTS urgentieniveau, een verlengde capillaire refill-tijd en een abnormale CDS-score.

Optimaliseren: implementatie van richtlijnen en interventies op de spoedeisende hulp (doel 2)

Na het verbeteren van het vroeg herkennen van risicopatiënten kan het proces van diagnose en behandeling verder worden verbeterd door optimaliseren van implementatie en vervolgens gebruik van up-to-date richtlijnen. Dit wordt beschreven in hoofdstuk 6 'Urineweginfectie bij kinderen: impactanalyse van een evidence-based richtlijn' en hoofdstuk 7 'Implementatie van een schriftelijk vangnetadvies voor ouders van kinderen met koorts met risico op een ernstige infectie op de spoedeisende hulp'. Hoe implementatie verder kan worden verbeterd wordt beschreven in hoofdstuk 8 'Acceptatie van twee klinische beslissingsmodellen op de spoedeisende hulp met behulp van het ' Ottawa Acceptability of Decision Rules Instrument (OADRI)'.

Implementatie van een gestandaardiseerde diagnostische strategie voor het diagnosticeren van een urineweginfectie (UWI) bij kinderen met koorts op de SEH, ontwikkeld volgens een op wetenschappelijke literatuur gebaseerd implementatieplan, toonde een significant betere naleving van de richtlijn, vooral bij kinderen van 3 tot 24 maanden. Toename in het volgen van de richtlijn werd beïnvloed door de leeftijd en het tijdstip van presentatie van de patiënt op de SEH, met het beste resultaat bij patiënten 3-24 maanden oud en bij kinderen die zich presenteerden buiten kantooruren. Deze studie onderstreept ook de noodzaak van een welomschreven implementatiestrategie na het

uitbrengen van een (inter)nationale richtlijn. Vervolgens hebben we een gestandaardiseerd ontslagadvies voor ouders geïmplementeerd na bezoek aan de SEH. Een afname van het aantal controle bezoeken of ziekenhuisopnamen werd niet waargenomen. Dit kon deels worden verklaard door setting- gerelateerde implementatieproblemen, uitgebreid beschreven in hoofdstuk 7. In de toekomst moeten gezondheidszorgmedewerkers worden geoutilleerd om beknopte en gestructureerde informatie aan te bieden aan ouders over de ziekte van hun kind en hen te betrekken bij de ontwikkeling.

Om een implementatiestrategie te optimaliseren en zorgprofessionals daadwerkelijk gebruik te laten maken van de interventie, moeten barrières en facilitators worden geïdentificeerd, bij voorkeur vooraf. Tijdens het implementatieproces kunnen deze worden gemonitord om het implementatieproces waar en wanneer nodig aan te passen. Dit is beschreven in hoofdstuk 8 'Het meten van de aanvaardbaarheid van twee klinische beslissingsmodellen op de afdeling spoedeisende hulp met behulp van het ' Ottawa Acceptability of Decision Rules Instrument (OADRI)'. Hoewel verdere validatie nodig is, hebben we adequate antwoorden op afzonderlijke items ontvangen, die voldoende bruikbaar zijn om verdere verbeteringen aan te brengen in het implementatieproces.

Verbeteren van ontslaginstructies – het bouwen van een veiligheidsnet (doel3)

