
improvements
of
PAEDIATRIC TRIAGE
at the
EMERGENCY DEPARTMENT
N. SEIGER

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COLOFON
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Improvements of Paediatric Triage at the Emergency Department

Verbeteringen van triage bij kinderen op de spoedeisende hulp

Proefschrift

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CHAPTER 1

Introduction, aims and outline

INTRODUCTION

The practice of triage, originated from the French word "trier" which means to sort, was conceived around 1792 by Baron Dominique-Jean Larrey, Surgeon in Chief to Napoleon's Imperial Gard.[1] In these days, triage was used to identify soldiers whose injuries were readily treatable in order to return them to battlefield at the earliest opportunity.[2] In 1846, the British naval surgeon John Wilson was the first who argued that treatment should be given first to patients who need immediate and potentially successful treatment.[3]
During World War I, the introduction of new weapons created an unprecedented number of potentially treatable mass casualties.[3] This led to a wide introduction of the term "triage" and to a new definition of its concept, in which triage was not only aimed at sorting treatable patients from untreatable patients, but also took into account the complexity of treatable patients in order to save as much patients as possible.[3]
Nowadays, triage aims to prioritise patients according to their medical presentation in situations with modest scarcity of health care resources. This scarcity of resources is not only present at the military battlefield or in case of mass casualties and disasters, but can also occur at the emergency department (ED) or in the hospital settings with limited numbers of beds such as the intensive care unit. Although all these settings have distinguishing features, each requires the presence of a trained health care worker ("triage nurse") to assess the patient's medical needs, and an established system or plan to determine patient's priority.[3]

At the ED, the most commonly used triage systems are the Australasian Triage Scale (ATS)[4], the Canadian Triage and Acuity Scale[5] (CTAS), the Emergency Severity Index (ESI)[6], and the Manchester Triage System (MTS)[7]. All triage systems allocate patients to one out of five urgency categories, i.e. the time frame in which they should be seen by a physician. The triage assessment should be conducted by emergency care nurses who fulfilled a training programme offered by the authors of the triage systems.
The ATS, formally known as the National Triage Scale, was developed in 1993 and is widely used in Australia. Nurses select an algorithm based on patient's presenting signs and symptoms or suspected diagnosis. Each algorithm consists of several clinical descriptors which, if present, determine the urgency category of the patient.[4] The final urgency category represents a waiting time up to 120 minutes.
The original CTAS was first published in 1998[8] and in 2001, a separate paediatric version, the pedCTAS, was published for children younger than 17 years. In both versions of the CTAS, nurses classify patients' presenting problems into one out of 17 subgroups: substantial abuse, mental health and psychosocial, neurological, ophthalmology, ENT – nose, ENT – ears, ENT – other, cardiovascular, gastrointestinal, obstetrics/gynaecology, genitourinary, orthopaedic, trauma, environmental, skin, and general and minor. Each subgroup consists of several presenting complaints which are grouped into an urgency classification table. Nurses select the complaint comparable to the patient's presenting signs and symptoms to determine the appropriate urgency category. The urgency categories represent waiting times up to 120 minutes.[5] The CTAS has become a mandatory practice in Canadian EDs.[8]
The ESI was introduced at the ED in 1999 and is widely used to triage paediatric and adult patients in the United States of America. The triage system uses one algorithm. The highest urgency categories (levels I and II) are allocated to patients with abnormal vital signs, patients in need for life-saving interventions, patients in high-risk situations, or patients with severe pain or distress. The lowest urgency levels (levels III, IV, and V) are allocated based on the

number of expected resources .[9]
The MTS, introduced in the United Kingdom in 1997, is commonly used in European EDs to classify paediatric and adult patients.[7] Patients are allocated to an urgency category by one of the 52 presentational flowcharts, which incorporate the range of patient's presenting problems at EDs without making any assumptions about diagnosis. All flowcharts include additional signs and symptoms (discriminators) ranked by priority. During the triage process, nurses gather this information from top to bottom until one of the discriminators is present. This positive discriminator stops the triage process and assigns to the patient the corresponding triage category.
Figure 1 shows the flowcharts "Worried parent" and "Diarrhoea and vomiting". As illustrated in these flowcharts, several general discriminators exist for patients with different presenting symptoms such as the discriminators airway compromise, shock, or hot child. These general discriminators are present in most of the flowcharts and always allocate patients to the same urgency level, irrespective of their presenting complaint. The MTS urgency categories are 1) Immediate: immediate evaluation by a physician; 2) Very urgent: evaluation within 10 minutes; 3) Urgent: evaluation within one hour; 4) Standard: evaluation within two hours; 5) Non-urgent: evaluation within four hours.

It is important to evaluate the performance of triage systems, because all triage systems are developed by expert opinion. Evaluation of triage systems can be made by using methodologies of diagnostic research.[10] This involves technical accuracy (reliability), diagnostic accuracy (validity), impact on patient outcome, and cost-effectiveness.[11]
Reliability is the ability to obtain the same result on repeated testing (reproducibility).[11] The reliability of triage systems has been evaluated in both adult and paediatric patients by written case scenarios and by simultaneous triage.[12-14] The reliability of the CTAS, ESI and MTS was moderate to good and seemed slightly better than that of the ATS in both adult and paediatric patients.[12-14]
Validity of a triage system is the ability of to correctly detect patients who need immediate care and the patients who can safely wait. To date, different approaches have been used to assess the validity of triage systems. Most often, surrogate markers for patient's acuity have been used, such as hospitalisation, ICU admission, resource use, length of stay, or outcome in specific subgroups.[14] However, these surrogate markers can only be used to assess associations with the allocated triage category, but cannot be used to modify triage systems.

To improve research in the field of triage, a multi-level reference standard as proxy for patients' true urgency was needed.[10] In 2006, an independent reference standard was developed to assess the validity of the MTS in paediatric emergency care.[15, 16] This reference standard was based on abnormal vital signs, potential life-threatening working diagnosis, resource utilization, hospitalisation, and follow-up.[15, 16] The introduction of this reference standard enabled a direct comparison between MTS urgency categories and categories of the reference standard for each individual child presenting at the ED. A first study on the validity of the MTS in 17 600 children showed a moderate validity of the MTS proving that there is room for improvements of the MTS in paediatric emergency care.[16]

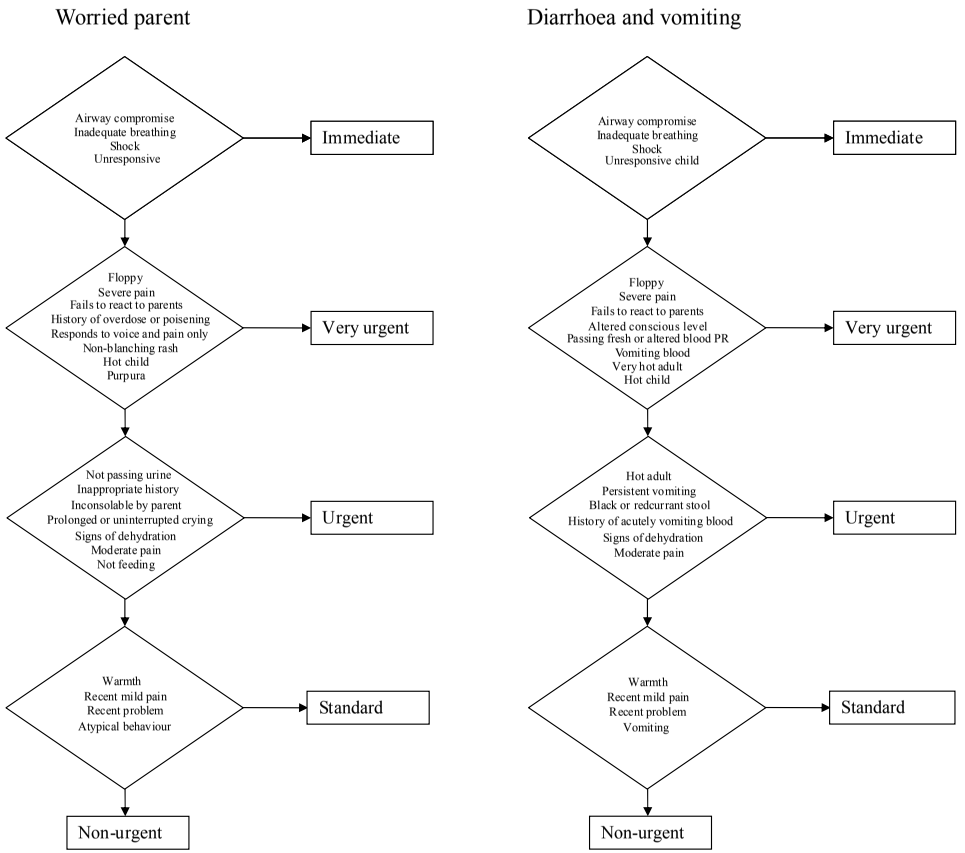


FIGURE 1: The flowcharts "worried parent" and "diarrhoea and vomiting" of the Manchester Triage System
Reprinted with permission from Blackwell Publishing Ltd (Mackway-Jones K, Manchester Triage Group. Emergency Triage, 2nd edition. London: BMJ Publishing Group; 2006).

The overall aim of this thesis was to improve triage for paediatric patients at the emergency department.

AIMS

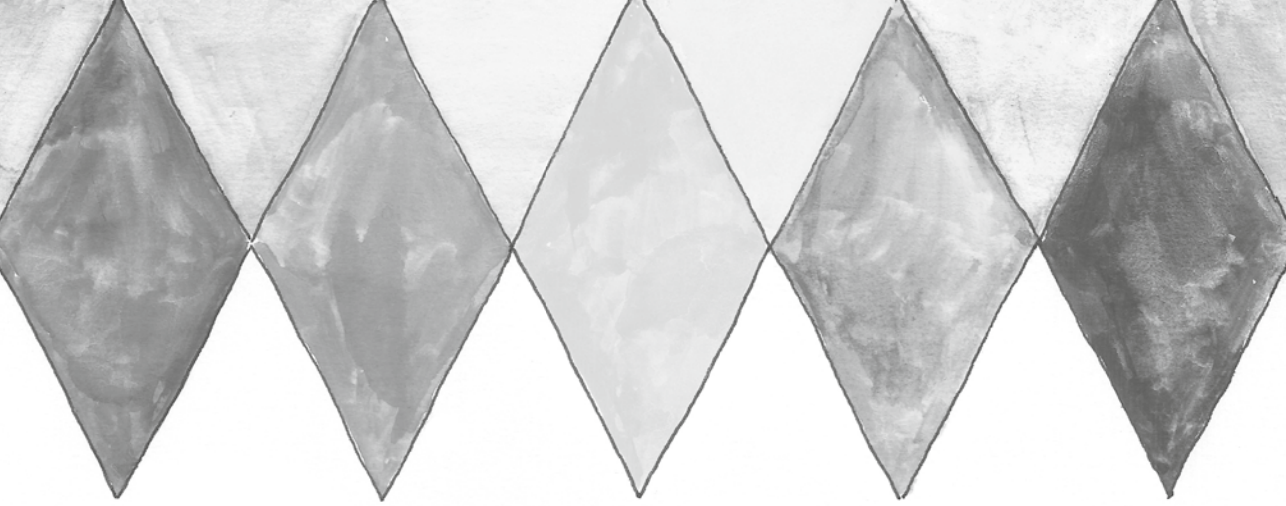
1. To identify children at risk of severe undertriage by the Manchester Triage System and to assess the clinical severity of this undertriage.
2. To improve the MTS by developing and validating modifications of the MTS for children.
3. To evaluate and provide tools that support the assessment of children's severity of illness at the ED.

OUTLINE

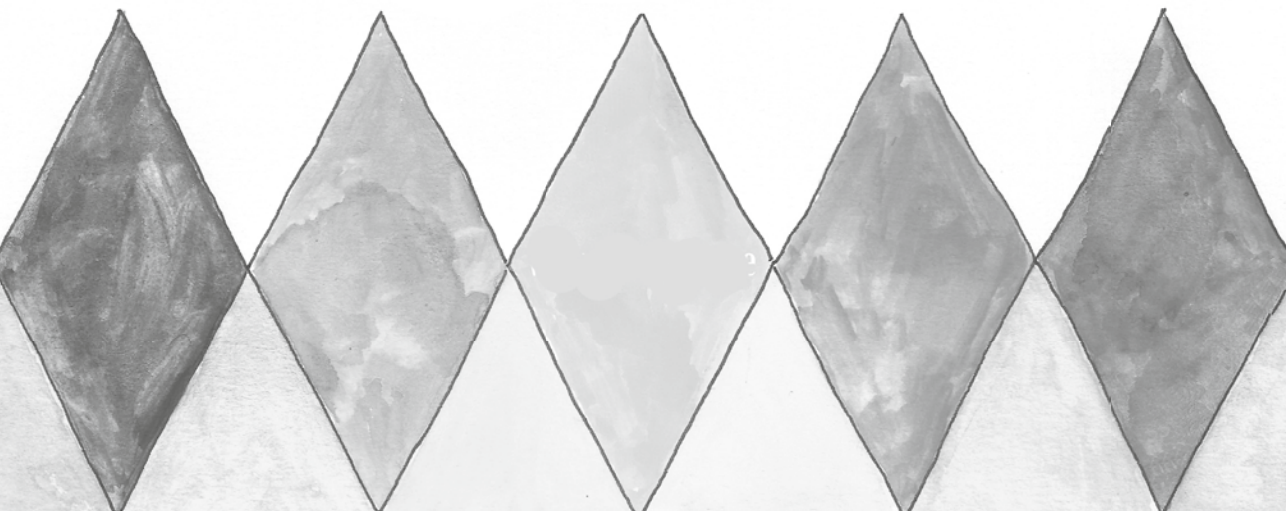
Following the general introduction in **Chapter 1**, part I of this thesis investigates opportunities to develop modifications of the MTS for paediatric emergency care. This starts is **Chapter 2**, in which the clinical severity and determinants of undertriage are assessed in severely undertriaged children. **Chapter 3** explores the need for a neonatal flowchart by comparing the use and validity of the MTS in neonates and older children. In **Chapter 4** and **Chapter 5**, the influences of referral type (chapter 4) and chronic illness (chapter 5) on patient's acuity are investigated for children presenting with infectious symptoms. **Chapter 6** shows the broad external validation of a modified version of the MTS in four different EDs in three European countries. **Chapter 7** focuses on improvement of the MTS by altering the urgency levels of some discriminators in combination with patient characteristics by using machine learning approaches.

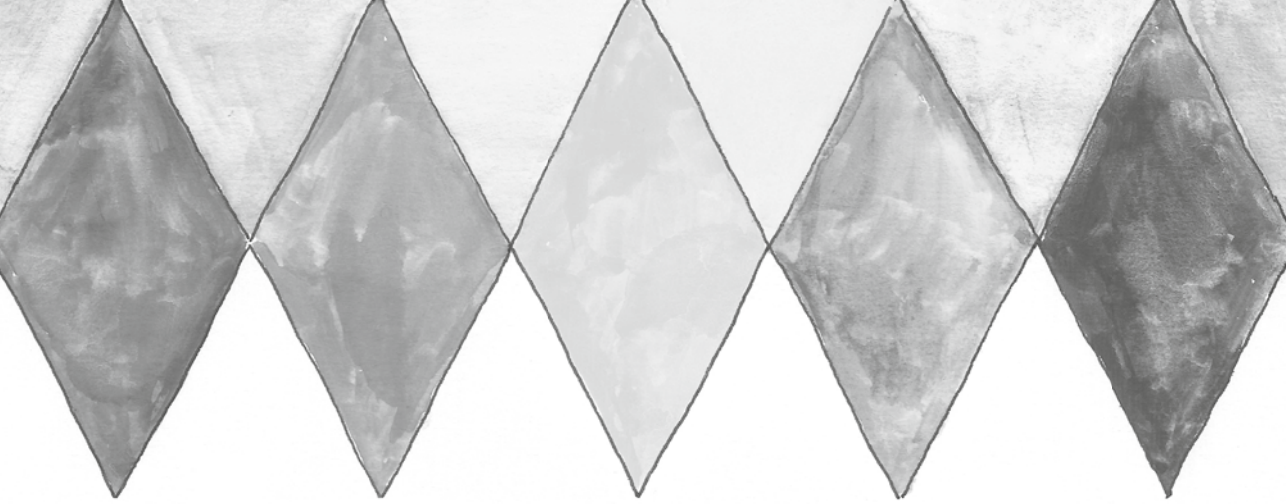
Part II of this thesis focuses on tools to assess patient's severity of illness at the ED. In **Chapter 8**, we analyse if alarming signs for serious illness available in the MTS can predict hospitalisation in febrile children. In **Chapter 9**, we derive heart rate and respiratory rate centile charts for children, which are corrected for age and Manchester pain scores, to improve patient's assessment of vital signs. **Chapter 10** explores if a physiology-based scoring systems (paediatric early warning scores) can be used to predict ICU admission and hospitalisation in paediatric patients at the emergency department.

C**hapter 11** summarizes the results and **Chapter 12** provides a general discussion based on the different studies. Recommendations and implications for future research are presented.

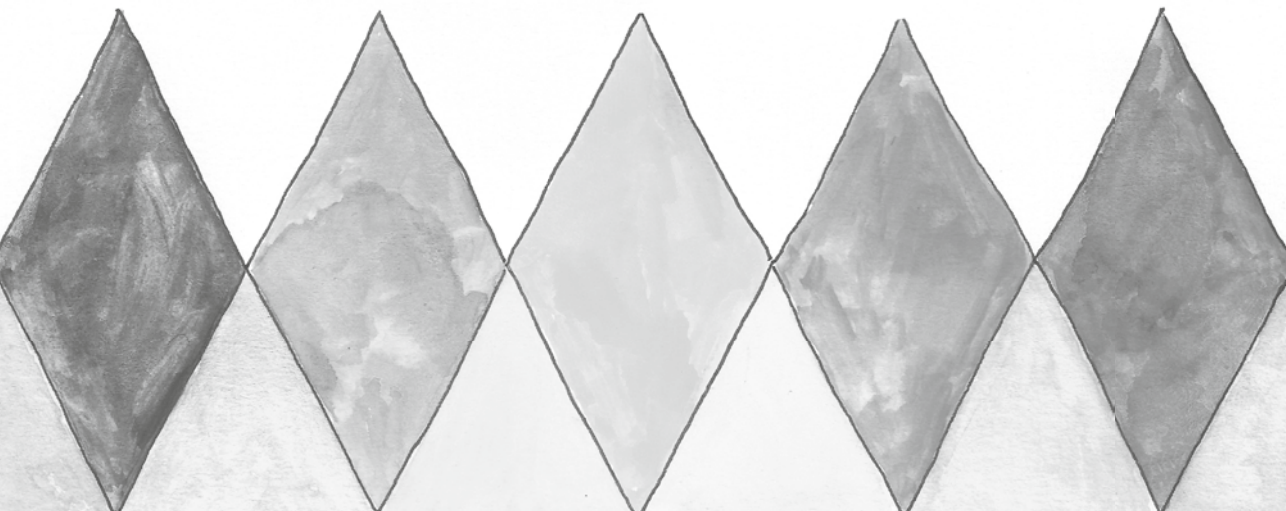


PART I





Improvements of the Manchester Triage System for paediatric care



CHAPTER 2

Undertriage in the Manchester Triage System: An assessment of severity and options for improvements

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ABSTRACT

Background The Manchester Triage System (MTS) determines an inappropriately low level of urgency (undertriage) to a minority of children. The aim of the study was to assess the clinical severity of undertriaged patients in the MTS and to define the determinants of undertriage.

Methods Patients who had attended the emergency department (ED) were triaged according to the MTS., Undertriage was defined as a 'low urgent' classification (levels 3, 4 and 5) under the MTS; as a 'high urgent' classification (levels 1 and 2) under an independent reference standard based on abnormal vital signs (level 1), potentially life-threatening conditions (level 2), and a combination of resource use, hospitalisation, and follow-up for the three lowest urgency levels. In an expert meeting, three experienced paediatricians used a standardised format to determine the clinical severity. The clinical severity had been expressed by possible consequences of treatment delay caused by undertriage, such as the use of more interventions and diagnostics, longer hospitalisation, complications, morbidity, and mortality. In a prospective observational study we used logistic regression analysis to assess predictors for undertriage.

Results In total, 0.9% (119/13,408) of the patients were undertriaged. In 53% (63/119) of these patients, experts considered undertriage as clinically severe. In 89% (56/63) of these patients the high reference urgency was determined on the basis of abnormal vital signs. The prospective observational study showed undertriage was more likely in infants (especially those younger than three months), and in children assigned to the MTS 'unwell child' flowchart (adjusted $OR_{<3\ months}$ 4.2, 95% CI 2.3 to 7.7 and adjusted $OR_{unwell\ child}$ 11.1, 95% CI 5.5 to 22.3).

Conclusions Undertriage is infrequent, but can have serious clinical consequences. To reduce significant undertriage, the authors recommend a systematic assessment of vital signs in all children.

BACKGROUND

Emergency departments (EDs) need triage systems to prioritise patients.[17] The Manchester triage system (MTS) is a five-level triage system that allocates a clinical priority to adult and paediatric patients.[7, 18] It was introduced in the UK in 1996 and its translated versions have been adapted and are currently used around the world.[7] The MTS applies 52 flowcharts which represent presenting complaints such as 'worried parent', 'limping child' and 'shortness of breath in children'. Each flowchart contains general as well as problem specific signs and symptoms (discriminators) that discriminate between the different urgency categories. The selection of a discriminator allocates the patient to one of five urgency levels, each indicating the maximum time a patient should wait before seeing a physician.[7, 18] Patients allocated to urgency level 'immediate' demand immediate medical evaluation, 'very urgent' need evaluation within 10 min, 'urgent' within 60 min, 'standard' within 120 min and 'non-urgent' patients can wait for up to 240 min prior to clinical assessment.

Earlier studies on the validity of the MTS calculated the sensitivity by detecting highly urgent cases or patients with specific conditions.[19-22] In a previous study conducted in a paediatric setting, the authors expressed sensitivity and specificity of the MTS as the capacity to distinguish between high (levels 1 and 2) and low urgency (levels 3, 4 and 5) defined by an independent five-level reference standard.[16] The sensitivity of the MTS to detect highly urgent children was 63% and the specificity 79%. The agreement with the reference standard was 34%, with overtriage in 54% and undertriage in 12% (mostly by one category).[16] Although overtriage can cause increased waiting times for truly urgent patients because of overcrowding, there is no direct harm for the overtriaged patient.[23] To date, no study has been performed examining the consequences of undertriage for patients who had attended EDs, but it is expected that undertriage might increase morbidity and mortality.[24, 25] Therefore this study focuses on the possible consequences of undertriage and how to reduce these in clinical practice. The aim is to assess clinical severity of undertriage by expert opinion and to define determinants for undertriage in paediatric patients at the ED in a large observational study.

METHODS

Study design

This study contained two parts, an expert opinion (case study) and a prospective observational study.

In the first part, experienced experts discussed the possible impact of treatment delay in undertriaged cases to determine the clinical severity.

In the second part, a logistic regression analysis was performed in a large prospective cohort to define determinants of undertriage. The study was approved by the institutional medical ethical committee; the requirement for informed consent was waived.

Setting and selection of participants

The Erasmus MC–Sophia Children's Hospital in Rotterdam, The Netherlands is a university, inner-city hospital with a specific paediatric ED that receives 9 000 patient visits a year. The MTS was implemented in 2005. The Haga Hospital–Juliana Children's Hospital in The Hague is a general teaching hospital with approximately 30 000 patient visits a year of which 15 000 are paediatric visits. In the Haga Hospital, the MTS was implemented in 2003. Both hospitals are comparable when it comes to availability of diagnostic resources and specialties

and they have the same opening hours (24 h).
We included children aged 0–16 who had attended the ED at Haga Hospital–Juliana Children's Hospital between 1 January 2006 and 1 August 2006 and the ED at Erasmus MC–Sophia Children's Hospital between 1 January 2006 and 1 February 2007. Trained nurses experienced in both paediatric nursing and ED nursing (median experience 10 years (IQR 7–14 years)) triaged the patients with the official Dutch translation of the first edition of the MTS.[18]

Reference standard
Prior to the study, a reference standard was defined on the basis of the literature and expert opinion.[15, 16] The reference standard consisted of five urgency levels, which estimate patients' true urgency. Patients were considered to be level 1 if their vital signs (heart rate, blood pressure, pulse oximetry and respiratory rate) were abnormal according to the Paediatric Risk of Mortality III (PRISM III) score (see table 1)[26] or in cases of hyperpyrexia (temperature >41°C) or altered level of consciousness. If vital signs were not recorded, they were assumed to be normal.

TABLE 1: Vital signs, normal values according to PRISM III

AGE	RESPIRATORY RATE (bpm)	SYSTOLIC BP (mmHG)	HEART RATE (bpm)
< 1 month	15-90	55-160	80-215
1-11 months	15-90	65-160	60-215
1-11 years	10-70	75-200	45-185
>12 years	10-70	85-200	40-145

Heart rhythm: arrhythmia; respiration pattern: inspiratory stridor, respiratory insufficiency
Temperature: ≤33°C or >41°C
Oxygen saturation: absolute percentage, cut-off=<90%
Level of consciousness: decreased, convulsive at arrival, coma
PRISM, Paediatric Risk of Mortality

Level 2 was allocated to patients with normal vital signs, but potentially life-threatening conditions diagnosed by the paediatrician at the end of the ED visit. Most of these conditions are described in the Advanced Paediatric Life Support workbook as emergent conditions.[27] In a systematic review, it was suggested that children with an apparent life-threatening event (ALTE) be monitored for 24 h. An ALTE is defined as an episode characterised by the combination of apnoea, colour change, marked change in muscle tone, choking, or gagging. Therefore ALTE was added as a level 2 condition to the reference standard.[28]
Patients were allocated to levels 3 or 4 depending on the combination of diagnostic and therapeutic resource use, hospitalization and if a follow-up visit was scheduled. Resource use was associated with the urgency levels of the Emergency Severity Index.[29] Category 5 was assigned if no resources were required. A classification matrix of the reference standard and detailed definitions of the reference urgencies have been published before.[15, 16] The reference standard was allocated independently of the MTS by using a computerised application of the classification matrix.

Undertriage
Undertriage was defined as a 'low urgent' classification (levels 3, 4 and 5) under the MTS; as a 'high urgent' classification (levels 1 and 2) under the reference standard; or at least a difference of two urgency levels between the MTS level and the reference urgency level. In the event of undertriaged cases presenting with similar problems (MTS flowchart and

discriminator, and reference urgency classification) and within similar age categories, one case was randomly selected as a representative case for the expert meeting.

Expert meeting

Three paediatricians evaluated the undertriaged cases at a meeting using anonymous ED forms. The ED forms included information on the assigned MTS and reference urgency levels and clinical notes about presenting symptom(s), history, physical examination, working diagnosis, therapy, diagnostics and suggested follow-up.

First, the experts scored the clinical severity of undertriage on a scale from 0 to 10. Zero represented 'the absolute minimum severity' and 10 'the maximum severity of undertriage'. Second, the experts evaluated the possible clinical consequences of undertriage by using a six-item questionnaire. For each case the experts assessed the probability of more interventions or diagnostics, a longer duration of hospitalisation, complications, and long-term morbidity and mortality because of treatment delay when the MTS protocol was followed instead of maximum waiting times assigned by the reference standard. The questionnaire was designed in a 'yes and no' format.

The experts had been working as paediatricians for at least 15 years and had clinical experience in emergency medicine. They were working at the Erasmus MC–Sophia Children's Hospital and the Haga Hospital–Juliana Children's Hospital at the time of the study.

Data collection

The study used a computerised version of the official Dutch translation of the MTS.[16] Data were collected on patients' characteristics, the selected flowcharts/discriminators and the MTS urgency levels.

Nurses and physicians used structured electronic and paper ED forms and they recorded data on vital signs measured directly after triage, diagnosis, diagnostic resources, therapeutic intervention and follow-up. Trained medical students entered these data in a separate database independently of triage outcome by using SPSS Data entry version 4. The data were checked for inconsistencies and outliers. Data on laboratory tests were obtained from the hospital information system.

Data analysis

The study assumed that the experts would have scored similar cases in an equal manner. The results of the discussed cases were therefore multiplied by the number of similar cases.

Undertriage was defined as severe if the experts' severity score was high (≥7) or if the patient could experience at least one consequence of undertriage. A univariate and multivariable logistic regression analysis was subsequently performed to define determinants for undertriage.

Age, gender and frequently assigned MTS flowcharts specific to the patient's presenting problem were considered as possible determinants of undertriage. Because the relation between age and risk of undertriage was non-linear, age was categorised as younger than 3 months, 3–11 months, 1–4 years, 4–8 years, and older than 8 years. SPSS version 15.0 was used for statistical analysis.

RESULTS

Undertriage

In total, 17600 children attended the EDs. Complete data of MTS triage and reference

standard were available for 13408 children. Two per cent (189/9582) of the children triaged as 'urgent', 'standard' or 'non-urgent' according to the MTS were assigned to reference urgency levels 1 or 2.
In 37% (70/189) the difference between the MTS level and the reference urgency level was only one level. In total, 0.9% (119) undertriaged cases remained for analysis (figure 1). If patients had similar medical problems, one was randomly selected for evaluation in the expert meeting. This resulted in 20 cases for discussion by the expert panel.

Clinical severity of undertriage
Table 2 shows the items discussed by the experts. Undertriage was considered severe in 53% (63/119) of the undertriaged patients, and 89% (56/63) of these severely undertriaged patients had a high reference urgency level because of abnormal vital signs (heart rate, blood pressure, pulse oximetry, respiratory rate).
According to the experts, 50% (60/119) of the undertriaged patients could potentially have experienced at least one consequence of undertriage; 45% (54/119) might have undergone more interventions; 40% (48/119) might have experienced more diagnostic investigations because of treatment delay; 34% (40/119) would have been likely to have complications; 6% (7/119) might have been hospitalised for longer; 11% (13/119) might have experienced long-term morbidity; and 3% (3/119) might have died because of treatment delay caused by undertriage. Fifty-one of the undertriaged patients had an ALTE. All these patients were considered non-severe by the experts (severity score 1 and no consequences caused by undertriage).

Determinants of undertriage
The patients assigned to the MTS 'unwell child' flowchart had an increased OR of 10.7 (95% CI 5.4 to 20.9) for undertriage when compared with patients assigned to the MTS 'general' flowchart (Table 3). This $OR_{unwell\ child}$ was adjusted for age in a multivariate analysis. This raised the adjusted $OR_{unwell\ child}$ to 11.1 (95% CI 5.5 to 22.3).
Infants (≤12 months) were at higher risk of undertriage than children aged 8–16 years ($OR_{<3\ months}$ 9.6, 95% CI 5.6 to 16.7 and $OR_{3–11\ months}$ 2.6, 95% CI 1.4 to 4.9). When these ORs were adjusted for flowcharts that were frequently used in undertriaged cases, children under the age of 3 months still had a higher adjusted $OR_{<3\ months}$ of 4.2 (95% CI 2.3 to 7.7) for undertriage.

DISCUSSION
This study aimed to assess the clinical severity of treatment delay caused by undertriage and to define determinants for undertriage in paediatric patients at the ED. Undertriage was assessed by comparing the MTS with an independent reference standard. In total, 0.9% (119) of patients were undertriaged. These undertriaged cases were discussed by experts who considered 53% (63/119) as clinically severe, and that 50% (60/119) might experience at least one consequence because of undertriage. Eighty-nine per cent (56/63) of these clinically severe undertriaged patients had abnormal vital signs.
Rather than measuring abnormal vital signs, the MTS uses the following discriminators to describe their symptoms: shock, inadequate breathing, compromised airway and unresponsiveness. Because not all patients with abnormal vital signs were assigned to one of these discriminators, they were not always recognised as highly urgent patients.[16] This is consistent with Cooke and Jinks,[20] who demonstrated that misclassification in the MTS

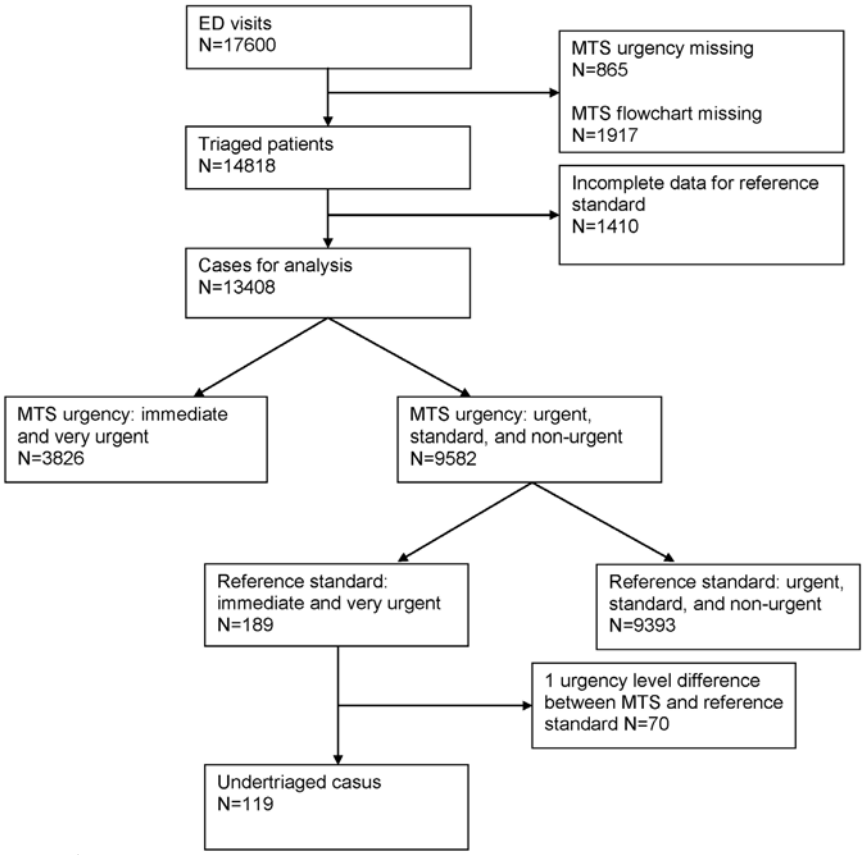

Figure 1: Population

TABLE 2: Experts' determination of the clinical severity of undertriaged patients

UNDERTRIAGED PATIENTS			ITEMS DISCUSSED BY EXPERT PANEL						
Vital sign or life-threatening condition[a]	**Undertriaged Patients**	**EP[b]**	**Severity[c]**	**More interventions[d]**	**More diagnostics[e]**	**Longer admission[e]**	**Complications[e]**	**Morbidity[e]**	**Mortality[e]**
ALTE[5]	51	4	1 (1-1)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Sepsis	5	2	1 (1-9)	2 (40%)	2 (40%)	0 (0%)	2 (50%)	2 (40%)	0 (0%)
Near drowning	3	2	0 (0-0)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Intoxication	1	1	10 (10-10)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1 (100%)	0 (0%)
Abnormal heart rate	32	4	9 (9-9)	32 (100%)	29 (91%)	3 (9%)	29 (91%)	3 (9%)	3 (9%)
Abnormal blood pressure	6	2	10 (3-10)	0 (0%)	0 (0%)	4 (67%)	4 (67%)	4 (67%)	0 (0%)
Pulse oximetry deviated	8	2	8 (5-8)	8 (100%)	5 (63%)	0 (0%)	3 (38%)	3 (38%)	0 (0%)
Abnormal respiratory rate	12	2	4 (4-4)	12 (100%)	12 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hyperpyrexia	1	1	7 (7-7)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)
Total	119	20	4 (1-9)	54 (45%)	48 (40%)	7 (6%)	40 (34%)	13 (11%)	3 (3%)

[a] Patient's characteristics determining the reference standard.
[b] Number of cases discussed by expert panel (EP)
[c] Clinical severity: median of the marks scored by experts on a scale from 1 to 10; 10 is considered as highest severity (25^{th}-75^{th} percentiles)
[d] Number of undertriaged patients who could have experienced consequences (% of undertriaged patients)
[e] ALTE, apparently life-threatening event

was due to the presence of abnormal vital signs in adults. If pulse oximetry had been part of the triage assessment, they would have been able to assign three patients with chest pain to the correct urgency level. This suggests that the MTS should include vital signs to reduce undertriage.

One of the findings of this study was relevant to the definition of the reference standard. Reference level 2 is defined by the presence of potential life-threatening conditions. One of these conditions is an ALTE. In the expert opinion study the experts agreed that increased waiting time in patients with an ALTE does not influence patients' outcome. ALTE was skipped from the list of life-threatening conditions in the reference standard (urgency level 2).

In the observational part of the study, children younger than 3 months and those assigned to the MTS 'unwell child' flowchart were shown to be more likely to be undertriaged than other patients. Although 'unwell appearance' is an important predictor for serious infections in children,[30] it is not a very sensitive and objective clinical feature.[31] Children who had been assigned to the MTS 'unwell child' flowchart could have attended the ED with a variety of problems, while the flowchart mainly focuses on children with infectious diseases based on the discriminators fever, signs of meningitis, purpura and signs of dehydration. As a result children with conditions other than infectious problems are difficult to assign to an urgency level and therefore undertriage may occur more frequently in the MTS 'unwell child' flowchart than other flowcharts.

Infants are also more difficult to allocate to urgency levels because they have non-specific signs and symptoms at presentation for several diseases, for example, fever.[32] In the revisions of the paediatric Canadian Triage and Acuity Scale, systematic assessment of level of consciousness, respiratory rate, heart rate and circulatory status were recommended for infants and young children to assist with the assessment of severity of illness.[32]

Systematic assessment of vital signs for selected groups of children (children younger than 3 months) could prevent 21% (13/63) of clinically severe undertriage and the workload would increase to 8.0% extra measurements (1072/13408 of patients). The number needed to treat (NNT) is 82 (1072/13). If we measure vital signs in the MTS 'unwell child' flowchart as well, the NNT decreases to 60 (1 200/20). Only systematic assessment of the vital signs in all children could prevent clinically severe undertriage in nearly all children (89%) (NNT 213).

Limitations

Although the value of expert opinion as evidence in biomedical research has been criticised, it remains the best available method for evaluating the consequences of undertriage for individual patients. To improve the validity of the judgement of cases, standardised questionnaires were used and paediatricians experienced in emergency medicine were selected as experts. To determine undertriage, a measure for patients' 'true' urgency was needed. The reference standard is based on patients' characteristics at ED presentation and at the end of their ED visit. Characteristics gathered at the end of consultation might be less suitable to define urgency because patients' conditions might change over time. However, assessment of true urgency requires more information than available at presentation (triage). The reference standard used in this study is the best available approximation of an ideal reference standard.[10]

Despite these limitations, the authors believe a reference standard is a reasonable best approach to determine the urgency with which particular patients should be seen and assessed.[10]

TABLE 3: Determinants of undertriage

DETERMINANTS	LOW URGENT PATIENTS[a] (N=9582)	UNDERTRIAGED CASES (N=119)	OR, UNIVARIATE OR (95% CI)	ADJUSTED OR OR (95% CI)[b]
Gender				
Male	5489	59	Reference	-
Female	4093	60	1.3 (0.9-1.9)	-
Age				
<3 months	774	47	9.6 (5.6-16.7)	4.2 (2.3-7.7)
3-11 months	1215	21	2.6 (1.4-4.9)	1.4 (0.7-2.8)
1-4 years	2903	24	1.2 (0.7-2.3)	1.0 (0.5-1.9)
4-8 years	1993	9	0.7 (0.3-1.5)	0.7 (0.3-1.7)
8-16 years	2697	18	Reference	Reference
Flowchart				
Diarrhoea and vomiting	1109	17	0.6 (0.3-1.2)	0.7 (0.4-1.4)
General	827	20	Reference	Reference
Headache	139	3	0.9 (0.3-3.0)	1.5 (0.4-5.2)
Shortness of breath	808	20	1.0 (0.6-1.9)	1.2 (0.6-2.3)
Unwell child	91	19	10.7 (5.4-20.9)	11.1 (5.5-22.3)
Worried parent	744	32	1.8 (1.0-3.2)	1.6 (0.9-2.9)
Other	5864	8	-	-

[a] Urgent, standard and non-urgent according to the Manchester triage system.
[b] Adjusted for age or flowchart, respectively.

CONCLUSIONS

Although serious undertriage in the MTS occurs in very small numbers of patients (approximately 1%), the experts believed that it could have serious consequences. To reduce significant undertriage, the authors recommend a systematic assessment of vital signs in all children.

CHAPTER 3

Does the Manchester Triage Sytem need a neonatal flowchart?

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ABSTRACT

Introduction The Manchester Triage System (MTS) is a five-level triage system developed to allocate urgency at the emergency department (ED). Of the 52 MTS flowcharts, 49 are suitable for children. However, there is no specific flowchart for neonates, while these children attend the emergency department with different presenting complaints to those seen in older children and mortality rates are higher in the first month of life. For this reason, the aim of this study was to explore the need of a neonatal flowchart in the MTS.

Methods This multicentre retrospective observational study, included children (<16 years) presented at four European paediatric EDs between 2006 and 2010. Descriptive statistics of the neonatal population (<1 month) and risk ratios (RR) were calculated to quantify the use of the general triage items. The validity of MTS in the neonatal population, determined by hospitalization, was compared with the validity of MTS in older children.

Results Neonates accounted for 2.7% of ED patients and were more often assigned to general MTS flowcharts (RR2.6, 95%CI2.5-2.7). Positive LRs of the overall MTS were 3.6 (95%CI3.0-4.4) for neonates and 2.7 (95%CI2.7-2.8) for older children. Negative LR and DORs were not statistically significant different. The validity of the general flowcharts was better for neonates (DOR6.9 (4.7-10.0) than for older children (DOR2.2 (2.0-2.5)).

Conclusion The number of neonates at the ED was considerable and neonates were more frequently triaged by general triage items. The validity of MTS for neonates was comparable with those of older children.

INTRODUCTION

The Manchester Triage System (MTS) is a five-level triage system developed to allocate the urgency and related to the maximum waiting time for patients' assessment at the ED.[18] Urgency is determined by a flowchart which represents the presenting problem, e.g. shortness of breath in children and a series of clinical indicators of acuity of illness. These clinical indicators are known as discriminators. The discriminators assign the triage urgency category, i.e. the time frame in which they should be seen. In the MTS, there are 52 flowcharts of which 49 are suitable for children.[7, 18] Figure 1, shows the flowcharts for 'abdominal pain in children'. Nurses start at the top of the flowchart until one of the discriminators is positive. This stops the triage process and assigns the triage urgency category.