Aangezien bij een aanzienlijk aantal patiënten na een SEH-bezoek onzekerheid blijft bestaan over de diagnose of het beloop van de ziekte, moeten risicopatiënten worden geïdentificeerd. Zij hebben een controleafspraak nodig en daarnaast dienen de instructies voor ontslag te worden verbeterd om (ouders van) patiënten adequaat te informeren over thuismanagement van de ziekte van hun kind en op het juiste moment hulp te zoeken of een controle bezoek te initiëren. Dit wordt beschreven in hoofdstuk 9 'Handvaten voor het creëren van een vangnet bij veelvoorkomende kinderziekten: een systematische review in spoedeisende geneeskunde'. We hebben het beschikbare wetenschappelijke bewijs beoordeeld als heterogeen. Sterke determinanten voor controlebezoeken werden geïdentificeerd, wat patiënten met deze kenmerken identificeert als hoog-risico patiënten. Vervolgens hebben we getracht een vangnetprotocol samen te stellen bij kinderen met koorts, braken/diarree en benauwdheid in hoofdstuk 10 ' Kenmerken van controle bezoeken van kinderen met een risico op ernstige infecties op de spoedeisende hulp'. Hoewel we niet in staat waren om een gestandaardiseerd bruikbaar protocol te ontwikkelen, hebben we vastgesteld dat jonge leeftijd, ouderlijke bezorgdheid en een aantal specifieke alarmsymptomen (intrekkingen, zieke indruk, klinische tekenen van uitdroging en snelle ademhaling) verband houden met bezoeken aan de spoedeisende hulp. We hebben ook vastgesteld dat een controlebezoek na ontslag van de SEH inderdaad ziekte-specifiek is en dat het post-ontslaginterval korter lijkt te zijn voor kinderen met braken/diarree.

DISCUSSIE

Wetenschappelijk onderzoek binnen de spoedeisende kindergeneeskunde is een uitdaging. Elke stap in het proces van het uitvoeren van wetenschappelijk onderzoek, het implementeren van nieuwe inzichten en het evalueren van de impact heeft zijn eigen winst in de praktijk, evenals zijn barrières en beperkingen. We bespreken enkele problemen die verband houden met de wetenschappelijke studies, beschreven in dit proefschrift.

Na het bespreken van verschillende hoofdstukken, bespreken we methodologische uitdagingen in wetenschappelijk onderzoek in de spoedeisende kindergeneeskunde. Ten eerste is het includeren van pediatrische patienten op een overvolle SEH een complex proces. Dit vereist 1) de correcte identificatie van alle in aanmerking komende patienten 2) rekening gehouden wordt met de eigenschappen van de instelling 3) het op de juiste manier benaderen van angstige ouders om informed consent te verkrijgen en 4) dat volledig aan alle vereisten wordt voldaan. Dit proces kan worden bemoeilijkt wanneer specifiek onderzoekspersoneel ontbreekt en onderzoek niet is ingebed in routinematige patiëntenzorg (hoofdstuk 7). Op de SEH van een academisch ziekenhuis heeft een groot aantal patiënten complexe co-morbiditeit, wat een belangrijk exclusiecriterium kan zijn. Bij niet-academische ziekenhuizen kunnen er grotere hoeveelheden geschikte patiënten zijn, maar ontbreekt vaak onderzoekservaring op de SEH. Overweeg daarom om onderzoekservaring in het academische centrum te combineren met het hogere aantal beschikbare patiënten in het niet-academisch ziekenhuis. Ten tweede moet generalisatie of pooling van resultaten met zorg gebeuren, omdat gegevens en uitkomstmaten kunnen worden beïnvloed door verschillen in land en behandelingsniveau (eerste, tweede en derde lijn). Ten derde is meervoudige imputatie een goede optie wanneer gegevens ontbreken, mits er goed geïnformeerd wordt over de ontbrekende gegevens, het proces van meerdere imputaties, en de impact van de ontbrekende gegevens op de resultaten.

Concluderend, na tientallen jaren van onderzoek, voornamelijk gericht op de diagnose en behandeling van voorheen gezonde kinderen die zich presenteerden op de SEH, is het nu tijd om te concentreren op vroege herkenning van ernstige ziekte door ouders, ouders adequaat te informeren en ontslaginstructies te optimaliseren.