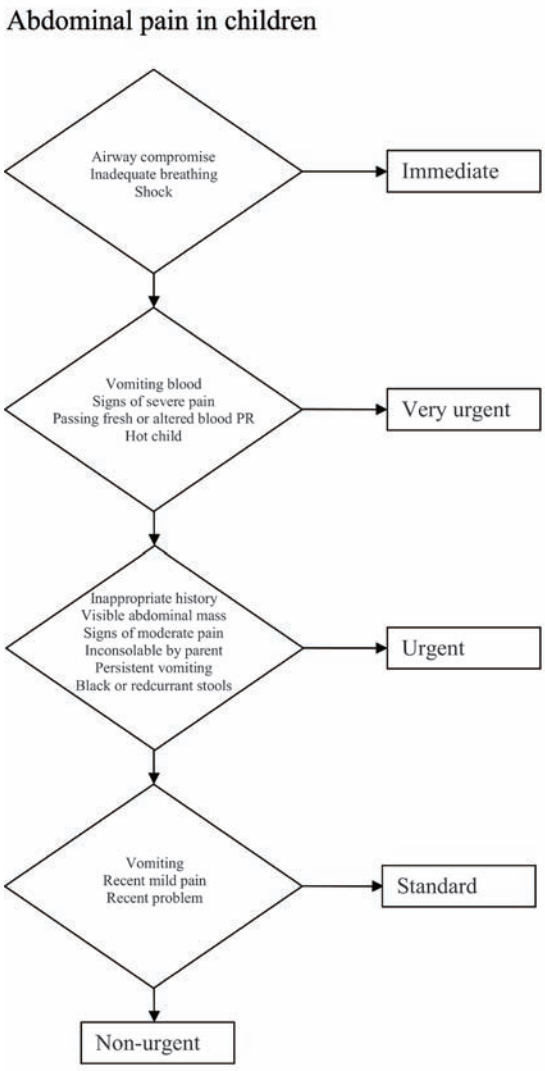

FIGURE 1: Flowchart 'Abdominal pain in children'

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Although neonates present the ED with different presenting (non-specific) complaints to those seen in older children[27], there is no specific flowchart for neonates. Moreover, neonates are often more severely ill than older children, since mortality rates are higher in the first month of life mainly due to immaturity and congenital abnormalities.[27] Triage nurses experience difficulties in allocating a triage category to neonates because of these possibly non-specific complaints and the tendency not to undertriage these young children.
Therefore, the aim of this study was to explore in a multicentre observational study if a neonatal flowchart was needed to improve the MTS. A neonatal flowchart should only be created if 1) the numbers of neonates presenting to ED are substantial; 2) the flowcharts and discriminators available in the MTS are insufficient to allocate a triage category; and 3) the validity of the MTS in neonates was low.

METHODS

Study design

In this multicentre retrospective observational study, we compared the use of the MTS in neonates (children younger than 1 month) with those in older children in order to explore the need of a neonatal flowchart. The criteria for creating a new flowchart was based on three items: 1) a substantial proportion of neonates; 2) the use of general triage criteria as proxy for difficulties to allocate a triage category; and 3) the validity of the MTS for neonates. The validity of the MTS was determined by hospitalisation and an independent reference standard based on abnormal vital signs, life-threatening working diagnosis, and a combination of therapeutic and diagnostic resource use and follow-up.[16] The datasets were partly used before for studies to the validity of the MTS.[16, 33, 34] This study was approved by the institutional medical ethical committees of the hospitals; the requirement for informed consent was waived.

Settings and participants

All children younger than 16 years who presented at the ED of Erasmus MC-Sophia Children's Hospital in Rotterdam between January 2006 and December 2010; at the ED of Haga Hospital-Juliana Children's Hospital in The Hague between January and April 2006 or between August and December 2007; at the ED St Mary's Hospital in London between June and November 2010; or at the ED of Fernando Fonseca Hospital in Lisbon between November and December 2010, were included.
Erasmus MC-Sophia Children's Hospital in Rotterdam, the Netherlands is an inner-city university hospital. The paediatric ED receives approximately 9000 children annually and is open 24 hours a day.
The Haga Hospital-Juliana Children's Hospital in The Hague, the Netherlands is a general teaching hospital in and its mixed adult-paediatric ED is open 24 hours a day and receives approximately 30000 patient-visits per year, of whom 18000 are paediatric patients.
The St. Mary's Hospital in London, UK is a general teaching hospital in North West London. The paediatric emergency department sees 26000 children a year and is open 24 hours a day.
The Fernando Fonseca Hospital in Lisbon, Portugal is an inner-city university hospital and its paediatric ED receives nearly 60000 children per year.
Patients were triaged with the MTS first edition.[18] In the Dutch and Portuguese hospitals a translation of this first edition was used.

Definitions

Neonates were defined as children younger than 1 month.

The proportion of neonates was considered substantial if the proportion of neonates was ≥1.7% of the total population. This cut-off level was chosen, because this percentage represents the number of children assigned to the tenth most frequently used flowchart in an earlier study on validity of the MTS in children.[16]

Difficulties in allocating a triage category due to insufficient flowcharts and discriminators was defined by the use of 'general' flowcharts and 'general' discriminators, since these flowcharts and discriminators tend to be used when the triaging nurses find difficulty in applying specific flowcharts and/or discriminators for the presenting complaints. General flowcharts were defined as the MTS flowcharts "worried parents" and "unwell child". General discriminators were defined as MTS discriminators "recent problem", "recent injury" and "no criteria", which all allocate patients to "standard" or "non-urgent".

We considered the validity of the MTS in neonates low, if likelihood ratios and/or diagnostic odds ratios were significantly lower than those of older children.

Outcome measures

Hospitalisation was used as outcome measure in all four settings to validate the MTS. Criteria for hospitalisation were abnormal or threatened vital signs; monitoring of vital signs when deterioration of patient's condition can be expected ; requirement of intravenous medication or fluids; inability to ingest prescribed medication or fluids (e.g. need for nasogastric tube); or requirements for surgery.

Another outcome measure was an independent reference standard developed as a proxy for true urgency.[16] This reference standard consists of five urgency levels ranging from one 'immediate' to five 'non-urgent'. The levels were defined by 1) 'immediate', abnormal vital signs according to the Paediatric Risk of Mortality Score version 3 (PRISM III)[26]; 2) 'very urgent', a working diagnosis of a life-threatening condition such as meningitis, sepsis, high energetic trauma, substantial blood loss, aorta dissection, >10% dehydration, (near)drowning, electric trauma, possible dangerous intoxication, >10% burns, and facial burns or possible inhalation trauma; 3 and 4) 'urgent' and 'standard, a combination of resource use at the ED, hospitalization, and follow-up (See appendix 1); 5) 'non-urgent', discharge without a planned follow-up visit and no diagnostics or treatment at the ED.

Data collection

Data on MTS triage categories and the allocated flowchart was collected from computerized systems of the MTS by trained triage nurses, experienced in both paediatric and emergency care.[18] The positive discriminator, which determines the MTS triage category, was only collected in the hospitals in the Netherlands and in the Fernando Fonseca hospital.

Data on the reference standard was collected in the Dutch Hospitals, because structured paper (2006-2009) and electronic (2009-2010) ED templates on vital signs values, resource use, and follow-up were only available in these hospitals. Trained medical students gathered and entered the data of the paper templates on a separate database, independent of the triage outcome, using SSPS data entry version 4.

Data analysis

The proportion of neonates was calculated as percentage of the total paediatric ED population. Descriptive statistics and risk ratios (RR) were used to quantify the use of the general triage

items as compared with specific triage items.
To assess the validity of the MTS in neonates, positive and negative likelihood ratios (LRs), and diagnostic odds ratios (DORs) were calculated for hospitalisation and for 'high urgency' defined as the levels 'immediate' and 'very urgent' of the independent reference standard. Positive likelihood ratios summarises how many times more likely patients are hospitalised or are classified as 'high urgent' when they are triaged as 'immediate' or 'very urgent' by the MTS. Negative likelihood ratios summarises how many times less likely patients are hospitalised or classified as 'high urgent' when they are triaged as 'urgent', 'standard' or 'non-urgent' by the MTS.[35]
The DOR combines the positive likelihood ratio and the negative likelihood ratio (positive likelihood ratio/negative likelihood ratio) and is an overall measure of test performance.[36]
All analyses were performed using SPSS software (version 17.0, SPSS, IL).

RESULTS

Settings and participants

69038 children under the age of sixteen years presented to one of the EDs, 2.7% (N=1873) were neonates. The proportion of neonates per hospital was 2.7% (N=889/32365) in Sophia Children's Hospital; 3.5% (N=581/16488) in Haga Hospital-Juliana Children's Hospital; 3.2% (N=276/8759) in St. Mary's Hospital; and 1.1% (N=127/11426) in Fernando Fonseca hospital.

MTS urgency, flowcharts, and discriminators allocated to neonatal patients

The distribution of triage categories was comparable for neonates and older children. (See table 1)
MTS flowcharts were available for 92% (N=63533) of patients. Fifty percent of neonatal patients were allocated to general flowcharts compared with 20% of older children. (RR 2.6, 95%CI 2.5-2.7)
The positive discriminator was available for 91% (N=54656) of children attending the EDs of the Dutch hospitals or the ED of Fernando Fonseca Hospital (Total population is 60279 children, of whom 1597 neonates and 58682 older children). Neonates were more often assigned to general discriminators than older children. (RR 1.5, 95% CI 1.5-1.7) Moreover, twenty-eight percent of all neonates (N=395/1425) were assigned to both a general flowchart as well as a general discriminator compared with eight percent of children of older age.

Validity of the MTS in neonates

Thirty-six percent of neonates (N=669) were hospitalised compared with 13% of older children (N=8977).
The reference standard was available for 46268 children (95%) attending the ED of the Dutch hospitals (N=48853). The distribution of the reference categories for neonates and older children are presented in Figure 2.
When hospitalisation was used as outcome measure, the positive LR of the overall MTS in neonates was 3.6 (95%CI 3.0-4.4) and the positive LR of the MTS in older children was 2.7 (95%CI 2.7-2.8). The negative likelihood ratio and the DOR were not significantly different in neonates compared with older children. These results were similar to when the reference standard was used as outcome measure (positive $LR_{neonates}$ 4.9 (95%CI 4.1-5.8) versus positive $LR_{older\ children}$ 3.7 (95%CI 3.6-3.9)). (See table 2)
Moreover, general flowcharts performed better in neonates than in older children. This was

statistically significant for the positive LR and the DOR in both outcome measures. (See table 2) For specific flowcharts, the results showed no statistically significant differences between the two age groups.

Neonates assigned to both a general flowchart and a general discriminator (N=395) were at risk of being undertriaged. When the reference standard was used, 32% of neonates assigned to both a general flowchart and a general discriminator were undertriaged compared with 12% of neonates

assigned to a specific flowchart and specific discriminator. (Figure 3) Neonatal problems like apparent life threatening events (ALTE), jaundice, upper respiratory tract infection by Respiratory Synctycial virus (RS-virus), or abnormal neonatal screening tests were the most common explanation for the differences in undertriage.

TABLE 1: Patients characteristics

	NEONATAL POPULATION		OLDER CHILDREN	
	N=1873	(2.7%)	N=67165	(97.3%)
MTS triage category				
Immediate	57	(3%)	945	(1%)
Very urgent	300	(16%)	12226	(18%)
Urgent	523	(28%)	19879	(30%)
Standard	850	(45%)	29791	(44%)
Non-urgent	26	(1%)	781	(1%)
Missing	117	(6%)	3543	(5%)
MTS flowchart				
General flowchart	937	(50%)	13113	(20%)
Shortness of breath	173	(9%)	7871	(12%)
Diarrhoea and vomiting	170	(9%)	5150	(8%)
Crying baby	81	(4%)	461	(1%)
Abscesses and local infections	63	(3%)	1010	(2%)
Rashes	58	(3%)	2118	(3%)
Abdominal pain	50	(3%)	3631	(5%)
Eye problems	28	(2%)	619	(1%)
Limb problems	24	(1%)	9899	(15%)
Urinary problems	17	(1%)	1217	(2%)
Testicular pain	12	(1%)	319	(<1%)
Wounds	11	(1%)	2997	(4%)
Other flowcharts	77	(4%)	13427	(20%)
Missing	172	(9%)	5333	(8%)
MTS discriminator[a]				
General discriminator	499	(31%)	12202	(21%)
Specific discriminator	926	(58%)	41029	(70%)
Missing	172	(11%)	5451	(9%)
Follow-up				
Hospitalisation	669	(36%)	8977	(13%)
Discharged	1201	(64%)	58004	(86%)
Missing	3	(<1%)	184	(<1%)

[a] Only available in Fernando Fonseca hospital, Juliana Children's Hospital, and Sophia Children's hospital
N_{total}=60279; $N_{neonaten}$=1597 en $N_{older\ children}$=58682

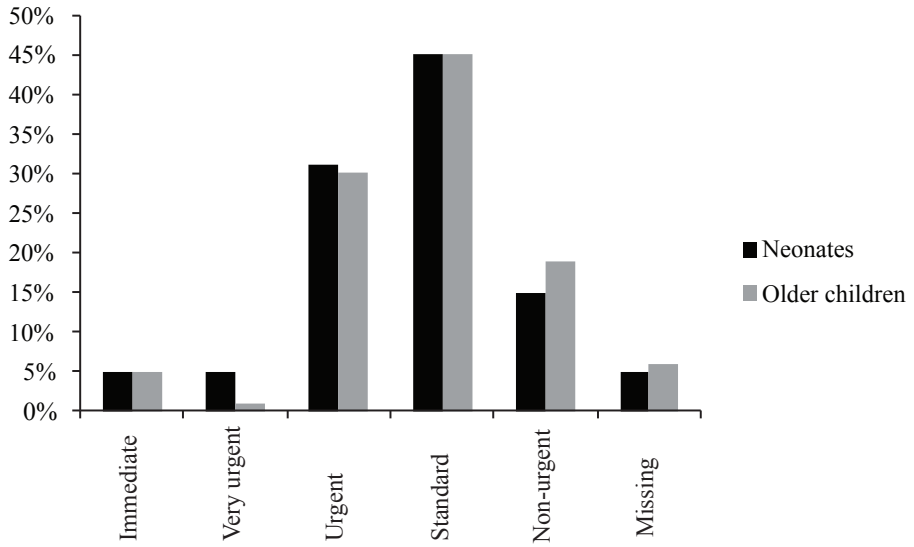

FIGURE 2: Distribution of the reference standard for neonates and older children

DISCUSSION

The number of neonates at the ED was considerable and neonates were more frequently triaged by general triage items, which indicate difficulties in allocating urgency by triage nurse. However, this does not lead to misclassification of neonates when compared with older children. The validity of the MTS for neonates was comparable with the validity of older children. The general flowcharts perform even better in neonates than general flowchart in older children and therefore there is no need to develop a neonatal flowchart.

Only when neonates were assigned to both a general flowchart as well as a general discriminator (N=395), neonates were at risk to be undertriaged in comparison with older children. This undertriage was mainly caused by the hospitalisation criteria 'monitoring of vital signs for deterioration of patient's condition', while this reason was less common in older children. We doubt if these neonates are truly undertriaged, since hospitalisation in these cases does not always reflect acuity of illness at the moment of presentation at the ED.

This study was conducted to explore the need for a new flowchart in the MTS. One criteria to create a new flowchart was that the proportion of patients who can be allocated to this new flowcharts was substantial. Which number of patients is substantial, is still open for debate. In a study by Balosinni et al., the prevalence of headache in children presenting at the ED was between 5.9 and 37.7% and considered high enough by the authors to modify the MTS flowchart 'Headache'.[37] In our study, we considered a proportion of two percent of neonates substantial, because this was comparable to the proportion of children allocated to the tenth most frequently used flowchart in the MTS (Flowchart 'urinary problems') and represents a common ED presenting problem.[38]

The second criteria for creating a new flowchart was that the flowcharts and discriminators available in the MTS are insufficient to allocate a triage category. Since this study was conducted retrospectively, we could not ask questions to the triage nurses concerning difficulties in allocating a triage category. For this reason, we had to develop a proxy and defined that nurses allocated patients to a general flowchart or discriminator if no specific

TABLE 2: Validity of the MTS for neonates and for older children

	NEONATES			OLDER CHILDREN		
	Total	Specific flowcharts	General flowcharts	Total	Specific flowcharts	General flowcharts
Hospitalisation						
Positive LR (95%CI)	3.6 (3.0-4.4)	2.6 (2.0-3.0)	4.7 (3.5-6.5)	2.7 (2.7-2.8)	3.3 (3.2-3.4)	1.6 (1.5-1.7)
Negative LR (95% CI)	0.69 (0.65-0.74)	0.72 (0.64-0.80)	0.69 (0.63-0.75)	0.65 (0.64-0.66)	0.63 (0.62-0.65)	0.74 (0.71-0.77)
DOR (95% CI)	5.3 (4.1-6.7)	3.6 (2.5-5.1)	6.9 (4.7-10.0)	4.2 (4.0-4.4)	5.3 (5.0-5.6)	2.2 (2.0-2.5)
Reference standard						
Positive LR (95%CI)	4.9 (4.1-5.8)	4.4 (3.3-5.8)	5.3 (4.2-6.7)	3.7 (3.6-3.9)	4.8 (4.7-5.0)	2.0 (1.9-2.1)
Negative LR (95% CI)	0.31 (0.23-0.42)	0.39 (0.26-0.59)	0.26 (0.17-0.40)	0.33 (0.31-0.35)	0.31 (0.28-0.33)	0.43 (0.38-0.49)
DOR (95% CI)	15.7 (10.3-24.0)	11.1 (5.8-21.1)	20.3 (11.3-36.4)	11.4 (10.4-12.5)	15.9 (14.3-17.7)	4.6 (3.8-5.6)

flowchart or discriminator represents the problem of the patient.
We are aware that this proxy is susceptible for bias, since neonates are not able to explain their problem and therefore more frequently present the ED with non-specific problems than older children. However, the most common ED presentations of at term born babies are feeding difficulties manifesting by vomiting or failure to thrive, breathing difficulties, crying, rash, or jaundice.[39] Despite these specific symptoms, which account for more than 70% of the neonatal ED presentations[39], this study showed that 50% of neonates are assigned to general flowcharts. For this reason, we believe that our proxy represents nurses inability to allocate a specific triage flowchart.

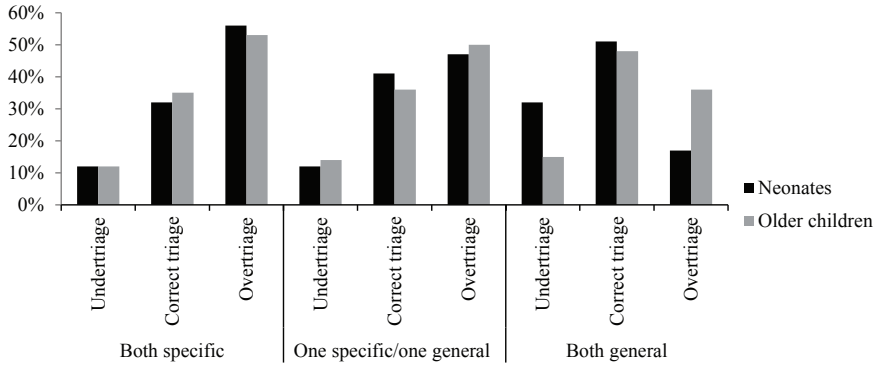

FIGURE 3: Undertriage, correct triage and overtriage of neonates and older children allocated to two specific triage items (flowchart or discriminator), to one specific and one general triage item or to two general triage items.

The validity of the MTS in neonates was comparable with children of older age. To asses validity, a predefined reference standard that combines prognostic markers, disease severity and case complexity is preferred.[40] However, the items needed for the reference standard were not available in all settings. Therefore, hospitalisation was chosen as a second outcome measure. Hospitalisation showed a trend with urgency categories in other paediatric triage validation studies[29, 41-43] and was available in all settings.
Because neonates are at risk for being hospitalised for less urgent reasons than older children, we are aware that this outcome measure could have biased our results. However, if this was the case, we expected a lower validity of the MTS in neonates than in older children. Moreover, if both the reference standard and hospitalisation were used as outcome measures, the validity of the MTS for neonates was comparable to the validity in older children.

Strength and limitations
This study included 69038 children selected from four different international hospitals in different time periods, represents a good case-mix, and is generalisable to other European paediatric ED-populations.
The main limitation of this study is the retrospective study design which has ensured that some data were not available in all hospitals. However, missing of data was not different for neonates and older children and therefore the main disadvantage of a retrospective study design 'information bias' was not likely to appear.

CONCLUSION

Although the number of neonates that attends the emergency department was substantial and nurses had difficulties to triage neonates, the validity of the MTS for neonates was comparable with the validity of older children and therefore there was no need to develop a neonatal flowchart.

CHAPTER 4

Self-referral and serious illness in children with fever

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ABSTRACT

Background The goal of this study was to evaluate parents' capability to assess their febrile child's severity of illness and decision to present to the emergency department. We compared children referred by a general practitioner (GP) with those self-referred on the basis of illness-severity markers.

Methods This was a cross-sectional observational study conducted at the emergency departments of a university and a teaching hospital. GP-referred or self-referred children with fever (aged,16 years) who presented to the emergency department (2006–2008) were included. Markers for severity of illness were urgency according to the Manchester Triage System, diagnostic interventions, therapeutic interventions, and follow-up. Associations between markers and referral type were assessed by using logistic regression analysis. Subgroup analyses were performed for patients with the most common presenting problems that accompanied the fever (i.e., dyspnoea, gastrointestinal complaints, neurologic symptoms, fever without specific symptoms).

Results Thirty-eight percent of 4609 children were referred by their GP and 62% were self-referred. GP-referred children were classified as high urgency (immediate/very urgent categories) in 46% of the cases and self-referrals in 45%. Forty-three percent of GP-referrals versus 27% of self-referrals needed extensive diagnostic intervention, intravenous medication/aerosol treatment, hospitalization, or a combination of these (odds ratio: 2.0 [95% confidence interval: 1.75–2.27]). In all subgroups, high urgency was not associated with referral type. GP-referred and self-referred children with dyspnoea had similar frequencies of illness-severity markers.

Conclusions Although febrile self-referred children were less severely ill than GP-referred children, many parents properly judged and acted on the severity of their child's illness. To avoid delayed or missed diagnoses, recommendations regarding interventions that would discourage self-referral to the emergency department should be reconsidered.

INTRODUCTION

Worldwide, emergency departments (EDs) are challenged by increasing numbers of patients who bypass primary care and present to the ED on their own initiative (self-referral).[16, 44-51] For adult patients, self-referral has been associated with nonurgent symptoms that can easily be handled in primary care[50, 52] Consequently, interventions to redirect self-referrals to fast-track areas, placement of primary care facilities next to EDs, or governmental policies for self-payment of ED visit costs by self-referrals have been introduced.[44, 53] Such interventions will reduce the number of adult self-referrals; however, they may also discourage parents from self-referring their child to the ED, even though knowledge on the severity of illness of self-referred children is scarce.

Fever is one of the main presenting problems at paediatric EDs.[54-56] Among febrile children, ~15% are diagnosed with bacterial infections (e.g., meningitis, bacteraemia, urinary tract infection), severe dehydration (caused by gastroenteritis), or dyspnoea.[30] For these illnesses, diagnostic or therapeutic interventions or hospitalization are often required.[30, 45, 57, 58] Delay in diagnosing these conditions by discouraging parents from self-referring their child to the ED may result in significant morbidity and mortality.[59-61]

This study aimed to assess the severity of illness of febrile children who were self-referred to the ED by their parents compared with those referred by the general practitioner (GP). We hypothesized that parents are capable of assessing their child's severity of illness and adequately decide to present their child to the ED. Urgency according to the Manchester Triage System (MTS), diagnostic interventions, therapeutic interventions, and follow-up were used as markers for severity of illness and were compared between GP-referred and self-referred children.

METHODS

Study design

In this cross-sectional observational study, we compared severity of illness of children with fever referred by a GP with those who presented to the ED on their parent's initiative on the basis of markers for severity of illness. This study is part of an ongoing prospective study on triage of paediatric patients.[16] Institutional medical ethics committees reviewed the study, and the requirement for informed consent was waived.

Health care system in the Netherlands

In the Netherlands, both primary care (provided by GPs) and secondary care (provided by medical specialists [e.g., paediatricians]) function as emergency care facilities. All inhabitants are registered with a local GP, who is available during office hours. Out-of-hours primary care (5 PM to 8 AM daily and the entire weekend) is organized in general practitioner cooperatives, in which GPs rotate shifts.[62, 63] Similar large-scale cooperatives have been observed in the United Kingdom, Scandinavia, and Australia.[64-66]

In principle, patients should first consult their local GP or telephone the general practitioner cooperative. After (telephone) triage by a trained nurse, the patient receives telephone advice or consultation. The availability of acute diagnostic and therapeutic interventions in primary care is predominantly limited to analysis of urine dipstick test results and administration of rescue medication (e.g., adrenaline, antihistaminic agents). In the event a specialist consultation, laboratory examinations, radiologic examinations, or extensive therapeutic interventions (e.g., aerosol treatment, intravenous [IV] medication) are necessary, the patient is referred to the ED, accompanied with a referral note (i.e., gatekeeping). Referral

is required for ~5% to 10% of all primary care consultations,[63, 67] similar to data from the United Kingdom, the United States, and Canada.[68, 69]
In addition, patients can directly present to the ED on their own initiative (self-referral). Only in life-threatening situations should patients call the national emergency number for ambulance services. Ambulance personnel judge the patient's acuity of illness on arrival and bring the patient directly to the ED when necessary. At the ED, all children with medical problems are consulted by a paediatrician or resident in paediatrics supervised by a paediatrician.

Study setting and participants
Our study population comprised all GP-referred or self-referred children with fever (aged,16 years) who presented to the ED of 2 large inner-city hospitals located in the southwest of the Netherlands. The Erasmus MC/Sophia Children's Hospital (Rotterdam) is a university hospital with a paediatric ED that provides 90% general paediatric care to ~9000 patients annually.[55] The inclusion period at this hospital ran from January 2006 to January 2007 and May 2007 to April 2008. The Haga Hospital/Juliana Children's Hospital (The Hague) is a large teaching hospital with a mixed paediatric–adult ED that delivers care to nearly 15 000 children annually. In this hospital, the inclusion period ran from January to August 2006 and August to December 2007. To avoid inclusion of patients who did not receive "usual care," we excluded children "referred by others." This group mainly comprised children with comorbidities and children referred by paediatric specialists (e.g., cardiologist, oncologist).

Manchester Triage System
The MTS is a triage algorithm that consists of 49 flowchart diagrams suitable for children. Each flowchart is specific to a patient's presenting problem and contains 6 key discriminators (life threat, pain, haemorrhage, acuteness of onset, consciousness level, and temperature) and specific discriminators (signs and symptoms) relevant to the presenting problem. Selection of a discriminator leads to 1 of the 5 urgency categories and maximum waiting time. Both participating hospitals used the first edition of the MTS (official Dutch translation).[18] Compliance with triage with the MTS was 99% (14078 of 14276), as in our MTS validation study.[16]

Data collection
We obtained information on demographic and contact characteristics, referral type, flowchart, discriminators, and urgency category from the computerized MTS. Parents were informed about the assigned urgency level. Only 0.5% of the parents left before being seen by the physician. These patients were not followed up because this number was very small. Over a 2-month period, the reason for self-referral was recorded by the triage nurses at Sophia Children's Hospital. Clinical data on diagnostic and therapeutic interventions and follow-up were recorded on structured electronic or paper ED forms by nurses or physicians. We obtained data on laboratory tests from the hospital information systems. Trained medical students entered these data in a separate database (SPSS data entry version 4.0 [SPSS Inc., Chicago, IL]), independent of triage outcome or referral type. The database was checked for outliers and consistency.
Referral type was documented for 13922 of 14078 (99%) triaged children. Demographic and clinical characteristics were comparable between patients with missing data (n = 354) and complete data (n = 13922). Selection of all febrile self-referred and GP-referred children

resulted in a study population of 4609 children (Figure 1). Eight percent (354 of 4609) of all eligible children presented to the ED more than once during the study period. Only 14 (0.3%) children presented frequently (≥4 presentations). Children who presented more than once were younger (median age: 1.4 vs. 1.8 years) and slightly more frequently self-referred (68% vs. 61%) than those who presented once. Because the MTS urgency distribution and frequency of hospitalization (as measures of severity of illness) were similar for both groups and the number of children with >1 visit was small, we decided not to exclude these patients.

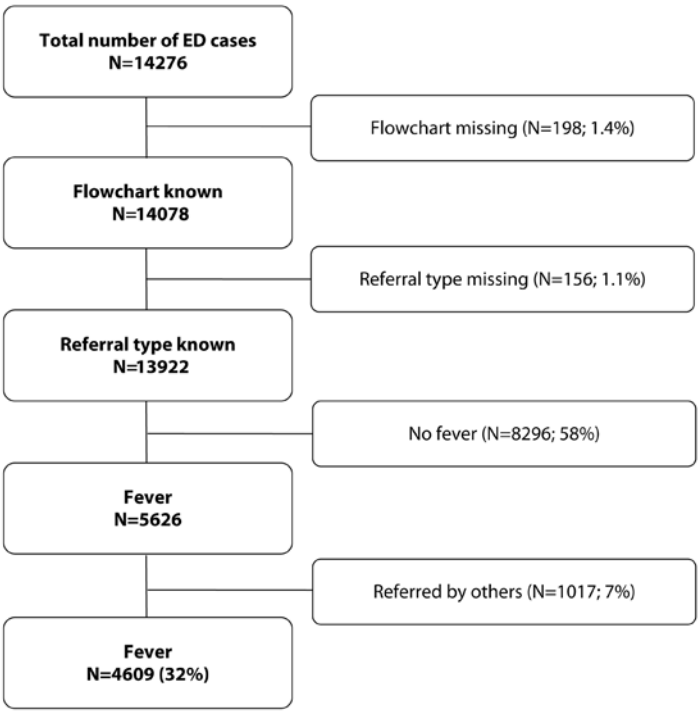

FIGURE 1: Selection of the study population

Definitions

Fever was defined as "fever as reason for attendance,"[70,71] "fever selected as triage discriminator," or a body temperature rectally measured at the ED ≥38.5°C. Referral type was recoded into the following: (1) self-referred: children who presented to the ED on their parent's initiative and children brought in by ambulance after their parents had telephoned the national emergency number; (2) referred by GP: children referred to the ED after consultation by a GP; and (3) referred by others: children referred to the ED by other health care workers (e.g., paediatric specialists [e.g., cardiologist, oncologist], police physician, or midwife). MTS flowcharts were categorized into 9 presenting problems (Table 1). We defined high MTS urgency as "immediate" or "very urgent" classification. As reported in our MTS validation study, diagnostic interventions were categorized into simple laboratory (complete blood cell count, electrolytes, liver enzymes, renal function, urine/stool cultures, and nasal swabs), simple radiology (radiograph or ultrasound imaging), extensive laboratory (blood culture,

cerebral spinal fluid puncture, or a combination of ≥2 simple laboratory tests), and extensive radiology (computed tomography or MRI).

Therapeutic interventions were categorized into self-care advice (no medication), medication on prescription (e.g., antibiotics), oral medication at ED (e.g., prednisone), and extensive therapeutic interventions (e.g., IV medication, aerosol treatment). Follow-up was categorized into no follow-up, hospital admission, outpatient clinic appointment, and other (e.g., telephone appointment, appointment by GP). Both EDs used similar criteria for hospitalization: (1) abnormal or threatened vital signs; (2) requirement of IV medication or IV fluids; and (3) inability to ingest prescribed medication (e.g., need for nasogastric tube). Hospitalization was further subdivided into admission to the medium care unit or intensive care unit. MTS urgency, diagnostic interventions, therapeutic interventions, and follow-up were considered as markers for severity of illness.

TABLE 1: MTS Flowcharts categorised into presenting problems

PRESENTING PROBLEM	FLOWCHART
Dyspnoea	Asthma, shortness of breath, shortness of breath in children
Gastrointestinal	Vomiting, abdominal pain, abdominal pain in children, diarrhoea, gastrointestinal bleeding
Neurological	Headache, fits, neck pain, unwell child, irritable child, behaving strangely
Ear, nose, and throat	Sore throat, nasal problems, ear problems
Rash	Rashes
Urinary tract	Urinary problems
Local infection/abscess/wound	Local infection/abscess, wounds, burns
Fever without specific symptoms	General, worried parent or crying baby with a positive 'fever' discriminator
Other	Other remaining flowcharts

Sample size

We assumed that the percentage of GP- referred patients who needed extensive medical interventions or hospitalization was 50%.[45, 47, 58] To find at least a 5% difference in outcome measure between GP-referred and self-referred children, we calculated the sample size for each referral group to be at least 1561 patients (α= 0.05; β = 0.20).

Statistical analysis

Where appropriate, demographic characteristics, contact characteristics, and illness-severity markers of GP-referred and self-referred patients were compared by using χ^2 tests (categorical variables) and Mann-Whitney *U* tests (continuous variables). To evaluate the association between referral type and illness-severity markers, multivariate logistic regression analyses were performed. Self-referred children were chosen as the reference category. We considered age (continuous), gender, presenting problem, time of contact (day, evening, or night), and day of contact (weekday or weekend) as potential confounders, as they may be related to both the decision to refer the child to the ED (by GP or parent) and physicians' decisions on diagnostic or therapeutic interventions or hospitalization. The associations between illness severity markers and referral type did not significantly change when children brought in by ambulances (n = 378) were excluded from the analysis (data not shown). We included these children in our main analyses. Statistical analyses were performed by using SPSS PASW software version 17.0.2. P values <.05 were considered significant.

RESULTS

Thirty-eight percent of the 4609 eligible children with fever were referred by a GP and 62% were self-referred. Gender was comparable between groups (Table 2). Median age was 1.5 years interquartile range: 0.7–3.8) for GP-referred children and 1.9 years (interquartile range: 1.0–3.8) for self-referred children (P = .16). Self-referred children were presented significantly more often during out-of-hours periods and more of them were brought in by ambulance services than GP-referred children (P<.01). In both referral groups, the most common presenting problems that accompanied the fever were dyspnoea, gastrointestinal complaints, neurologic symptoms, and fever without specific symptoms. Table 2 displays differences in illness-severity markers between GP-referred and self-referred children. Parents of a subsample of 88 self-referred children (response: 68%) were asked to give their main reason for ED attendance. Eighty-five percent of them reported that they considered the ED to be the most appropriate place to present their child (i.e., they thought their child would need a paediatrician's expertise or diagnostic and therapeutic interventions only available at the ED), 8% had been unable to contact their own GP or general practitioner cooperative, and 4% had other reasons.

TABLE 2: Distribution of illness-severity markers in GP-referred and self-referred children

CHARACTERISTICS	GP-REFERRED (N=1774)		SELF-REFERRED (N=2835)		*P*
Gender[a]					
Male	997	(56)	1630	(58)	.40
Age, y[b]					
≤ 1	655	(37)	759	(27)	<.01
1-3	707	(40)	1399	(49)	<.01
4-7	265	(15)	489	(17)	.04
8-16	147	(8)	188	(7)	.04
Time of consultation					
Out-of-hours	917	(52)	2203	(78)	<.01
Transport to ED					
Ambulance services	64	(4)	314	(11)	<.01
Presenting problem[b]					
Dyspnoea	387	(22)	396	(14)	<.01
Gastro-intestinal	240	(14)	323	(11)	.03
Neurological	131	(7)	317	(11)	<.01
Ear, nose, and throat	53	(3)	178	(6)	<.01
Rash	59	(3)	79	(3)	.30
Urinary tract problems	60	(3)	45	(2)	<.01
Local infection/abscess/wound	11	(1)	13	(1)	.46
Fever without specific symptoms	611	(34)	1101	(39)	<.01
Other problem	222	(13)	383	(14)	.33
MTS urgency[b,c]					
Immediate	28	(2)	69	(2)	.05
Very urgent	783	(44)	1216	(43)	.41
Urgent	610	(34)	861	(30)	<.01
Standard	341	(19)	658	(23)	<.01
Nonurgent	12	(1)	31	(1)	.15
Diagnostic interventions[b]					
No diagnostic intervention	555	(31)	1435	(51)	<.01

TABLE 2: Continued

CHARACTERISTICS	GP-REFERRED (N=1774)		SELF-REFERRED (N=2835)		*P*
Simple laboratory[d]	461	(26)	661	(23)	.04
Simple radiology[e]	310	(18)	318	(11)	<.01
Extensive laboratory or extensive radiology[f]	284	(16)	292	(10)	<.01
Extensive laboratory and any radiology	164	(9)	129	(5)	<.01
Therapeutic interventions[b]					
No therapy	159	(9)	259	(9)	.84
Self-care advice	256	(14)	425	(15)	.60
Medication on prescription	756	(43)	1470	(52)	<.01
Oral medication at ED[g]	171	(10)	262	(9)	.65
IV medication/aerosol treatment[h]	432	(24)	419	(15)	<.01
Follow-up[b]					
No follow-up	696	(39)	1723	(61)	<.01
Outpatient clinic	375	(21)	396	(14)	<.01
Hospital admission[b]					
MCU[i]	444	(25)	396	(14)	<.01
ICU	13	(1)	15	(1)	.39
Other follow-up	246	(14)	305	(11)	<.01

Data are presented as *n* (%). MCU: medium care unit; ICU: intensive care unit.
[a] One missing value.
[b] Overall χ^2 P <.01.
[c] MTS urgency classification (and maximum waiting time): immediate: 0 min, very urgent: 10 min, urgent: 60 min, standard: 120 min, and non-urgent: 240 min.
[d] Complete blood cell count, electrolytes, liver enzymes, renal function, urine/stool cultures, nasal swabs.
[e] Radiography and/or ultrasound.
[f] Extensive laboratory: blood culture, cerebrospinal fluid puncture, or combination of ≥ 2 simple laboratory tests. Extensive radiology: computed tomography and/or MRI.
[g] Examples include oral rehydration salts, prednisone, or antibiotics.
[h] Examples of IV medication include fluids and antibiotics.
[i] All admissions to the hospital other than ICU admissions

Associations between referral type and illness-severity markers

Forty-three percent of GP-referred children needed extensive diagnostic interventions, IV medication/aerosol treatment, hospitalization, or a combination of these compared with 27% of self-referred children (odds ratio [OR]: 2.0 [95% confidence interval (CI): 1.75–2.27]). Table 3 displays the associations between referral type and illness-severity markers separately. GP-referred children were classified as high urgency in 46% of the cases and self-referred children in 45% (OR: 1.2 [95% CI: 1.02–1.35]). Compared with self-referrals, GP-referred children required significantly more extensive diagnostic interventions (OR: 2.0 [95% CI: 1.74–2.38]) and IV therapy or aerosol treatments (OR: 1.6 [95% CI: 1.39–1.93]) more frequently hospitalized (OR: 2.0 [95% CI: 1.74–2.39]). Due to small numbers, we could not analyse medium care unit and intensive care unit admissions separately in our regression analysis (Table 2).

Presenting problems

Table 4 presents a subgroup analysis of children with the 4 most common presenting problems that accompanied the fever. The proportion of children classified according to the MTS as high urgency was comparable between GP-referred and self-referred children in all presenting problem groups. The odds of requiring extensive diagnostic interventions or IV medication were higher for GP-referred children than for self-referred children with gastrointestinal complaints, neurologic symptoms, or those without specific symptoms that

TABLE 3: Associations between referral type and illness-severity markers for children who presented to the ED with fever

ILLNESS-SEVERITY MARKERS	GP-REFERRED (N=1774)		SELF-REFERRED[a] (N=2835)		UNADJUSTED OR		ADJUSTED OR[b]	
	N	(%)	N	(%)	OR	(95% CI)	OR	95% CI
High MTS urgency[c]	811	(46)	1285	(45)	1.0	(0.90-1.14)	1.2	(1.02-1.35)
Extensive diagnostic interventions[d]	448	(25)	421	(15)	1.9	(1.67-2.25)	2.0	(1.74-2.38)
IV therapy/aerosol treatment	432	(24)	419	(15)	1.9	(1.60-2.16)	1.6	(1.39-1.93)
Hospital admission	457	(26)	411	(15)	2.1	(1.76-2.38)	2.0	(1.74-2.39)

[a] Reference category: self-referred children.
[b] Adjusted for gender, age, presenting problem, time of contact (day, evening, or night), and day of contact (weekday or weekend).
[c] High MTS urgency (maximum waiting time): immediate (0 min) or very urgent (10 min).
[d] Extensive laboratory or radiology examinations.

accompanied the fever. In these subgroups, hospitalization ranged from 20% to 37% among GP-referred children and from 11% to 22% among self-referred children. The frequencies of all illness-severity markers for feverish children with dyspnoea were comparable between GP-referrals and self-referrals.

DISCUSSION

Our study revealed that even though self-referred children with fever were less severely ill than GP-referred children, at least 1 in4 self-referrals needed extensive diagnostic interventions, IV medication/aerosol treatment, or hospitalization. The most common presenting problems that accompanied the fever as well as classification according to the MTS as high urgency were similar for GP-referred and self-referred children. Our subgroup analyses further revealed that for children with fever and dyspnoea, severity of illness was similar in both referral groups. Obviously, many parents properly judged and acted on their child's severity of illness by presenting their child to the ED on their own initiative.

The majority of parents self-referred their child because they thought their child needed paediatrician's expertise or diagnostic or therapeutic interventions, for which they had to visit the ED anyway, which is comparable to previous reports.[46, 72] We further observed that 11% of the self-referred children were brought in by ambulance services. In all of these cases, the ambulance dispatch centre assessed and agreed on the urgent need for medical care, indicating the child was seriously ill and parents adequately decided to telephone the national emergency number.

Comparison with literature

Our results support, to some extent, the findings of Rinderknecht et al[47] that GP-referred children with fever are more severely ill than self-referred children; however, the magnitude of the difference in our population was much smaller. Their study revealed that febrile children referred by a GP to their quaternary, international referral centre had higher triage acuities and higher frequencies of abnormal vital signs and hospitalizations than self-referred children. On the basis of these results, they suggested incorporating referral type in triage algorithms used at the ED.

It is likely that our much smaller difference in severity of illness between GP-referred and self-referred children can be explained by the difference in study settings. Children referred to their quaternary care centre are likely to be more seriously ill and to need more specialized care than children referred to our study EDs, which mainly provide basic paediatric care.[55] According to our finding that the frequency of high-urgent classification was comparable between GP-referred and self-referred children, we disagree with the recommendation to use referral type alone to influence triage algorithms at community EDs.

Although the health care system is organized differently in the Netherlands compared with other countries, we think our results are generalisable to community EDs of countries in which primary care and ED care are both available as emergency care facilities. In other European countries,[45, 46, 66, 73] Australia,[48, 49] the United States,[50, 51] and Canada,[47, 74] ED populations constitute a case-mix of referred and nonreferred children, with numbers of self-referrals ranging from about 30% to 80%,[45, 50, 73-77] comparable with the frequency of self-referrals in the Netherlands.[16, 72, 78]

Our finding that 1 in 4 self-referred children required some form of extensive intervention or hospitalization is much higher than one would expect if parents were unable to judge their child's medical need. In addition, it is only slightly lower than the frequency found among

GP-referred children. Primary care, which is only provided by GPs in the Netherlands, has been shown to be adequate,[63, 67] safe,[79] and satisfactory.[63, 66, 80] Because in our health care system GPs only refer patients who need specialist care, we have used GP-referred children as a reference group of true severely ill patients. This study revealed that many parents, who could choose between primary or secondary care facilities for emergency care, presented to the ED adequately and were capable of judging their child's severity of illness. Therefore, we believe that our results and the medical implications are important for community EDs in other countries as well.

Because increasing numbers of self-referrals at the ED cause a high workload for ED nurses and physicians, future research should focus on demographic and clinical characteristics of self-referred febrile children that point toward severe illness. By knowing these characteristics, one can distinguish severely ill from nonseverely ill children on arrival at the ED. For example, our subgroup analyses already revealed that GP-referred and self-referred children with fever and dyspnoea were equally ill. Such determinants, rather than general measures on the basis of referral type alone, should be used to guide decisions on accepting or diverting self-referrals at the ED.

Study weaknesses and strengths

The first limitation of this study is our use of MTS urgency, diagnostic interventions, therapeutic interventions, and follow-up as proxies for severity of illness. However, because such proxies have been extensively used to validate triage systems worldwide,[15, 29, 41, 81] we believe this method is valid to approximate true severity of illness.

Second, we had no information on whether self-referred children were seen by a GP (but not referred) before their presentation at the ED. Possibly, parents were instructed by the GP about specific symptoms to be aware of or to go to the ED when symptoms worsened. Potentially, this information could have influenced our results toward more severely ill patients in the self-referred group.

Third, our interpretation that 1 in 4 self-referred children who required at least some extensive medical intervention or hospitalization is a significant number is primarily based on our own clinical experience and intuition. We concluded that discouragement of all parents to self-refer their feverish child to the ED is unacceptable. Unfortunately, this statement is not evidence based, because cut-off values for what we generally consider to be an acceptable number of patients to delay or miss diagnosis in (e.g., by discouragement of self-referral) are unavailable.

We are, however, to the best of our knowledge, the first to report differences in severity of illness between GP-referred and self-referred children with fever who presented to a large community ED. Our study sample constitutes a good case-mix selected from a multicultural, inner-city ED population of >14 000 children. In addition, our subgroup analysis is the first to demonstrate that self-referral is justifiable for a considerable number of febrile children with specific accompanying symptoms, especially for those with dyspnoea.

Data collection was complete for 98% of all children who presented to the ED during our study period. General patient and clinical characteristics of children with and without missing data were comparable, indicating that selection bias was unlikely.

Differences in the level of expertise between residents and paediatricians may have led to differences in diagnostic management. At our study EDs, all residents were supervised by a paediatrician, and we found no differences in the number of diagnostic interventions performed by residents or paediatricians (χ^2-test: P = .28 [data not shown]).

The magnitude of the difference in diagnostic and therapeutic interventions performed between self-referred and GP-referred children is similar to that of the number of hospitalizations required.

Because hospitalization depends on the patient's clinical condition rather than referral type, information bias (i.e., paediatricians will perform more diagnostic and therapeutic interventions when they know a child is referred by a GP) is unlikely.

TABLE 4: Association between referral type and illness-severity markers categorized according to the most common presenting problems among children who presented at the ED with fever

ILLNESS-SEVERITY MARKERS	DYSPNEA					GASTROINTESTINAL				
	GP (N=387)		SR (N=396)		OR[a] (95% CI)	GP (N=240)		SR (N=323)		OR[a] (95% CI)
High MTS urgency[b]	199	(51)	200	(51)	1.1 (0.82-1.48)	13	(5)	12	(4)	1.4 (0.59-3.25)
Extensive diagnostic interventions[c]	52	(13)	46	(12)	1.2 (0.77-1.92)	65	(27)	47	(15)	2.0 (1.27-3.04)
IV medication/ aerosol treatment	168	(43)	160	(40)	1.1 (0.79-1.44)	36	(15)	31	(10)	1.7 (1.02-2.98)
Hospital admission	111	(29)	102	(26)	1.3 (0.92-1.79)	49	(20)	45	(14)	1.5 (0.97-2.45)

ILLNESS-SEVERITY MARKERS	NEUROLOGICAL					FEVER WITHOUT SPECIFIC SYMPTOMS				
	GP (N=131)		SR (N=317)		OR[a] (95% CI)	GP (N=611)		SR (N=1101)		OR[a] (95% CI)
High MTS urgency[b]	99	(76)	252	(80)	0.8 (0.49-1.34)	382	(63)	648	(59)	1.2 (0.97-1.48)
Extensive diagnostic interventions[c]	56	(43)	99	(31)	1.6 (1.06-2.52)	180	(30)	151	(14)	2.4 (1.90-3.13)
IV medication/ aerosol treatment	38	(29)	58	(18)	1.9 (1.17-3.10)	127	(21)	110	(10)	2.1 (1.61-2.85)
Hospital admission	49	(37)	68	(22)	2.5 (1.55-3.89)	174	(29)	125	(11)	2.9 (2.22-3.80)

GP: GP-referred patients; SR: self-referred patients.
[a] Adjusted for age, gender, time of contact (day, evening, or night) and day of contact (weekday or weekend). Reference category: self-referred children.
[b] High MTS urgency (maximum waiting time): immediate (0 min) or very urgent (10 min).
[c] Extensive laboratory or radiology examinations.

CONCLUSIONS

Our study emphasized that many parents properly judged and acted on their febrile child's severity of illness by presenting to the ED on their own initiative. Self-referred children with fever must not be generalized and approached as a uniform group of nonseverely ill patients. General measures to discourage self-referrals from presenting to the (community) ED are undesirable for children with fever; this action may result in delayed or missed diagnoses and potentially increase morbidity and mortality.

CHAPTER 5

Accuracy of triage for children with chronic illness and infectious symptoms

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ABSTRACT

Objective This prospective observational study aimed to assess the validity of the Manchester Triage System (MTS) for children with chronic illnesses who presented to the emergency department (ED) with infectious symptoms.

Methods Children (<16 years old) presenting to the ED of a university hospital between 2008 and 2011 with dyspnoea, diarrhoea/vomiting, or fever were included. Chronic illness was classified on the basis of International Classification of Diseases, Ninth Revision, Clinical Modification, codes. The validity of the MTS was assessed by comparing the urgency categories of the MTS with an independent reference standard on the basis of abnormal vital signs, life-threatening working diagnosis, resource utilization, and follow-up. Overtriage, undertriage, and correct triage were calculated for children with and without a chronic illness. The performance was assessed by sensitivity, specificity, and diagnostic odds ratios, which were calculated by dichotomizing the MTS into high and low urgency.

Results Of the 8592 children who presented to the ED with infectious symptoms, 2960 (35%) had a chronic illness. Undertriage occurred in 16% of children with chronic illnesses and in 11% of children without chronic illnesses (P< .001). Sensitivity of the MTS for children with chronic illnesses was 58% (95% confidence interval [CI]: 53%–62%) and was 74% (95% CI: 70%–78%) for children without chronic illnesses. There was no difference in specificity between the 2 groups. The diagnostic odds ratios for children with and without chronic illnesses were 4.8 (95% CI: 3.9–5.9) and 8.7 (95% CI: 7.1–11), respectively.

Conclusions In children presenting with infectious symptoms, the performance of the MTS was lower for children with chronic illnesses than for children without chronic illnesses. Nurses should be particularly aware of undertriage in children with chronic illnesses.

INTRODUCTION

New insights in biomedical science for children have improved treatments for previously untreatable conditions and increased survival. Although these improved treatments have led to a decline in mortality, there has been a simultaneous increase in children with chronic illnesses[82] who tend to be sicker during acute infectious diseases than those who were previously healthy.[83-85]

At the emergency department (ED), triage systems aim to recognize patients who need immediate care to prevent deterioration while patients are waiting. The Manchester Triage System (MTS), commonly used in Europe, was developed for both adults and paediatric emergency care.[7, 18] The MTS consists of 52 flowcharts that together represent the range of patients presenting symptoms at the ED. All flowcharts contain additional signs and symptoms (discriminators), the presence of which defines the patient's urgency category. The 5 urgency categories correspond to the maximum waiting times before being seen by a physician. The urgency categories of the MTS are as follows: (1) immediate, immediate evaluation; (2) very urgent, evaluation within 10 min; (3) urgent, evaluation within 60 min; (4) standard, evaluation within 120 min; and (5) nonurgent, evaluation within 240 min.[7, 18]

Although some MTS flowcharts include the discriminator "significant medical history," defined as "any pre-existing medical condition requiring continual medication or other care,"[18] children with chronic illnesses are triaged in the same manner as previously healthy children. However, the validity of the MTS for children with chronic illnesses has not yet been evaluated. Therefore, the aim of the current study was to assess the performance of the MTS for children with chronic illnesses who presented to the ED with infectious symptoms. The performance of the MTS for children with chronic illnesses was compared with that of the MTS in previously healthy children by using an independent reference standard as the outcome measure.[16, 33]

METHODS

Study design

We conducted a prospective observational study on the validity of the MTS in children with chronic illnesses defined according to a list of diagnostic codes for congenital and chronic acquired disorders.[86]

Settings and selection of participants

Included were all children aged ≤16 years who presented at the ED of Sophia Children's Hospital (Rotterdam, The Netherlands) between January 2008 and January 2012. This paediatric ED is part of the Erasmus University Medical Centre, is open 24 hours a day, and receives ~9000 children annually. All children were triaged with the Dutch translation of the first (January 2008 through July 2009) or second (August 2009 through December 2011) edition of the MTS.[7, 18] Both versions of the MTS contained the same validated adjustments for triage of febrile children.[33] Eligible children were those who presented at the ED with diarrhoea and/or vomiting, shortness of breath, or fever.

Ethical Approval

This study is part of an ongoing study on validation of the MTS. The Medical Ethics Committee of the Erasmus MC approved the study, and the requirement for informed consent was waived.

Definitions

Diarrheal and/or vomiting and shortness of breath were defined according to whether children were allocated to the MTS flowcharts "diarrhoea and vomiting" or "shortness of breath in children," respectively. defined as follows: fever as reason for attendance, fever selected as triage discriminator, or a body temperature of ≥38.5°C rectally measured at the ED according to our previous studies.[87, 88]

Chronic illnesses are coded according to a widely used list of diagnostic codes for congenital and chronic acquired disorders.[86] This list was based on the International Classification of Diseases, Ninth Revision, Clinical Modification, codes that represent chronic illnesses that can be "reasonably expected to last at least 12 months (unless death intervenes) and to involve either several different organ systems or 1 organ system severely enough to require specialty paediatric care and probably some period of hospitalization in a tertiary care centre".[86]

In summary, the list distinguishes the following: (1) neuromuscular illnesses, divided into brain and spinal cord malformations, mental retardation, central nervous system degeneration and diseases, infantile cerebral palsy, and muscular dystrophies and myopathies; (2) cardiovascular illnesses, divided into heart and great vessel malformations, cardiomyopathies, conduction disorders, and dysrhythmias; (3) respiratory illnesses, divided into respiratory malformations, chronic respiratory diseases, and cystic fibrosis; (4) renal illnesses, divided into congenital anomalies and chronic renal failure; (5) gastrointestinal illnesses, divided into congenital anomalies, chronic liver diseases and cirrhosis, and inflammatory bowel diseases; (6) hematologic or immunologic illnesses, divided into sickle cell disease, hereditary anaemias, hereditary immunodeficiencies, and acquired immunodeficiencies; (7) metabolic illnesses, divided into amino acid metabolic disorders, carbohydrate metabolic disorders, lipid metabolic disorder, storage disorders, and other metabolic disorders; (8) other congenital or genetic defects divided into chromosomal anomalies, bone and joint anomalies, diaphragm and abdominal wall anomalies, and other congenital anomalies; and (9) malignancy or malignant neoplasms. Patients were only categorized into this last category if they received treatment at the time of presentation to the ED.

Outcome Measures

An independent reference standard with 5 urgency categories was used as proxy for true urgency.[16, 33] Details of the reference standard and the actual reference matrix have been published earlier.[16, 33] The 5 urgency categories were as follows:

1. immediate (patients who had abnormal vital signs according to the Paediatric Risk of Mortality Score III[26]);
2. very urgent (patients who were diagnosed with life-threatening conditions defined as meningitis, sepsis, high energetic trauma, substantial blood loss, aorta dissection, >10% dehydration, (near) drowning, electric trauma, possible dangerous intoxication, >10% burns, and facial burns or possible inhalation trauma);
3. urgent (patients who received intravenous [IV] medication [including aerosols and fluids] or casting or inguinal hernia reposition or luxation reposition or gastrolavage at the ED; patients who had some diagnostic workup or received oral medication or small surgical interventions, e.g., bandage at the ED, and were admitted to hospital; patients who had extended laboratory diagnostics including blood culture, cerebrospinal fluid puncture or multiple laboratory tests, or imaging and who received therapy at the ED or small surgical interventions; patients who had imaging and extended laboratory diagnostics; patients who had extended

laboratory diagnostics or imaging at the ED, received some therapy [including medication on prescription or simple advice] at the ED, and had a planned follow-up visit within 24 h);
4. standard (patients who had some diagnostic workup or therapy at the ED or were admitted to hospital or had a planned follow-up visit without meeting the criteria for urgent; and
5. nonurgent (patients with no diagnostic workup, no treatment at the ED, and who were discharged without a planned follow-up visit).

Statistical analysis

First, we compared the performance of the first edition of the MTS with the performance of the second edition of the MTS to investigate whether the 2 data sets of children presenting with infectious symptoms could be combined.

Second, we compared the MTS urgency categories with the categories of the independent reference standard to calculate percentages of overtriage, correct triage, and undertriage. These percentages of children with a chronic illness were compared with those of children without a chronic illness by using a χ^2 test. A P value ≤.05 was considered statistically significant.

In addition, we compared sensitivity, specificity, and the diagnostic odds ratio (DOR). The DOR (with a range from zero to infinity) is a measure that combines sensitivity and specificity (DOR = [sensitivity/1-sensitivity]/[1-specificity/specificity]) and represents the ratio of the odds of positivity in diseased patients relative to the odds of positivity in nondiseased patients.[36] To calculate sensitivity, specificity, and the DOR, patients were categorized as high urgent ("immediate" or "very urgent") and low urgent ("urgent," "standard," and "nonurgent"). The differences between the DORs of children with and without a chronic illness were tested by using interaction terms in logistic regression. A P value ≤.05 was considered statistically significant.

Finally, we performed a subgroup analysis for the 9 categories of chronic illnesses, infectious condition, and age (divided into 5 categories: 0–3 months, 3–12 months, 1–4 years, 4–8 years, and .8 years). To correct for multiple testing, for differences in DORs a P value ≤.01 was considered statistically significant.

Analyses were performed with the IBM SPSS software, version 20 (IBM SPSS Statistics, IBM Corporation, Armonk, NY).

RESULTS

A total of 26312 children had visited the ED, 7208 (27.4%) of whom had a chronic illness. Infectious symptoms were present in 8592 (33%) of all children, including 2960 (35%) with a chronic illness. Of this latter group, 531 (18%) patients had a neuromuscular illness, 326 (11%) had a cardiovascular illness, 262 (9%) had a respiratory illness, 266 (9%) had a renal illness, 390 (13%) had a gastrointestinal illness, 131 (4%) had a hematologic or immunologic illness, 247 (8%) had a metabolic illness, 467 (16%) had a congenital or genetic defect, and 340 (12%) children had a malignancy.

The overall performance of the first edition of the MTS (January 2008 through July 2009) was slightly better than that of the second edition of the MTS (August 2009 through December 2011) for children presenting with infectious symptoms (P = .02). However, because this finding showed no interaction with the presence of a chronic illness (P = .73), we combined the 2 data sets for the analysis of children with and without a chronic illness.

Children with and without a chronic illness

Children with a chronic illness were more often male and were older than children without a chronic illness (P =.04 and <0.001, respectively). Moreover, children with chronic illnesses received more extensive diagnostics, more IV therapy, and were more often hospitalized than children without a chronic illness (all P ≤.001) (Table 1).

Validity

The MTS urgency was not available for 1% (n = 25) of the children, and the reference standard could not be provided for 93 children. Therefore, 8374 children with infectious symptoms remained for analysis of the validity of the MTS.

The performance of the MTS in children with a chronic illness differed from that in children without a chronic illness. In patients with a chronic illness, the Manchester Triage category agreed with the reference standard in 35% of patients, compared with in 30% of the children without a chronic illness. Undertriage was more common in children with a chronic illness than in those without chronic illness (17% vs. 11%), whereas overtriage was more frequent in children without a chronic illness than in those with a chronic illness (59% vs. 48%). Figure 1 presents the percentages for overtriage, correct triage, and undertriage per chronic illness subgroup.

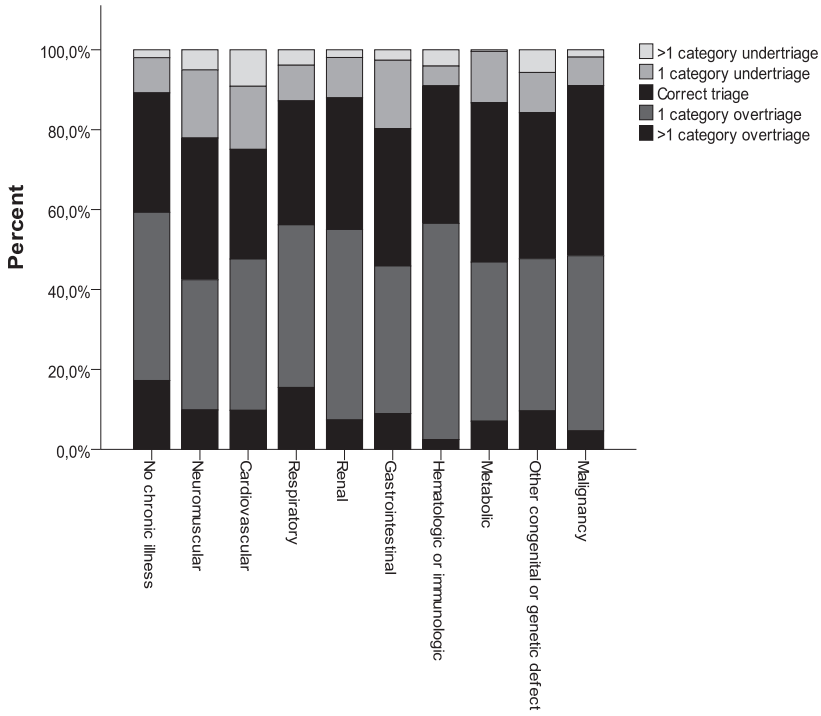

FIGURE 1: Percentages for overtriage, correct triage, and undertriage per chronic illness subgroup.

TABLE 1: Characteristics of the study population.

CHARACTERISTIC	CHRONIC ILLNESS (N= 2960)		NO CHRONIC ILLNESS (N=5632)		P-VALUE
Male Gender, n (%)	1773	(60)	3244	(58)	0.04
Age, mean (IQR), y	3.1	(1.1-6.5)	1.8	(0.7-4.3)	<0.001
MTS urgency, n (%)					<0.001[a]
Immediate	104	(4)	166	(3)	0.145
Very urgent	702	(24)	1464	(26)	0.026
Urgent	1601	(54)	2529	(45)	<0.001
Standard	500	(17)	1368	(25)	<0.001
Non-urgent	3	(<1)	30	(<1)	0.002
Missing	50	(2)	75	(1)	
Diagnostics, n (%)					<0.001[a]
No diagnostics	540	(18)	1961	(35)	<0.001
Simple laboratory	724	(25)	1747	(31)	<0.001
Simple radiology	454	(15)	668	(12)	<0.001
Extensive laboratory or extensive radiology	725	(25)	761	(14)	<0.001
Extensive laboratory and any radiology	501	(17)	467	(8)	<0.001
Missing	16	(1)	28	(1)	
Therapy, n (%)					<0.001[a]
No therapy	1080	(37)	2046	(36)	0.873
Self-care advice/ medication on prescription	643	(22)	1335	(24)	0.039
Oral medication at ED[4]	364	(12)	831	(15)	0.002
Intravenous medication/aerosol[5]	857	(29)	1392	(25)	<0.001
Missing	16	(1)	28	(1)	
Follow-up, n (%)					<0.001[a]
No follow-up	365	(12)	2288	(41)	<0.001
Outpatient clinic	974	(33)	1351	(24)	<0.001
Hospital admission	1037	(35)	1078	(19)	<0.001
ICU admission	121	(4)	93	(2)	<0.001
Other follow-up (mostly by telephone)	461	(16)	819	(15)	0.201
Missing	3	(<1)	4	(<1)	

[a] p-value of overall Chi-square test

The sensitivity of the MTS for children without chronic illness was 74% (95% confidence interval [CI]: 70%–78%) and was 58% (95% CI: 53%–62%) for children with chronic illness. There was no significant difference in specificity between the 2 groups: the specificity was 75% (95% CI: 74%–77%) for children without chronic illness and 78% (95% CI: 76%–79%) for children with chronic illness. The DOR of the MTS in children without chronic illness was 8.7 (95% CI: 7.1–11), which was higher (P , .001) than the DOR of the MTS in children with a chronic illness, i.e., 4.8 (95% CI: 3.9–5.9).

TABLE 2: Validity per subgroup of patients.

SUBGROEP	NUMBER OF PATIENTS	HIGH URGENCY %		UNDER-TRIAGE	CORRECT TRIAGE	OVER-TRIAGE	SENSITIVITY		SPECIFICITY		DOR		P[a]
	(N=8374)	MTS	Reference	%	%	%	(95% CI)		(95% CI)		(95% CI)		
Chronic illness													
No chronic illness	5502	29.3	9.7	10.8	29.9	59.3	74	(70-78)	75	(74-77)	8.7	(7.1-10.7)	Ref
Neuromuscular	516	37.0	21.2	22.1	35.5	42.4	73	(69-77)	73	(69-77)	8.1	(5.0-13.1)	0.772
Cardiovascular	317	34.6	24.5	24.9	27.4	47.6	58	(47-69)	73	(67-78)	3.8	(2.2-6.5)	0.004
Respiratory	258	39.8	12.3	12.8	31.0	56.2	60	(42-75)	63	(56-69)	2.5	(1.2-5.5)	0.002
Renal	258	16.4	7.3	12.0	32.9	55.0	42	(23-64)	86	(81-90)	4.4	(1.6-11.7)	0.178
Gastrointestinal	379	17.0	14.7	19.8	34.3	45.9	31	(20-44)	85	(81-87)	2.6	(1.3-4.9)	<0.001
Hematologic or immunologic	122	20.2	10.2	9.0	34.4	56.6	50	(25-75)	84	(76-89)	5.1	(1.5-17.7)	0.403
Metabolic	241	21.8	8.6	13.3	39.8	46.9	86	(65-95)	85	(79-89)	32.8	(9.2-117.6)	0.045
Other congenital or genetic defect	457	31.5	17.8	15.8	36.5	47.7	54	(44-65)	73	(69-78)	3.3	(2.0-5.4)	<0.001
Malignancy	324	19.9	6.9	9.0	42.6	48.5	41	(23-61)	82	(77-86)	3.2	(1.3-7.8)	0.032
Age													
No chronic illness,<3 months	506	41.1	14.3	17.4	31.8	55.7	79	(69-87)	65	(61-70)	7.3	(4.0-13.3)	Ref
Chronic illness,<3 months	121	35.5	20.5	12.5	32.2	50.4	64	(62-80)	72	(62-80)	4.5	(1.8-11.5)	0.402
No chronic illness, 3 months-1 year	1270	24.4	8.8	10.1	35.7	59.4	72	(77-81)	79	(77-81)	9.8	(6.3-15.2)	Ref
Chronic illness, 3 months-1 year	540	26.6	12.7	16.1	30.6	48.1	70	(58-80)	79	(75-83)	9.0	(5.1-15.9)	0.819
No chronic illness, 1-4 years	2234	32.7	11.3	12.4	26.5	61.1	77	(72-82)	73	(71-75)	9.1	(6.7-12.4)	Ref
Chronic illness, 1-4 years	1031	27.1	16.4	16.2	33.7	50.1	53	(46-61)	78	(75-81)	4.1	(2.9-5.7)	0.448

TABLE 2: Continued

SUBGROEP	NUMBER OF PATIENTS	HIGH URGENCY %		UNDER-TRIAGE	CORRECT TRIAGE	OVER-TRIAGE	SENSITIVITY		SPECIFICITY		DOR		P[a]
	(N=8374)	MTS	Reference	%	%	%	(95% CI)		(95% CI)		(95% CI)		
No chronic illness, 4-8 years	857	22.7	6.6	7.9	33.1	58.9	61	(48-73)	80	(77-82)	6.1	(3.5-10.7)	Ref
Chronic illness, 4-8 years	651	27.7	13.7	15.8	36.4	47.8	54	(44-64)	77	(73-80)	3.9	(2.4-6.2)	0.638
No chronic illness, 8-16 years	635	24.9	6.4	9.1	34.3	56.5	68	(53-80)	78	(74-81)	7.6	(3.8-15.1)	Ref
Chronic illness, 8-16 years	529	28.3	14.8	18.5	36.3	45.2	59	(48-70)	77	(73-81)	5.0	(3.1-8.3)	0.658
Presenting symptom													
No chronic illness, shortness of breath	1464	50.5	15.4	17.7	28.5	53.8	85	(80-89)	56	(53-59)	7.4	(5.0-10.8)	Ref
Chronic illness, shortness of breath	784	55.9	24.4	22.3	28.7	49.0	81	(74-86)	52	(48-56)	4.5	(3.0-6.7)	0.08
No chronic illness, diarrhoea/vomiting	1138	13.3	4.6	9.1	40.1	50.8	40	(28-54)	89	(85-90)	4.9	(2.8-8.8)	Ref
Chronic illness, diarrhoea/vomiting	717	14.3	8.6	17.9	43.7	38.5	37	(26-50)	88	(85-90)	4.2	(2.4-7.5)	0.713
No chronic illness, fever	2900	25.0	8.8	8.0	26.6	65.4	71	(65-76)	79	(65-76)	9.4	(7.1-12.5)	Ref
Chronic illness, fever	1371	18.7	13.0	12.6	34.3	53.1	40	(33-48)	85	(83-87)	3.8	(2.7-5.3)	<0.001

P-values <.01 were considered significant. Ref, reference.
[a] P value for comparison between the subgroup DOR and the DOR of the reference group.

Subgroup analyses revealed that the performance of the MTS was significantly lower in children with a cardiovascular illness, a respiratory illness, a gastrointestinal illness, or another congenital or genetic defect, compared with children without a chronic illness (Table 2). In addition, of all children who presented at the ED with fever without dyspnoea or vomiting/diarrhoea, children with a chronic illness were less often correctly classified than those without a chronic illness.

DISCUSSION

The overall performance of the MTS in patients with infectious symptoms was lower among children with a chronic illness than in those without a chronic illness. Moreover, children with a chronic illness were at higher risk of being undertriaged when the MTS categories were compared with an independent reference standard. Our subgroup analyses revealed that, compared with the performance of the MTS in children without a chronic illness, the performance of the MTS was significantly lower in children with a cardiovascular illness, a respiratory illness, a gastrointestinal illness, or another congenital or genetic defect. In addition, of all children who presented to the ED with fever without dyspnoea or vomiting/diarrhoea, children with a chronic illness were less often correctly classified than those without a chronic illness.

Despite the identification of certain patient subgroups in which the MTS validity was low, it was not feasible to propose specific modifications for children with a chronic illness from our database: the heterogeneity in these subgroups was too large to identify urgency by a few discriminators. Therefore, more studies are needed to identify specific features of these undertriaged children with chronic illness. Currently, we can only recommend that nurses take into account an individual patient's chronic illness when triaging and, if necessary, use their experience to overrule the MTS.

The validity of the MTS depends on the accuracy of the nurse who applies the system (interrater agreement). A previous study in our hospital revealed that the interrater agreement of the MTS (expressed by a weighted κ) was 0.83 (95% CI: 0.74–0.91) for written case scenarios and 0.65 (95% CI: 0.56–0.72) for simultaneous triage of actual patients.[89] Although we did not include chronic illnesses in the written case scenarios, children with chronic illnesses were included during simultaneous triage. The interrater agreement was the same for children with and without chronic illness (data not shown).

Second, in the current study, children with a chronic illness had increased resource utilization and were more frequently hospitalized than children without a chronic illness. These results are in line with other studies on hospitalization and utilization in children with chronic illnesses.[90-92]

This finding can partly be explained by the difference in decision-making around admission and resource utilization between children with and without a chronic illness. For example, children with a chronic illness might more frequently be hospitalized because of challenges in clinical assessment that require longer observation.[91] On the other hand, children with chronic illness may have advanced medical care at home and therefore stay at home, whereas previously healthy children are hospitalized.

However, despite these different strategies for hospitalization and resource use, we believe that this did not affect the final urgency level as assessed by the reference standard. The reference standard only classifies hospitalized children as urgent if the reason for hospitalization

was medical, e.g., abnormal vital signs, requirement of IV medication or fluids, failure to ingest medication (e.g., need for a nasogastric tube), or a surgical intervention. For this reason, the decision to identify patients as urgent was made on the basis of the patient's clinical condition without taking into account nonmedical factors. Therefore, conclusions concerning the validity of the MTS in children with and without a chronic illness are likely to be unbiased.

To our knowledge, this is the first study to examine the validity of the MTS in children with a chronic illness. The study included a good case mix of nearly 9000 children, selected from a multicultural, inner-city, university ED population. Because our percentages of children with chronic illnesses are comparable to the 20% to 35% reported in earlier studies on chronic illness,[4, 91-93] we believe that our results are probably generalisable to other Western tertiary paediatric EDs. It should be noted that our results might have been biased by the way in which chronic illness was defined. In the current study, children were classified into chronic illness subcategories according to the International Classification of Diseases, Ninth Revision, Clinical Modification, codes. This method implies that children should have previously visited the hospital to be classified as having a chronic illness; therefore, children with a chronic illness might be incorrectly classified as a child without chronic illness. The difference between the validity of the MTS in children with and without a chronic illness can therefore be underestimated.

In addition, the way in which chronic illnesses were defined might influence why we were unable to improve the MTS for children with chronic illness in whom the validity was low. We created subgroups on the basis of diagnostic groups, whereas a recent study on chronic illnesses created subgroups on the basis of patients' complexity.[91] Classification based on patients' complexity might have led to a more homogenous group of patients who need to be quickly seen by a physician.

CONCLUSIONS

In children presenting with infectious symptoms, the performance of the MTS was lower for those with a chronic illness than in those without a chronic illness. Particularly for children with a cardiovascular illness, respiratory illness, gastrointestinal illness, or another congenital or genetic defect, nurses should bear in mind that the prioritizing of the MTS might be suboptimal.

CHAPTER 6

Improving the Manchester Triage System for paediatric emergency care: An international multicenter study

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ABSTRACT

Objectives This multicentre study examines the performance of the Manchester Triage System (MTS) after changing discriminators, and with the addition use of abnormal vital sign in patients presenting to paediatric emergency departments (EDs).

Design International multicentre study

Settings EDs of two hospitals in The Netherlands (2006–2009), one in Portugal (November–December 2010), and one in UK (June–November 2010).

Patients Children (<16 years) triaged with the MTS who presented at the ED.

Methods Changes to discriminators (MTS 1) and the value of including abnormal vital signs (MTS 2) were studied to test if this would decrease the number of incorrect assignment. Admission to hospital using the new MTS was compared with those in the original MTS. Likelihood ratios, diagnostic odds ratios (DORs), and c-statistics were calculated as measures for performance and compared with the original MTS. To calculate likelihood ratios and DORs, the MTS had to be dichotomized in low urgent and high urgent.

Results 60375 patients were included, of whom 13% were admitted. When MTS 1 was used, admission to hospital increased from 25% to 29% for MTS 'very urgent' patients and remained similar in lower MTS urgency levels. The diagnostic odds ratio improved from 4.8 (95%CI 4.5–5.1) to 6.2 (95%CI 5.9–6.6) and the c-statistic remained 0.74. MTS 2 did not improve the performance of the MTS.

Conclusions MTS 1 performed slightly better than the original MTS. The use of vital signs (MTS 2) did not improve the MTS performance.

INTRODUCTION

The Manchester Triage System (MTS) is widely used in European emergency departments (EDs) and is based on 52 flowcharts, which incorporate the range of patients' presenting problems. [7, 18] Of these flowcharts, 49 flowcharts are suitable for children. The flowchart that best fits the child's presentation e.g. 'abdominal pain in children' or 'abscesses and local infections' is used by triage nurses to determine the urgency by which they should be seen by a physician.

Triage nurses work down this flowchart until one of the features (discriminators) is positive. This stops the triage process at that stage and the child needs to be seen within the allocated waiting time, corresponding to the triage category.[7, 18] The MTS triage categories are: 1) Immediate: immediate evaluation by a physician; 2) Very urgent: evaluation within 10 minutes; 3) Urgent: evaluation within one hour; 4) Standard: evaluation within two hours; and 5) Non-urgent: evaluation within four hours.

Misclassifying the MTS triage category for a patient can result in a longer waiting time (undertriage) or a shorter waiting time (overtriage). Undertriage, which can result in a patient's condition deteriorating whilst waiting to be seen, is more frequent in children with abnormal vital signs.[94] Overtriage may lead to delay in the assessment of truly unwell patients, particularly when there is a large number of patients (particularly of lesser urgency) waiting to be seen.[23]

Earlier studies on the MTS in children established an independent reference standard for use as proxy for the true urgency of the patient to be seen.[15, 16] When comparing the original MTS with this reference standard, overtriage was more common in children older than 1 year presenting with medical problems, e.g. fever.[16] Modifying the MTS discriminators for these children improved MTS performance in terms of reducing overtriage without increasing undertriage in the Netherlands.[33]

Modifications to the discriminators as presented in our previous study were made, and MTS version 1 was produced.[33] The addition of using vital signs (from an updated ranges of abnormal vital sign values taken from a recent systematic review) to the original MTS is termed MTS version 2 in this paper.[95] This international multicentre study evaluated the MTS performance of two modified versions of MTS for triaging paediatric patients at the ED.

METHODS

Study design

Two adaptations of the MTS in three different countries were studied to see if they could improve overall performance. The adaptations were called 'discriminator modifications, MTS version 1' and with additional 'vital sign modifications', MTS version 2.

The study population was composed of children who had presented at the EDs of four European hospitals, triaged by the original first edition of the MTS. In Portugal and the Netherlands the official Portuguese or Dutch translated versions of MTS were used.[18]

Triage categories, according to MTS version 1 and MTS version 2, were produced by adapting the original MTS triage categories on the basis of allocated MTS flowchart, positive discriminator, age, or vital sign values. Thus, we retrospectively applied MTS 1 and MTS 2 on data that was prospectively collected by using the original MTS.

This study is part of an ongoing study on validation of the MTS [16, 33]; approved by the medical ethics committee of Erasmus MC. Requirement for informed consent was waived.

Settings and selection of participants

Data collection included all children younger than 16 years in the following ED open for 24 hours a day.

Erasmus MC-Sophia Children's Hospital in Rotterdam, the Netherlands (May 2007–July 2009) is an inner-city university hospital with a multi-socio-economic and multi-ethnic population consisting of two million habitants. The paediatric ED receives approximately 9000 children annually (44% self-referrals).

The Haga Hospital-Juliana Children's Hospital in The Hague, the Netherlands (August–December 2007) is a general teaching hospital in The Hague. The mixed adult-paediatric ED receives approximately 30000 patient-visits per year, of whom 18000 are paediatric patients (63% self-referrals). Since 1999, the ED has served as a trauma centre with a catchment area of approximately one million habitants.

The St. Mary's Hospital in London, UK (June–November 2010) is a general teaching acute hospital with a catchment area of nearly 2 million habitants. It is the major trauma centre for North West London. The paediatric emergency department sees 26000 children a year (88% self-referrals).

The Fernando Fonseca Hospital in Lisbon, Portugal (November–December 2010) is an inner-city university hospital with a catchment area of 700000 habitants. The paediatric ED receives nearly 60000 children per year, predominantly self-referrals.

Modifications of the MTS

MTS version 1

In the previous study, modifications to the discriminators for patient groups with high percentages of misclassification were evaluated in two hospitals in The Netherlands and improved the MTS performance.[33] In the MTS, there are general discriminators, e.g. hot child, which occur in most flowcharts and allocate to the same triage category, irrespective of their presenting problem. Our previous modifications were adjusted to this concept. The modifications (MTS version 1) are provided in table 1.[7, 18]

MTS version 2

Vital signs were included as an additional discriminator to the original MTS, to produce MTS version 2.[94] Heart rates and respiratory rates were considered abnormal if the first measured heart rate or respiratory rate was lower than the first percentile or higher than the 99th percentile values published by Fleming et al.[95]. The cut-off levels are presented in the supporting information file Appendix 1. The presence of abnormal heart or respiratory rates leads to a triage category of 'very urgent'.

The discriminators 'very low saturation' and 'low saturation' were defined as peripheral oxygen saturation in air lower than 90% and lower than 95% respectively. If present, patients were triaged to MTS version 2 'very urgent' and MTS version 2 'urgent' triage categories. These discriminators were added to all flowcharts.

Although abnormal vital sign measurements were included in all flowcharts, vital sign recording was left to the nurse's discretion.

Data collection

Data on MTS triage categories, the flowchart used for each patient, and the positive discriminator was collated from the computerized systems of MTS by trained triage nurses,

TABLE 1: Discriminator modifications for patients with high percentage of misclassification (MTS version 1)

DISCRIMINATOR ORIGINAL MTS	ORIGINAL MTS TRIAGE CATEGORY	MTS VERSION 1 DISCRIMINATORS	MTS VERSION 1 TRIAGE CATEGORY	CUT-OFF LEVEL[b]
Hot child	Very urgent	Hot child < 3 months	Very urgent	-
		Hot child > 3 months	Urgent	86%
		Febrile child[a]	Very urgent	-
Persistent vomiting	Urgent	Persistent vomiting < 3 months	Urgent	-
		Persistent vomiting > 3 months	Standard	70%
Not feeding	Urgent	Not feeding < 1 year	Urgent	-
		Not feeding > 1 year	Standard	76%
Prolonged or uninterrupted crying	Urgent	Prolonged or uninterrupted crying < 1 year	Urgent	-
		Prolonged or uninterrupted crying > 1 year	Standard	100%
Scalp hematoma	Standard	Scalp hematoma < 1 year	Standard	-
		Scalp hematoma > 1 year	Non-urgent	66%
Unable to talk in sentences	Very urgent	Unable to talk in sentences	Urgent	75%
Wheeze	Standard	Wheeze	Urgent	53%[c]

[a] This discriminator is present in the neurological flowcharts: fits, irritable child, headache, crying baby, neck pain or behaving strangely.
[b] Proportion of children that were allocated to a lower urgency triage category according to the independent reference standard
[c] Proportion of children that were allocated to a higher urgency triage category according to the independent reference standard

experienced in both paediatric and emergency care.[18] The positive discriminator is the one that determines the MTS triage category.
Nurses recorded data on vital signs values, admission to hospital, and follow-up on structured ED templates. Heart rates, oxygen saturation, and temperature were collected in all four hospitals. Respiratory rates were not collected in the Fernando Fonseca Hospital in Lisbon, Portugal, because it was too time-consuming to measure respiratory rates routinely.
Triage categories, according to MTS version 1 and MTS version 2, were altered by adapting the original MTS triage categories on the basis of allocated MTS flowchart, positive discriminator, age, or vital sign values.

Data analysis
MTS version 1 was initially derived for febrile children. To analyse the effect of this version, analysis on a febrile population was first performed. This population was defined as children who presented with a temperature higher than 38.4ºC or had fever selected as triage discriminator. The next step was to analyse the performance of MTS version 1 in the total population to determine the overall improvement.
To assess the performances of MTS version 1 and MTS version 2, percentages of hospitalisation of the original MTS categories were compared with the percentages of hospitalisation of the new MTS categories. The MTS was deemed to have been improved if the hospitalisation proportions increased in the higher urgency levels and/or lowered in the lower urgency levels.

Subsequently, the positive and negative likelihood ratios, diagnostic odds ratios (DORs), c-statistics (area under the receiver operator-curve), and R^2 were calculated as measures for performance. The DOR is a measure of test performance that combines the sensitivity and specificity (sensitivity/1-sensitivity)/(1-specificity/specificity).[36]
To calculate the DOR and likelihood ratios the triage categories were ordered into 'high urgent' (MTS levels 'immediate' and 'very urgent') and 'low urgent' (MTS levels 'urgent', 'standard', and 'non-urgent'). The c-statistics of the original MTS and the adapted versions of the MTS were compared by using the nonparametric approach of DeLong et al.[96] A p-value of less than 0.05 was considered significant.
Missing vital signs were imputed using a multiple imputation model including age, vital sign values, MTS category, presenting problem, and follow-up. This imputation process resulted in ten databases on which statistical analysis were performed and pooled for a final result.[97] Imputation was performed by using Design and Hmisc (AregImpute function) in R packages version 2.15.2. Statistical Packages for the Social Sciences (SPSS) version 20.0 (Chicago, IL) was used for the statistical analysis.

RESULTS
Study population
In total 64653 children had presented to the EDs. Ninety-four percent (N = 60800) were triaged using the MTS. Data on discharge or hospitalisation were available for 60735 patients. In total, 6895 (11%) patients were admitted to hospital, of whom 29 died in the ED. Patients' characteristics are provided in table 2.

TABLE 2: Patients' characteristics per hospital

	SOPHIA CHILDREN'S HOSPITAL		JULIANA CHILDREN'S HOSPITAL		ST. MARY'S HOSPITAL		FERNANDO FONSECA HOSPITAL		TOTAL POPULATION	
	N=14507 (%)		N=5299 (%)		N=29524 (%)		N=11405 (%)		N=60735 (%)	
Age (years)										
Median (IQR)	4.0	(1.3 to 9.2)	2.7	(0.9 to 6.7)	3.8	(1.5 to 8.5)	4.5	(1.7 to 9.0)	3.8	(1.4 to 8.6)
Presenting problem										
Trauma	2856	(20)	873	(17)	6171	(32)	983	(9)	10883	(18)
Dyspnoea	1428	(10)	1033	(20)	3520	(12)	2484	(22)	8465	(14)
Gastro-intestinal	2042	(14)	819	(16)	5075	(17)	1665	(15)	9601	(16)
Ear, nose, throat	362	(3)	215	(4)	1805	(6)	1830	(16)	4212	(7)
Wounds	1111	(8)	349	(7)	1405	(5)	242	(2)	3107	(5)
Neurological	1115	(8)	208	(4)	1448	(5)	409	(4)	3180	(5)
Fever without source	845	(6)	493	(9)	928	(3)	54	(1)	2320	(4)
Rash	358	(3)	164	(3)	2671	(9)	579	(5)	3772	(6)
Urinary tract problems	335	(2)	102	(2)	292	(1)	247	(2)	976	(2)
Local infection/ abscess	232	(2)	91	(2)	186	(1)	183	(2)	692	(1)
Other problems	3823	(26)	952	(18)	6023	(20)	2729	(24)	13527	(22)
Original MTS triage category										
Immediate	329	(2)	102	(2)	297	(1)	51	(0)	779	(1)
Very urgent	2855	(20)	942	(18)	3537	(12)	2288	(20)	9622	(16)
Urgent	6253	(43)	1283	(24)	4338	(15)	2277	(20)	14151	(23)
Standard/non-urgent	5070	(35)	2972	(56)	21352	(72)	6789	(60)	36183	(60)
Follow-up										
No follow-up	5572	(38)	3104	(59)	15383	(52)	6573	(58)	30632	(50)
Outpatient clinic/ GP	5055	(35)	1192	(22)	8387	(28)	3999	(35)	18633	(31)
Hospital admission	2720	(19)	755	(14)	2866	(10)	554	(5)	6895	(11)
Other follow-up	1160	(8)	248	(5)	2888	(10)	279	(2)	4575	(8)

MTS version 1 in the febrile population

Among the 6836 febrile children eligible for analyses, 19% (N = 1302) were hospitalised. One percent (N = 80) were triaged 'immediate'; 63% (N = 4310) 'very urgent'; 18% (N = 1259) 'urgent'; 17% (N = 1184) 'standard'; and less than 1% (N= 3) 'non-urgent'. In total, 3162 (46%) children were reclassified to either a higher or lower triage category.

The proportions of hospitalisation increased in the MTS 'very urgent' level from 20% to 37% and decreased in the MTS 'urgent' level from 23% to 16%, while there were no differences in the other MTS urgency levels. The positive likelihood ratio increased from 1.1 (95%CI 1.1–1.2) to 2.6 (95%CI 2.4–2.9) and the negative likelihood ratio decreased from 0.80 (95%CI 0.73–0.87) to 0.71 (95%CI 0.68–0.74). The DOR improved from 1.4 (95%CI 1.2–1.6) to 3.7 (95%CI 3.3–4.7), the R^2 improved from 0.05 to 0.10 and the c-statistic increased significantly from 0.56 (95%CI 0.55–0.58) to 0.66 (95%CI 0.64–0.67, p-value, 0.001). (Table 3)

MTS version 1 in the total population

Using the MTS version 1 in the total population (N =60735), 4526 (7%) children were reclassified of whom 3991 were allocated to a lower urgency level. Hospitalisation increased in the MTS 'very urgent' triage category from 25% to 29%, while they remained similar in the other MTS urgency levels. Table 4 shows the total reclassification. The overall positive likelihood ratio of the MTS improved significantly from 3.2 (95%CI 3.0–3.3) to 4.3 (95%CI 4.1–4.4). The DOR increased from 4.8 (95%CI 4.6–5.1) to 6.2 (95%CI 5.9–6.6), the R^2 changed from 0.17 to 0.18 and the c-statistic remained 0.74. (Table 3)

If percentages of hospitalisation were compared for the three hospitals separately, similar trends in percentages of hospitalisation were found. (Figure 1) The likelihood ratios, DORs, R^2 and c-statistics for the separate hospitals are shown in table 5. In all hospitals, the modifications showed the same results although the results of the Fernando Fonseca hospital were not statistically significant.