Appendices

List of abbreviations
List of publications
Training Supervision Plan

LIST OF ABBREVIATIONS

AAP	American Academy of Pediatrics
AGE	acute gastroenteritis
CDS	Clinical Dehydration Scale
CFU	colony forming units
CRT	capillary refill time
CTG	Central Disciplinary Committee
ED	emergency department
FWS	fever without source
GP	general practitioner
Hib	Haemophilus Influenza B
IRB	Institutional Review Board
LOS	length of stay
MTS	Manchester Triage System
NICE	National Institute of Clinical Health and Excellence
OADRI	Ottawa Acceptability of Decision Rules Instrument
ORS	oral rehydration salts
PC7	7-valent pneumococcal vaccine
PEM	pediatric emergency medicine
RTG	Regional Disciplinary Committee
SBI	serious bacterial infection
SI	serious infection
SPA	suprapubic aspiration
UTI	urinary tract infection

LIST OF PUBLICATIONS

1. Alarm symptoms of meningitis in children with fever.
Geurts DHF, Moll HA.
Ned Tijdschr Geneeskd. 2011;155:A2293. Dutch. General introduction

2. Malpractice in pediatric emergency medicine: what can be learned?
Tuchtrecht in de kindergeneeskunde; Hoofdstuk 7: Tuchtrecht en de spoedzorg.
DHF Geurts, A de Koning, HA Moll
ISBN: 9789462510449, 1e druk
Redactie: A.M. de Koning, W.G. Leeuwenburgh-Pronk, M.C. de Vries

3. Do we need weight in the assessment of dehydration in children with acute gastroenteritis at the emergency department?
Geurts DHF, Moll H, Oostenbrink R.
Eur J Pediatr. 2017 Nov 7.

4. Implementation of clinical decision support in young children with acute gastroenteritis: a randomized controlled trial at the emergency department.
Geurts DHF, de Vos-Kerkhof E, Polinder S, Steyerberg E, van der Lei J, Moll H, Oostenbrink R.
Eur J Pediatr. 2017 Feb;176(2):173-181.

5. How to predict failure of rehydration in children with acute gastroenteritis.
Geurts DHF, Steyerberg EW, Moll H, Oostenbrink R
J Pediatr Gastroenterol Nutr. 2017 Nov;65(5):503-508.

6. Impact analysis of an evidence-based guideline on diagnosis of urinary tract infection in infants and young children with unexplained fever.
Geurts DHF, Vos W, Moll HA, Oostenbrink R.
Eur J Pediatr. 2014 Apr;173(4):463-8

7. Lessons learned from implementation of a written safety netting advice for parents of febrile children at the emergency department.
Geurts DHF, de Vos-Kerkhof E, Wiggers MBL, Manai B, Lakhanpaul M, Moll HA, Oostenbrink, R
Submitted

8. Measuring acceptability of two clinical decision models in the emergency department using the Ottawa Acceptability of Decision Rules Instrument (OADRI)
de Vos-Kerkhof, E, Geurts, DHF, Vergouwe Y, Korfage I, Slager-Lodders A, Moll HA, Oostenbrink R
Int Arch Nurs Health Care 2016; 2:044.gffs

9. Tools for 'safety netting' in common paediatric illnesses: a systematic review in emergency care.
de Vos-Kerkhof E, Geurts DHF, Wiggers M, Moll HA, Oostenbrink R.
Arch Dis Child 2016 feb; 101(2): 131-139.

10. Characteristics of revisits of children at risk for serious infections in paediatric emergency care.
de Vos-Kerkhof E, Geurts DHF, Steyerberg EW, Lakhanpaul M, Moll HA, Oostenbrink R
Eur J Pediatr, Febr 3, 2018

TRAINING SUPERVISION PLAN

Training and supervision plan

Name PhD student: D Geurts	PhD period: 2010-2017
Erasmus MC department: Pediatrics	Promotor Prof dr HA Moll
Research school: NIHES	Supervisor:dr R Oostenbrink