MTS version 2

Heart rates were measured in 52% (N = 31707) of the total population (N = 60735); respiratory rates were measured in 48% (N = 23513) of patients who visited the hospitals in the Netherlands and the UK (N = 49330 patients); and oxygen saturation was measured in 46% (N = 28066) of patients. Heart rate modifications reclassified 7,298 patients (12%) to the higher MTS 'very urgent' triage category when compared to the original MTS. Eleven percent (N= 829) of the reclassified patients were hospitalised.

Respiratory rate modification reclassified 4,949 patients (10%). Thirteen percent (N= 666) of these were hospitalised.

Oxygen saturation modifications reclassified 130 patients (<1%) to the MTS 'very urgent' triage category (of whom 47 (36%) were hospitalised) and 220 patients (<1%) to the MTS 'urgent' triage category (of whom 57 (26%) were hospitalised).

The performance of MTS version 2 did not improve irrespective of the use of heart rate and respiratory rate. (Table 3) The addition of oxygen saturation slightly changed the R^2 and the c-statistics; however there were no statistically significant improvements of likelihood ratios and diagnostic odds ratios.

TABLE 3: Performance of the original MTS, MTS version 1, and MTS version 2

DATA	MTS EDITION	POSITIVE LIKELIHOOD	NEGATIVE LIKELIHOOD	DIAGNOSTIC ODDS RATIO[b]	C-STATISTIC	R^2
MTS version 1						
Fever (N=6,836)	Original MTS	1.1 (1.1 to 1.2)	0.80 (0.73 to 0.87)	1.4 (1.2 to 1.6)	0.56 (0.55 to 0.58)	0.05
	MTS version 1	2.6 (2.4 to 2.9)	0.71 (0.68 to 0.74)	3.7 (3.3 to 4.3)	0.66 (0.64 to 0.67)	0.10
Total population (N=60,735)	Original MTS	3.2 (3.0 to 3.3)	0.66 (0.64 to 0.67)	4.8 (4.6 to 5.1)	0.74 (0.73 to 0.74)	0.17
	MTS version 1	4.3 (4.1 to 4.4)	0.69 (0.67 to 0.70)	6.2 (5.9 to 6.6)	0.74 (0.74 to 0.75)	0.18
MTS version 2						
Heart rate (N=60,735)	Original MTS	3.2 (3.0 to 3.3)	0.66 (0.64 to 0.67)	4.8 (4.6 to 5.1)	0.74 (0.73 to 0.74)	0.17
	MTS version 2	2.2 (2.1 to 2.2)	0.74 (0.74 to 0.75)	3.6 (3.4 to 3.8)	0.71 (0.71 to 0.72)	0.16
Respiratory rate (N=49,330)[a]	Original MTS	3.5 (3.3 to 3.6)	0.65 (0.64 to 0.66)	5.3 (5.0 to 5.7)	0.74 (0.74 to 0.75)	0.19
	MTS version 2	2.4 (2.3 to 2.5)	0.60 (0.58 to 0.61)	4.0 (3.8 to 4.2)	0.73 (0.72 to 0.73)	0.16
Oxygen saturation (N=60,735)	Original MTS	3.2 (3.0 to 3.3)	0.66 (0.64 to 0.67)	4.8 (4.6 to 5.1)	0.74 (0.73 to 0.74)	0.17
	MTS version 2	3.2 (3.1 to 3.3)	0.65 (0.64 to 0.66)	4.9 (4.6 to 5.1)	0.74 (0.74 to 0.75)	0.18

[a] Respiratory rates were measured in the Sophia Children's Hospital, Juliana Children's Hospital, and St. Mary's hospital
[b] Diagnostic odds ratio=DOR=((sensitivity/1-sensitivity)/(1-specificity/specificity))

DISCUSSION

This international multicentre study showed that discriminator modifications of the MTS (MTS version 1) improved the performance of the MTS when hospitalisation was used as surrogate marker for urgency. Moreover, MTS version 1 did not increase the hospitalisation percentages in the lowest urgency levels. Vital signs modifications (MTS version 2) did not improve the performance of MTS.

MTS version 1

MTS version 1, reclassified only 7% of the total population. This seems a small number and therefore the impact on the total performance may be minimal. However, 88% of those patients were reclassified to a lower urgency level and therefore influences on workflow and pressure could be substantial, as maximum waiting times are extended to at least 50 minutes. The modifications were initially developed for children with infectious presenting symptoms. When analyses were performed on the febrile population 46% patients were reclassified and both DOR as c-statistic increased significantly.

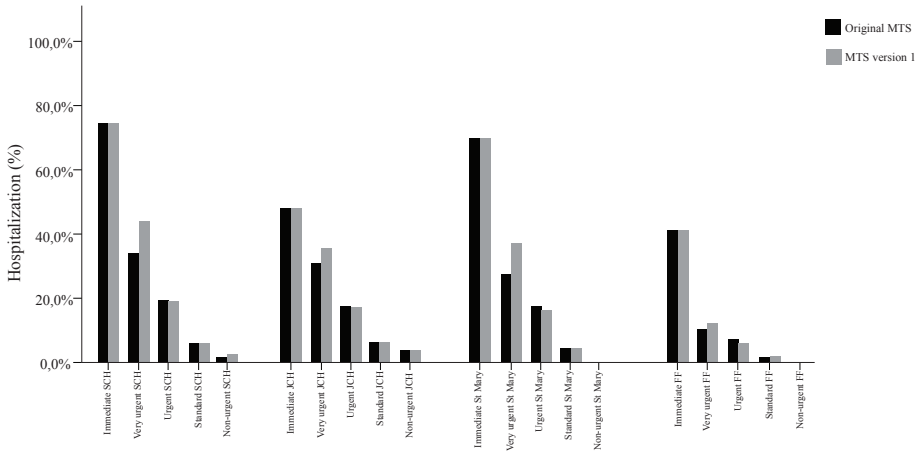

FIGURE 1: Percentages of hospitalisation per urgency level in Sophia Children's Hospital (SCH), Juliana Children's Hospital (JCH), St. Mary's Hospital, and in Fernando Fonseca Hospital (FF).

In the paediatric Canadian Triage and Acuity Scale (CTAS) and the Emergency Severity Index (ESI), modifications for febrile children were implemented as well.[9, 32] In the paediatric CTAS, waiting times for febrile children older than three months without signs of 'toxicity', toxicity meaning unexplained crying before examination, difficulty awakening, or poor response to the physical evaluation, were extended from 15 minutes to 30 minutes and waiting times for febrile children older than three years were extended from 30 minutes to 60 minutes.[32]

TABLE 4: Reclassification table: The original MTS compared with MTS version 1

	MTS VERSION 1					
ORIGINAL MTS	**Immediate**	**Very urgent**	**Urgent**	**Standard**	**Non urgent**	**Total**
Immediate	779	0	0	0	0	779
Hospitalization (%)	552 (67.0)					552 (67.0)
Very urgent	0	6562	3061	0	0	9623
Hospitalization (%)		2068 (31.5)	402 (13.1)			2470 (25.7)
Urgent		0	13221	930	0	14151
Hospitalization (%)			2211 (16.7)	147 (15.8)		2358 (16.7)
Standard	0	0	535	35254	119	35908
Hospitalization (%)			89 (16.6)	1449 (4.1)	1 (0.8)	1539 (4.3)
Non urgent	0	0	0	0	274	274
Hospitalization (%)					6 (2.2)	6 (2.2)
Total	779	6562	16817	36184	393	60735
Hospitalization (%)	552 (67.0)	2068 (31.5)	2702 (16.0)	1596 (4.4)	7 (1.8)	6895 (11.4)

TABLE 5: Performance of the original MTS, MTS version 1, and MTS version 2 per hospital

DATA	MTS EDITION	POSITIVE LIKELIHOOD	NEGATIVE LIKELIHOOD	DOR	C-STATISTIC	R^2
Sophia Children's Hospital (N=14507)	Original MTS	2.7 (2.5-2.8)	0.67 (0.64-0.69)	4.0 (3.7-4.4)	0.71 (0.70-0.72)	0.17
	MTS version 1	4.1 (3.8-4.4)	0.68 (0.66-0.70)	6.1 (5.5-6.7)	0.72 (0.71-0.73)	0.19
	MTS version 2 (heart rate)	2.0 (1.9-2.2)	0.60 (0.55-0.65)	3.4 (2.9-4.0)	0.70 (0.69-0.71)	0.15
	MTS version 2 (respiratory rate)	1.9 (1.8-2.0)	0.63 (0.60-0.66)	3.0 (2.8-3.3)	0.69 (0.67-0.71)	0.14
	MTS version 2 (oxygen saturation)	2.7 (2.5-2.8)	0.66 (0.64-0.68)	4.0 (3.7-4.4)	0.71 (0.70-0.72)	0.17
Juliana Children's Hospital (N=5299)	Original MTS	2.9 (2.6-3.2)	0.65 (0.61-0.70)	4.4 (3.8-5.2)	0.71 (0.69-0.73)	0.14
	MTS version 1	3.6 (3.2-4.0)	0.68 (0.64-0.72)	5.2 (4.4-6.2)	0.72 (0.70-0.74)	0.15
	MTS version 2 (heart rate)	2.9 (2.6-3.2)	0.65 (0.61-0.70)	4.4 (3.8-5.2)	0.69 (0.67-0.71)	0.11
	MTS version 2 (respiratory rate)	2.1 (2.0-2.2)	0.57 (0.52-0.62)	3.7 (3.2-4.4)	0.70 (0.69-0.73)	0.12
	MTS version 2 (oxygen saturation)	3.0 (2.7-3.3)	0.64 (0.60-0.68)	4.6 (3.9-5.5)	0.72 (0.70-0.74)	0.15
St. Mary's Hospital (N=29524)	Original MTS	4.1 (3.9-4.4)	0.65 (0.63-0.67)	6.3 (5.8-6.9)	0.74 (0.73-0.75)	0.18
	MTS version 1	6.5 (6.0-7.0)	0.69 (0.67-0.71)	9.4 (8.6-10.3)	0.74 (0.73-0.75)	0.20
	MTS version 2 (heart rate)	4.3 (4.0-4.7)	0.78 (0.77-0.78)	4.3 (4.0-4.7)	0.72 (0.71-0.73)	0.15
	MTS version 2 (respiratory rate)	2.7 (2.6-2.9)	0.61 (0.59-0.63)	4.5 (4.2-4.9)	0.72 (0.71-0.73)	0.15
	MTS version 2 (oxygen saturation)	4.1 (4.0-4.3)	0.65 (0.63-0.67)	6.4 (5.9-6.9)	0.74 (0.73-0.75)	0.18
Fernando Fonseca Hospital(N=11405)	Original MTS	2.5 (2.2-2.7)	0.65 (0.60-0.71)	3.8 (3.2-4.5)	0.72 (0.69-0.74)	0.10
	MTS version 1	2.9 (2.7-3.2)	0.64 (0.59-0.69)	4.6 (3.9-5.5)	0.71 (0.69-0.74)	0.10
	MTS version 2 (heart rate)	1.8 (1.6-1.9)	0.64 (0.58-0.70)	2.8 (2.3-3.3)	0.68 (0.65-0.70)	0.08
	MTS version 2 (oxygen saturation)	2.5 (2.2-2.7)	0.65 (0.60-0.70)	3.8 (3.2-4.5)	0.71 (0.69-0.74)	0.11

The modifications of the ESI were on the basis of the guideline "Clinical Policy for Children Younger than 3 Years Presenting to the Emergency Department with Fever" published by The American College of Emergency Physicians.[98] Children older than three months with a temperature higher than 39.0°C could be down-triaged at least one triage category.[9] Modifications of the ESI were based on literature review, but the impact of these specific modifications for children was, to our knowledge, not evaluated after implementation.
The changes in MTS version 1 are similar to the modifications implemented in other triage systems and are evaluated in four different settings in three different countries. The implementations improved the MTS ability to distinguish the degree of urgency and therefore we recommend incorporation of the modifications in the next version of the MTS.

MTS version 2
Before the introduction of formal triage systems, vital signs were often used as a decision making tool to determine how quickly a patient should be seen.[6] Since the introduction of five-level triage scales, the role of vital signs as an urgency marker still exists, but is not predominant as decision making tool anymore.
In the Australasian Triage Scale (ATS), the paediatric CTAS, and ESI, vital signs are measured in less urgent triage categories to upgrade patients with abnormal vital signs.[4, 6, 32]
In the original MTS, vital signs are only incorporated in specific flowcharts and therefore only measured in patients presenting with specific presenting symptoms.[7, 18] Vital signs have been thought to be an essential component of paediatric triage.[99] Our previous study[94] suggested that vital sign measurement might help reduce undertriage rates. Given these two factors, the values for normal and abnormal vital signs were added to all flowcharts. In contrast to our expectations, our study showed that MTS version 2 did not benefit from introducing vital signs measurements.
These results can partially be explained by knowledge of abnormal vital sign values at triage assessment. Studies have shown that in six to eight percent of patients, triage decisions were affected by knowledge of vital signs.[100, 101] These percentages were 11.4% for younger children.[101] However, none of these studies have analysed the correctness of changing the triage decision. Moreover, no cut-off levels for abnormal vital signs were given to these nurses[101] and therefore change in triage decision in these studies were not based on evidence based cut-off values, but on the interpretation by the nurse. In our study, the cut-off levels of abnormal vital signs were on the basis of evidence-based reference ranges.[95] Cut-off level for abnormal vital sign were the first and 99th percentile of these reference ranges, because these extreme levels are associated with the most severely ill population.

Strength and limitations
The modifications were evaluated in four different settings. Although the included time period varied per hospital and therefore case-mix could have affected our results, the modifications showed the same results for MTS version 1 and MTS version 2 in all hospitals. Moreover, the seasonal influences upon the evaluation of the triage decisions were not statistically significant in the hospitals in which data was collected for at least one year. (Data not shown) This indicates that modifications of the MTS can be generalized to other developed countries regardless of health care system or MTS translation.
In this study, the modifications of the MTS were not implemented in the triage process itself and therefore the modifications were not evaluated in practice. As the modifications to the MTS are small and simple, we expect comparable performance in practice.

In earlier studies, we argued that it is preferred to evaluate triage systems with an independent reference standard.[10, 15, 16, 33] However, this reference standard is based on many different items which were not available in the various settings. Since MTS version 2 has incorporated vital signs to the MTS, a reference standard including vital signs is not independent of MTS version 2 and therefore not suitable. For these reasons, hospitalisation was used as a surrogate marker for severity. Criteria for hospitalisation were abnormal or threatened vital signs, requirements of intravenous medication or fluids, failure to ingest medication (e.g., need for a nasogastric tube), and requirements for surgery. We are aware that hospitalisation may not always mean the patient must be seen within 10 minutes or that discharged patients can wait for at least one hour.[102] For example, patients with respiratory distress stabilized after receiving a nebulizer should be seen within 10 minutes after arrival, but the patient may be subsequently discharged. Despite this limitation, the marker of hospitalisation is associated with patients being classified as 'urgent' in other studies on paediatric triage.[29, 42, 103]
Vital signs were only measured in 50% of patients. Literature showed that there is a correlation between triage nurse measurement of vital signs and the severity of the presenting illness and thus missing at random on x (vital signs) and y (hospitalisation).[104, 105] A valid method to deal with missing at random is a multiple imputation model that replaces the missing value by a value that is drawn from an estimate of the distribution of the variable.[97, 106]

CONCLUSIONS

Discriminator modifications (MTS version 1) improve the performance of the MTS in this broad validation study in different international EDs.
We recommend implementing these modifications in the next version of the MTS. The addition of vital signs to the MTS (MTS version 2) did not improve triage classifications.

APPENDIX 1: Reference values for normal heart rates and respiratory rates by Fleming et al.[95]

	HEART RATE (beats per minute)	RESPIRATORY RATE (breaths per minute)
Age range		
0-3 months	107 to 181	25 to 66
3 to 6 months	104 to 175	24 to 64
6 to 9 months	98 to 168	23 to 61
9 to 12 months	93 to 161	22 to 58
12 to 18 months	88 to 156	21 to 53
18 to 24 months	82 to 149	19 to 46
2 to 3 years	76 to 142	18 to 38
3 to 4 years	70 to 136	17 to 33
4 to 6 years	65 to 131	17 to 29
6 to 8 years	59 to 123	16 to 27
8 to 12 years	52 to 115	14 to 25
12 to 15 years	47 to 108	12 to 23
15 to 16 years	43 to 104	11 to 22

CHAPTER 7

Exploring the possibilities of improving triage for paediatric patients by machine learning

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ABSTRACT

Background The Manchester Triage System (MTS), a five-level triage system used to prioritize patients at the emergency department (ED), showed moderate validity. To optimize triage, this study explored machine learning approaches to predict 'true urgency' defined by a reference standard for urgency classification.

Methods Children (<16years) who visited the ED of the Erasmus MC–Sophia Children's Hospital (2006-2010) and were allocated to the MTS flowchart 'Shortness of breath', 'Worried parent' and 'Fits' were included. Machine learning algorithms CART and RIPPER were applied to classify children according to a reference standard based on abnormal vital signs, resource utilization, and follow-up. The validity of the models was expressed by sensitivity, specificity and area under the curve (AUC). The algorithms OPUS and EXPLORE were used to search for association and decision rules for undertriaged and overtriaged patients that could improve the current MTS flowcharts.

Results In the flowchart 'Shortness of breath', CART and RIPPER generated models with an AUC of 0.58 (95%CI 0.57-0.59) and 0.53 (95%CI 0.52-0.53), respectively. In the flowchart 'Worried parent', the AUC of CART was 0.50 (95%CI 0.49-0.51) and of RIPPER 0.50 (95%CI 0.48-0.51). In the flowchart 'Fits' these were 0.58 (95%CI 0.57-0.60) and 0.53 (95%CI 0.52-0.54). None of these AUCs were higher than those of the original MTS flowchart. The algorithms OPUS and EXPLORE induced four association rules that might improve the MTS.

Conclusion The validity of three MTS flowcharts could not be improved by using the Machine learning algorithms CART, RIPPER, OPUS and EXPLORE on discriminators of the MTS in combination with patient's characteristics.

BACKGROUND

Triage systems are important tools in emergency departments (EDs) to identify patients with life-threatening conditions and to manage flows of patients with lower acuity safely.[7, 18]

The Manchester Triage system (MTS) is a consensus based five-level triage system widely used in European emergency departments (EDs).[7] It is based on 52 flowcharts, which incorporate the range of patients' presenting problems. The flowchart that best fits the patient's presentation is used to allocate one out of five triage categories. The first positive sign or symptom (positive discriminator) in the flowchart determines the triage category that expresses the maximum waiting time for patients to be seen by the physician.[7, 18]. The five triage urgency categories of the MTS are: 1) Immediate, direct evaluation; 2) Very urgent, evaluation within 10 minutes; 3) Urgent, evaluation within one hour; 4) Standard, evaluation within two hours; 5) Non-urgent, evaluation within four hours.

In paediatric patients, the MTS showed moderate validity, i.e. more overtriage than undertriage when compared with a reference standard based on a combination of abnormal vital signs, diagnostic and therapeutic resource use, hospitalisation, and discharge.[16] The sensitivity was 63% and the specificity 79%.[16] A recent study found that specificity can be increased to 87% without decreasing the sensitivity by adding age specific adaptations to the fever discriminator of the MTS for children.[33] This improvement by age specific adaptations suggests that the MTS might be further improved by moving certain discriminators to a higher or lower urgency category in combination with patients characteristics like age.

Since the development of a triage system can be compared with that of clinical prediction rules[10], it might be possible to optimize the MTS model by estimating the reference outcome by using all possible predictors of the MTS (discriminators) and additional patients' characteristics present at triage. Traditionally, logistic regression models are the standard approach to develop such decision rules.[107] However, the probability estimates of these models can be biased if the model is not correctly specified due to problems like non-linear robust estimation of individual probabilities, large numbers of predictors, or unknown interactions within the predictors.[108]

To improve classifications, Machine Learning algorithms might be of value. These flexible methods may recognize complex patterns in data for probability estimation and classification.

The aim of this study was to explore the value of machine learning algorithms CART, RIPPER, OPUS, and EXPLORE for optimizing the MTS by predicting 'true urgency' defined by an independent reference standard for paediatric urgency classification at the ED.

METHODS

Study design

In this observational study, we used machine learning for two different strategies. First, we applied the CART and RIPPER algorithms to classify patients into urgency levels according to an independent reference standard by using the discriminators of the MTS in combination with patient's characteristics.

Secondly, we searched for combinations of discriminators and patient's characteristics that can be moved to a higher or lower triage category in the current MTS flowcharts by searching with OPUS and EXPLORE for association and decision rules respectively that focused on the miss-classifications with the highest impact, e.g., patients that were classified by the MTS as low urgency and a high urgency based on the reference standard (undertriage) and the other way around (overtriage).

This study was part of an ongoing study on the validity of the MTS that was approved by the Medical Ethical Committee of Erasmus MC, who waived requirements for informed consent.[16, 33, 34, 109]

Study population

Our study population comprised all children (<16 years) who attended the ED of a large inner-city university hospital in the Southwest of the Netherlands and who were allocated to the MTS flowcharts 'Worried parent', 'Shortness of breath', or 'Fits'. The inclusion period started in January 2006 and ran until at least 1000 patients per flowchart were included, which was reached in December 2010.

The paediatric ED of Erasmus MC - Sophia Children's Hospital (Rotterdam) is open 24/7 and receives approximately 9000 children annually. The MTS has been used since August 2005 by trained triage nurses experienced in paediatrics and emergency care.

Manchester Triage System, version and adaptations

In this study, an adapted version of the MTS (official Dutch translation) was used. The adaptations included nine changes to discriminators which were applied to flowcharts that showed low validity. The adaptations were mainly for children presenting the ED with infectious symptoms.[33] In figure 1, the flowcharts 'Shortness of breath in children (22 discriminators) ', 'Worried parent'(25 discriminators), and 'Fits' (22 discriminators) including the adaptations can be seen.

Reference standard

The independent reference standard used as proxy for true urgency was developed on the basis of expert opinion and literature.[16, 33] The reference standard consist of five urgency levels comparable with the urgency levels of the MTS and included the following items which were collected during patient's ED visit:

1) Immediate, patients who had abnormal vital signs according to the Paediatric Risk of Mortality Score[26]
2) Very urgent, patients who were diagnosed with life-threatening conditions defined as meningitis, sepsis, high energetic trauma, substantial blood loss, aorta dissection, > 10% dehydration, (near)drowning, electric trauma, possible dangerous intoxication, >10% burns, and facial burns or possible inhalation trauma
3) Urgent, patients who had one of the following combinations;
   - Intravenous medication (including aerosols and fluids) OR casting OR gastrolavage, inguinal hernia reposition OR luxation reposition
   - Some diagnostic work-up OR oral medication at the ED OR small surgical interventions e.g. bandage AND admission to hospital
   - Extended laboratory diagnostics including blood culture, CSF puncture or multiple laboratory tests OR imaging AND therapy at the ED OR small surgical interventions.
   - Extended laboratory diagnostics AND imaging
   - Extended laboratory diagnostics OR Imaging AND planned follow-up visit within 24 hours AND some therapy including medication on prescription or simple advices
4) Standard, patients who had some diagnostic work-up, therapy at the ED or a planned follow-up visit or who were admitted to hospital without meeting the criteria for

urgent.
5) Non-urgent, patients with no diagnostic work-up, no treatment at the ED, and who were discharged without a planned follow-up visit.

In earlier studies, details about the development of the reference standard and the actual reference matrix were published.[16, 33, 109]

Data collection

To apply machine learning, we had to collect possible predictors of acuity. Discriminators of the MTS could be considered as predictors of acuity and therefore information about the presence or absence of all discriminators in a flowchart was needed. Therefore nurses had to select in a computerized version of the MTS the allocated flowchart and positive discriminator and had to gather information on all the other discriminators that represent additional signs and symptoms during triage.

Data on patients' characteristics, vital signs, resource utilization, and follow-up were collected on structured paper (2006-2009) and later electronic ED forms (2009-2010). The information collected on paper ED forms were gathered and entered by trained medical students using SPSS Data Entry 4.0.

Data analyses

Missing data on the presence or absence of discriminators were imputed using a single imputation model including age, gender, referrer, medical specialty, vital sign values, MTS category, discriminators, reference standard, time of arrival, and follow-up.[97] The number of imputed discriminators are shown in table 1.

For each flowchart, Classification And Regression Tree (CART) and Repeated Incremental Pruning to Procedure Error Reduction (RIPPER) classifiers available in WEKA Data Mining Software[110] were induced using ten-fold cross-validation.

CART generates a decision tree by determining a sequence of logical 'if-then' conditions that split the data into two classes. This process continues until regions with examples of mainly the same class are obtained. Finally, a global optimization step is applied to prune the decision tree to reduce overfitting which could improve the accuracy of the tree on unseen data.[111]

RIPPER generates a large number of rules based on patterns in the data using a covering approach. This pattern is assessed by learning first the best conjunctive rule. This rule will be supplemented by a new rule extracted from the remaining samples after removal of the positive samples from the first rule. This process continues until enough rules are added to classify the dataset. Secondly, the algorithm prunes the rule set systematically and incrementally until there is a concise set of best classification rules.[112]

Percentages of overtriage, correct triage, and undertriage were calculated when patients were classified into five categories. The discriminative ability of CART and OPUS were expressed by the area under the curve (AUC) for ordinal data.[113] Sensitivity and specificity were calculated when patients were classified into two categories e.g. 'high urgency' (reference categories 'immediate' and 'very urgent') and 'low urgency' (reference categories 'urgent', 'standard', and 'non-urgent').

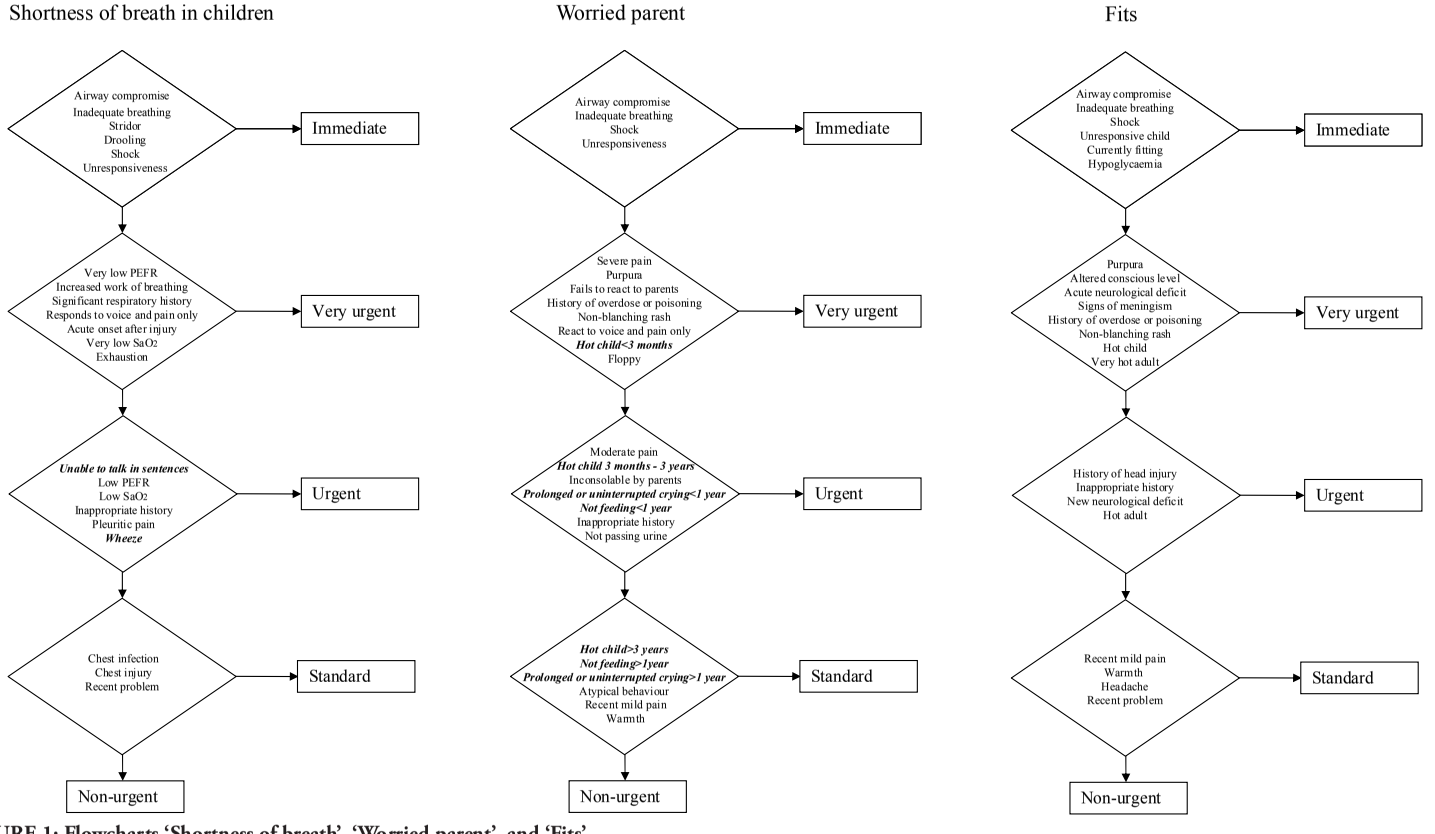


FIGURE 1: Flowcharts 'Shortness of breath', 'Worried parent', and 'Fits'

Adaptations are displayed in bold/italic. Reprinted with permission from Blackwell Publishing Ltd (Mackway-Jones K, Manchester Triage Group. Emergency Triage, 2nd edition. London: BMJ Publishing Group; 2006).

TABLE 1: Presence, absence and missing of discriminators per flowchart

DISCRIMINATOR	PRESENT		ABSENT		MISSING	
	N	(%)	N	(%)	N	(%)
Flowchart 'Shortness of breath'						
Airway compromise	45	(2)	2606	(98)	0	(0)
Inadequate breathing	75	(3)	2574	(97)	0	(0)
Stridor	113	(4)	2535	(96)	3	(<1)
Drooling	5	(<1)	2646	(>99)	0	(0)
Shock	10	(<1)	2617	(99)	24	(1)
Unresponsiveness	22	(1)	2628	(99)	1	(<1)
Increased work of breathing	1335	(50)	1287	(49)	29	(1)
Significant respiratory history	548	(21)	1930	(73)	173	(7)
Responds to voice and pain only	26	(1)	2469	(93)	156	(6)
Acute onset after injury	8	(<2)	2555	(96)	88	(3)
Very low SaO_2	144	(5)	2502	(94)	5	(<1)
Exhaustion	91	(3)	2434	(92)	126	(5)
Unable to talk in sentences	322	(12)	1998	(75)	331	(12)
Low SaO_2	833	(31)	1785	(67)	33	(1)
Inappropriate history	20	(1)	2466	(93)	165	(6)
Pleuritic pain	535	(20)	1701	(64)	415	(16)
Wheeze	998	(38)	1344	(51)	309	(12)
Chest infection	992	(37)	930	(35)	728	(28)
Chest injury	9	(<1)	2432	(92)	210	(8)
Recent problem	2346	(89)	125	(5)	180	(7)
Flowchart 'Worried parent'						
Airway compromise	1	(<1)	1425	(>99)	0	(0)
Inadequate breathing	3	(<1)	1423	(>99)	0	(0)
Shock	0	(0)	1424	(>99)	2	(<1)
Unresponsiveness	0	(0)	1424	(>99)	2	(<1)
Severe pain	2	(<1)	1420	(>99)	4	(<1)
Purpura	3	(<1)	1420	(>99)	3	(<1)
Fails to react to parents	5	(<1)	1417	(>99)	4	(<1)
History of overdose or poisoning	3	(<1)	1419	(>99)	4	(<1)
Non-blanching rash	11	(1)	1412	(99)	3	(<1)
Responds to voice and pain only	2	(<1)	1420	(>99)	4	(<1)
Hot child <3 months	22	(2)	1403	(98)	1	(<1)
Floppy	7	(1)	1417	(99)	2	(<1)
Moderate pain	124	(9)	1235	(87)	67	(5)
Hot child 3 months-3 years	275	(19)	1151	(81)	0	(0)
Inconsolable by parents	93	(7)	1310	(92)	23	(2)
Prolonged or uninterrupted crying <1year	106	(7)	1310	(92)	10	(1)
Not feeding <1 year	87	(6)	1313	(92)	26	(2)
Inappropriate history	126	(9)	1268	(89)	32	(2)
Not passing urine	23	(2)	1369	(96)	34	(2)
Hot child >3 years	110	(8)	1315	(92)	1	(<1)
Not feeding >1 year	99	(7)	1293	(91)	34	(2)
Prolonged or uninterrupted crying >1year	61	(4)	1326	(93)	39	(3)
Atypical behaviour	129	(9)	1186	(83)	111	(8)
Recent mild pain	131	(9)	1218	(85)	77	(5)
Warmth	478	(34)	928	(65)	20	(1)

TABLE 1: Continued

DISCRIMINATOR	PRESENT		ABSENT		MISSING	
	N	(%)	N	(%)	N	(%)
Flowchart 'Fits'						
Airway compromise	17	(2)	992	(98)	0	(0)
Inadequate breathing	46	(5)	963	(95)	0	(0)
Shock	4	(<1)	970	(96)	35	(4)
Unresponsive child	70	(7)	938	(93)	1	(<1)
Currently fitting	176	(17)	818	(81)	15	(2)
Hypoglycaemia	2	(<1)	920	(91)	87	(9)
Purpura	6	(1)	920	(91)	83	(8)
Altered conscious level	329	(33)	678	(67)	2	(<1)
Signs of meningism	7	(<1)	891	(88)	111	(11)
History of overdose or poisoning	2	(<1)	894	(89	113	(11)
Non-blanching rash	11	(1)	909	(90)	89	(9)
Hot child	410	(41)	565	(56)	34	(3)
History of head injury	25	(3)	785	(78)	199	(20)
Inappropriate history	8	(1)	824	(82)	177	(18)
New neurological deficit	300	(30)	473	(47)	236	(23)
Recent mild pain	195	(19)	494	(49)	320	(32)
Warmth	291	(29)	546	(54)	172	(17)
Headache	90	(9)	372	(37)	547	(54)
Recent problem	612	(61)	26	(3)	371	(37)

Additionally, we induced association and decision rules by the Optimized Pruning for Unordered Search (OPUS) and Exhaustive Procedure for Logical Rule Extraction (EXPORE) to find anomalies in the data that could trigger improvements for the MTS.

We applied the Optimized OPUS algorithm [114] to find association rules that focused on undertriaged and overtriaged patients. Undertriage was defined as patients allocated to the MTS categories 'immediate' or 'very urgent' and were classified as 'urgent', standard' or 'non-urgent' by the reference standard and vice versa is called overtriage. For this case we then tried to create rules based on combinations of discriminators that were only part of the lower levels of the MTS to estimate high urgency. This strategy was also applied for overtriage.

The OPUS algorithm searches for probabilistic rules that contain combinations of attribute values that occur at a frequency greater than could be expected by change. Each rule is composed of two parts. The left-hand-side (LHS) appears before the arrow and the right-hand-side (RHS) appears after the arrow. A number of statistics are estimated that describe the relationship between the LHS and RHS. The *coverage* is the proportion of patients that meet the criteria of the LHS of the rule;

the *support* of the rule is the number of cases that contain both the LHS and the RHS; the *strength* is the support divided by the coverage which represents the proportion of the cases that contain the LHS that also contain the RHS. We assessed rules if at least 1% of patients meet the criteria of the rule (support) and if the strength was higher than 50%.

Furthermore, decision rules were estimated using the EXPLORE which is an algorithm designed for binary classification. The algorithm exhaustively generates all possible rules of a user-specified length that fulfil user-specified performance constraints. The maximal length of a rule was set on three parameters. The performance constraint was set at a specificity of 90% , the mean for all flowcharts.[33] For each rule the sensitivity, specificity, and positive and negative predictive values were calculated. The rule might be useful if the sensitivity of the rule was higher than the sensitivity of
the individual flowcharts.

RESULTS

Population

The MTS was applied in 30518 of 32365 children (94%) who had attended the ED. The reference standard did not differ between children with a triage category and children of whom the triage category was missing. Nurses overruled the triage category in 1414 children (5%), of whom 659 children (47%) were up-triaged and 755 (53%) children were down-triaged. The reference standard could not be obtained in 795 children (3%) due to incompleteness of data. Therefore, 28309 children were eligible, of whom 2651 children (9%) were allocated to the flowchart 'Shortness of breath in children, 1426 children (5%) to the flowchart 'Worried parent', and 1009 (4%) to the flowchart 'Fits'. Patient's characteristics of the total population and per flowchart are shown in table 2.

The distribution of the reference standard for children allocated to the MTS flowchart 'Shortness of breath in children' was: immediate, 458 children (17%); very urgent, 32 children (2%); urgent, 1,243 children (47%); standard, 644 children (24%); and non-urgent, 274 children (10%).
For the flowchart 'Worried parent' this was: immediate, 33 children (2%); very urgent, 11 children (1%); urgent, 160 children (11%); standard, 750 children (53%); and non-urgent, 472 children (33%). And for the flowchart 'Fits' this was: immediate, 354 children (35%); very urgent, 3 children (1%); urgent, 186 children (18%); standard, 408 children (40%); and non-urgent, 58 children (6%).
The comparison of the MTS triage categories with the reference standard categories expressed by sensitivity, specificity, AUC, undertriage, correct triage, and overtriage are shown in table 2.

Machine learning used for classification (CART and RIPPER)

Table 3 shows the urgency distribution according to CART and RIPPER and the percentages overtriage, correct triage, undertriage, sensitivity, specificity and AUC per flowchart. The CART decision trees and RIPPER rules generated from the data per flowchart are shown in appendix 1-6. The classifications according to these decision trees or rules were compared with the reference standard and these results are shown in Appendix 7. The matrices of appendix 7 show the average result of the ten-fold cross-validation experiment, which all may have resulted in different classifiers. The final CART and RIPPER models are the one trained when taking the whole dataset.
The algorithms CART and RIPPER did not significantly improve the discriminative ability of the MTS. The original MTS flowchart 'Shortness of breath' had an AUC of 0.60 (95% CI 0.59-0.61) and this was 0.58 (95% CI 0.57-0.59) for the decision tree generated by CART

TABLE 2: Patients characteristics of the total population and per flowchart

	STUDY POPULATION		SHORTNESS OF BREATH		WORRIED PARENT		FITS	
	N=28309 (%)		N=2651 (%)		N=1426 (%)		N=1009 (%)	
Gender								
Female	11842	(42)	1027	(39)	694	(49)	423	(42)
Age (years)								
Median (IQR)	4.1	(1.4-9.4)	1.8	(0.7-4.6)	1.1	(0.3-3.2)	3.3	(1.6-8.1)
MTS triage category								
Immediate	646	(2)	178	(7)	4	(0)	209	(21)
Very urgent	3943	(14)	1279	(48)	90	(6)	450	(45)
Urgent	13114	(46)	632	(24)	586	(41)	201	(20)
Standard	10122	(36)	557	(21)	561	(39)	148	(15)
Non-urgent	484	(2)	5	(0)	185	(13)	1	(0)
Follow-up								
No follow-up	11030	(39)	668	(25)	654	(46)	231	(23)
Outpatient clinic/GP	9788	(35)	715	(27)	422	(30)	317	(31)
Hospital admission	4573	(16)	845	(32)	186	(13)	346	(34)
IC admission/Mortality at ED	511	(2)	139	(5)	14	(1)	59	(6)
Telephonic follow-up	2103	(7)	279	(11)	130	(9)	52	(5)
Other follow-up	304	(1)	5	(0)	20	(1)	4	(0)
Comparison MTS triage categories with reference standard								
Undertriage	3391	(12)	472	(18)	181	(13)	199	(20)
Correct triage	11591	(41)	730	(28)	460	(32)	340	(34)
Overtriage	13327	(47)	1449	(55)	785	(55)	470	(47)
Sensitivity (95% CI)[a]	71.9	(69.8-73.9)	89.0	(85.9-91.5)	25.0	(14.6-39.4)	93.3	(90.2-95.4)
Specificity (95% CI)[a]	87.8	(87.4-88.2)	52.8	(50.7-54.9)	94.0	(92.6-95.1)	50.0	(46.2-53.8)
AUC (95% CI)	0.58	(0.57-0.58)	0.60	(0.59-0.61)	0.57	(0.54-0.60)	0.60	(0.59-0.61)

[a] To calculate sensitivity and specificity both variables 'MTS triage categories' and 'reference categories' have to be dichotomized in 'high urgency' and 'low urgency'

and 0.53 (95%CI 0.52-0.53) for the rules generated by RIPPER. For the MTS flowchart 'Worried parent', CART and RIPPER provided an AUC of 0.50 (95% CI 0.49-0.51) and 0.50 (95% CI 0.48-0.51) respectively, while the AUC of the original MTS flowchart was 0.57 (95% CI 0.54-0.60). The original MTS flowchart 'Fits' had an AUC of 0.60 (95% CI 0.59-0.61) , CART an AUC of 0.58 (95% CI 0.57-0.60) and RIPPER 0.53 (95% CI 0.52-0.54). Moreover, in all three flowcharts CART and RIPPER decreased the sensitivity and increased the specificity.

Machine learning to extract information for improving the current MTS flowcharts (OPUS and EXPLORE)

The OPUS algorithm generated 77 rules with a support of 1% that allocated patients to 'high urgency' according to the reference standard for the flowchart 'Shortness of breath', 1 rule for the flowchart 'Worried parent', and 45 rules for the flowchart 'Fits'. The exact rules generated by OPUS are shown in Appendix 8. There were no rules extracted that allocated patients to the reference category 'low urgency'.

Only four of the extracted rules, all generated for the flowchart 'Shortness of breath', had a strength higher than 50%. These rules were:

1. Unable to talk in sentences=present AND Low SaO2=present AND Chest infection=present -> Reference standard='high urgency'
2. Unable to talk in sentences=present AND Low SaO2=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency'
3. Unable to talk in sentences=present AND Low SaO2=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency'
4. Unable to talk in sentences=present AND Significant respiratory history=present AND Low SaO2=present AND Chest infection=present -> Reference standard='high urgency'

The EXPLORE algorithm generated for high and low urgency are shown in appendix 9. Only the EXPLORE rule 'Prolonged or uninterrupted crying > 1 year=present AND Warmth=absent' OR 'Prolonged or uninterrupted crying < 1 year=present' which allocates patients to 'low urgency' in the flowchart 'Worried parent' had a higher sensitivity compared to the sensitivity of the current flowchart 'Worried parent'. However, since it is not possible for a patient to be younger and older than 1 year at the same time addition of this rule to the flowchart 'Worried parent' will not improve the discriminative ability of the MTS.

DISCUSSION

In this study, we used the machine learning approaches CART, RIPPER, OPUS and EXPLORE to improve the validity of the MTS flowcharts 'Shortness of breath in children', 'Worried parent' and 'Fits'. The discriminative ability for these flowcharts was low, the AUC varied between 0.50-0.58. In none of these flowchart, there was an improvement of the discriminative ability by CART and RIPPER. Moreover, in all flowcharts CART and RIPPER decreased the sensitivity strongly, while the specificity increased, which means that these algorithms increases undertriage and thus potential morbidity.[94]

TABLE 3: Validity of the flowcharts when applying the machine learning algorithms CART and RIPPER

	URGENCY DISTRIBUTION	NUMBER (%)		OUTCOME[a]	PERCENTAGE (95% CI)	
Flowchart 'Shortness of breath'						
CART	Immediate	273	(10.3)	Undertriage	17.3	(15.8-18.7)
	Very urgent	0	(0.0)	Correct triage	57.1	(55.3-59.0)
	Urgent	1716	(64.7)	Overtriage	26.1	(24.4-27.8)
	Standard	606	(24.9)	Sensitivity	41.4	(37.2-45.8)
	Non-urgent	2	(0.1)	Specificity	96.8	(95.9-97.4)
	High urgency	273	(10.3)	AUC	0.58	(0.57-0.59)
	Low urgency	1064	(89.7)			
RIPPER	Immediate	282	(10.6)	Undertriage	12.2	(11.0-13.5)
	Very urgent	0	(0.0)	Correct triage	53.7	(51.8-55.6)
	Urgent	2219	(83.7)	Overtriage	34.7	(32.9-36.5)
	Standard	150	(5.7)	Sensitivity	44.7	(40.4-49.1)
	Non-urgent	0	(0.0)	Specificity	97.1	(96.3-97.7)
	High urgency	282	(10.6)	AUC	0.53	(0.52-0.53)
	Low urgency	2369	(89.4)			
Flowchart 'Worried parent'						
CART	Immediate	1	(0.1)	Undertriage	14.0	(12.2-15.8)
	Very urgent	0	(0.0)	Correct triage	52.5	(49.9-55.0)
	Urgent	13	(0.9)	Overtriage	33.6	(31.1-36.0)
	Standard	1411	(98.9)	Sensitivity	0.0	(0.0-8.0)
	Non-urgent	1	(0.1)	Specificity	99.9	(99.9-100.0)
	High urgency	1	(0.1)	AUC	0.58	(0.57-0.60)
	Low urgency	1425	(99.9)			
RIPPER	Immediate	2	(0.1)	Undertriage	7.5	(6.5-8.5)
	Very urgent	0	(0.0)	Correct triage	28.2	(26.5-29.9)
	Urgent	9	(0.6)	Overtriage	18.0	(16.6-19.5)
	Standard	1415	(99.2)	Sensitivity	0.0	(0.0-8.0)
	Non-urgent	0	(0.0)	Specificity	99.9	(99.5-100.0)
	High urgency	2	(0.2)	AUC	0.50	(0.48-0.51)
	Low urgency	1424	(99.9)			
Flowchart 'Fits'						
CART	Immediate	377	(37.4)	Undertriage	29.2	(26.4-32.0)
	Very urgent	0	(0.0)	Correct triage	47.6	(44.5-50.7)
	Urgent	0	(0.0)	Overtriage	27.0	(24.2-29.7)
	Standard	632	(62.6)	Sensitivity	51.3	(46.1-56.4)
	Non-urgent	0	(0.0)	Specificity	70.3	(66.6-73.6)
	High urgency	377	(37.4)	AUC	0.58	(0.57-0.60)
	Low urgency	632	(62.6)			
RIPPER	Immediate	274	(27.2)	Undertriage	34.5	(31.6-37.4)
	Very urgent	0	(0.0)	Correct triage	48.2	(45.1-51.2)
	Urgent	3	(0.3)	Overtriage	19.9	(17.5-22.4)
	Standard	732	(72.5)	Sensitivity	40.3	(35.4-45.5)
	Non-urgent	0	(0.0)	Specificity	80.1	(76.8-83.0)
	High urgency	274	(27.2)	AUC	0.53	(0.52-0.54)
	Low urgency	735	(72.8)			

[a] Machine learning distribution compared with the reference standard

The question is why these algorithms were not able to improve the MTS. First, CART and RIPPER are not built to induce classifiers such as the MTS, i.e. an ordered classifier containing a disjunction of discriminators. For example CART builds a decision tree containing nodes of single discriminators and is not taking the order of the urgency levels into account. More research is needed in developing machine learning algorithms tuned for
learning these kind of classifiers. RIPPER induces an ordered list but is not taking the predefined order of urgency levels into account. Furthermore, both algorithms are sensitive to the strong class imbalance in the datasets.

A second reason why these algorithms were not able to improve the MTS could be the result of suboptimal MTS discriminators to predict the reference standard. For this reason future studies should focus on new discriminators that could predict true urgency. In previous studies, we found that the addition of abnormal vital signs could reduce severe undertriage[94], but did not improve the validity of the MTS due to an increase of overtriage when vital signs were applied to the total ED population.[34] The vital signs in this study were limited to heart rate, respiratory rate and oxygen saturation.[34] Since a combination of several vital signs are provided in Paediatric Early Warning Scores (PEWS) and these PEWS are suitable to detect the critically ill at the ED[115], the addition of the combination of several vital signs might improve the MTS.
The OPUS and EXPLORE algorithms were used in a completely different strategy. With these two algorithms we tried to answer the question: "Can combinations of low urgency discriminators predict high urgency and vice versa?". We applied frequent pattern search (OPUS) and exhaustive search (EXPLORE) on, e.g., a dataset containing only the discriminators of the low urgency discriminators taking high urgency as the positive class. Using this approach we did not try to build a new MTS classifier but searched for ways of improvement of the original MTS by looking at the false positives in more detail. This strategy was able to find anomalies in the data as the result of coding errors and proved to be of value for cleaning the data. (data not shown) Furthermore, OPUS found four association rules for the flowchart 'Shortness of breath' that could possibly improve the MTS. In the flowchart 'Shortness of breath', the combination of inability to talk in sentences with a low oxygen saturation and a chest infection led to a classification of 'high urgency', while the individual items allocate patients to 'low urgency'. However, the addition of this rule to the MTS reclassifies only 0.4% (N=144) of the total population.

Limitations
Ideally, we would have performed the machine learning algorithms on every flowchart in the MTS. However, a substantial number of patients was needed to have enough power to train the machine learning algorithms. For this reason, machine learning algorithms were applied to only three MTS flowcharts. The flowcharts chosen were all in the top ten of most frequently used flowcharts in a previous study[16] and were used for 18% of patients visiting the ED. The inclusion period ran until at least 1000 patients were included. The flowcharts represented both specific ('Shortness of breath' and 'Fits') and non-specific ('Worried parents') presenting problems.
The validity of the MTS depends on the predictive value for "true urgency" for each individual patient. Since a golden standard for this correct urgency level does not exist[102], it is important to agree on a 'silver' standard in order to compare studies on the validity of triage systems.[40, 116, 117] In this study, a five-level reference standard was used that combined different

prognostic markers abnormal vital signs, disease severity (admission, conditions in need of early treatment), and case complexity (resource use), which were collected during patient's ED visit. In our opinion, this reference standard is the best 'silver' standard available, because it is independent of triage, it correlates to patient's severity of illness and it is applicable to patients with a wide range of presenting problems.[40]

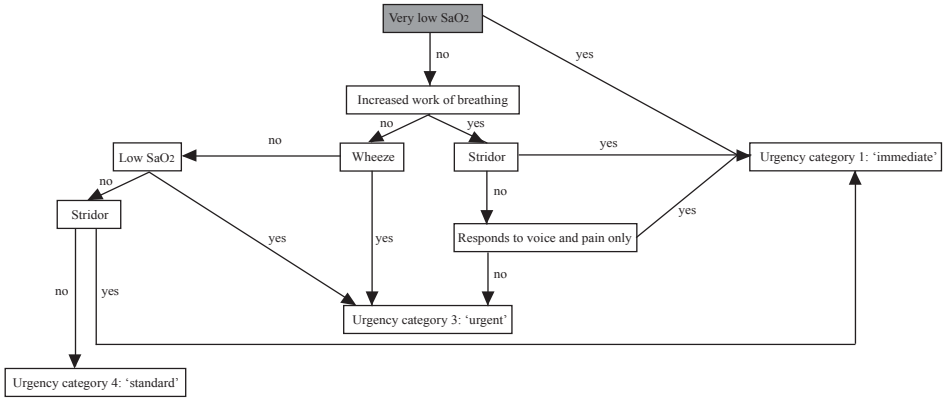
The CART and RIPPER models were developed by a10-fold cross-validation experiment. To prevent the decision trees and classification rules from overfitting, the algorithms used pruning. Ideally, we should have performed an extra internal validation step by bootstrapping or cross-validation to prevent the final CART and RIPPER models from overfitting.[118] However, the generated decision trees and classification rules did not improve the MTS and for this reason correction for overfitting was not necessary since the models will not be used in practice anyway.

Moreover, we did not validate the results externally.[119] The study sample was selected for an ED population that constitutes more than 30000 children and represents a good case-mix of a multicultural, inner-city ED population. However, patients included were attending the ED of one single hospital in Rotterdam. For this reason, it might be possible that the algorithms provide different results when they were applied to a different population.

CONCLUSION

The performance of the three MTS flowcharts 'Shortness of breath', 'Worried parents' and 'Fits' cannot be improved by remodelling these flowcharts using Machine learning algorithms CART, RIPPER, OPUS, and EXPLORE in combination with patients characteristics.

APPENDIX 1: CART Decision tree 'Shortness of breath'



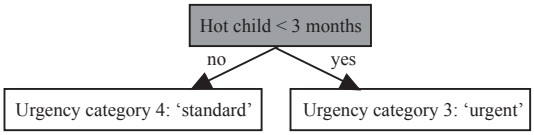
APPENDIX 2: RIPPER rules 'Shortness of breath'

Rules that allocate patient to urgency category 1 'immediate' are:
1) The presence of 'very low SaO_2'
2) The presence of 'stridor'
3) The presence of 'increased work of breathing' AND 'exhaustion' AND 'unable to talk in sentences AND the absence of 'pain'
4) The presence of 'increased work of breathing' AND 'unable to talk in sentences' AND 'responds to voice and pain only' AND the absence of 'inappropriate history'
5) The presence of 'low SaO_2'AND 'airway compromise' and the absence of 'pain'

Rules that allocate patient to urgency category 4 'standard' are:
1) The presence of 'pain' AND 'chest infection' AND the absence of 'increased work of ' AND 'wheeze' AND 'low SaO_2'AND 'significant respiratory history'.

All patient who did not meet the criteria of the RIPPER rules mentioned above, were allocated to urgency category 3 'urgent'.

APPENDIX 3: CART Decision tree 'Worried parent'



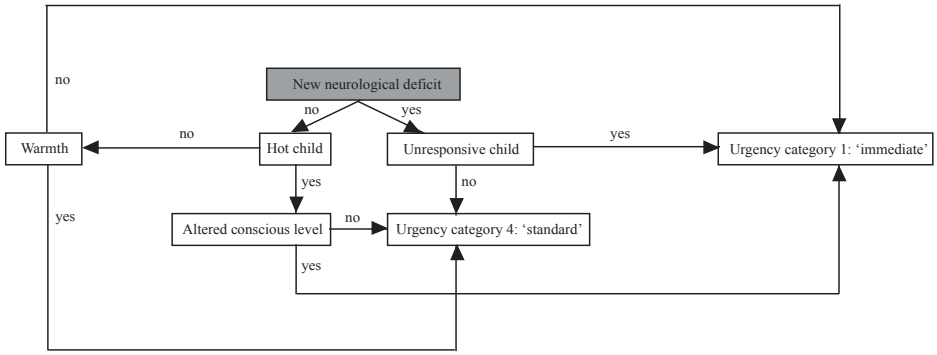
APPENDIX 4: RIPPER rules 'Worried parent'

Rules that allocate patient to urgency category 1 'immediate' are:
1) The presence of 'fails to react to parents'
2) The presence of 'atypical behaviour' AND 'floppy'

Rules that allocate patient to urgency category 3 'urgent' are:
1) The presence of 'hot child < 3 months' AND 'Not feeding < 1 year'

All patient who did not meet the criteria of the RIPPER rules mentioned above, were allocated to urgency category 4 'standard'.

APPENDIX 5: CART Decision tree 'Fits'



APPENDIX 7: Machine learning algorithm applied to classify patients into the five levels of the reference standard for the flowchart 'Shortness of breath'

	REFERENCE STANDARD					
	Immediate	**Very urgent**	**Urgent**	**Standard**	**Non-urgent**	**Total**
Flowchart 'Shortness of breath'						
CART						
Immediate	196	7	51	12	7	273
Very urgent	0	0	0	0	0	0
Urgent	235	20	1022	334	105	1716
Standard	27	5	169	297	162	660
Non-urgent	0	0	1	1	0	2
Total	458	32	1243	644	274	2651
RIPPER						
Immediate	214	5	44	11	8	282
Very urgent	0	0	0	0	0	0
Urgent	240	27	1146	569	237	2219
Standard	4	0	53	64	29	150
Non-urgent	0	0	0	0	0	0
Total	458	32	1243	644	274	2651
Flowchart 'Worried parent'						
CART						
Immediate	0	0	1	0	0	1
Very urgent	0	0	0	0	0	0
Urgent	0	1	5	6	1	13
Standard	33	10	154	743	471	1411
Non-urgent	0	0	0	1	0	1
Total	33	11	160	750	472	1426
RIPPER						
Immediate	0	0	1	1	0	2
Very urgent	0	0	0	0	0	0
Urgent	0	2	3	4	0	9
Standard	33	9	156	745	472	1415
Non-urgent	0	0	0	0	0	0
Total	33	11	160	750	472	1426
Flowchart 'Fits'						
CART						
Immediate	182	1	65	110	19	377
Very urgent	0	0	0	0	0	0
Urgent	0	0	0	0	0	0
Standard	172	2	121	298	39	632
Non-urgent	0	0	0	0	0	0
Total	354	3	186	408	58	1009
RIPPER						
Immediate	.	0	51	66	13	274
Very urgent	0	0	0	0	0	0
Urgent	3	0	0	0	0	3
Standard	207	3	135	342	45	732
Non-urgent	0	0	0	0	0	0
Total	354	3	186	408	58	1009

APPENDIX 6: RIPPER rules 'Fits'

Rules that allocate patient to urgency category 1 'immediate' are:

1) The presence of 'pain' AND 'purpura'
2) The presence of 'unresponsive child' AND absence of 'currently fitting'
3) The presence of 'pain' AND the absence of 'altered conscious level' AND 'headache'
4) The absence of 'new neurological deficit' AND 'hot child' AND 'warmth' AND 'inappropriate history'

All patient who did not meet the criteria of the RIPPER rules mentioned above, were allocated to urgency category 4 'urgent'.

APPENDIX 8: Extracted OPUS rules

OPUS rules with a support of 1% for the flowchart 'Shortness of breath' are:

1. Recent problem=present -> Reference standard='high urgency' [Coverage=0.939 (2489); Support=0.164 (435); Strength=0.175]
2. Low SaO2=present -> Reference standard='high urgency' [Coverage=0.317 (841); Support=0.103 (274); Strength=0.326]
3. Low SaO2=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.304 (806); Support=0.099 (263); Strength=0.326]
4. Chest infection=present -> Reference standard='high urgency' [Coverage=0.532 (1410); Support=0.089 (236); Strength=0.167]
5. Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.487 (1292); Support=0.082 (218); Strength=0.169]
6. Wheeze=present -> Reference standard='high urgency' [Coverage=0.439 (1165); Support=0.074 (197); Strength=0.169]
7. Unable to talk in sentences=present -> Reference standard='high urgency' [Coverage=0.182 (483); Support=0.074 (196); Strength=0.406]
8. Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.406 (1077); Support=0.070 (185); Strength=0.172]
9. Unable to talk in sentences=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.170 (450); Support=0.068 (181); Strength=0.402]
10. Low SaO2=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.168 (446); Support=0.052 (137); Strength=0.307]
11. Low SaO2=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.158 (420); Support=0.049 (129); Strength=0.307]
12. Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.263 (698); Support=0.046 (122); Strength=0.175]
13. Unable to talk in sentences=present AND Low SaO2=present -> Reference standard='high urgency' [Coverage=0.093 (247); Support=0.045 (120); Strength=0.486]
14. Unable to talk in sentences=present AND Low SaO2=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.088 (234); Support=0.043 (113); Strength=0.483]
15. Significant respiratory history=present -> Reference standard='high urgency' [Coverage=0.237 (627); Support=0.042 (112); Strength=0.179]
16. Pain=present -> Reference standard='high urgency' [Coverage=0.244 (648); Support=0.042 (111); Strength=0.171]
17. Wheeze=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.240 (635); Support=0.042 (111); Strength=0.175]
18. Low SaO2=present AND Wheeze=present -> Reference standard='high urgency' [Coverage=0.148 (392); Support=0.041 (109); Strength=0.278]
19. Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.231 (613); Support=0.040 (107); Strength=0.175]
20. Low SaO2=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.141 (373); Support=0.039 (104);

Strength=0.279]
21. Significant respiratory history=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.223 (592); Support=0.038 (102); Strength=0.172]
22. Unable to talk in sentences=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.090 (238); Support=0.038 (102); Strength=0.429]
23. Unable to talk in sentences=present AND Wheeze=present -> Reference standard='high urgency' [Coverage=0.098 (260); Support=0.035 (93); Strength=0.358]
24. Unable to talk in sentences=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.081 (216); Support=0.035 (92); Strength=0.426]
25. Unable to talk in sentences=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.091 (242); Support=0.032 (86); Strength=0.355]
26. Low SaO2=present AND Pain=present -> Reference standard='high urgency' [Coverage=0.105 (278); Support=0.027 (72); Strength=0.259]
27. Significant respiratory history=present AND Low SaO2=present -> Reference standard='high urgency' [Coverage=0.083 (221); Support=0.027 (71); Strength=0.321]
28. Unable to talk in sentences=present AND Significant respiratory history=present -> Reference standard='high urgency' [Coverage=0.077 (205); Support=0.026 (70); Strength=0.341]
29. Low SaO2=present AND Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.102 (271); Support=0.026 (69); Strength=0.255]
30. Significant respiratory history=present AND Wheeze=present -> Reference standard='high urgency' [Coverage=0.138 (366); Support=0.026 (68); Strength=0.186]
31. Significant respiratory history=present AND Low SaO2=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.079 (209); Support=0.025 (66); Strength=0.316]
32. Significant respiratory history=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.124 (330); Support=0.024 (64); Strength=0.194]
33. Low SaO2=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.084 (223); Support=0.024 (64); Strength=0.287]
34. Unable to talk in sentences=present AND Significant respiratory history=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.071 (188); Support=0.023 (62); Strength=0.330]
35. Significant respiratory history=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.129 (343); Support=0.023 (61); Strength=0.178]
36. Low SaO2=present AND Wheeze=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.079

(209); Support=0.023 (60); Strength=0.287]

37. Unable to talk in sentences=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.054 (144); Support=0.022 (59); Strength=0.410]
38. Significant respiratory history=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.116 (307); Support=0.022 (57); Strength=0.186]
39. Pain=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.132 (350); Support=0.021 (56); Strength=0.160]
40. Unable to talk in sentences=present AND Low SaO2=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.041 (110); Support=0.021 (56); Strength=0.509]
41. Pain=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.123 (325); Support=0.020 (53); Strength=0.163]
42. Unable to talk in sentences=present AND Wheeze=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.049 (130); Support=0.020 (53); Strength=0.408]
43. Unable to talk in sentences=present AND Low SaO2=present AND Wheeze=present -> Reference standard='high urgency' [Coverage=0.048 (127); Support=0.020 (53); Strength=0.417]
44. Unable to talk in sentences=present AND Pain=present -> Reference standard='high urgency' [Coverage=0.068 (180); Support=0.020 (52); Strength=0.289]
45. Unable to talk in sentences=present AND Low SaO2=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.038 (101); Support=0.020 (52); Strength=0.515]
46. Unable to talk in sentences=present AND Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.066 (174); Support=0.019 (50); Strength=0.287]
47. Unable to talk in sentences=present AND Low SaO2=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.046 (121); Support=0.019 (50); Strength=0.413]
48. Pain=present AND Wheeze=present -> Reference standard='high urgency' [Coverage=0.119 (316); Support=0.018 (48); Strength=0.152]
49. Unable to talk in sentences=present AND Significant respiratory history=present AND Low SaO2=present -> Reference standard='high urgency' [Coverage=0.041 (108); Support=0.017 (45); Strength=0.417]
50. Pain=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.111 (295); Support=0.017 (44); Strength=0.149]
51. Significant respiratory history=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.074 (196); Support=0.016 (43); Strength=0.219]
52. Unable to talk in sentences=present AND Significant respiratory history=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.036 (95); Support=0.016 (42); Strength=0.442]
53. Significant respiratory history=present AND Low SaO2=present AND

Wheeze=present -> Reference standard='high urgency' [Coverage=0.054 (143); Support=0.015 (41); Strength=0.287]

54. Unable to talk in sentences=present AND Significant respiratory history=present AND Low SaO2=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.038 (101); Support=0.015 (41); Strength=0.406]
55. Significant respiratory history=present AND Low SaO2=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.043 (113); Support=0.015 (40); Strength=0.354]
56. Unable to talk in sentences=present AND Significant respiratory history=present AND Wheeze=present -> Reference standard='high urgency' [Coverage=0.046 (123); Support=0.015 (39); Strength=0.317]
57. Significant respiratory history=present AND Wheeze=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.068 (179); Support=0.014 (37); Strength=0.207]
58. Significant respiratory history=present AND Low SaO2=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.051 (134); Support=0.014 (37); Strength=0.276]
59. Significant respiratory history=present AND Low SaO2=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.039 (104); Support=0.014 (37); Strength=0.356]
60. Unable to talk in sentences=present AND Significant respiratory history=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.032 (85); Support=0.014 (37); Strength=0.435]
61. Unable to talk in sentences=present AND Significant respiratory history=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.043 (114); Support=0.013 (34); Strength=0.298]
62. Unable to talk in sentences=present AND Low SaO2=present AND Pain=present -> Reference standard='high urgency' [Coverage=0.034 (90); Support=0.013 (34); Strength=0.378]
63. Pain=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.067 (177); Support=0.012 (33); Strength=0.186]
64. Low SaO2=present AND Pain=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.050 (133); Support=0.012 (32); Strength=0.241]
65. Unable to talk in sentences=present AND Low SaO2=present AND Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.033 (87); Support=0.012 (32); Strength=0.368]
66. Low SaO2=present AND Pain=present AND Wheeze=present -> Reference standard='high urgency' [Coverage=0.052 (137); Support=0.012 (31); Strength=0.226]
67. Unable to talk in sentences=present AND Low SaO2=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.023 (62); Support=0.012 (31); Strength=0.500]
68. Significant respiratory history=present AND Pain=present -> Reference standard='high urgency' [Coverage=0.095 (251); Support=0.011 (30);

Strength=0.120]

69. Pain=present AND Wheeze=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.062 (164); Support=0.011 (30); Strength=0.183]
70. Low SaO2=present AND Pain=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.048 (128); Support=0.011 (30); Strength=0.234]
71. Unable to talk in sentences=present AND Pain=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.035 (93); Support=0.011 (29); Strength=0.312]
72. Significant respiratory history=present AND Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.091 (242); Support=0.011 (28); Strength=0.116]
73. Low SaO2=present AND Pain=present AND Wheeze=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.049 (131); Support=0.011 (28); Strength=0.214]
74. Unable to talk in sentences=present AND Pain=present AND Chest infection=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.033 (88); Support=0.011 (28); Strength=0.318]
75. Unable to talk in sentences=present AND Significant respiratory history=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.023 (61); Support=0.011 (28); Strength=0.459]
76. Significant respiratory history=present AND Low SaO2=present AND Wheeze=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.028 (75); Support=0.010 (26); Strength=0.347]
77. Unable to talk in sentences=present AND Significant respiratory history=present AND Low SaO2=present AND Chest infection=present -> Reference standard='high urgency' [Coverage=0.018 (49); Support=0.010 (26); Strength=0.531]

OPUS rules with a support of 1% for the flowchart 'Worried parent' are:

1. Recent problem=present -> Reference standard='high urgency' [Coverage=0.866 (1235); Support=0.022 (31); Strength=0.025]

OPUS rules with a support of 1% for the flowchart 'Fits' are:

1. Recent problem=present -> Reference standard='high urgency' [Coverage=0.876 (884); Support=0.302 (305); Strength=0.345]
2. Pain=present -> Reference standard='high urgency' [Coverage=0.332 (335); Support=0.136 (137); Strength=0.409]
3. Headache=present -> Reference standard='high urgency' [Coverage=0.320 (323); Support=0.112 (113); Strength=0.350]
4. Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.266 (268); Support=0.104 (105); Strength=0.392]
5. Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.296 (299); Support=0.099 (100); Strength=0.334]
6. Warmth=present -> Reference standard='high urgency' [Coverage=0.337 (340); Support=0.096 (97); Strength=0.285]
7. New neurological deficit=present -> Reference standard='high

urgency' [Coverage=0.367 (370); Support=0.091 (92); Strength=0.249]
8. Warmth=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.297 (300); Support=0.085 (86); Strength=0.287]
9. Pain=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.209 (211); Support=0.077 (78); Strength=0.370]
10. Pain=present AND Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.195 (197); Support=0.069 (70); Strength=0.355]
11. New neurological deficit=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.306 (309); Support=0.068 (69); Strength=0.223]
12. Pain=present AND Warmth=present -> Reference standard='high urgency' [Coverage=0.116 (117); Support=0.048 (48); Strength=0.410]
13. New neurological deficit=present AND Warmth=present -> Reference standard='high urgency' [Coverage=0.185 (187); Support=0.041 (41); Strength=0.219]
14. Pain=present AND Warmth=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.100 (101); Support=0.041 (41); Strength=0.406]
15. New neurological deficit=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.131 (132); Support=0.038 (38); Strength=0.288]
16. History of head injury=present -> Reference standard='high urgency' [Coverage=0.100 (101); Support=0.038 (38); Strength=0.376]
17. Warmth=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.114 (115); Support=0.037 (37); Strength=0.322]
18. Inappropriate history=present -> Reference standard='high urgency' [Coverage=0.101 (102); Support=0.036 (36); Strength=0.353]
19. New neurological deficit=present AND Warmth=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.163 (164); Support=0.034 (34); Strength=0.207]
20. Warmth=present AND Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.108 (109); Support=0.034 (34); Strength=0.312]
21. New neurological deficit=present AND Pain=present -> Reference standard='high urgency' [Coverage=0.105 (106); Support=0.034 (34); Strength=0.321]
22. History of head injury=present AND Pain=present -> Reference standard='high urgency' [Coverage=0.075 (76); Support=0.033 (33); Strength=0.434]
23. New neurological deficit=present AND Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.122 (123); Support=0.032 (32); Strength=0.260]
24. Pain=present AND Warmth=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.079 (80); Support=0.029 (29); Strength=0.362]
25. Pain=present AND Warmth=present AND Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.075 (76); Support=0.028 (28); Strength=0.368]
26. New neurological deficit=present AND Pain=present AND Recent problem=present

-> Reference standard='high urgency' [Coverage=0.079 (80); Support=0.025 (25); Strength=0.312]

27. Inappropriate history=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.063 (64); Support=0.022 (22); Strength=0.344]
28. New neurological deficit=present AND Pain=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.071 (72); Support=0.021 (21); Strength=0.292]
29. Inappropriate history=present AND Pain=present -> Reference standard='high urgency' [Coverage=0.053 (53); Support=0.020 (20); Strength=0.377]
30. New neurological deficit=present AND Pain=present AND Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.067 (68); Support=0.019 (19); Strength=0.279]
31. New neurological deficit=present AND Pain=present AND Warmth=present -> Reference standard='high urgency' [Coverage=0.054 (54); Support=0.017 (17); Strength=0.315]
32. History of head injury=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.049 (49); Support=0.016 (16); Strength=0.327]
33. Inappropriate history=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.047 (47); Support=0.016 (16); Strength=0.340]
34. New neurological deficit=present AND Warmth=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.062 (63); Support=0.015 (15); Strength=0.238]
35. History of head injury=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.041 (41); Support=0.015 (15); Strength=0.366]
36. New neurological deficit=present AND Pain=present AND Warmth=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.046 (46); Support=0.014 (14); Strength=0.304]
37. History of head injury=present AND Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.040 (40); Support=0.014 (14); Strength=0.350]
38. History of head injury=present AND Pain=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.035 (35); Support=0.014 (14); Strength=0.400]
39. New neurological deficit=present AND Warmth=present AND Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.059 (60); Support=0.013 (13); Strength=0.217]
40. Inappropriate history=present AND Headache=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.042 (42); Support=0.013 (13); Strength=0.310]
41. Inappropriate history=present AND Pain=present AND Recent problem=present -> Reference standard='high urgency' [Coverage=0.031 (31); Support=0.012 (12); Strength=0.387]
42. Inappropriate history=present AND Warmth=present -> Reference standard='high urgency' [Coverage=0.029 (29); Support=0.012 (12); Strength=0.414]
43. History of head injury=present AND New neurological deficit=present ->

Reference standard='high urgency' [Coverage=0.033 (33); Support=0.010 (10); Strength=0.303]

44. Inappropriate history=present AND History of head injury=present -> Reference standard='high urgency' [Coverage=0.029 (29); Support=0.010 (10); Strength=0.345]
45. Inappropriate history=present AND Pain=present AND Headache=present -> Reference standard='high urgency' [Coverage=0.023 (23); Support=0.010 (10); Strength=0.435]

APPENDIX 9: Extracted EXPLORE rules

EXPLORE rules for the flowchart 'Shortness of breath' that allocate patients to 'high urgency' according to the reference standard are:

1. Airway compromise=present
   [Sensitivity:0.5553, specificity:93.27, positive predicted value:26.67, and negative predicted value:17.54]
2. Acute onset after injury=present
   [Sensitivity:1.897, specificity:90.41, positive predicted value:46.59, and negative predicted value:17.28]
3. Inadequate breathing=absent AND Exhaustion=present
   [Sensitivity:2.082, specificity:90.41, positive predicted value:48.91, and negative predicted value:17.31]
4. Unable to talk in sentences=present AND Increased work of breathing=absent
   [Sensitivity:3.008, specificity:94.08, positive predicted value:69.15, and negative predicted value:18.03]
5. Drooling=absent AND Unable to talk in sentences=present AND Increased work of breathing=absent
   [Sensitivity:3.008, specificity:94.08, positive predicted value:69.15, and negative predicted value:18.03]
6. Inadequate breathing=absent AND Unable to talk in sentences=present AND Increased work of breathing=absent
   [Sensitivity:3.008, specificity:95.71, positive predicted value:75.58, and negative predicted value:18.28]
7. Shock=absent AND Unable to talk in sentences=present AND Increased work of breathing=absent
   [Sensitivity:3.008, specificity:94.69, positive predicted value:71.43, and negative predicted value:18.12]
8. Unable to talk in sentences=present AND Increased work of breathing=absent AND Very low PEFR=not measured
   [Sensitivity:3.008, specificity:94.08, positive predicted value:69.15, and negative predicted value:18.03]
9. Unable to talk in sentences=present AND Increased work of breathing=absent OR Unresponsiveness=present
   [Sensitivity:3.054, specificity:90.41, positive predicted value:58.41, and negative predicted value:17.45]
10. Unable to talk in sentences=present AND Increased work of breathing=absent OR Shock=present
    [Sensitivity:3.1, specificity:91.02, positive predicted value:60.36, and negative predicted value:17.56]

EXPLORE rules for the flowchart 'Shortness of breath' that allocate patients to 'low urgency' according to the reference standard are:

1. Inappropriate history=present
   [Sensitivity:3.878, specificity:97.96, positive predicted value:30.16, and negative predicted value:81.8]
2. Recent problem=absent
   [Sensitivity:5.102, specificity:93.66, positive predicted value:15.43, and negative predicted value:81.32]

3. Significant respiratory history=present AND Low SaO2=present
   [Sensitivity:15.31, specificity:93.24, positive predicted value:33.94, and negative predicted value:82.92]
4. Low SaO2=present AND Pain=present
   [Sensitivity:15.51, specificity:90.65, positive predicted value:27.34, and negative predicted value:82.55]
5. Significant respiratory history=absent AND Low SaO2=present AND Chest infection=absent
   [Sensitivity:23.67, specificity:92.09, positive predicted value:40.42, and negative predicted value:84.18]
6. Low SaO2=present AND Pain=absent AND Wheeze=absent
   [Sensitivity:26.94, specificity:91.86, positive predicted value:42.86, and negative predicted value:84.72]

EXPLORE rules for the flowchart 'Worried parent' that allocate patients to 'high urgency' according to the reference standard are:

1. Airway compromise=present
   [Sensitivity:0.07236, specificity:100, positive predicted value:100, and negative predicted value:3.088]
2. Floppy=present
   [Sensitivity:0.3618, specificity:93.18, positive predicted value:62.5, and negative predicted value:2.891
3. Hot child < 3 months=present
   [Sensitivity:1.375, specificity:93.18, positive predicted value:86.36, and negative predicted value:2.92]
4. Airway compromise=present OR Hot child < 3 months=present
   [Sensitivity:1.447, specificity:93.18, positive predicted value:86.96, and negative predicted value:2.922]
5. Severe pain=present OR Hot child < 3 months=present
   [Sensitivity:1.52, specificity:93.18, positive predicted value:87.5, and negative predicted value:2.924]
6. History of overdose or poisoning=present OR Hot child < 3 months=present
   [Sensitivity:1.592, specificity:93.18, positive predicted value:88, and negative predicted value:2.926]
7. Fails to react to parents=absent AND Non-blanching rash=present OR Hot child < 3 months=present
   [Sensitivity:1.954, specificity:90.91, positive predicted value:87.1, and negative predicted value:2.867]

EXPLORE rules for the flowchart 'Worried parent' that allocate patients to 'low urgency' according to the reference standard are:

1. Not feeding < 1 year=present
   [Sensitivity:11.36, specificity:93.7, positive predicted value:5.435, and negative predicted value:97.08]
2. Prolonged or uninterrupted crying < 1 year=present
   [Sensitivity:15.91, specificity:92.69, positive predicted value:6.481, and negative predicted value:97.19]
3. Atypical behaviour=present

[Sensitivity:18.18, specificity:90.01, positive predicted value:5.479, and negative predicted value:97.19]

4. Prolonged or uninterrupted crying < 1 year=present OR Not passing urine=present
   [Sensitivity:20.45, specificity:90.23, positive predicted value:6.25, and negative predicted value:97.27]
5. Not passing urine=present OR Not feeding > 1 year=present
   [Sensitivity:22.73, specificity:90.23, positive predicted value:6.897, and negative predicted value:97.35]
6. Moderate pain=absent AND Prolonged or uninterrupted crying > 1 year=present OR Not feeding > 1 year=present
   [Sensitivity:22.73, specificity:90.09, positive predicted value:6.803, and negative predicted value:97.34]
7. Inconsolable by parents=absent AND Prolonged or uninterrupted crying > 1 year=present OR Not feeding > 1 year=present
   [Sensitivity:25, specificity:90.09, positive predicted value:7.432, and negative predicted value:97.42
8. Prolonged or uninterrupted crying > 1 year=present AND Warmth=absent OR Prolonged or uninterrupted crying < 1 year=present
   [Sensitivity:27.27, specificity:90.16, positive predicted value:8.108, and negative predicted value:97.5]

EXPLORE rules for the flowchart 'Fits' that allocate patients to 'high urgency' according to the reference standard are:

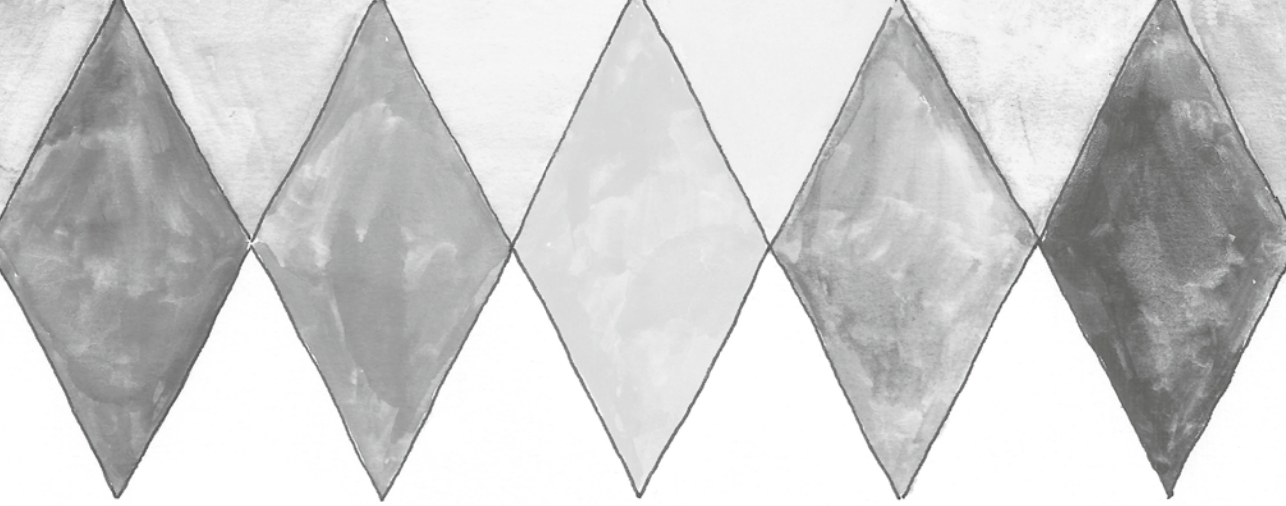
1. Airway compromise=present
   [Sensitivity:1.534, specificity:98.04, positive predicted value:58.82, and negative predicted value:35.28]
2. Inadequate breathing=present
   [Sensitivity:3.834, specificity:94.12, positive predicted value:54.35, and negative predicted value:34.89]
3. Hypoglycaemia=present
   [Sensitivity:4.601, specificity:94.12, positive predicted value:58.82, and negative predicted value:35.07]
4. Non-blanching rash=present
   [Sensitivity:6.442, specificity:92.72, positive predicted value:61.76, and negative predicted value:35.18]
5. Airway compromise=present OR Non-blanching rash=present
   [Sensitivity:6.902, specificity:91.6, positive predicted value:60, and negative predicted value:35.01]
6. Shock=present OR Non-blanching rash=present
   [Sensitivity:7.362, specificity:91.88, positive predicted value:62.34, and negative predicted value:35.19]
7. Inadequate breathing=present AND History of overdose or poisoning=absent OR Non-blanching rash=present
   [Sensitivity:7.669, specificity:90.48, positive predicted value:59.52, and negative predicted value:34.92]
8. Unresponsive child=absent AND Hypoglycaemia=present OR Non-blanching rash=present

[Sensitivity:7.975, specificity:90.48, positive predicted value:60.47, and negative predicted value:34.99]

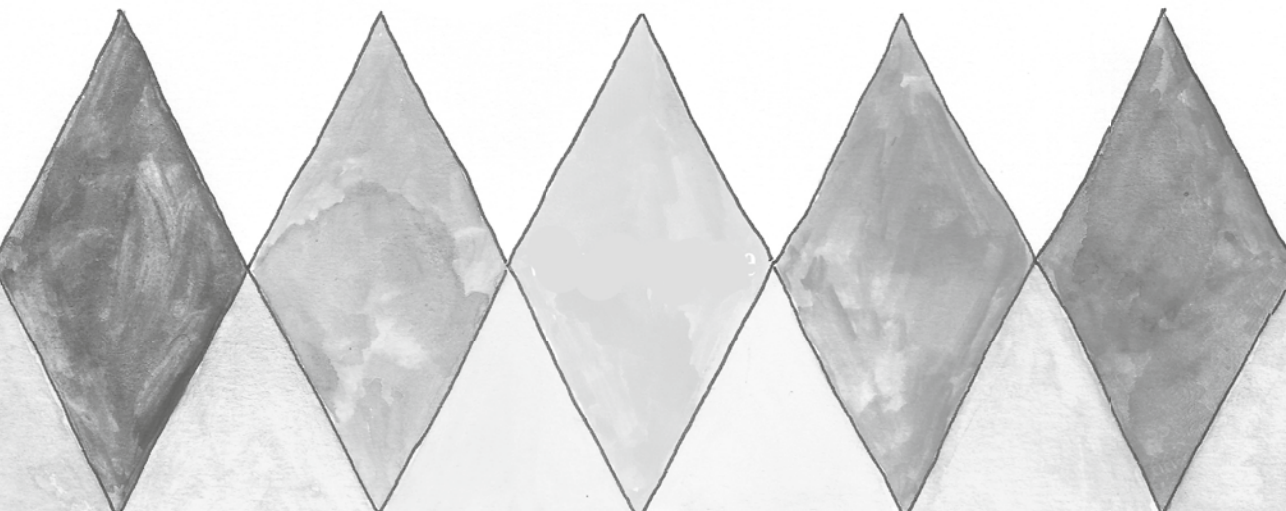
9. Unresponsive child=absent AND History of overdose or poisoning=present OR Non-blanching rash=present
   [Sensitivity:8.589, specificity:90.76, positive predicted value:62.92, and negative predicted value:35.22]

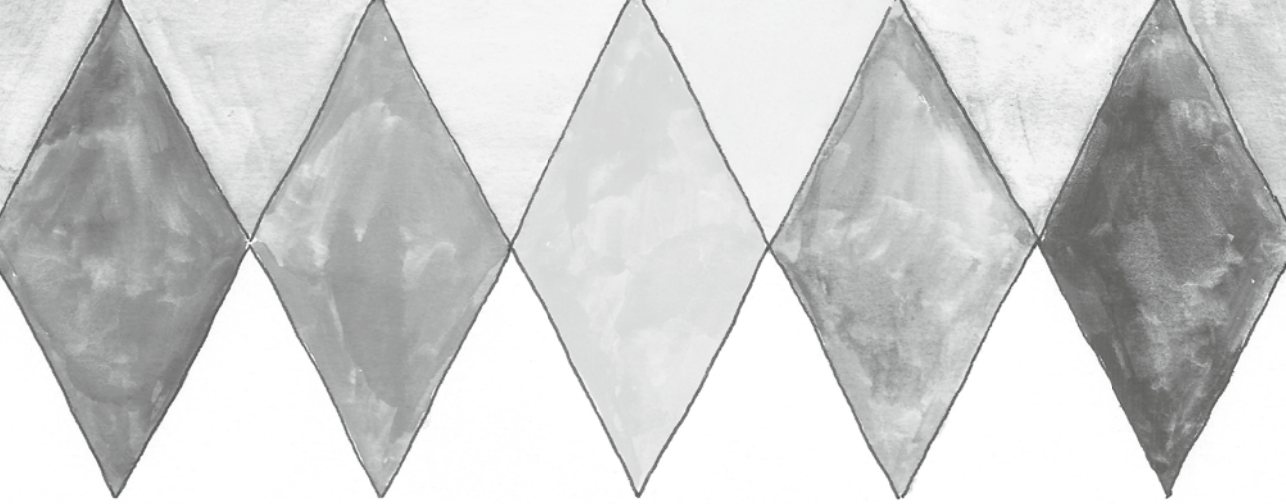
EXPLORE rules for the flowchart 'Fits' that allocate patients to 'low urgency' according to the reference standard are:

1. Airway compromise=present
   [Sensitivity:1.961, specificity:98.47, positive predicted value:41.18, and negative predicted value:64.72]
2. Inadequate breathing=present
   [Sensitivity:5.882, specificity:96.17, positive predicted value:45.65, and negative predicted value:65.11]
3. Unresponsive child=present
   [Sensitivity:10.64, specificity:94.94, positive predicted value:53.52, and negative predicted value:65.99]
4. Signs of meningism=present
   [Sensitivity:10.92, specificity:93.4, positive predicted value:47.56, and negative predicted value:65.7]
5. Airway compromise=present OR Signs of meningism=present
   [Sensitivity:12.04, specificity:92.79, positive predicted value:47.78, and negative predicted value:65.83]
6. Inadequate breathing=present OR Purpura=present
   [Sensitivity:13.17, specificity:93.87, positive predicted value:54.02, and negative predicted value:66.38]
7. Inadequate breathing=present OR Signs of meningism=present
   [Sensitivity:14.57, specificity:90.95, positive predicted value:46.85, and negative predicted value:66.04]
8. Unresponsiveness=present OR Purpura=present
   [Sensitivity:15.41, specificity:92.94, positive predicted value:54.46, and negative predicted value:66.74]
9. Unresponsiveness=present OR Non-blanching rash=present
   [Sensitivity:15.69, specificity:90.64, positive predicted value:47.86, and negative predicted value:66.26]
10. Signs of meningism=present OR History of overdose or poisoning=present
    [Sensitivity:16.25, specificity:90.49, positive predicted value:48.33, and negative predicted value:66.37]
11. Airway compromise=absent AND Unresponsiveness=present OR Signs of meningism=present
    [Sensitivity:17.37, specificity:90.34, positive predicted value:49.6, and negative predicted value:66.63]
12. Shock=absent AND Signs of meningism=present OR Unresponsiveness=present
    [Sensitivity:17.93, specificity:90.34, positive predicted value:50.39, and negative predicted value:66.78]

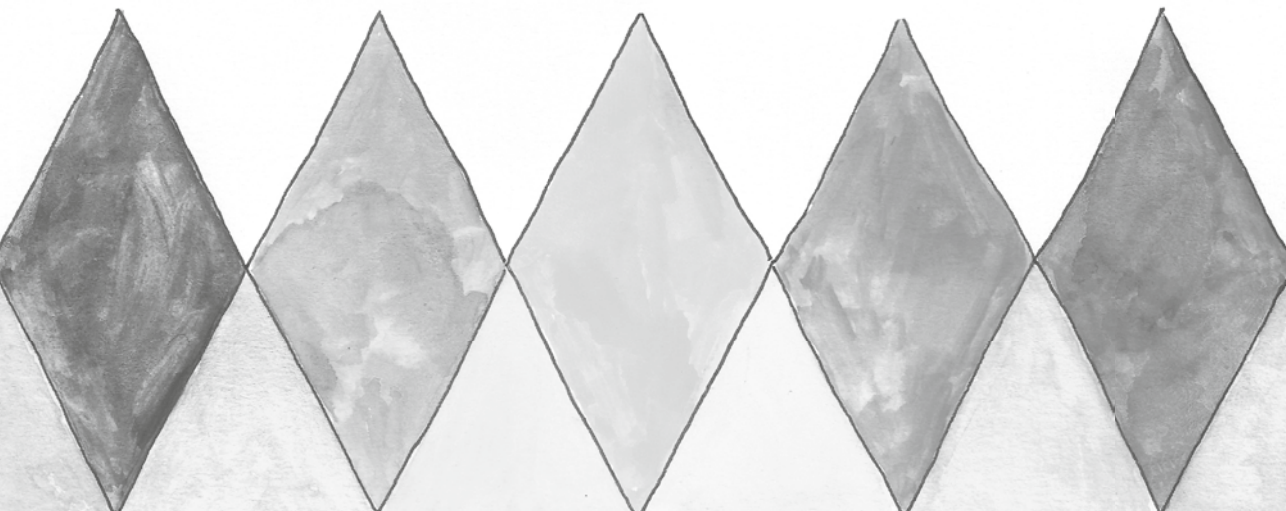


PART II





Specific Tools to Assess Patient's Severity of Illness at the Emergency Department



CHAPTER 8

Alarming signs in the Manchester Triage System: A tool to identify febrile children at risk of hospitalisation

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ABSTRACT

Objectives To assess whether the flowcharts and discriminators of the Manchester Triage System (MTS) can be used as indicators of alarming signs of serious febrile illness to predict the risk of hospitalization for febrile children who present at the emergency department (ED).