PhD training	Year	Workload (ECTS)
General courses		
Introduction clinical research/ funding	2012	0.5
Research Integrity (Prof dr I.D. de Beaufort)	2016	1.0
BROK	2017	1.0
Specific courses		
NIHES 'Methods of Clinical Research' (ESP10).	2011	1.5
NIHES 'Introduction to data analysis' (ESP03) ;	2011	1.5
Research meetings		
Internal Research meetings, Department of General Pediatrics	2010-2017	2.0
Joint Research Meetings, Department General Pediatrics, Medical Informatics and Medical Decision Making	2010-2017	1.0
Research meetings REPEM annual	2012-2017	1.0
Seminars and workshops		
Research Masterclass, ESPID, The Hague.	2012	1.0
Presentations (inter)national conferences		
• Malpractice lawsuits in pediatric emergency medicine in The Netherlands: what can we learn? Oral presentation EUSEM, Torino, Italy.	2015	1.0
• Zal orale rehydratie op de spoedeisende hulp bij dit kind met acute gastro-enteritis succesvol zijn? NVK, Veldhoven, Nederland.	2014	1.0
• Will oral rehydration at the emergency department in this young child with acute gastroenteritis fail? EAPS, Barcelona, Spain.	2014	1.0
• Implementation of a written safety netting advice for parents of feverish children at risk for serious infections at the emergency department. EUSEM, Amsterdam, The Netherlands.	2014	1.0
• Vroege rehydratie met behulp van klinische beslisondersteuning door verpleegkundigen op de spoedeisende hulp bij jonge kinderen met acute gastroenteritis: een randomised controlled trial. NVK, Veldhoven, Nederland.	2013	1.0
• CDSS-guided Early Rehydration by Nurses in Young Children with Acute Gastroenteritis at the Emergency Department: a Randomised Controlled Trial. Oral presentation at EAP, Lyon, Frankrijk.	2013	1.0
• CDSS-guided early rehydration by nurses in young children with gastroenteritis at the emergency department. PREM, Ghent, Belgium.	2013	1.0
• Impact analysis of an evidence based guideline on urinary tract infection (UTI) in children: determinants of implementation. EAP, Istanbul, Turkije	2012	1.0
• Safety netting in children at risk for serious illness in paediatric emergency care. EUSEM Antalya, Turkey.	2012	1.0
• Diagnosis of urinary tract infection in children: impactanalysis of an evidence based guideline. ESPID, Thessaloniki, Greece. (poster)	2012	0.5
• Diagnostiek van urineweginfectie bij kinderen: impactanalyse van een evidence based richtlijn. NVK, Veldhoven, Nederland.	2011	1.0

• Predictors of hospitalisation in children with gastroenteritis. ESPID, Den Haag, Nederland. (poster)	2011	0.5
• Hyperglycemia and increased mortality in the pediatric intensive care. ESPNIC, Brussel. (poster)	2005	0.5
• Outcome of critically ill children treated with insulin in the pediatric intensive care. NVIC, Ede, Nederland.	2005	1.0
• Outcome of critically ill children treated with insulin in the pediatric intensive care. ESPNIC, Londen.	2004	1.0

International conferences		
EUSEM, Athens, Greece	2017	0.5
PREM, Ghent, Belgium	2017	0.5
EUSEM, Vienna, Austria	2016	0.5
EUSEM, Torino, Italy	2015	0.5
PREM, Ghent, Belgium	2015	0.5
EUSEM, Amsterdam, The Netherlands	2014	0.5
EAPS, Barcelona, Spain	2014	0.5
EAP, Lyon, France	2013	0.5
EAPS, Istanbul, Turkey	2012	0.5
EUSEM, Antalya, Turkey	2012	0.5
ESPID, The Hague, The Netherlands	2012	2.0

Teaching		
• Peer review of manuscripts for international scientific journals	2015-2017	3.0
• Supervising master's thesis	2012-2016	3.0
• Nascholing kinderartsen PAO-K	2011, 2014,	1.0
• Voordracht PAO-H Utrecht 'Vroege alarmsymptomen van kinderen met meningitis.'	2017 2012	0.5
• Voordracht jaarlijks congres Nederlandse Vereniging voor Spoedeisende Hulp Verpleegkundigen ' Vroege symptomen van ernstige infectie bij kinderen.'	2012	

ECTS European Credit Transfer and Accumulation System

1 ECTS = 28 hours