Study design Observational study, which included 2455 children (<16 years) who came to the ED of a university hospital with fever as their main complaint (May 2007-July 2009). Alarming signs for serious febrile illness were matched with MTS flowcharts and discriminators. At triage, the percentage of alarming signs positive was calculated. The diagnostic ability of the percentage of alarming signs positive to identify children at risk of hospitalization was assessed by calculating positive and negative likelihood ratios.

Results Thirty percent of children had at least 1 alarming sign positive at triage. Twenty-three percent were hospitalized. Positive likelihood ratios of hospitalization were 5.0 (95% CI: 3.9-6.5) for children with >20% of alarming signs positive at triage and 12.0 (95% CI: 5.2-27.6) for those with >40% of alarming signs positive. Negative likelihood ratios were 0.8 (95% CI: 0.8-0.8) and 1.0 (95% CI: 0.9-1.0), respectively.

Conclusions By alternatively using the flowcharts and discriminators of the MTS as alarming signs, rather than urgency classifiers, the MTS can function as a simple, readily available tool to identify febrile children at risk of hospitalization nearly in the care process. This knowledge may help to improve ED throughput times as well as admission and discharge management at paediatric EDs.

INTRODUCTION

Paediatric emergency departments (EDs) are becoming more and more crowded.[120] Febrile children constitute one of the major patient groups at paediatric EDs and are at risk of serious illnesses, like meningitis, sepsis, or pneumonia.[30, 45] Prevalence of such infections ranges from about 7%-15%.[30, 45, 57, 121] Early detection of serious febrile illnesses is important, because delaying or missing such diagnoses may lead to morbidity or even mortality and hospitalization is often required.[59-61] Recently, a systematic review has identified several alarming signs for serious illnesses in children with fever.[30]

Because the need for strategies to improve patient flows at paediatric EDs is growing, Asplin et al have proposed a conceptual input-throughput-output model to find areas for improvement of ED work flows.[122] One of the model's suggestions is that if one can already predict whether a patient will likely be admitted during the intake-phase (e.g., triage), timeliness of admission to the ward or discharge management can be improved.[120, 122]

The Manchester Triage System (MTS)[18, 123] is implemented in a large scale and used to prioritize patients according to acuity.[16, 45, 124-127] The MTS contains flowcharts (presenting problem) and discriminators (other signs and symptoms) for triage of both adult and paediatric patients and collects clinical information at the moment of arrival at the ED.

This study aimed to assess whether the flowcharts and discriminators of the MTS can be used as indicators of alarming signs of serious febrile illness, rather than urgency classifiers alone, to predict the risk of hospitalization for febrile children who present at the ED.

METHODS

This observational study is part of an ongoing study on validation of the MTS, for which standardized clinical information is prospectively and electronically collected.[16, 94] The institution's medical ethics committee approved the study and the requirement for informed consent was waived.

We included all children up to 16 years of age who had come to the ED of the Sophia Children's Hospital, Rotterdam, The Netherlands, from May 2007-July 2009. This ED is part of the Erasmus University Medical Centre and provides care to approximately 9000 children annually (i.e., 50% general paediatrics, 40% surgery, 10% other specialties).[55] Eligible contacts were those who had general paediatric problems and: (1) fever as the reason for contact; (2) fever selected as triage discriminator; or (3) a rectal temperature ≥38.5°C measured at the ED. Revisits for the same complaint within 7 days were excluded, as were children who died at the ED.

All children who presented at the ED were routinely triaged with the MTS. The MTS consists of 49 flowchart-diagrams which represent main problems with which children present to the ED (e.g., 'crying baby' or 'shortness of breath'). Each flowchart is built up of a specific combination of discriminators (i.e., signs and symptoms that often go hand-in-hand with the presenting problem). Within each flowchart, the discriminators are arranged from most urgent (U1, top) to least urgent (U5, bottom) (Figure 1). At triage, trained nurses first have to select the most appropriate flowchart for the child. Next, the patient's urgency level is assessed by selection of the most relevant discriminator, starting from the top of the flowchart moving downwards.

For the purpose of this study, triage nurses also had to indicate whether the other discriminators within the flowchart were present or absent ('triage remaining items'). In our hospital, a modified version of the first edition of the MTS (official Dutch translation)[18] was used, which contained several adjustments for triage of febrile children. Compliance with triage was 97%

(7311/7573). Inter-rater agreement (agreement in triage urgency level if multiple nurses triage one patient) and intra-rater agreement (agreement in triage urgency level if 1 triage nurse triages 1 case scenario at different time points) have been shown to be good for the MTS, both at our own ED and other setting[87, 128] and were not influenced by nurses' work experience.[128]

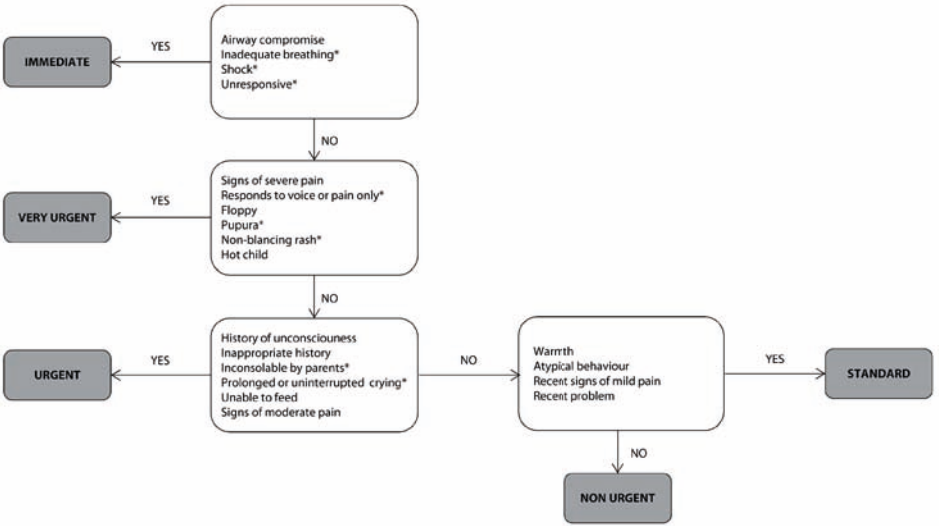

FIGURE 1: Example of the MTS flowchart 'crying baby'
Urgency categories and maximum waiting time: 'immediate': 0 minutes, 'very urgent': 10 minutes, 'urgent': 60 minutes, 'standard': 120 minutes, 'non urgent': 240 minutes. Eight discriminators (*) function as a proxy for 6 alarming signs for serious illness. Reprinted with permission from the BMJ Publishing Group (Mackway-Jones K, Manchester Triage Group.Emergency Triage, 1st edition. London: BMJ Publishing Group; 1997).

Patient's characteristics, selected flowchart, selected discriminators, urgency category, and hospitalization were extracted from the computerized MTS. Medical records were checked manually for children who missed 1 or more triage remaining items (N = 262; 3.5%). For 47 (1.8%) patients, some triage remaining items remained missing and were assumed to be absent. Among all evaluated in the ED, 0.5% left before being seen by a physician. These patients were not followed up, because this number was very small and will not have influenced our results.

We matched alarming signs for serious illness, as identified in a systematic review (positive likelihood ratio >5 or negative likelihood ratio <0.2),[30] with flowcharts and discriminators of the MTS. Three flowcharts and 20 discriminators were considered as valid proxies for 14 alarming signs (Table 1). The alarming signs 'child moaning,' 'crackles,' and 'decreased breathing sounds' could not be matched with any flowchart or discriminator. Two alarming signs were excluded from the analysis: 'decreased skin elasticity' was specific for only gastro-enteritis with subsequent dehydration and 'any abnormal finding in history or physical examination' we found too unspecific for triage purposes.

Because every flowchart contains a unique combination of discriminators, relevant for the presenting problem, the maximum number of alarming signs that could have been selected at triage of a child was dependent on the assigned flowchart and ranged from 1-7. For example, in the flowchart 'crying baby' (Figure 1), 8 discriminators are valid proxies for 6 alarming signs in total.

TABLE 1: Flowcharts and discriminators of the MTS as proxies for alarming signs for serious illness[30]

ALARMING SIGNS FOR SERIOUS ILLNESS[a]	FLOWCHART OR DISCRIMINATOR OF THE MTS
Global assessment	
Parental concern	Flowchart 'Worried parent'
Child appears ill/Clinical impression/Clinician instinct something is wrong	Flowchart 'Unwell child' Flowchart 'Irritable child'
Child behaviour	
Changed crying pattern/Inconsolable child	Prolonged or uninterrupted crying Inconsolable by parents Not distractible
Child drowsy	Altered conscious level Responds to voice or pain only Fails to react to parents
Child moaning	-
Circulatory and respiratory features	
Cyanosis	Very low SaO2 Low SaO2
Poor peripheral circulation/Hypotension	Shock
Crackles	-
Decreased breathing sounds	-
Shortness of breath/Rapid breathing	Inadequate breathing Stridor Increased work of breathing Unable to talk in sentences Wheeze
Miscellaneous	
Meningeal irritation	Signs of meningism
Petechial rash	Non-blanching rash Purpura
Seizures	Currently fitting
Unconsciousness	Unresponsive child Unresponsive

SaO_2 percentage of available haemoglobin that is saturated with oxygen.
[a] Alarming signs 'decreased skin elasticity' (gastroenteritis only) and 'any abnormal finding in history or physical examination' (unspecific) are excluded from the Table.

To correct for the difference in the maximum number of alarming signs between flowcharts, we calculated the percentage of alarming signs positive at triage as follows:

$$\text{Percentage of alarming signs positive} = \frac{\text{number of alarming signs present at triage, given the assigned flowchart}}{\text{maximum number of alarming signs available in the assigned flowchart}}$$

The primary outcome measure of this study was hospitalization. At our study ED, the admission policy was based on medical indications only: (1) abnormal or threatened vital signs; (2) requirement of intravenous (IV)-medication or IV-fluids; or (3) failure to ingest medication (e.g., need for a nasogastric tube). To validate our assumption that hospitalization could be used as a proxy for serious febrile illness, we evaluated the number of diagnostic and therapeutic interventions performed during hospital admission and the definite diagnosis in a random subsample of admitted children (January 2008-July 2009; N = 356).

Statistical analyses

The majority of patients (77%) were assigned to flowcharts in which the maximum number of alarming signs that could be selected was 5 (flowcharts 'general,' 'shortness of breath,' and 'vomiting and diarrhoea') or 7 (flowcharts 'worried parent' and 'fits'). In our analyses, we, therefore, categorized the percentage of alarming signs positive as such that for children assigned to these flowcharts the categories corresponded with 'no alarming signs positive at triage' (0%; 'none'), '1 alarming sign positive at triage' (≤20%, 'low'), '2 alarming signs positive at triage' (≤40%, 'intermediate'), and '3 or more alarming signs positive at triage' (>40%, 'high').

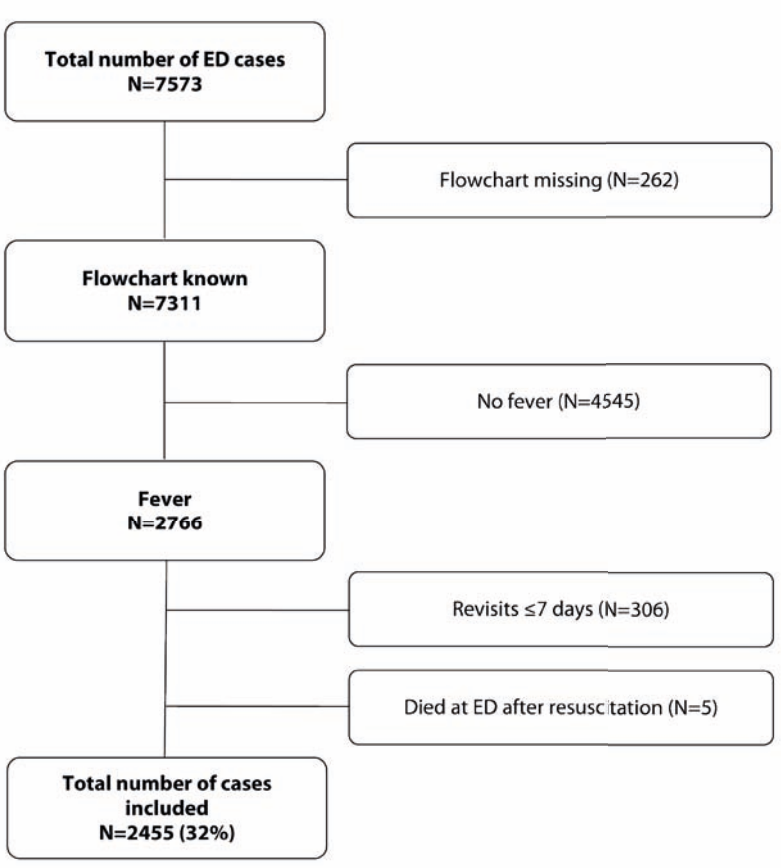

FIGURE 2: Selection of the study population

Two-by-two contingency tables were constructed to show the distribution of hospitalizations among the 4 percentage groups. To determine the diagnostic value of the percentage of alarming signs to assess the need for hospitalization, as if it were a diagnostic test, we calculated sensitivity, specificity, and positive and negative likelihood ratios with 95% CIs (VassarStats Clinical Calculator; http://vassarstats.net/clin1.html). To indicate a 'positive' and 'negative' test result, we dichotomized the percentage of alarming signs at the 3 cut-off points: (1) >0% versus no alarming signs; (2) more than 20% of alarming signs positive (>20% vs. ≤20%); or (3) more than 40% of alarming signs positive (>40% vs. ≤40%). For descriptive statistics we used SPSS PASW statistics software (v. 17.0.2; SPSS Inc., Chicago, Illinois).

RESULTS

In total, 2455 (32%) of 7573 children were eligible for analyses (Figure 2). No differences in age, sex, temperature, and frequency of hospitalization were found between children included in the study and those with missing flowchart (N =262; data not shown). Patient's and triage characteristics of the study population are shown in Table 2. Hospitalization was required for 563 (23%) children. Main reasons for hospitalization were: (1) a diagnosis of serious bacterial infection (32%); (2) requirement of IV-medication/fluids or oxygen/dose-aerosol treatment (42%); (3) failure of therapy compliance at home (4%); (4) observation, awaiting diagnostic test results (14%); and (5) other reasons (7%). Eleven percent of children had a revisit for the same complaint within 7 days. Hospitalization after a revisit occurred in 77 (3%) of children.

TABLE 2: Patients' and triage characteristics of the total study population

CHARACTERISTICS		
Male sex (N; %)	1423	(58)
Age in years (median; IQR)	2.2	(1.0 - 4.6)
Temperature in °C (median; IQR)	38.9	(38.1 - 39.5)
MTS urgency (N; %)		
Immediate	64	(3)
Very urgent	725	(30)
Urgent	1232	(50)
Standard	422	(17)
Non urgent	12	(1)
MTS flowchart (N; %)		
General	824	(34)
Shortness of breath in children	363	(15)
Worried parent	281	(11)
Vomiting & diarrhoea	236	(10)
Fits	187	(8)
Urinary problems	78	(3)
Other flowcharts[a]	486	(20)
Hospitalisation (N; %)	563	(23)

Sex: 1 missing value; Temperature: 83 missing values.
[a] Other flowcharts (n): abdominal pain in children (69), haematological disorder (61), rashes (60), unwell child (53), ear problems (50), throat ache (41), headache (41), crying baby (27), local infection/abscess (15), neck pain (14), asthma (8), thoracic pain (8), irritable child (7), shortness of breath (6), limping child (5), extremity problems (5), nose problems (3), back pain (3), abdominal pain (2), foreign body (2), apparently drunk (2), strange behaviour (1), gastro-intestinal bleeding (1), severe trauma (1), unwell adult (1).

Alarming signs for serious illness and hospitalization

For 733 (30%) children, at least 1 alarming sign was selected at triage. Among these, 544 (74%) had 1 alarming sign positive, 158 (22%) had 2, 20 (3%) had 3, 9 (1%) had 4, and 2 (0.3%) had 5. For children assigned to the 5 most commonly used flowcharts, the relation between the percentage of alarming signs positive and hospitalization is depicted in Figure 3.

Table 3 shows the diagnostic performance of the percentage of alarming signs positive, as if we would use it as a diagnostic tool. The presence of more than 20% alarming signs at triage showed a high specificity (>95%) for hospitalization. The positive likelihood ratios for patients with more than 20% and more than 40% of alarming signs positive at triage indicate that hospitalization is 5 and 12 times as likely to be required for children in these groups compared with those who had lower percentages. Negative likelihood ratios were approximately one for all three cut-off levels.

DISCUSSION

Over the past years, much effort has been put into finding alarming signs, which identify febrile children at risk of a serious illness.[30, 45, 57] This study showed that by alternatively using the flowcharts and discriminators of the MTS, as indicators of alarming signs rather than urgency classifiers, the system has the potential to identify children at risk of hospitalization early in the ED care process. We found the majority of alarming signs for serious illness to be represented in flowcharts or as discriminators in the MTS. A percentage of alarming signs positive at triage above 20% was useful for 'ruling-in' hospitalization (high specificity and positive likelihood ratio). For children with more than 40% of alarming signs positive the likelihood of hospitalization was even higher, although this analysis was based on small numbers. On the contrary, a low percentage or absence of alarming signs was not helpful in excluding ('ruling-out') hospitalization, as shown by the low sensitivities and high negative likelihood ratios. These patients should still be assessed with caution and one should look for other clinical measures to judge their risk of serious illness.

In principal, triage systems have been developed to prioritize patients according to their acuity upon arrival at the ED. Others have previously demonstrated that a high MTS urgency level could not well discriminate between children with or without serious bacterial infections.[45, 121] Both authors explained this limited discriminative ability by the fact that assessing a patient's level of urgency is different from predicting severity of illness or diagnosing a disease.[45, 102, 121]. In this study, we focused on the more specific and detailed information available in the MTS (i.e., the presence of alarming signs of serious febrile illness specifically instead of a high urgency classification only), which resulted in a higher diagnostic value to predict the need for hospitalization.

We certainly realize that the MTS may not be the most optimal tool for recognizing children at risk for hospitalization. However, more sophisticated tools, such as computerized decision support systems, often require additional clinical characteristics not available from the triage assessment.[129] Besides, such tools are scarce for general complaints such as fever, because their development and implementation is difficult and time-consuming.[119, 129]

In practice, the percentage of alarming signs can be automatically calculated by the computerized MTS or by hand. Next, the observed likelihood ratios can be applied to Bayes nomogram[130] to calculate the post-test probabilities of hospitalization for febrile children at comparable ED settings.

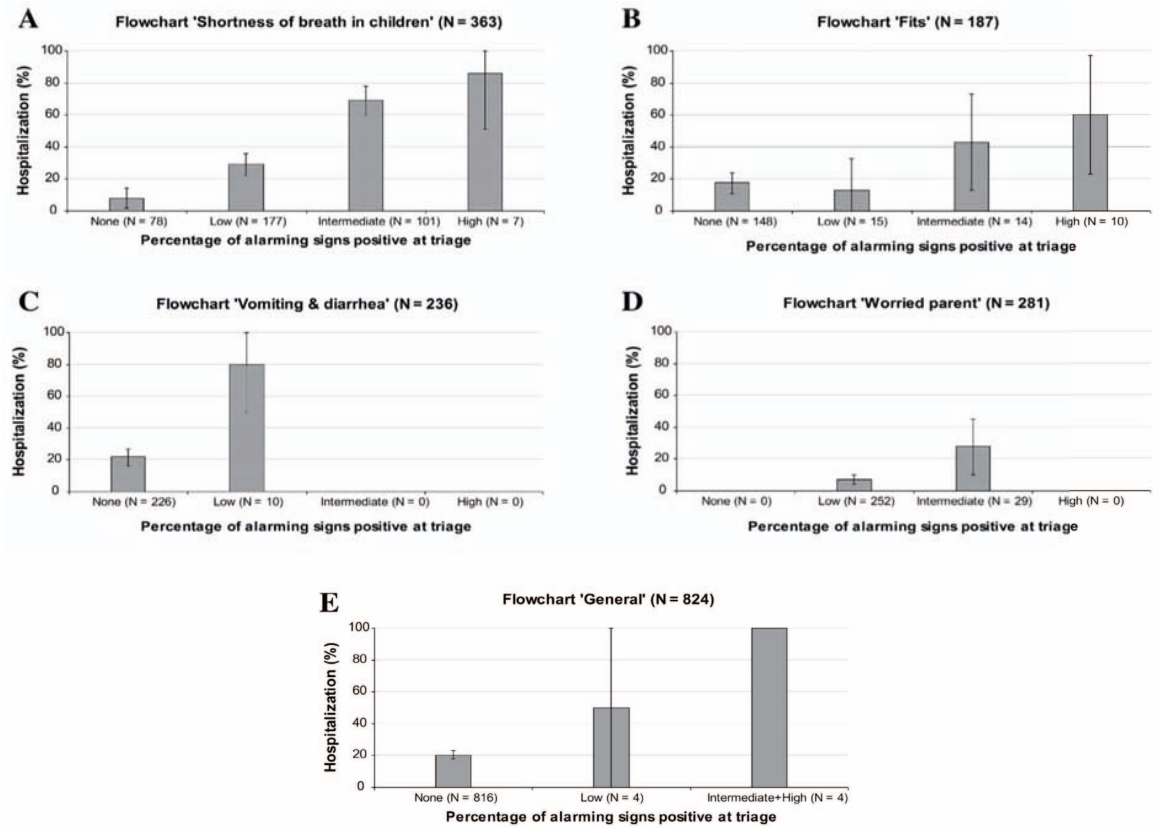

FIGURE 3: Hospitalization per percentage group of alarming signs positive at triage for the most commonly chosen flowcharts.
The intermediate and high percentage groups are displayed as one group because of small group numbers.

For example, in a particular ED-setting with a pre-test probability of hospitalization of 15%, the probability of hospitalization will increase to 45% for a febrile child with >20% of alarming signs positive and 70% in case >40% of alarming signs are positive at triage (Figure 4).

Early identification of children at risk of hospitalization, as a proxy for serious illness, may be useful in further prioritizing patients at the ED, accelerating the application of diagnostic or therapeutic interventions, or deciding to perform interventions after the patient is first admitted to the inhospital ward.[120, 122] Before broad implementation in practice, our findings should be validated in other settings where the MTS is used for triage of febrile children. Subsequently, impact studies must evaluate the improvement of throughput and output flows of febrile children at the paediatric ED.

Our study population comprised a good case mix of nearly 2500 children, selected from a multicultural, inner-city ED population. Even though in The Netherlands we have a well-preserved primary care system (general practitioners), which functions as a gatekeeper for specialist care, nearly one-half of our ED population was self-referred.[88] Therefore, we think our results are likely to be generalisable to other Western paediatric EDs with a case mix population of referred and nonreferred children. Besides, hospital admission was defined for medical indications only at our study ED. From this perspective, the choice of being admitted is independent of referral status or the prevalence of disease.

Selection bias seems unlikely, because compliance with triage was high and general patients' characteristics and hospitalization frequencies of children excluded because of missing flowcharts were comparable with those of children included in the study.

We only had information on revisits, which had taken place at our study ED, even though in practice patients may have visited other health care facilities subsequently. Because our study ED is the major paediatric emergency care facility of the Rotterdam district with 24/7 availability, we do not expect to have missed many revisits.

Selection of alarming signs at triage was restricted by the flowchart chosen. It might have been possible that additional alarming signs were present at triage, which could not have been selected because of the absence of these discriminators in that particular flowchart. Because we primarily focused on alternative use of the available content of the MTS, rather than the exact number of alarming signs present at triage, this will not have influenced our results and its clinical implications.

Lastly, some alarming signs were strongly associated with the outcome (e.g., abnormal vital signs) and mainly applied to children classified as 'immediate (U1).' Analyses without this patient group resulted in comparable findings (data not shown), which indicates that inclusion of these children in our main analyses was of no major threat to the validity of our results.

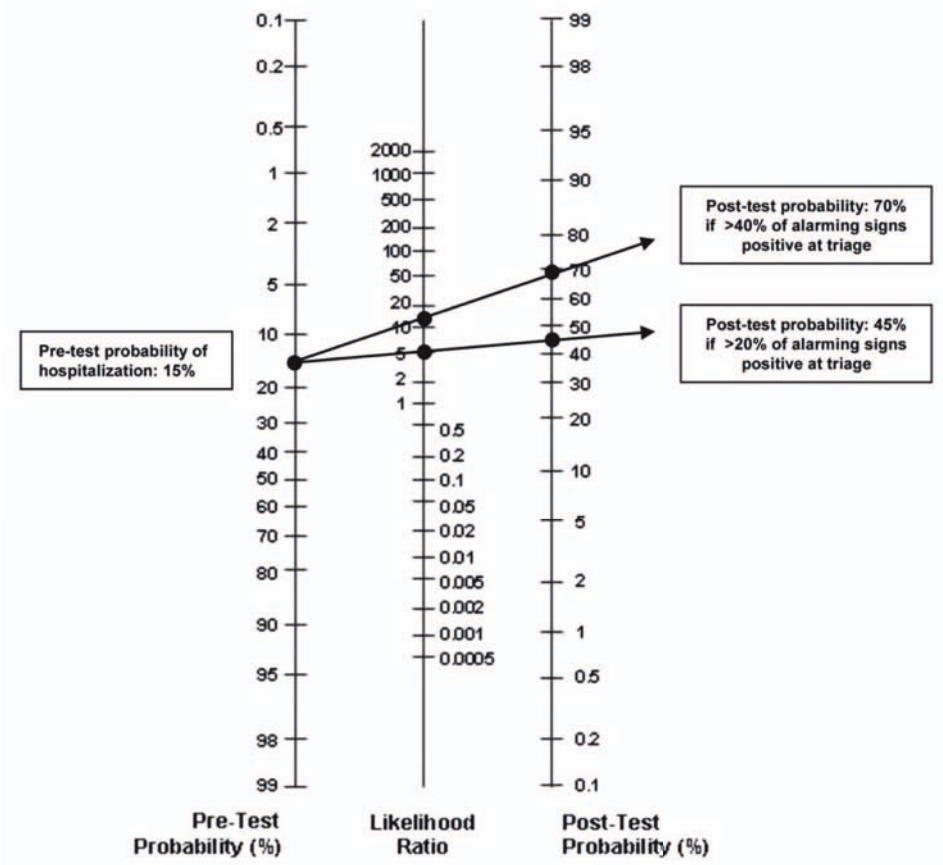

FIGURE 4: Example of the calculation of post-test probabilities of hospitalization using Bayes nomogram.

CHAPTER 9

Heart rates and respiratory rates are associated with Manchester pain scores in children presented at the emergency department

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ABSTRACT

Introduction This multicenter observational study aims to determine the association between respiratory rates or heart rates and Manchester pain scores and to derive age and pain appropriate centiles for children presenting at EDs.

Methods Included were children (<16 years) presenting at two EDs in the Netherlands (2006-2012) or one ED in the UK (2010-2012). Pain scores were obtained by the Manchester pain scale (range 0-10) during triage. This pain scale combines a visual analogue scale, a verbal descriptor scale, and a pain behaviour tool. Age and pain appropriate heart rate and respiratory rate centile charts were derived.

Results In total 87,291 children were included to develop heart rate and respiratory centile charts. These centiles showed that pain influenced vital signs in younger children, but not in older children. In comparison with no pain, the median heart rates of children younger than 1 year was 10 bpm (IQR 8-14) higher when in severe pain; the median heart rates of children between 1-2 years was 11 bpm (IQR 7-16) higher; the median heart rates of children between 2-5 years was 5 bpm (IQR 4-7) higher; and in children older than five this effect disappeared. Respiratory rates per age category showed similar trends as the heart rates per age category, although not as evident.

Conclusions In new derived centile charts for children, the associations between heart rates or respiratory rates and Manchester pain scores were quantified. Especially in younger children, clinicians should reinterpret patient's heart rate if patients are in pain.

INTRODUCTION

Respiratory rates and heart rates are key vital signs to assess the physiological status of children and are widely used in routine clinical care to identify critical illnesses.[95] To prevent overdiagnosing or underdiagnosing of tachycardia and tachypnoea, the use of accurate reference ranges are essential, and therefore reference ranges for children were recently published based on a systematic review.[95] However, these reference ranges do not take into account the experience of pain[131], while there is evidence that acute pain induces activation of the autonomic nervous system which leads to increased heart rates, blood pressures, and respiratory rates.[132]

To measure the level of pain, different pain scales for children have been developed.[133, 134] The Manchester pain scale is one of those scales and was developed for pain assessment of paediatric and adult patients who presented at the emergency department (ED).[18] The Manchester pain scale is a pain ruler which combines a visual analogue scale, a verbal descriptor scale and a pain behaviour tool and is part of the Manchester Triage System (MTS).[7, 18] The Manchester pain scale showed good convergent validity to the Oucher Scale[135], one of the most comprehensively validated pain scales, and can therefore be used to assess pain in children presented at the ED.[136]

To our knowledge, vital sign reference ranges have never been adjusted for pain scores, whilst up to 78% of all patients who visits the ED experience pain.[137-139] Therefore, we aimed to determine the relationship between respiratory rates or heart rates, age and Manchester pain scores in children up to 16 years of age. We further aimed to derive age and pain corrected reference values and centile charts for heart rate and respiratory rates in this patient population.

METHODS

Study design

In this multicenter observational study, anonymous ED records data of three European hospitals were used to assess the relationship between respiratory rates or heart rates (vital signs) and Manchester pain scores in children. The final association between vital signs and pain score were expressed by heart rate and respiratory rates centiles for different age groups. The centiles were created by using generalized additive models for location, scale and shape (GAMLSS).[140-143]

Some parts of the databases were used before to assess the performance of a modified version of the Manchester Triage System (MTS) in children.[16, 33] The study was approved by the institutional medical ethical committees; the requirement for informed consent was waived.

Population and setting

Eligible children (0-15 years) included children presenting consecutively at the ED of Erasmus MC-Sophia Children's Hospital in Rotterdam, The Netherlands between 01-01-2006 and 1-12- 2012; or at the ED of Juliana's Children's Hospital in The Hague, The Netherlands between 1-6-2006 and 31-7-2006 or between 1-8-2007 and 31-12-2007; or the ED of St. Mary's Hospital in London, United Kingdom between 17-06-2010 and 30-06-2012. The data collection was consecutive but interrupted for four months in the Sophia Children's Hospital and for five months in the St. Mary hospital due to software changes.

The EDs of St Mary and Sophia Children's Hospital are independent paediatric EDs and the ED of Juliana Children's hospital is a mixed paediatric-adult ED. All EDs are open 24-

hours a day. Sophia Children's Hospital is a university hospital and its ED sees 9000 patients annually. St. Mary's Hospital and Juliana Children's Hospital are general teaching hospitals and their EDs receive approximately 26000 and 12000 paediatric patients respectively.
We excluded children allocated to the 'immediate' triage category according to the MTS. Moreover, we excluded children who presented at the ED with dyspnoeic problems defined as children assigned to the MTS flowcharts 'shortness of breath in children' or 'asthma') for the respiratory rate analyses.

Manchester pain scale

The Manchester pain scale is a pain assessment tool derived for use in the ED during the triage process.[136] It is implemented in the five-level MTS, which is commonly used triage system in and outside Europe.[7, 18] The Manchester pain scale combines three types of pain assessments tools: a visual analogue scale, a verbal descriptor scale and a pain behaviour tool and can be supplemented by panda facial images for small children.[7, 18] The visual analogue scale is a pain ruler in the form of a ladder rising from zero to ten. The verbal descriptor scale describes the level in pain in words, for instance "no pain" or "worst pain ever". The pain behaviour component described how activities are influenced by pain, for instance "the pain is disabling the patient". The visual analogue scale and the verbal descriptor scale are self-report scales. The observational scale can be used in children too young to self-report.
Depending on the discretion of the nurse and age of the child, these different methods are used separately or combined and result in a pain score varying from zero to ten. Zero represents no pain and ten the worst pain possible. Details of the Manchester pain scale are shown in figure 1.

The Manchester pain scores could be categorized in four different pain categories corresponding to the triage categories used in the MTS: 1) no pain includes pain score zero; 2) mild pain includes pain scores one to four; 3) moderate pain includes pain score five to seven; 4) severe pain includes pain scores eight to ten.[144]

Data collection

Data on patients' characteristics, Manchester pain scores and presenting problems were recorded in computerized systems of the MTS. ED nurses measured vital signs (heart rate, respiratory rate, blood pressure, temperature, and level of consciousness) during triage assessment and recorded these values on structured paper (and from 2009 on electronic) ED forms. Heart rates were measured using electronic pulse oximeters and respiratory rates were measured by counting respiratory movements for 30 seconds. The measurement of vital signs was left to the discretion of the nurse or physician. Trained medical students gathered and entered data from the paper forms on a separate database, independent of pain scores, using data entry version 4.0.

Sample size

A sample size of approximately 60-80 children per pain category for all age groups (0-1 year, 1-2 years, 2-5 years, 5-12 years, and 12-16 years) was sufficient to create heart rate and respiratory rate centiles.[145] The age subdivisions were chosen as they were clinically relevant and similar to the age groups of the APLS.[27]

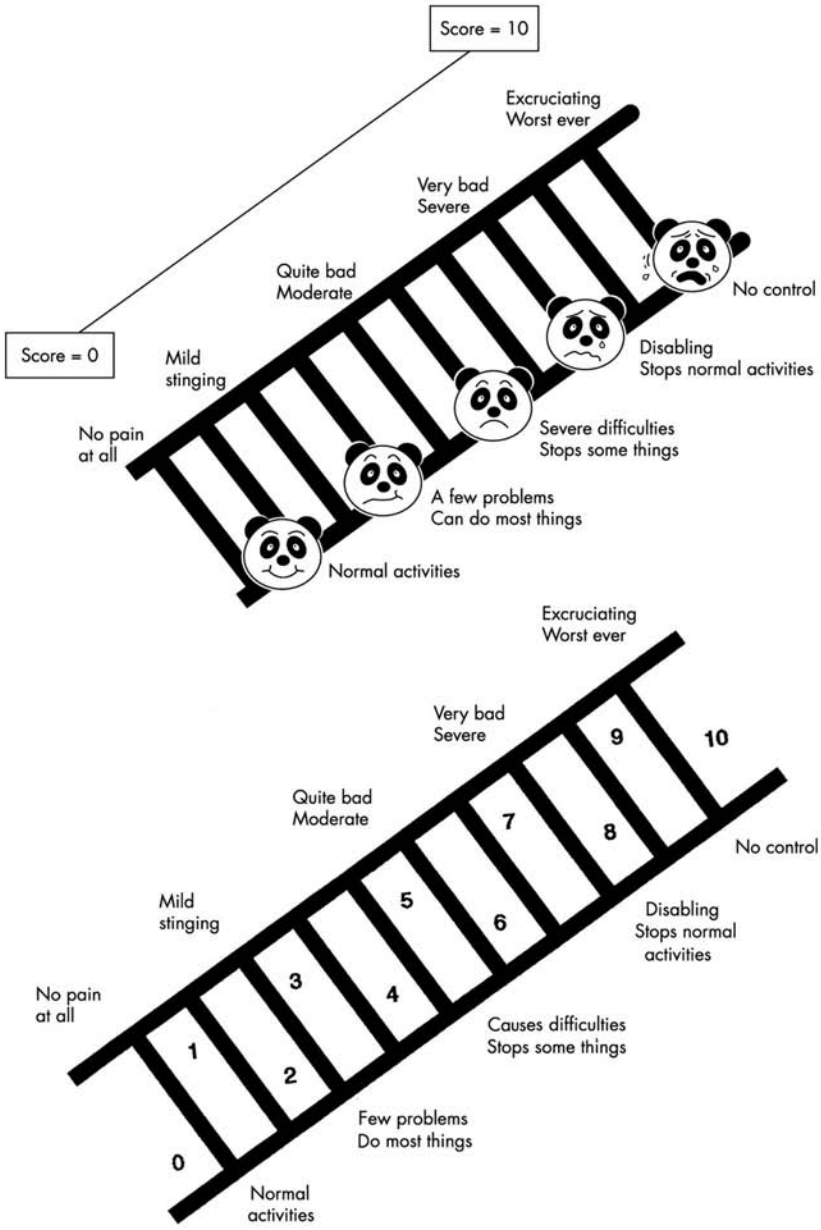

FIGURE 1: Manchester pain scale Reprinted with permission from the BMJ Publishing Group (Mackway-Jones K, Manchester Triage Group. Emergency Triage, 1st edition. London: BMJ Publishing Group; 1997).

Data analysis

To deal with missing vital signs values, a multiple imputation model was used to impute missing respiratory rates and heart rates. This means that missing data are replaced by a value that is drawn from an estimate of the distribution of the variable to create a complete database.[146] This process was executed ten times to generate ten complete databases. Statistical analysis on each database were performed and pooled for a final result. In our imputation model age, presenting problem, hospitalization, pain scores, heart rates, respiratory rates, and blood pressures values were used to impute missing values. Vital sign values of children whose vital signs were measured during crying or distress, were considered as missing and these values were imputed as well.

To analyze the association between vital signs and Manchester Pain scores, we truncated vital signs values which were more than three standard deviations (SDs) from the mean heart or respiratory rate for their age group and pain category to the value three SDs from the mean.[147]

First, we calculated Spearman's rho (rank correlation) for ordinal variables and secondly, we performed univariable and multivariable linear regression analysis to assess the relationship between vital signs and Manchester pain scores. In the multivariate model, age was considered as possible confounder. Interaction terms were added and tested for significant model improvement.

Finally, we developed pain score appropriate centile charts (2.5th, 10th, 25th, 50th, 75th, 90th, and 97.5th) of heart rates and respiratory rates for different age groups by using Generalized Additive Models for Location, Scale, and Shape (GAMLSS).[140-143] In contrast to generalized linear models, GAMLSS allows for skewness and kurtosis.[141] The four parameters for location (mean,μ), scale (coefficient of variance,σ), skewness (transformation to symmetry, ν), and kurtosis (power exponential parameter, τ) were modelled using cubic splines. The optimal effective degrees of freedom for each parameter were selected based on the Schwartz Bayesian information Criteria (SBC). The final models were checked using Z-score graphs, detrended Q-Q plots (worm plots) and Q-statistics for the parameters in the model.[141, 148]

Statistical analysis were performed using Statistical Packages for Social Sciences (SPSS) version 17.0 (Chicago, IL) and R package version 2.13.1, using the Design, Hmisc (AregImpute function), and GAMLSS packages. (www.r-project.org)

RESULTS

Population

In total 100913 patients had presented at the EDs of the three hospitals, of whom 96864 (96%) were triaged using the MTS. Manchester pain scores were recorded in 91850 (95%). From five percent (N=4553) of the patients, nurses could not obtain pain scores, because of altered level of consciousness or other factors and, in 6 patients, their age was unknown. After excluding patients allocated to the MTS category "immediate" (N=787), 86504 patients remained for analysis. Patient characteristics of the three hospitals are shown in table 1.

In total, 39206 (45%) children presented without pain, 37470 (43%) children with mild pain, 8645 (10%) children with moderate pain, and 1183 (1%) with severe pain. Eighteen percent (N=15725) of all patients were younger than one year; 13% (N=11594) of patients were between one and two years; 25% (N=21687) of patients were between two and five years; 30% (N=25551) of patients were between five and twelve years; and 14% (N=11947) of patients between twelve and sixteen years. The final distribution of patients per pain category per age group is shown in appendix 1.

Table 1: Patient's characteristics per hospital

	SOPHIA CHILDREN'S HOSPITAL	JULIANA CHILDREN'S HOSPITAL	ST. MARY'S HOSPITAL	TOTAL POPULATION
	N=35749	N=11446	N=39309	N=86504
Age (years, %)	$N_{available}$=35749 (100%)	$N_{available}$=11446 (100%)	$N_{available}$=39309 (100%)	$N_{available}$=86504 (100%)
Median (IQR)	4.6 (1.7-9.8)	3.1 (1.1-7.5)	3.8 (1.5-8.6)	4.0 (1.5-9.0)
Presenting problem (%)	$N_{available}$=35749 (100%)	$N_{available}$=11446 (100%)	$N_{available}$=39309 (100%)	$N_{available}$=86504 (100%)
Trauma	7889 (22)	1923 (17)	7543 (19)	17355 (20)
Gastro-intestinal	5044 (14)	2048 (18)	6253 (16)	13345 (15)
Dyspnoea	2862 (8)	1604 (14)	4164 (11)	8630 (10)
Wounds	2828 (8)	738 (6)	1745 (4)	5311 (6)
Rash	822 (2)	345 (3)	3229 (8)	4396 (5)
Ear, nose, throat	847 (2)	459 (4)	2311 (6)	3617 (4)
Neurological	1322 (4)	254 (2)	1609 (4)	3185 (4)
Fever without source	1247 (4)	557 (5)	1337 (3)	3141 (4)
Urinary tract problems	850 (2)	194 (2)	376 (1)	1420 (2)
Local infection/abscess	666 (2)	180 (2)	372 (1)	1218 (1)
Other problems	11372 (32)	3144 (28)	10370 (26)	24886 (29)
MTS triage category (%)	$N_{available}$=35749 (100%)	$N_{available}$=11446 (100%)	$N_{available}$=39309 (100%)	$N_{available}$=86504 (100%)
Very urgent	6762 (19)	1170 (10)	4349 (11)	12281 (14)
Urgent	15367 (43)	3455 (30)	6241 (16)	25063 (29)
Standard	13186 (37)	6666 (58)	27421 (70)	47274 (55)
Non-urgent	434 (1)	155 (1)	1298 (3)	1887 (2)
Follow-up (%)	$N_{available}$=35749 (100%)	$N_{available}$=11446 (100%)	$N_{available}$=39309 (100%)	$N_{available}$=86504 (100%)
No follow-up	14069 (39)	6526 (57)	20517 (52)	41112 (48)
Outpatient clinic/GP	12987 (36)	3043 (27)	11120 (28)	27150 (31)
Hospital admission	5515 (15)	1370 (12)	3669 (9)	10554 (12)
Other follow-up	3178 (9)	507 (4)	4003 (10)	7688 (9)
Manchester pain score (%)	$N_{available}$=35749 (100%)	$N_{available}$=11446 (100%)	$N_{available}$=39309 (100%)	$N_{available}$=86504 (100%)
Median (IQR)	3 (1-4)	0 (0-2)	0 (0-1)	1 (0-3)
Respiratory rates (bpm, %)	$N_{available}$=11453 (32%)	$N_{available}$=973 (9%)	$N_{available}$=24379 (62%)	$N_{available}$=36805 (43%)
Median (IQR)	28 (20-36)	40 (31-52)	26 (22-32)	28 (22-36)
Heart rates (bpm, %)	$N_{available}$=15798 (44%)	$N_{available}$=2678 (23%)	$N_{available}$=28154 (72%)	$N_{available}$=46630 (54%)
Median (IQR)	116 (96-140)	130 (110-153)	120 (100-140)	120 (98-140)

CI=confidence interval
IQR=interquartile range
bpm= beats/breaths per minute

Heart rate

Heart rates were significantly negatively correlated with Manchester pain score (rho=-0.29, p-value <0.001) and age (rho=-0.69, p-value<0.001). The correlation between heart rates and Manchester Pain scores was reduced to rho=-0.09, but remained significant when corrected for age (p-value=0.03).

Univariable analysis showed pain scores were non-linearly associated with heart rates and that increasing pain scores decreased the heart rate. (Model I, table 2) In multivariable analysis, when heart rates were corrected for age (Model II, table 2), the average heart rate of children with mild or moderate pain decreased significantly with 6.7 (95% CI 6.3-7.1) and 5.9 (95% CI 5.2-6.6) beats per minute respectively, while children with severe pain had increased heart rates (3.2 beats per minute, 95% CI 1.6-4.7) in comparison to patients without pain. The addition of interaction terms Twas statistically significant (p-value 0.03), which means that the effect of pain scores on vital signs differed per age category.

To display this association between heart rates and pain scores for individual age groups, reference centiles were created and shown in figure 2. In comparison with children without pain, the median heart rates of children younger than 1 year were 10 bpm (IQR 8-14) higher when in severe pain; the median heart rates of children between 1-2 years were 11 bpm (IQR 7-16) higher; the median heart rates of children between 2-5 years were 5 bpm (IQR 4-7) higher; and in children older than five this effect disappeared. The values of heart rate at the 2.5th, 10th, 25th 50th, 75th, 90th, and 97th centiles per age-pain category are shown in appendix 3. Especially children younger than five with severe pain will be overdiagnosed with tachycardia, when Fleming's reference ranges will be used. (Figure 2)

Table 2: Univariable and multivariable linear regression analysis pain score, age and heart rates

MODEL	MODEL I		MODEL II	
	Heart rate, pain scores		Heart rate, pain scores and age	
	β(SE)	*p-value*	*β(SE)*	*p-value*
Intercept	123.4 (0.2)	<0.001	91.5 (0.3)	<0.001
Pain scores				
No pain	Reference	NA	Reference	NA
Mild pain	-14.9 (0.2)	<0.001	-6.7 (0.2)	<0.001
Moderate pain	-19.9 (0.4)	<0.001	-5.9 (0.4)	<0.001
Severe pain	-11.1 (0.9)	<0.001	3.2 (0.8)	<0.001
Age				
0-1 year	NA	NA	51.3 (0.3)	<0.001
1-2 years	NA	NA	44.5 (0.3)	<0.001
2-5 years	NA	NA	31.9 (0.3)	<0.001
5-12 years	NA	NA	11.6 (0.3)	<0.001
12-16 years	NA	NA	Reference	NA
Pooled R square (change R square)	0.08	NA	0.44 (0.36)	<0.001

NA=not applicable

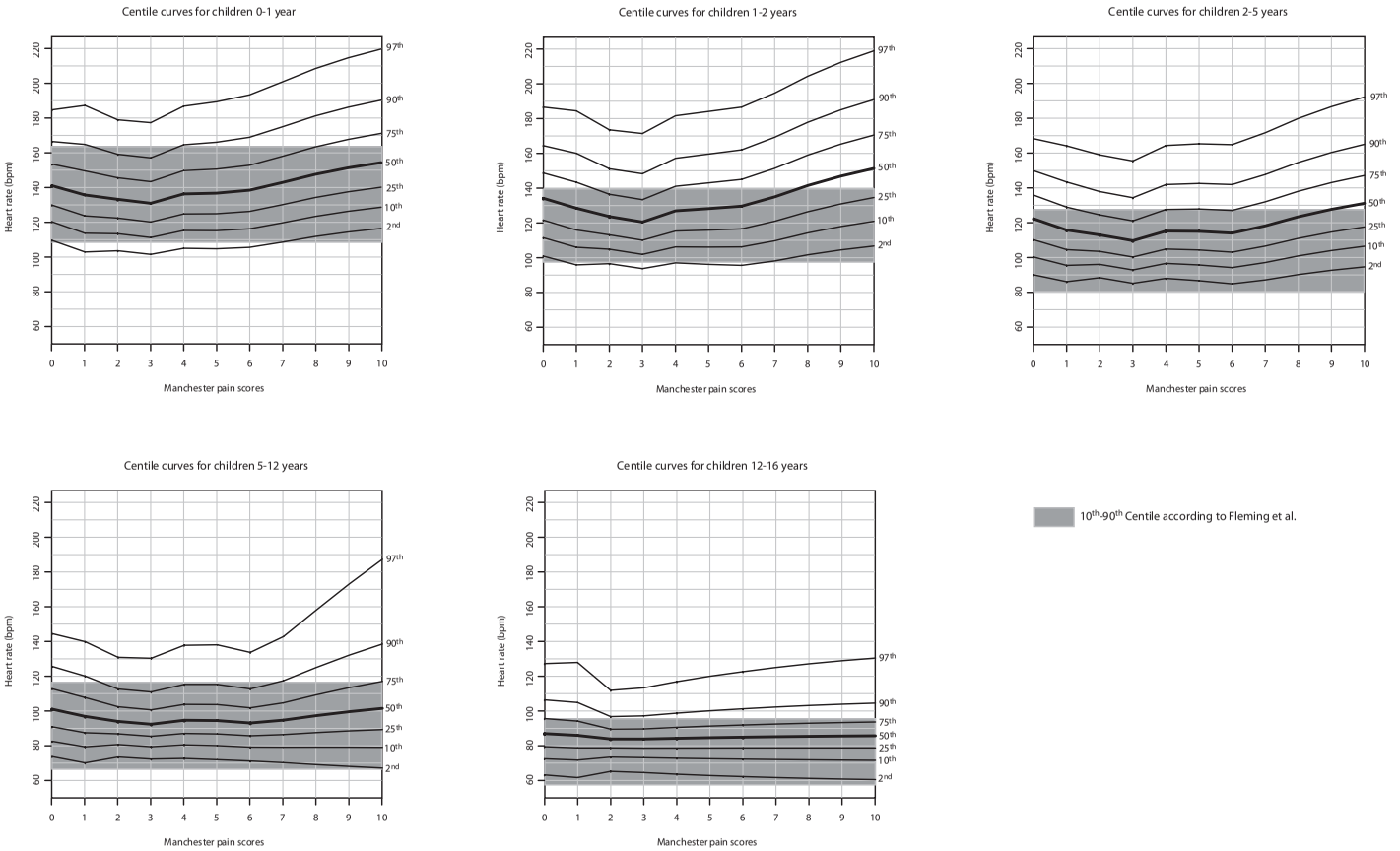

FIGURE 2: Centiles of heart rate for different Manchester Pain scores

10th-90th centiles according to Fleming et al.[95]: children 0-1 year, 109-164 bpm ; 1-2 years, 98-140; 2-5 years, 81-128 bpm; 5-12 years, 67-117 bpm; and 12-16 years, 58-96 bpm.

Respiratory rate

After excluding patients who presented with dyspnoea, 77874 (89%) patients remained for analysis. The final distribution of patients per pain category per age group is shown in appendix 2. The correlation between respiratory rate and pain scores was moderate (rho=-0.25, p-value <0.001) and strong for respiratory rates and age (rho=-0.68, p-value <0.001). The age corrected correlation coefficient for respiratory rate and pain scores was rho=-0.04 (p<0.001).

Univariable and multivariable analysis showed pain scores were not linearly associated with respiratory rates (Model I and II, table 3). The addition of interaction terms was significant (p-value=0.02).

Figure 3 shows the association between respiratory rates and pain scores for individual age groups expressed by centiles (2.5th, 10th, 25th 50th, 75th, 90th, and 97th) and appendix 4, the matching reference values.

TABLE 3: Univariable and multivariable linear regression analysis pain score, age and respiratory rates

MODEL	MODEL I		MODEL II	
	Respiratory rates, pain scores		Respiratory rates, pain scores and age	
	β(SE)	*p-value*	*β(SE)*	*p-value*
Intercept	29.2 (0.1)	<0.001	20.4 (0.1)	<0.001
Pain scores				
No pain	Reference	NA	Reference	NA
Mild pain	-3.8 (0.1)	<0.001	-1.2 (0.1)	<0.001
Moderate pain	-5.4 (0.1)	<0.001	-1.1 (0.1)	<0.001
Severe pain	-3.8 (0.4)	<0.001	0.8 (0.4)	0.02
Age				
0-1 year	NA	NA	16.8 (0.1)	<0.001
1-2 years	NA	NA	11.4 (0.1)	<0.001
2-5 years	NA	NA	7.5 (0.1)	<0.001
5-12 years	NA	NA	2.8 (0.1)	<0.001
12-16 years	NA	NA	Reference	NA
Pooled R square (change R square)	0.05	NA	0.38 (0.33)	<0.001

NA=not applicable

DISCUSSION

In this analysis, pain affected heart rate and respiratory rates in a complex, non-linear relationship way. Both respiratory rates and heart rates decreased when children had mild to moderate pain according to the Manchester pain scale, while they increased in children with severe pain. Especially in younger children with severe pain, the adjustment of heart rates leads to better classification of children with tachycardia. The adjusted heart rates per age groups were provided in reference centiles. The association between respiratory rates and Manchester pain scores showed similar trends as the curves for heart rates. However, the changes in respiratory rates were not large enough to be clinically relevant.

To our knowledge, this is the first study that aimed to determine the association between heart rates or respiratory rates and pain severity in children at the ED. Adult studies on correlation between vital signs and pain severity by simple correlation or univariable linear regression analyses showed minimal to no effect.[149-151]

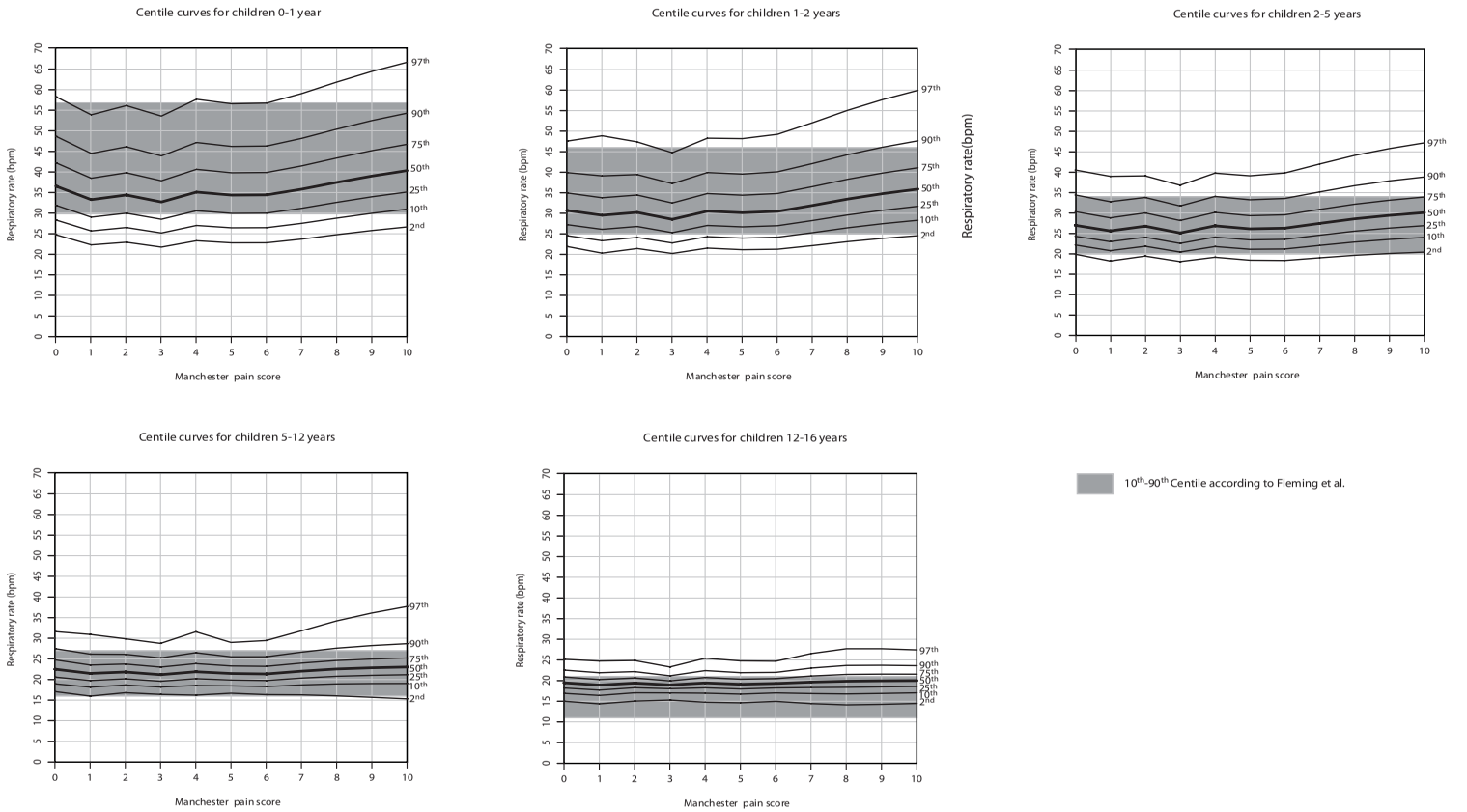

FIGURE 3: Centiles of respiratory rate for different Manchester Pain scores

10^{th}-90^{th} centile according to Fleming: children 0-1 year, 30-57 bpm ; 1-2 years, 25-46; 2-5 years, 20-34 bpm; 5-12 years, 16-27 bpm; and 12-16 years, 11-21 bpm.

Although we found a significant association between vital signs and pain severity, this association was minimal for respiratory rates and disappeared for heart rates, when children were older than five years of age. An explanation could be that the heart rate variability of children is influenced by the maturation of the autonomic nervous system.[152, 153] This may account for heart rate variability of children to decrease with age. Moreover, infants have a high sympathetic activity that rapidly decreases between the age of five and ten.[153, 154]

The centiles display an association between the absolute value of pain-intensity scores and vital sign values. At his moment, they can only be used to correctly interpret patient's heart rates and respiratory rates. However, the clinical impact of these centiles is larger, if the centiles could be used as an objective guidance for anaesthetic treatment, since we expect that vital sign values will decrease after treatment. To use the centiles in such way, further validation of the centiles is needed.

Strengths and limitations

This study provides age and pain appropriate centile charts for children derived from a large cohort consisting of 87,291 children visiting three European EDs. Therefore, these reference values can be considerate as stable and precise. However, our reference values are not validated in a different time period or different settings and therefore the generalisability of this study may be limited.

The definition of pain according to the international association for the study of pain is: "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[155] The use of experience of the patient in this definition ensures that pain is subjective. Moreover, there is no golden standard to measure pain in children at the ED. In the literature, two different tools to assess pain are described: observational scales like behavioural measurement scales[133] and self-report scales like facial scales, numeric scales, or visual analogue scales.[134] The advantages of observational scales like the well-validated COMFORT scale developed for critical care is that it can be used in children too young to use self-report scales, in children with cognitive impairment or in children with an altered level of consciousness.[133] The disadvantage is that the COMFORT scale requires baseline measurements, which are not available at the ED.[156]

The Manchester pain ruler, combines a self-report scale with an observational scale, and it has the advantage to be quick and easy to use at the ED.[7, 18] Although the Manchester pain scale showed good convergent validity with the Oucher scale[136], the inter-rater and intra-rater observer agreement of the scale have never been tested for the paediatric population. Since a systematic review on face scales of self-report in children has shown the reproducibility of most scales to be moderate to good[134], we have no reason to believe that the reproducibility of the Manchester pain scale was low.

Next, vital signs were not measured in all patients, because we left the decision to measure vital signs to the discretion of the nurse. We solved this problem by using a multiple imputation.[146] We are aware that imputation of outcome variables would have led to similar result as a complete case with covariate adjustment.[157] However, GAMLSS is a method used for univariable regression[140-143]; therefore covariate adjustment was not possible and thus multiple imputation was chosen to avoid selection.

Respiratory rates were measured by counting respiratory movements for 30 seconds, which is less accurate then counting them twice or by electronic devices.[158-160] Although respiratory rate variability consequently probably slightly increased, this reflected common clinical

practice and therefore increased the face validity of the centile charts. Moreover, vital sign values were not measured in all children, since the measurement was left to the discretion of the nurse. We solved this problem validly by using a multiple imputation model that can be used when the outcome measure and predictor are correlated.[106]
Finally, the final reference centiles for children are corrected for age and pain severity. We excluded patients with distress or crying. A more detailed description of patient's well-being would have added to the validity of the centiles. However, these data were not recorded. Another factor that showed increasingly effects on vital signs is temperature.[161-163] The addition of temperature did not interfere the association of pain scores and vital signs (data not shown). To make centile charts useful for clinical practice, we choose to only present centile charts corrected for age and pain scores.

CONCLUSIONS

In new derived centile charts for children, the association between heart rates or respiratory rates and Manchester pain scores was quantified for different age groups. Especially in younger children, heart rates increased when patients had severe pain. Respiratory rates increased as well in children with severe pain; however, this increase was too small to be clinically relevant.

APPENDIX 1: The distribution of complete heart rate cases per pain category per agegroup

	NO PAIN	MILD PAIN	MODERATE PAIN	SEVERE PAIN	TOTAL
Age					
0-1 year	10008 (64%)	5023 (32%)	589 (4%)	105 (1%)	15725 (100%)
1-2 years	6674 (58%)	4143 (36%)	673 (6%)	104 (1%)	11594 (100%)
2-5 years	10599 (49%)	9218 (43%)	1677 (8%)	193 (1%)	21687 (100%)
5-12 years	8667 (34%)	12997 (51%)	3487 (14%)	400 (2%)	25551 (100%)
12-16 years	3258 (27%)	6089 (51%)	2219 (19%)	381 (3%)	11947 (100%)

APPENDIX 2: The distribution of complete respiratory rate cases per pain category per agegroup

	NO PAIN	MILD PAIN	MODERATE PAIN	SEVERE PAIN	TOTAL
Age					
0-1 year	8371 (63%)	4348 (33%)	503 (4%)	71 (1%)	13293 (100%)
1-2 years	5507 (56%)	3791 (38%)	606 (6%)	71 (1%)	9975 (100%)
2-5 years	8826 (46%)	8613 (45%)	1579 (8%)	156 (1%)	19174 (100%)
5-12 years	7705 (32%)	12535 (52%)	3389 (14%)	377 (2%)	24006 (100%)
12-16 years	2966 (26%)	5916 (52%)	2177 (19%)	367 (3%)	11426 (100%)

APPENDIX 3: Predicted heart rate values at different pain categories in children

		HEART RATE CENTILES (BEATS PER MINUTE)						
		2nd	10th	25th	50th	75th	90th	97th
Age	**Pain category**							
0-1 year	No pain	109	120	130	141	153	166	184
	Mild pain	101	111	120	130	142	156	175
	Moderate pain	105	116	126	138	153	169	193
	Severe pain	114	126	137	151	167	186	214
1-2 years	No pain	101	111	122	134	149	164	187
	Mild pain	94	102	110	120	133	147	170
	Moderate pain	96	106	117	130	145	162	187
	Severe pain	104	118	131	147	165	185	212
2-5 years	No pain	90	100	110	122	136	150	168
	Mild pain	86	93	100	110	121	134	155
	Moderate pain	85	94	103	114	127	142	165
	Severe pain	93	104	115	128	143	160	187
5-12 years	No pain	74	83	92	101	113	126	145
	Mild pain	73	80	86	93	107	111	129
	Moderate pain	72	80	86	93	102	113	134
	Severe pain	68	79	89	100	114	132	173
12-16 years	No pain	64	73	80	87	96	107	127
	Mild pain	65	74	79	84	90	97	112
	Moderate pain	63	73	79	85	92	101	123
	Severe pain	61	72	79	86	94	104	129

APPENDIX 4: Predicted respiratory rate values at different pain categories in children

		RESPIRATORY RATE CENTILES (BREATHS PER MINUTE)						
		2nd	10th	25th	50th	75th	90th	97th
Age	**Pain category**							
0-1 year	No pain	25	28	32	36	42	48	58
	Mild pain	22	25	28	33	38	44	53
	Moderate pain	23	26	30	34	40	46	57
	Severe pain	26	30	34	39	45	52	64
1-2 years	No pain	22	24	27	31	35	40	46
	Mild pain	20	23	25	29	32	37	44
	Moderate pain	21	24	27	30	35	40	48
	Severe pain	24	27	31	35	40	46	56
2-5 years	No pain	20	22	24	27	30	34	40
	Mild pain	18	21	23	25	28	32	37
	Moderate pain	18	21	24	26	30	34	40
	Severe pain	20	23	26	29	33	38	46
5-12 years	No pain	17	19	21	23	25	28	32
	Mild pain	17	18	20	21	23	25	29
	Moderate pain	16	18	20	21	23	26	30
	Severe pain	16	19	21	23	25	28	36
12-16 years	No pain	15	17	18	20	21	23	25
	Mild pain	15	17	18	19	20	21	23
	Moderate pain	15	17	18	19	21	22	25
	Severe pain	14	17	19	20	22	24	28

APPENDIX 5: Mu, sigma, nu, and tau derived from the heart rate centiles per pain category

	0-1 YEAR				1-2 YEARS				2-5 YEARS			
	μ	σ	ν	τ	μ	σ	ν	τ	μ	σ	ν	τ
Pain score												
0	140.8	0.120	-0.255	12.23	134.1	0.146	-0.480	20.20	122.3	0.153	-0.144	32.39
1	135.5	0.136	-0.509	12.23	128.4	0.155	-0.650	20.20	115.8	0.152	-0.521	18.57
2	133.0	0.124	-0.593	12.23	123.6	0.136	-1.081	20.20	113.1	0.133	-1.142	15.43
3	130.8	0.127	-0.636	12.23	120.5	0.140	-1.126	20.20	109.7	0.135	-1.090	14.07
4	136.1	0.131	-0.661	12.23	126.9	0.146	-0.920	20.20	115.3	0.141	-0.905	13.30
5	136.6	0.134	-0.678	12.23	128.2	0.153	-0.707	20.20	115.1	0.146	-0.775	12.82
6	138.3	0.137	-0.690	12.23	129.6	0.159	-0.537	20.20	114.1	0.150	-0.679	12.48
7	142.7	0.139	-0.699	12.23	134.9	0.163	-0.405	20.20	118.3	0.154	-0.602	12.24
8	147.4	0.141	-0.706	12.23	141.5	0.167	-0.302	20.20	123.5	0.156	-0.540	12.05
9	151.1	0.142	-0.712	12.23	146.9	0.170	-0.220	20.20	127.7	0.159	-0.490	11.90
10	154.1	0.143	-0.716	12.23	151.3	0.172	-0.153	20.20	131.2	0.161	-0.449	11.78

	5-12 YEARS				12-16 YEARS			
	μ	σ	ν	τ	μ	σ	ν	τ
Pain score								
0	101.3	0.154	-0.386	13.31	87.3	0.124	-0.511	4.01
1	97.1	0.146	-0.377	7.34	86.2	0.117	-0.511	3.21
2	94.2	0.114	-1.052	6.02	84.2	0.083	-0.511	2.98
3	92.6	0.112	-1.192	5.45	84.2	0.085	-0.511	2.87
4	94.9	0.120	-1.130	5.14	84.6	0.091	-0.511	2.81
5	94.7	0.121	-1.050	4.94	84.9	0.096	-0.511	2.77
6	93.3	0.117	-0.981	4.80	85.2	0.099	-0.511	2.74
7	95.0	0.130	-0.923	4.70	85.5	0.103	-0.511	2.72
8	97.6	0.150	-0.876	4.62	85.7	0.106	-0.511	2.70
9	99.9	0.168	-0.838	4.558	85.9	0.109	-0.511	2.69
10	101.8	0.183	-0.806	4.409	86.0	0.111	-0.511	2.67

APPENDIX 6: Mu, sigma, nu, and tau derived from the respiratory rate centiles per pain category

	0-1 YEAR				1-2 YEARS				2-5 YEARS			
	μ	σ	ν	τ	μ	σ	ν	τ	μ	σ	ν	τ
Pain score												
0	36.4	0.204	-0.416	21.02	30.6	0.812	-0.681	19.57	27.0	0.157	-0.969	9.26
1	33.1	0.204	-0.416	14.09	29.4	0.812	-0.681	7.171	25.6	0.157	-0.717	6.04
2	34.3	0.204	-0.416	12.34	30.1	0.812	-0.681	14.54	26.7	0.157	-0.633	9.20
3	32.6	0.204	-0.416	11.54	28.4	0.812	-0.681	14.39	25.1	0.157	-0.591	8.27
4	35.0	0.204	-0.416	11.09	30.4	0.812	-0.681	12.27	26.8	0.157	-0.566	6.99
5	34.3	0.204	-0.416	10.80	30.0	0.812	-0.681	10.47	26.1	0.157	-0.549	6.08
6	34.3	0.204	-0.416	10.59	30.4	0.812	-0.681	9.168	26.3	0.157	-0.537	5.43
7	35.7	0.204	-0.416	10.44	30.8	0.812	-0.681	8.246	27.4	0.157	-0.528	4.97
8	37.3	0.204	-0.416	10.33	33.4	0.812	-0.681	7.574	28.5	0.157	-0.521	4.63
9	38.9	0.204	-0.416	10.24	34.7	0.812	-0.681	7.067	29.4	0.157	-0.515	4.38
10	40.2	0.204	-0.416	10.16	35.8	0.812	-0.681	6.675	30.1	0.157	-0.511	4.18

	5-12 years				12-16 years			
	μ	σ	ν	τ	μ	σ	ν	τ
Pain score								
0	22.6	0.127	-0.866	6.11	19.6	0.091	-0.192	3.54
1	21.6	0.115	-0.866	3.56	19.0	0.087	-0.192	2.96
2	21.9	0.111	-0.866	4.68	19.5	0.078	-0.192	2.79
3	21.3	0.109	-0.866	4.78	19.1	0.064	-0.192	2.71
4	22.0	0.108	-0.866	3.05	19.5	0.082	-0.192	2.66
5	21.6	0.107	-0.866	4.76	19.2	0.079	-0.192	2.63
6	21.5	0.107	-0.866	3.90	19.4	0.075	-0.192	2.61
7	22.1	0.106	-0.866	2.94	19.7	0.091	-0.192	2.59
8	22.7	0.106	-0.866	2.38	20.0	0.010	-0.192	2.58
9	23.0	0.106	-0.866	2.07	20.0	0.098	-0.192	2.57
10	23.2	0.106	-0.866	1.88	20.1	0.094	-0.192	2.56

CHAPTER 10

The performance of different paediatric early warning scores in the emergency department: An observational study

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ABSTRACT

Objective Paediatric early warning scores (PEWS) are being advocated for use in the emergency department (ED). The goal of this study was to compare the validity of different PEWS in a paediatric ED.

Methods Ten different PEWS were evaluated in a large prospective cohort. We included children aged ,16 years who had presented to the ED of a university hospital in The Netherlands (2009-2012). The validity of the PEWS for predicting ICU admission or hospitalization was expressed by the area under the receiver operating characteristic (ROC) curves.

Results These PEWS were validated in 17943 children. Two percent of these children were admitted to the ICU, and 16% were hospitalized. The areas under the ROC curves for predicting ICU admission, ranging from 0.60 (95% confidence interval [CI]: 0.5720.62) to 0.82 (95% CI: 0.79–0.85), were moderate to good. The area under the ROC curves for predicting hospitalization was poor to moderate (range: 0.56 [95% CI: 0.55–0.58] to 0.68 [95% CI: 0.66–0.69]). The sensitivity and specificity derived from the ROC curves ranged widely for both ICU admission (sensitivity: 61.3%–94.4%; specificity: 25.2%–86.7%) and hospital admission (sensitivity: 36.4%–85.7%; specificity: 27.1%–90.5%). None of the PEWS had a high sensitivity as well as a high specificity.

Conclusions PEWS can be used to detect children presenting to the ED who are in need of an ICU admission. Scoring systems, wherein the parameters are summed to a numeric value, were better able to identify patients at risk than triggering systems, which need 1 positive parameter.

INTRODUCTION

Paediatric early warning scores (PEWS) are physiology-based scoring systems developed to identify patients admitted to inpatient paediatric wards at risk for clinical deterioration.[164] A recent publication showed that early warning scores are needed to quickly identify critically ill patients in the emergency departments (EDs) so that treatment can be started without delay.[165] Moreover, the use of the same system in the ED and inpatient wards allows continuity for patient assessment.

According to an adult study performed in the United Kingdom, early warning scores are used in the majority of EDs, although the evidence for this claim is lacking.[165] To date, there are few data on the use of PEWS in children presenting to the ED.[166, 167] Bradman and Maconochie[166] validated only 1 of the several PEWS that are currently in use. Egdell et al[167] conducted a pilot study to validate a designed for initial assessment at the ED and showed that the system was able to identify children requiring ICU admission.

The goal of the current study was to compare the performance of different PEWS to predict ICU admission or hospitalization in a large population of children visiting the paediatric ED.

METHODS

Study design

Different versions of PEWS were evaluated in a large prospective cohort of children presenting to the ED. The different PEWS were based on patients' age and vital sign values (heart rate, respiratory rate, oxygen saturation, blood pressure, temperature, and level of consciousness) prospectively collected during the triage assessment.

The current study used data collected for an ongoing study on the validity of the Manchester Triage System (MTS) in paediatric patients.[16, 162] The medical ethics committee of Erasmus MC approved the study, and the requirement for informed consent was waived.

Setting and selection of participants

Data collection included all children aged <16 years who presented to the ED of the Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands, between August 2009 and June 2012. The Erasmus MC-Sophia Children's Hospital is a large inner-city university hospital with a paediatric ED that is open 24 hours a day. The ED receives ~8000 children annually from a catchment area with a multisocioeconomic and multi-ethnic population of 2 million inhabitants.

Paediatric Early Warning Scores

A PubMed search was performed in June 2012 using the terms "paediatric early warning," "paediatric early warning," "track and trigger," "trigger criteria," "calling criteria," "medical emergency team," "paediatric alert criteria," or "paediatric alert criteria." Studies were limited to children aged 0 to 18 years and a publication date within the past 10 years. Subsequently, the titles, abstract, and full text articles were screened, and the reference lists of systematic reviews and studies on the use of PEWS in the ED were scanned to complete the search.

The PEWS were included if the scores were newly developed for children presenting to the ED or admitted to an inhospital paediatric ward or if the original scores were adjusted.

TABLE 1: The Paediatric Early Warning Scores (PEWS) and their parameters

PEWS	ORIGIN	TYPE	NORMAL VITAL SIGN CUT-OFF LEVELS							OTHER PARAMETERS	EXCLUDED PARAMETERS
			Age range	Heart rate (bpm)	Respiratory rate (bpm)	Systolic Blood Pressure (mmHg)	Oxygen saturation	Temperature (°C)	Level of Consciousness		
Monaghan[168]	Original	Scoring (0-9)	<1y	120-190	35-50	NA	NA	NA	Sleeping; Irritable; Lethargic; Confused; Reduced response to pain	Capillary refill; Oxygen therapy; Work of breathing	¼ hourly nebulizers; Persistent vomiting after surgery
			1-2y	80-130	30-45	NA					
			3-4y	70-130	26-41	NA					
			5-11y	70-130	22-37	NA					
			12-16y	60-110	11-26	NA					
Akre[169]	Derived[168]	Scoring (0-9)	<1m	100-200	35-70	N A	NA	NA	Sleeping; Irritable; Lethargic; Confused; Reduced response to pain	Capillary refill; Cyanotic; Oxygen therapy; Work of breathing	¼ hourly nebulizers; Persistent vomiting after surgery
			1-12m	100-200	30-50	NA					
			13m-3y	70-130	20-40	NA					
			4-6y	70-130	16-33	NA					
			7-12y	70-130	14-31	NA					
			13-16y	55-110	11-28	NA					
Skaletzky[170]	Derived[168]	Scoring (0-9)	<3m	85-225	30-70	NA	NA	NA	Sleeping; Irritable; Lethargic; Confused; Reduced response to pain	Capillary refill; Oxygen therapy; Work of breathing	¼ hourly nebulizers; Persistent vomiting after surgery
			3m-1y	100-210	30-70	NA					
			1-2y	100-210	24-50	NA					
			2-3y	60-160	24-50	NA					
			4-5y	60-160	22-44	NA					
			6-10y	60-160	18-40	NA					
			10-12y	60-120	18-40	NA					
			13-16y	60-120	12-26	NA					
Duncan[171]	Original	Scoring (0-23)	<3m	110-150	30-60	60-80	>95%	36-38.5	Glasgow Coma scale ≤11	Pulses; Capillary refill; Oxygen therapy; bolus fluid	None (dynamic model was used)
			3-12m	100-150	25-50	80-100					
			1-4y	90-120	20-40	90-110					
			4-12y	70-110	20-30	90-120					
			>12y	60-100	12-16	100-130					
Parshuram[172]	Derived[171]	Scoring (0-26)	<3m	110-150	30-60	60-80	>95%	NA	NA	Capillary refill; Respiratory effort; Oxygen therapy;	
			3-12m	100-150	25-50	80-100					
			1-4y	90-120	20-40	90-110					
			4-12y	70-110	20-30	90-120					
			>12y	60-100	12-16	100-130					

TABLE 1: Continued

PEWS	ORIGIN	TYPE	NORMAL VITAL SIGN CUT-OFF LEVELS							OTHER PARAMETERS	EXCLUDED PARAMETERS
			Age range	Heart rate (bpm)	Respiratory rate (bpm)	Systolic Blood Pressure (mmHg)	Oxygen saturation	Temperature °C	Level of Consciousness		
Egdell[167]	Original	Scoring (0-21)	<1y	110-160	30-40	NA	≥93%	36-38	Responds to voice; Responds to pain; Unresponsive	Work of breathing; Capillary refill	
			1-2y	100-150	25-35	NA					
			2-5y	95-140	25-30	NA					
			5-12y	80-120	20-25	NA					
			>12y	60-100	15-20	NA					
Tibballs[173]	Original	Triggering	<3m	100-180	>60	<50	≥90% or ≥60% with cyanotic heart disease	NA	Acute change in neurological status or convulsion	Airway threat; Severe respiratory distress, apnoea, cyanosis; cardiac or respiratory arrest; Worried about clinical state	
			4-12m	100-180	>50	<60					
			1-4y	90-180	>40	<70					
			5-12y	80-140	>30	<80					
			>12y	60-130	>30	<90					
			1-2y	80-150	15-45	80-95	≥93%	NA	Responds to voice; Responds to pain; Unresponsive	Airway threat e.g. stridor; Work of breathing; Worried about clinical state	
			2-5y	75-140	15-40	80-100					
			5-12y	60-120	10-35	90-110					
			>12y	55-100	10-30	100-120					
Haines[174]	Derived[173]	Triggering	<6m	≥150	≥70	NA	≥92% or ≥75% with cyanotic heart disease	NA	Glasgow Coma scale ≤11; responds only to pain; convulsion;	Airway threat; Signs of shock e.g. prolonged capillary refill (3s); Worried about clinical state; Bolus fluid	Hyperkalaemia; suspected meningococcus; suspected keto-acidosis
			6-12m	≥150	≥60	NA					
			1-5y	≥150	≥40	NA					
			5-12	≥120	≥25	NA					
			>12	≥100	≥25	NA					
Brilli[175]	Derived[173]	Triggering	NA	NA	NA	NA	≥90%	NA	Agitation or decreased level of consciousness	Work of breathing; Cyanosis; Worried about clinical state	

The PubMed search retrieved a total of 75 articles. After exclusion of studies not addressing PEWS (n = 45), original research on PEWS (n = 8), or children (n =6), 16 studies remained. Eight studies described newly developed or derived PEWS and the remaining 8 studies validated these PEWS. Four studies were included after screening the reference lists, resulting in a total of 12 PEWS, of which 11 were developed for inpatient use[168-178] and 1 for use in the ED.[167]

The PEWS can be differentiated into scoring systems and triggering systems.[164] A scoring system contains different parameters (e.g., heart rates or respiratory rates). If these parameters show an increased deviation from normal values, the given scores are greater. The scores for all the different parameters are cumulated to 1 numeric value, which, depending on the cut-off level, determines a patient's risk for clinical deterioration. In a triggering system, the patient is considered at risk if 1 of the parameters is positive.

Six PEWS were considered as scoring systems[167-172] and 6 as triggering systems.[173-178]. Most PEWS were developed for inhospital patients and therefore not all parameters were available at triage assessment. Parameters that contain diagnostics, therapeutic interventions, or suspected diagnoses were removed from the scoring and triggering systems. Only therapeutic interventions such as oxygen therapy and bolus fluids remained in the model because these parameters are surrogate markers of low saturation and severe dehydration, which are features scored by triage nurses. The PEWS of Hunt et al[178] and Sharek et al[177] are not useful for triage assessment in the ED because continuous monitoring of vital signs is needed to assess acute change in vital signs. Therefore, 10 PEWS remained for analysis.

Details of parameters used in the remaining PEWS are shown in Table 1,and the contributions of individual parameters to the scoring systems are shown in Appendix 1.

Data collection

ED nurses specialized in both paediatric and emergency care collected standardized data on the different parameters of the PEWS during triage assessment and recorded this information on structured electronic or paper (2006-2009) ED forms. Heart rates, oxygen saturation, and blood pressure were measured by using electronic devices. Respiratory rates were measured by counting respiratory movements for 30 seconds. The measurement of vital signs was left to the discretion of the nurse. The database was checked for outliers (values <3 times the interquartile range above the 75th percentile and ,3 times the interquartile range below the 25th percentile[179]). Patient characteristics and data on follow-up were extracted from the electronic hospital system and merged in SPSS version 20.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) for analysis.

Data analysis

To impute missing vital signs values, we used a multiple imputation model, including age, gender, vital signs values, hospitalization, ICU admission, MTS category, and presenting problem. This method means that missing data are replaced by a value that is drawn from an estimate of the distribution of the variable to create a complete database.[97] This process was executed 10 times to generate 10 complete databases. Statistical analyses on each database were performed and pooled for a final result. A numeric score was calculated for the different scoring systems and a binary score for the triggering systems. The validity of the PEWS was expressed by the areas under the receiver operating characteristic (ROC) curves, sensitivity, specificity, and positive likelihood ratios and negative likelihood ratios for ICU admission and admission to the hospital. To calculate sensitivity, specificity, and likelihood ratios, the

numeric scores of the scoring systems had to be dichotomized at the most optimal cut-off level of the ROC curves.
Sensitivity, specificity, positive likelihood ratios, negative likelihood ratios, and the 95% confidence intervals (CIs) were calculated with the VassarStats Web site (http://vassarstats.net/clin1.html). Statistical analyses were performed by using SPSS and R package version 2.13.1 (R Foundation for Statistical Computing, Vienna, Austria) using the Design, Hmisc (AregImpute) function.

RESULTS

Study population

In total, 18073 children presented to the ED during the study period. Data were not available for 130 children. Therefore, 17943 children remained for analysis, of whom 16% (n = 2828) were admitted to the hospital and 2% (n=373) were admitted to an ICU or died in the ED. Patients' characteristics are shown in Table 2.

TABLE 2: Patient characteristics

CHARACTERISTIC	STUDY POPULATION N=17943	
Female gender, n (%)	7399	(41)
Median age (IQR), y	4.2	(1.4-9.5)
Presenting problem, n (%)		
Trauma	4438	(25)
Gastro-intestinal	2399	(13)
Fever without known source	1624	(9)
Dyspnoea	1566	(9)
Wounds	1186	(7)
Neurological	810	(5)
Urinary tract problems	438	(2)
Local infection/abscess	344	(2)
Rash	306	(2)
Ear, nose, throat	260	(1)
Other problems	3953	(22)
Missing	620	(4)
MTS triage category, n (%)		
Immediate	356	(2)
Very urgent	2237	(13)
Urgent	7887	(44)
Standard	6339	(35)
Non-urgent	504	(3)
Missing	620	(4)
Follow-up, n (%)		
No follow-up	6700	(37)
Outpatient clinic/GP	5835	(32)
Hospital admission	2828	(16)
IC admission/Mortality at ED	373	(2)
Other follow-up	2207	(12)

GP, general practitioner; IQR, interquartile range

Ninety-six percent of patients (n = 17289) had at least 1 vital sign measured. Heart rate was measured in 9062 (51%) children; respiratory rates in 6671 (37%); blood pressure in 3632 (20%); oxygen saturation in 4901 (27%); temperature in 10050 (56%); and level of consciousness in 16 319 (91%). The absence of vital signs was more frequent in patients allocated to lower MTS urgency categories and in patients presenting with traumatic problems than in those presenting with medical problems.

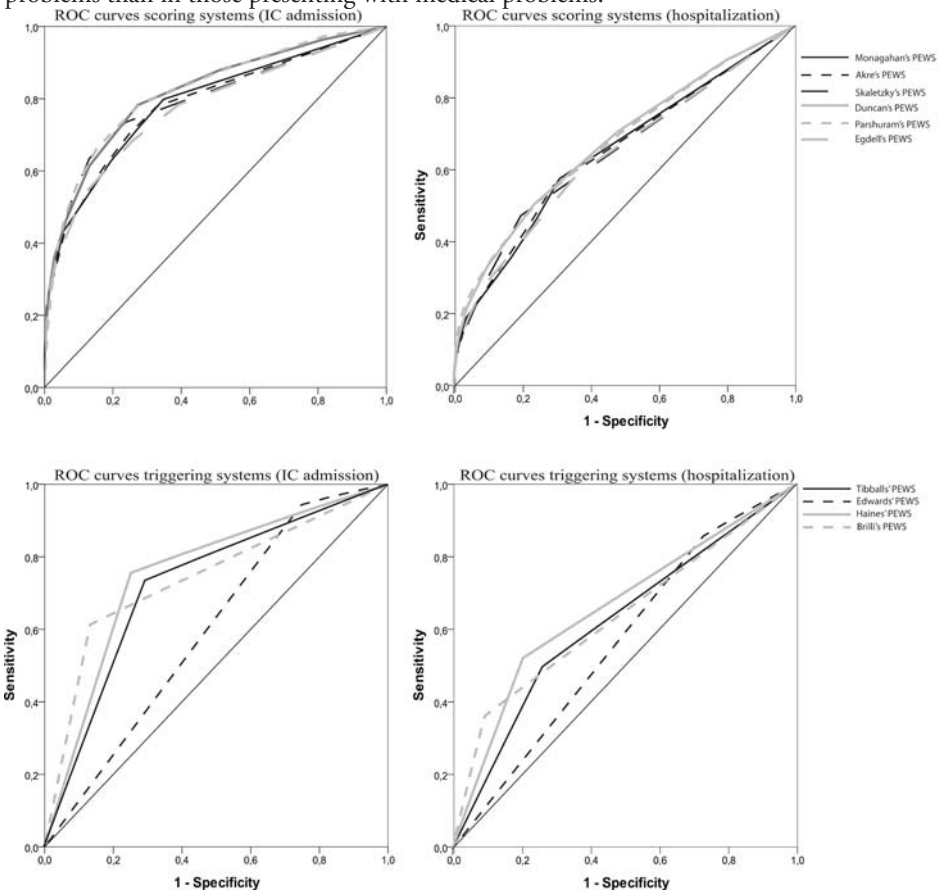


FIGURE 1: ROC curves of scoring systems and triggering systems for (left) ICU admission and (right) hospitalization.

Performances of PEWS in the total population

The ROC curves of the PEWS are shown in Figure 1. The discriminative ability to predict ICU admission and admission to the hospital was higher when scoring systems were used than when triggering systems were used (Table 3). Moreover, PEWS were better suited to predict ICU admission than admission to the hospital, because the areas under the ROC curves decreased significantly when admission to the hospital was used as the outcome measure.

For all PEWS, the optimal cut-off level to calculate sensitivity and specificity for both ICU admission and admission to hospital was set at 1, except for the PEWS of Duncan et al[171] and Parshuram et al,[172] for which the cut-off levels were set at 3 for ICU admission and 2 for

admission to the hospital (Table 3). The sensitivity and specificity at different cut-off levels of the scoring systems are shown in Appendix 2.
The sensitivity and specificity of the PEWS at the optimal cut-off levels varied widely. When ICU admission was used, the sensitivity of the different PEWS ranged from 61.3% to 94.4% and the specificity ranged from 25.2% to 86.7%. These findings resulted in a positive likelihood ratio between 1.3 and 4.6 and a negative likelihood ratio between 0.22 and 0.45.
When hospitalization was used, the sensitivity ranged from 36.4% to 85.7% and the specificity ranged from 27.1% to 90.5%. None of the PEWS showed both a high sensitivity and a high specificity. Sensitivity, specificity, positive likelihood ratios, and negative likelihood ratios of the individual PEWS are shown in Table 3.

DISCUSSION

Twelve different PEWS were described in the literature, of which 10 were potentially suited for use in the ED. The discriminative ability of the PEWS (area under the ROC curve) were moderate to good for ICU admission (range: 0.60-0.82) and poor to moderate for admission to the hospital (range: 0.56-0.68). Moreover, scoring systems with parameters leading to a numeric value were better able to identify patients at risk than triggering systems, which need 1 positive parameter. The c-statistics of the different scoring systems, however, were not statistically different. The choice of best PEWS in the ED should depend on other factors such as ease of use.
The scoring systems of Egdell et al[167] and Duncan et al[171] contain more parameters than the scores of Monaghan,[168] Akre et al,[169] Skaletzky et al,[170] and Parshuram et al[172] and thus are more time-consuming at initial assessment. Moreover, the PEWS of Duncan et al and Parshuram et al included blood pressure, which is difficult to obtain in a standardized manner in a busy ED. For this reason, the applicability of scoring systems should be evaluated for the individual setting before implementation. However, scoring systems with more parameters provide a wider range of sum scores and can therefore differentiate patients into >2 risk groups. This categorization can be important when PEWS are not only used to identify patients in need of ICU admission but also patients in need of admission to a paediatric ward. The PEWS of Duncan et al[171] and its bedside version from Parshuram et al[172] are the only scores with different optimal cut-off levels for hospitalization and ICU admission, and they are therefore best suited to allocate patients to >2 risk groups. Thresholds for abnormal vital signs influence the validity of the PEWS, because PEWS that only differ according to vital sign thresholds showed different c-statistics. This finding suggests that the PEWS could be optimized by choosing the optimal cut-off levels for vital sign values. At present, most PEWS use cut-off levels based on the Advanced Paediatric Life Support program.[27, 180] However, recent publications suggest that reference ranges for vital signs should be updated with new thresholds.[95, 161, 162]

TABLE 3: Performance of the different PEWS for ICU admission and for admission to hospital

PEWS	CUT-OFF LEVEL	HIGH-RISK PATIENTS		LOW-RISK PATIENTS		SENSITIVITY		SPECIFICITY	
		N	(%)	N	(%)	%	(95% CI)	%	(95% CI)
IC admission									
Monaghan et al.[168]	1	6415	(35.8)	11528	(64.2)	79.8	(75.3-83.7)	65.2	(64.5-65.9)
Akre et al.[169]	1	6073	(33.8)	11870	(66.2)	77.9	(73.3-81.9)	67.1	(66.4-67.8)
Skaletzky et al.[170]	1	4417	(24.6)	13526	(75.4)	73.4	(68.6-77.8)	76.4	(75.8-77.0)
Duncan et al.[171]	3	5083	(27.4)	12860	(72.6)	78.3	(73.7-82.3)	72.7	(72.1-73.4)
Parshuram et al.[172]	3	5152	(28,7)	12791	(71.3)	78.3	(73.7-82.3)	72.3	(71.7-73.0)
Egdell et al.[167]	1	7182	(40.0)	10761	(60.0)	78.4	(73.8-82.4)	60.8	(60.0-61.5)
Tibballs et al.[173]	NA	5447	(30.4)	12496	(69.6)	73.5	(68.7-77.8)	70.6	(69.9-71.2)
Edwards et al.[176]	NA	13497	(75.2)	4446	(24.8)	94.4	(91.4-96.4)	25.2	(24.5-25.8)
Haines et al.[174]	NA	4695	(26.1)	13248	(73.8)	75.6	(70.9-79.8)	74.9	(74.2-75.5)
Brilli et al.[175]	NA	2557	(14.3)	15384	(85.7)	61.3	(56.1-66.2)	86.7	(86.2-87.2)
Admission to hospital									
Monaghan et al.[168]	1	6415	(35.8)	11528	(64.2)	57.7	(56.0-59.4)	69.0	(68.3-69.8)
Akre et al.[169]	1	6073	(33.8)	11870	(66.2)	55.6	(53.9-57.4)	70.9	(70.1-71.6)
Skaletzky et al.[170]	1	4417	(24.6)	13526	(75.4)	47.4	(45.7-49.2)	80.3	(79.7-81.0)
Duncan et al.[171]	2	9317	(51.9)	8626	(48.1)	70.5	(69.0-72.1)	52.1	(51.3-52.9)
Parshuram et al.[172]	2	9449	(52.7)	8494	(47.3)	70.3	(68.7-71.9)	51.2	(50.4-52.0)
Egdell et al.[167]	1	7182	(40.0)	10761	(60.0)	58.7	(57.0-60.4)	64.0	(63.2-64.8)
Tibballs et al.[173]	NA	5447	(30.4)	12496	(69.6)	49.9	(48.1-51.6)	73.9	(73.2-74.6)
Edwards et al.[176]	NA	13497	(75.2)	4446	(24.8)	85.7	(84.5-86.9)	27.1	(26.4-27.8)
Haines et al.[174]	NA	4695	(26.1)	13248	(73.8)	52.3	(50.5-54.0)	79.5	(78.8-80.1)
Brilli et al.[175]	NA	2557	(14.3)	15384	(85.7)	36.4	(34.7-38.1)	90.5	(90.0-91.0)

TABLE 3: Continued

PEWS	CUT-OFF LEVEL	POSITIVE LIKELIHOOD RATIO		NEGATIVE LIKELIHOOD RATIO		AREA UNDER ROC CURVE	
		RATIO	(95% CI)	RATIO	(95% CI)	AUC	(95% CI)
IC admission							
Monaghan et al.[168]	1	2.3	(2.2-2.4)	0.31	(0.25-0.38)	0.79	(0.76-0.81)
Akre et al.[169]	1	2.4	(2.2-2.5)	0.33	(0.27-0.40)	0.78	(0.76-0.81)
Skaletzky et al.[170]	1	3.1	(2.9-3.3)	0.35	(0.29-0.41)	0.79	(0.76-0.82)
Duncan et al.[171]	3	2.9	(2.7-3.0)	0.30	(0.25-0.36)	0.82	(0.79-0.84)
Parshuram et al.[172]	3	2.8	(2.7-3.0)	0.30	(0.25-0.36)	0.82	(0.79-0.85)
Egdell et al.[167]	1	2.0	(1.9-2.1)	0.36	(0.29-0.43)	0.77	(0.74-0.80)
Tibballs et al.[173]	NA	2.5	(2.3-2.7)	0.38	(0.32-0.44)	0.72	(0.69-0.75)
Edwards et al.[176]	NA	1.3	(1.2-1.3)	0.22	(0.15-0.34)	0.60	(0.57-0.62)
Haines et al.[174]	NA	3.0	(2.8-3.2)	0.33	(0.27-0.39)	0.75	(0.72-0.78)
Brilli et al.[175]	NA	4.6	(4.2-5.1)	0.45	(0.39-0.51)	0.74	(0.71-0.77)
Admission to hospital							
Monaghan et al.[168]	1	1.9	(1.8-1.9)	0.61	(0.59-0.64)	0.65	(0.64-0.66)
Akre et al.[169]	1	1.9	(1.8-2.0)	0.63	(0.60-0.65)	0.65	(0.64-0.66)
Skaletzky et al.[170]	1	2.4	(2.3-2.5)	0.65	(0.63-0.68)	0.65	(0.64-0.66)
Duncan et al.[171]	2	1.5	(1.4-1.5)	0.56	(0.54-0.60)	0.68	(0.66-0.69)
Parshuram et al.[172]	2	1.4	(1.4-1.5)	0.58	(0.55-0.61)	0.68	(0.66-0.69)
Egdell et al.[167]	1	1.6	(1.6-1.7)	0.64	(0.62-0.67)	0.64	(0.63-0.65)
Tibballs et al.[173]	NA	1.9	(1.8-2.0)	0.68	(0.66-0.70)	0.62	(0.61-0.63)
Edwards et al.[176]	NA	1.2	(1.2-1.2)	0.53	(0.48-0.57)	0.56	(0.55-0.58)
Haines et al.[174]	NA	2.5	(2.4-2.7)	0.60	(0.58-0.62)	0.66	(0.65-0.67)
Brilli et al.[175]	NA	3.9	(3.6-4.1)	0.70	(0.68-0.72)	0.63	(0.62-0.65)

NA, not applicable

At present, conventional triage systems such as the MTS,[7, 18] the Emergency Severity Index (ESI)[9] the paediatric Canadian Triage and Acuity Scale (PedCTAS),[32] and the Australasian triage Scale (ATS)[4] are used in the ED to allocate the patient's acuity. In the MTS, PedCTAS, and ATS, trained triage nurses had to recognize patient's signs and symptoms to allocate acuity.[7, 18, 32, 4] In the ESI, the urgency categories are based on the need of life-saving interventions and resource use. In all triage systems, vital signs are included to allocate urgency. However, the use of these vital signs differed from the use in PEWS scoring systems, because they are dichotomized into normal and abnormal for the ATS, PedCTAS, and ESI, and in the MTS, they were included as discriminators such as "shock," "abnormal pulse," and "increased work of breathing"; thus, values for abnormality in children were not provided. In South Africa, an early warning score was included to allocate patients to the lowest urgency levels. This triage strategy is inexpensive and can be executed by an inexperienced staff.[181]

Although PEWS can identify patients at risk in the ED for ICU admission and, to a lesser extent, identify patients at risk for hospitalization, we do not advise using warning scores as triage tools to prioritize patients.[182] At present, there is no evidence that PEWS are better than conventional triage systems. To prove that PEWS as triage tools are better than conventional triage systems or that PEWS have added value to conventional triage systems, a direct comparison study should be conducted in which patient outcomes and costs are included.

Currently, PEWS in the ED should be an adjunct of conventional triage. They can be used as a tool to indicate ICU admission or as a monitoring tool to identify patient deterioration, due to their ability to continue a patient's assessment when admitted to the hospital.[165, 183]

The main limitation of the current study is that the different PEWS were not implemented in the ED itself and therefore were not evaluated in practice. Conversely, because the PEWS have not been implemented, clinicians did not know the PEWS scores when examining the patients. The decision to admit patients to the ICU or paediatric ward was not influenced by the outcome of the PEWS and therefore could not bias our results.

Second, ICU admission and admission to the hospital were chosen as a proxy for acuity because a golden standard for acuity does not exist. Worldwide, hospitalization and ICU admission have been used extensively as a proxy for severity of illness in the ED.[29, 103, 126, 184, 185]

Also, it is a limitation that vital signs were not measured in all patients. We resolved this problem by using a multiple imputation model that can be used when the outcome measure (ICU admission) and predictor (presence of vital signs) on X and Yare correlated.[106]

Lastly, the study population comprises children from 1 hospital, which could influence the generalisability of the results. However, the population included a varied case-mix of ~18 000 children, selected from a multicultural, inner-city ED population, and the result are therefore likely to be generalisable to other paediatric ED populations.

CONCLUSIONS

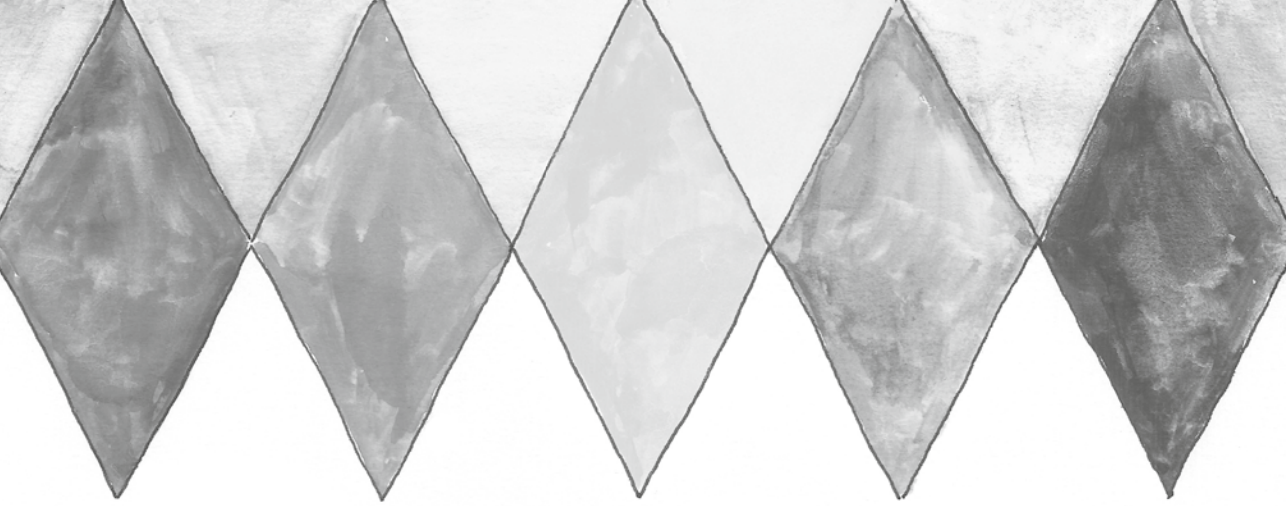
PEWS are capable of identifying children in need of ICU admission. Scoring systems, with parameters leading to a numeric value, were better able to identify patients at risk than triggering systems, which need 1 positive parameter.

APPENDIX 1: Contribution of single parameters to the scoring PEWS

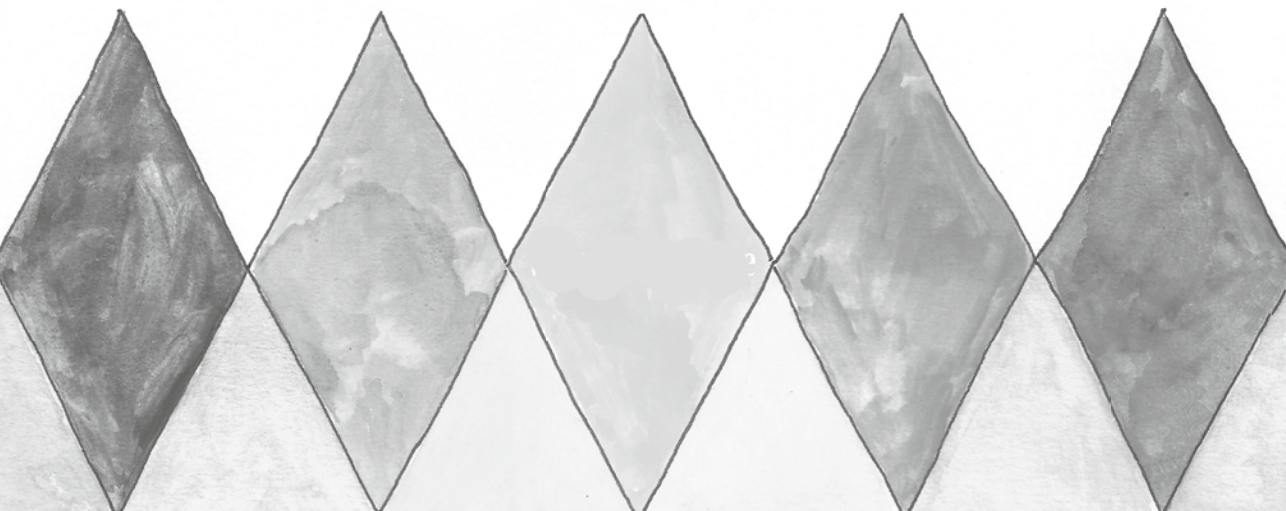
PEWS	INCLUDED PARAMETERS	SCORE
Monaghan et al.[168]/Akre et al.[169]/Skaletzky et al.[170]	Behaviour: level of consciousness	0-3
	Cardiovascular: capillary refill/heart rate	0-3
	Respiratory: work of breathing/oxygen therapy /respiratory rate	0-3
Duncan et al.[171]	Heart rate	0-2
	Respiratory rate	0-2
	Systolic Blood pressure	0-2
	Pulses	0-2
	Oxygen saturation	0-2
	Capillary refill	0-2
	Level of consciousness	0-2
	Oxygen therapy	0-2
	Bolus fluid	0-2
	Temperature	0-2
Parshuram et al.[172]	Heart rate	0-4
	Systolic blood pressure	0-4
	Capillary refill	0-4
	Respiratory rate	0-4
	Respiratory effort	0-4
	Oxygen saturation	0-2
	Oxygen therapy	0-4
Egdell et al.[167]	Respiratory rate	0-3
	Work of breathing	0-3
	Oxygen saturation	0-3
	Temperature	0-3
	Capillary refill	0-3
	Heart rate	0-3
	Level of consciousness	0-3

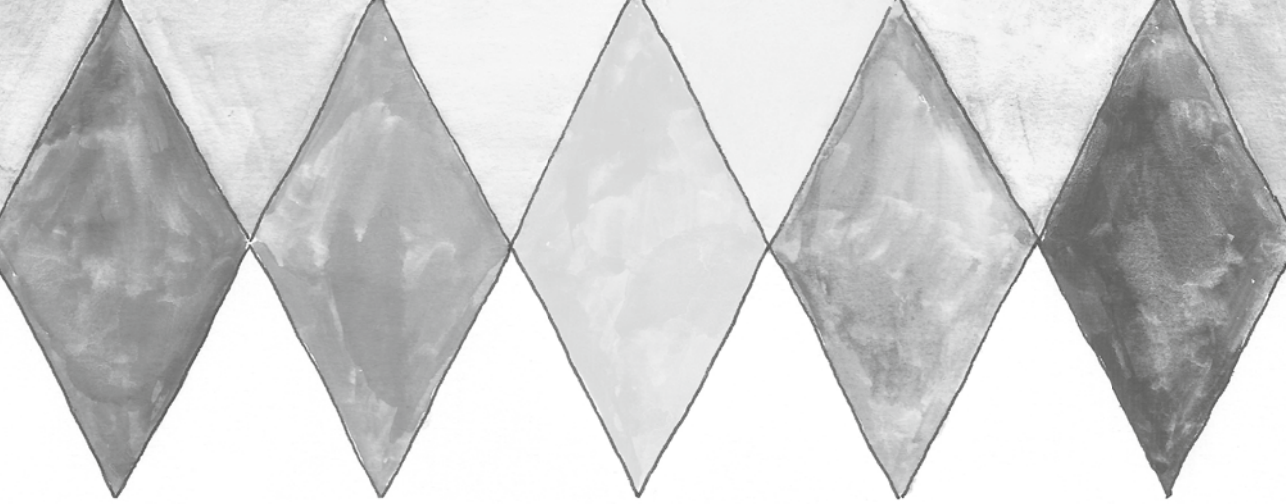
APPENDIX 2: Sensitivity and specificity at different cut-off levels for scoring PEWS

PEWS	CUT-OFF LEVEL	ICU ADMISSION		ADMISSION TO HOSPITAL	
		Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Monaghan et al.[168]	≥1	79.8	65.2	57.7	69.0
	≥2	71.8	72.6	46.6	75.7
	≥3	62.7	80.6	36.0	83.1
	≥4	43.0	94.6	18.9	96.6
Akre et al.[169]	≥1	77.9	67.1	55.6	70.9
	≥2	70.2	75.3	44.2	78.4
	≥3	60.5	83.5	34.0	85.7
	≥4	42.9	94.2	19.1	96.1
Skaletzky et al.[170]	≥1	73.4	76.4	47.4	80.3
	≥2	63.4	86.9	31.1	89.5
	≥3	52.3	91.9	22.0	93.8
	≥4	32.7	97.8	10.8	98.9
Duncan et al.[171]	≥1	96.4	18.6	90.5	20.1
	≥2	87.9	48.8	70.6	52.1
	≥3	78.2	72.7	50.5	76.5
	≥4	61.4	86.8	33.6	90.1
	≥5	46.2	93.8	22.0	96.2
Parshuram et al.[172]	≥1	97.3	18.2	90.6	19.7
	≥2	87.8	48.1	70.3	51.2
	≥3	78.3	72.3	50.7	76.1
	≥4	66.2	84.7	36.6	88.1
	≥5	56.0	90.6	28.6	93.6
Egdell et al.[167]	≥1	78.4	60.8	58.7	64.0
	≥2	68.1	74.6	43.4	77.4
	≥3	53.2	88.7	27.9	91.3
	≥4	41.2	93.9	18.9	95.8

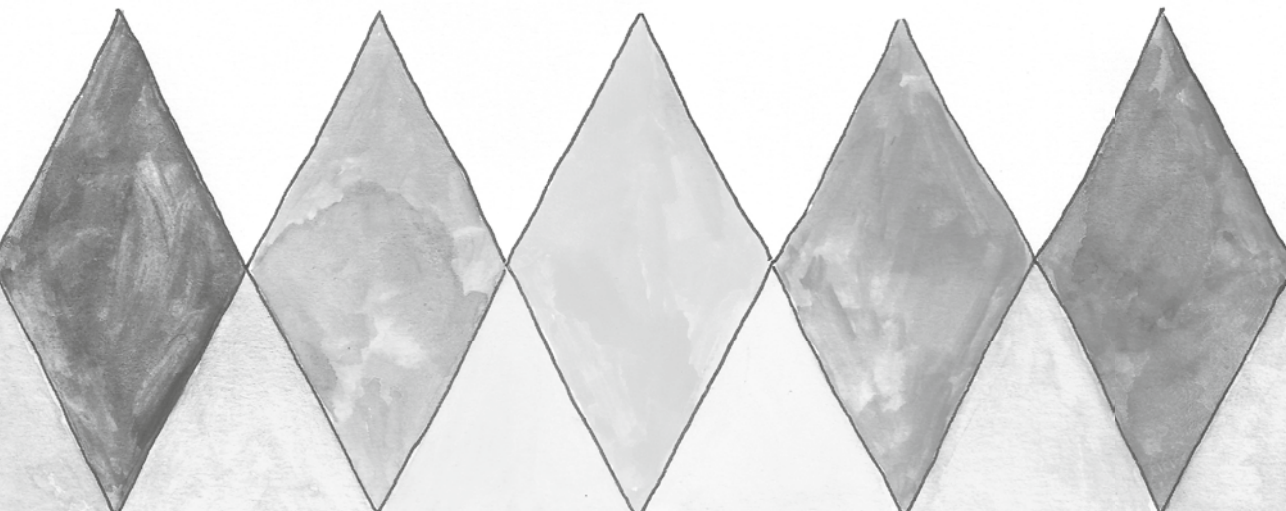


PART III





Discussion and Summary



CHAPTER 11

General discussion and future prospectives

Improvements of the Manchester triage system for paediatric patients

Emergency departments (EDs) throughout the world have to cope with increasing demands for care, changing populations, rising patient expectations, increasing financial pressure, and shortage of staff.[1] As an answer to some of these challenges, the Manchester Triage System (MTS) was introduced in the United Kingdom at the end of the twentieth century, to identify those who are at immediate risk and to prioritise patients who are clinically stable but seriously ill into the most appropriate order for treatment.[18]

However, the MTS was, like other triage systems, based on expert opinion and the evidence that it prioritises paediatric patients correctly was lacking. A study that evaluated the performance of the MTS, showed moderate validity with more overtriage than undertriage and concluded that there was room for improvement.[16]

Before conducting a study to improve the MTS, it was important to analyze if this moderate validity had severe consequences for individual patients and if adaptations were actually needed. In order to evaluate this, we focussed on patients with conditions that could have deteriorated in the waiting room and thus on patients that were severely undertriaged (Chapter 2). Since more than 50% of these patients could have expected clinical consequences of undertriage, we concluded that improvements were needed and that a promising intervention could be the introduction of vital signs measurements in the MTS (Chapter 2).

Vital signs can detect clinical deterioration of children in hospital and in emergency situations.[95] However, the way vital signs should be included in the MTS can be questioned. In Chapter 6, we defined abnormal vital signs by percentiles based on a systematic review[95] and had to conclude that the addition of abnormal vital signs reduce undertriage, but introduce overtriage in the total population. This overtriage is not unexpected, since we are aware that vital signs not only deviate if patients are critically ill, but are also influenced by high temperature[161, 162], and pain (Chapter 9). On the other hand, a combination of vital signs as provided in Paediatric Early Warning Scores (PEWS) were suitable to detect the critically ill at the ED (Chapter 10) and therefore future research may focus on the addition of a combination of vital signs to the MTS.

Another way to improve the MTS were specific adaptations for febrile children.[16] In the original MTS, all febrile children are assigned to a clinical priority with a maximum waiting time of ten minutes by a physician, while most acute febrile illness are caused by self-limiting viral infections, which do not require any treatment. Overtriage by the MTS is therefore very common in febrile children.[16] Since fever accounts for about 10% to 30% of all presenting complaints by children[16, 56], small adaptations have a major impact on the validity of the MTS.[33]

For this reason, age specific modifications for febrile children older than three months[33] needed broad validation in other European settings (Chapter 6). Moreover, literature suggested that referral by general practitioner[47] and the presence of chronic illness[83, 84 85] were associated with a more severe course of a febrile illness. Although this thesis confirmed these associations (Chapter 4 and 5), this we could not translate this into modifications of the MTS.

Referral status was not a characteristic that could be used to improve the MTS. Febrile children who attended the ED on their own initiative were less severely ill than those referred by a general practitioner, but still one in four self-referrals needed extensive diagnostic interventions, intravenous medication, nebulizers, or were hospitalised (Chapter 4). Since this is a considerable number of patients, we believe that self-referred children must not be considered as comparable and approached as a uniform group of non severely ill patients.

Therefore, we feel that down-triaging patients based on their referral status alone, might lead to an increase of severe undertriage. This conclusion was in contrast to the study of Rinderknecht et al., which showed a much larger difference between the severity of illness of self-referred children and children referred by their general practitioner (in their quaternary, international referral centre) and therefore recommended to add referral status to triage algorithms.[47]

The study in febrile children with a chronic illness provided no specific modifications due to limited information of general and clinical characteristics of patients with a chronic illness. The febrile children with chronic illness showed a large heterogeneity, and therefore it was infeasible to propose specific modifications (Chapter 5). For this reason, it would be interesting to search for modifications for these children in a larger study in different settings with more patients characteristics to identify those patients with chronic illnesses at risk of undertriage.

Age specific modifications for febrile children older than three months were previously (developed and) validated in two EDs in the Netherlands[33] and improved the performance of the MTS. In this thesis, the modifications were broadly validated in four EDs in three different European countries and showed again improvement of the validity of the MTS (Chapter 6). We investigated if the validity of the MTS could be further improved by using the same technique as in previous studies: moving current MTS discriminators to a higher or lower triage category whether or not in combination with patients characteristics like age and sex. Because the earlier study using this technique was limited by the number of patients to detect substantial misclassification[33], machine learning techniques were applied to frequent used flowcharts of the MTS to overcome this problem of limited data (Chapter 7). Moreover, learning techniques were not only used to search for combinations of discriminators, but also if the flowchart based structure of the MTS was the most optimal model to triage patients. Although this search did not provide modifications to improve triage at the ED, this study confirmed the need for new discriminators to identify patient's true urgency and thus to increase the validity of triage systems.

Methodological challenges of observational cohort studies to validate triage systems

Outcome measures to validate triage systems

Based on:

- How to evaluate a triage system in emergency care? A systematic review on outcome measures by M. van Veen, N. Seiger, J.M. Zachariasse, K. Mackway-Jones, H.A. Moll [Submitted]
- Triage systems: Outcome measures to validate by N. Seiger, H.A. Moll, a letter published in Ann Emerg Med. 13Mar;61(3):372-3.

Triage systems are usually based on literature, guidelines and expert opinion and evaluated for reliability and validity after application in practice.[13] Reliability of the system refers to the system's reproducibility; when triaging the same patient, the triage system should give the same triage result, independent of the person performing triage. Validity determines if a test or system measures what it aims to measure and compares test results to a gold standard. At this moment, there is no single outcome measure that is found reliable and accurate as a prognostic measure of urgency for the various conditions treated at the ED and thus a gold standard for triage systems does not exists.

However, since it is important to evaluate triage systems, we need an outcome measure as the

best proxy for true urgency. Therefore we will use the term 'silver standard' instead of 'gold standard'. A silver standard is needed to compare triage systems, to compare performance of a system in different settings and to define options for improvement. The optimal 'silver standard' depends on the evaluated ED population as well. For example, in settings with a low prevalence of serious illness and high quality of health care, mortality does not appear to be a good outcome measure while follow-up or resource use might be more appropriate.[10]
To date no consensus exists on which outcome measure should be used to evaluate a triage system. Hence, we decided to investigate which outcome measures have been used in the past and to assess the quality of those standards.
We conducted a systematic review on the outcome measures used to evaluate a triage system at the ED. In this review, we identified 4260 papers of which 92 studies remained after evaluation of title and abstracts. Evaluation of the full text paper excluded another 43 papers, leaving 48 studies to include; 14 studies focused on children while 34 focused on adults.
In table 1, all outcome measures used to evaluate a triage system can be seen. The most commonly used outcome measure in children as well as in adults was hospitalisation. (children; 11 studies, 79%, adults; 24 studies, 71%).

TABLE 1: outcome measures used to evaluate a triage system

OUTCOME MEASURES	NUMBER OF PAPERS	PERCENTAGE
Adults	**34**	100%
Hospitalisation	24	71%
Resource use	16	47%
Length of stay	10	29%
Expert opinion	7	21%
Death	8	23%
Costs	2	6%
Immediate lifesaving intervention	2	6%
One year survival	1	3%
Vital signs	1	3%
Children	**14**	100%
Hospitalisation	11	79%
Length of stay	6	43%
Resource use	6	43%
Reference standard (combination of measures)	3	21%
Costs	3	21%
IC hospitalization	2	14%
Return visit for admission	1	7%
Need for significant hospital treatment	1	7%
PRISA score	1	7%
Left without being seen	1	7%

Although hospitalisation was the most frequently used outcome measure, this did not mean that the quality of this outcome measure was the best. In order to investigate the quality of outcome measures, it was decided that an outcome measure should at least be independent of triage; should reflect severity of illness of patients; and should be applicable to individual patients presenting with a wide range of problems.[10] These criteria were combined with general items used in a well-known checklist on how to evaluate diagnostic studies, the Standards for Reporting of Diagnostic Accuracy (STARD).[10, 40, 102, 186, 187]

This resulted in a checklist for quality containing the following items:

1. Is the outcome measure collected independently of (blinded to) the triage urgency level?
   Yes: 1 point No: 0 points [186]
2. What is the time period between the triage assessment and outcome measure?
   <12 hrs: 1 point, > 12 hrs: 0 points [10, 40, 187]
3. Does the outcome measure differentiate between urgency levels (3-5 levels)?
   Yes: 1 point, No: 0 points [40]
4. Is the triage system evaluated as a diagnostic test? (Using standards to evaluated diagnostic value?)
   Yes 1 point, No: 0 points [186]
5. Does the outcome measure depend on the setting?
   Yes: 0 points, No: 1 point [40, 102]

Although hospitalisation was independent of triage, correlated with patients' severity of illness, and showed a clear association between urgency level (Figure 1), the mean quality score of this outcome measure was low. (mean 1.6, 95% CI 1-1.3 for children and mean 2.0, 95% CI 1.5-2.5 for adults). Hospitalisation cannot discriminate patients into five reference urgency categories that are needed to modify the triage system[188] and it is not clear what the cut-off level of the correlation should be, to conclude that the system is valid. Moreover, there were some large differences between studies and triage systems, which were also reported in other reviews on triage systems.[102] Since the proportion of hospitalization might be dependent on the setting, it is difficult to compare different validity studies on hospitalization. Therefore, hospitalisation as outcome measure is in our opinion only suited to detect associations (trends) between urgency levels and to compare two different triage systems. The same arguments can be applied to the second most used outcome measure 'resource use' of which the quality score did not differ from that of hospitalisation.

Other commonly used outcome measures such as length of stay and number of patients left without being seen by a physician showed even lower quality scores, because these markers have an interdependency with the triage category, i.e. the period in which patients should be treated, and therefore are not suited to validate a triage system. Pacella and Yealy[188] suggested using time stamps of numerous moments of interventions, but these markers face the same problem.

Using our quality score, the highest ranked outcome measures were an independent multi-level reference standard for urgency (mean score 4.0, 95% CI 4.0-4.0), immediate lifesaving interventions (mean score 3.5, 95% CI 2.8-10), and expert opinion (mean score 3.3, 95% CI 2.6-4).

The multi-level reference standard for urgency was only applied in studies focusing on children and combines different prognostic markers (abnormal vital signs), disease severity (admission, conditions in need of early treatment), and case complexity (resource use) and provides a definition for all five urgency levels.[15, 16, 33] The vital signs and potential life threatening condition are objective measures, although the cut-off levels are subject to expert opinion. Vital signs are measured at the same time as the triage assessment. Therefore, other factors influencing the outcome measure besides the triage assessment are less likely to be of influence.

Vital signs are used in some triage systems to assess the urgency level. In that case, vital signs cannot be used as outcome measures. Van der Wulp et al. showed an association between vital

signs and ESI urgency levels. However, an important limitation of this study was that the decision to measure vital signs was dependent on the triage assessment.[187] Hospitalization and resource use are more dependent on the study's setting, secondly they are measured later in time, which makes them less closely related to the triage urgency level.

Immediate lifesaving intervention are used to identify high urgent patients. [189, 190] and are defined as 1) Airway and breathing support, including intubation or emergent non-invasive positive pressure ventilation; 2) Electrical therapy, including defibrillation, emergent cardioversion, or external pacing; 3) Procedures, including chest needle decompression, pericardiocentesis, or open thoracotomy; 4) Hemodynamic support, including significant intravenous fluid resuscitation in the setting of hypotension, blood administration, or control of major bleeding; or 5) Emergency medications, including Naloxone, Dextrose, Atropine, Adenosine, Epinephrine, or Vasopressors. The collected items are objective and less setting dependent than hospitalization or resource use. However, disadvantages are that this outcome measure was only used in studies performed in elderly [189, 190], that the measure does not define the low urgent categories, and that the items are defined by a clinician, while patients may rate other items such as severe pain higher than the conditions mentioned above.

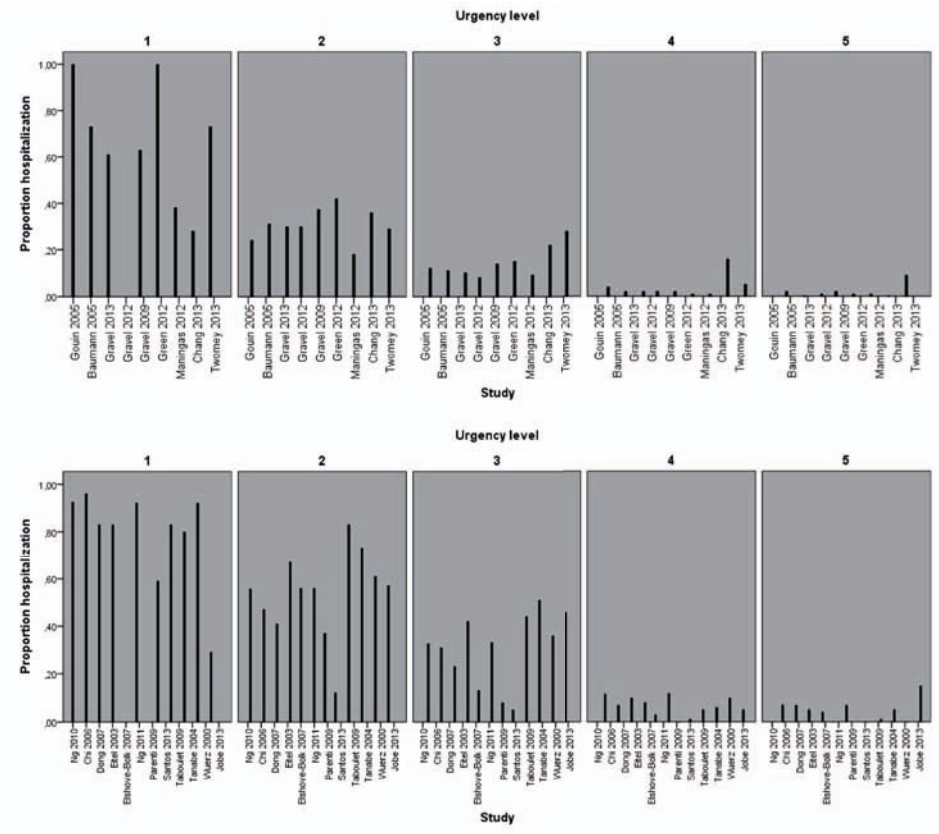


FIGURE 1: Proportion of hospitalisation per triage category per study
The upper figure represents studies conducted in children and the lower figure studies conducted in adult patients

Lastly, expert opinion uses a group of experts who evaluate written triage scenarios, leading to a 'correct urgency level'. Their concluded urgency level can make a distinction between different urgency levels. The experts' judgement will be influenced by the setting from which the expert comes. For example, if an expert works in a low prevalence setting, he will find it easier to categorise patients as low urgent. Secondly it is impractical to use this method for a large sample.
In conclusion, many different outcome measures have been used to compare, evaluate or improve triage systems. However, the most frequently used outcome measures are not always the ones with the highest quality. For this reason, we searched for an objective, non-setting dependent outcome measure that is applicable to patients presenting with a variety of problems, and is able to discriminate patients into five urgency categories.[16, 162] In our opinion, the multi-level reference standard for urgency, immediate lifesaving interventions, expert opinion, or a combination of those are the best options for a 'silver' standard to evaluate validity of triage systems.

Strength and limitations
In this thesis, we used large and detailed patient data from different EDs in different European countries and different time periods. This increases the generalisability of our results. Furthermore, these large databases had sufficient power to investigate options for improvement of the MTS for specific patient groups like neonates or patients with a chronic illness.
Despite these strengths because of the large database, some limitations need to be discussed. The first problem was that the different settings used their own translated version of the MTS. Therefore, flowcharts and discriminators used in the MTS in different settings might be interpreted in different ways and could have influenced our study results.
Further, it was not possible to implement all required variables into the patient record system or it was too time consuming for nurses and physicians to collect them. For this reason, it was not possible to address specific issues like referral status, children with chronic illnesses, or PEWS in an international multicentre study.
Especially our conclusions for children with a chronic illness, could have been influenced by the fact that the Sophia Children's Hospital is a tertiary hospital with high numbers of children with a chronic illness. Moreover, it is likely that children with a chronic illness who visit the ED of a general hospital face different problems than those presenting to the ED of a tertiary hospital. The results of this study are applicable to Western tertiary hospitals but probably not to general hospitals.
We left the measurement of vital signs to the discretion of the triage nurse, the 'real world' setting. This resulted in missing values of vital signs. In this thesis, we handled missing of vital sign values in two different ways. In studies in which vital sign values were used as part of the reference standard (Chapter 3, 5, and 7) we considered unmeasured vital sign values as normal and in studies in which vital signs were predictors of urgency or severity of illness (Chapter 6, 9 and 10) we used a multiple imputation model that replaces the missing value by a value that is drawn from an estimate of the distribution of the variable.[97, 106]
This difference in approach is caused by the way the vital sign value were used. If vital sign values were used to identify patients for the 'immediate' reference category, only extremely deviated vital signs were considered, since the cut-off levels chosen were according to the third version of the paediatric risk of mortality score (PRISM III), a score that identifies patients at risk for mortality at the intensive care unit.[16, 26] It is not likely that nurses would

not measure those values in such critically ill patients, because literature shows that there is a strong correlation between triage nurse measurement of vital signs and the severity of the presenting illness. Therefore missing values could be considered as normal. If the vital sign values were used as predictor of urgency or severity of illness, we needed an estimate of specific vital sign values in order to reduce bias. In that case, a valid method to deal with missing at random on x (vital signs) and y (outcome),[104, 105] is the use of a multiple imputation model.

Future prospective

In Europe, a wide variation of child health care exists due to complex interactions of cultural, social, economic factors resulting in different health care policies and risk exposures.[191, 192] Thus a wide variation of children presenting to European EDs exists.[192] As a consequence, healthcare factors and availability, patient characteristics, urgency of presenting problems, disease severity, and disease prevalence differ between countries. These differences were shown when patient characteristics from our multicentre studies were compared (Chapter 3, 6 and 9).

From studies on diagnostic tests and decision rules, it is known that performance expressed by sensitivity and specificity is influenced by the prevalence of outcome (e.g. disease) and predictors. Since triage systems are evaluated in the same way[10], it is likely that the performance of triage systems vary per country or ED setting due to health care differences. At this moment, commonly used triage systems such as the MTS are uniform and are not adapted to local setting in which they are used. For this reason, there is a tendency for countries to develop their own mostly consensus based triage system.[67, 181, 193] However, the development of new triage systems is very time consuming and requires a lot of research before its reliability and validity are demonstrated. We recommend the use of a uniform and well validated triage system in all European countries.

Moreover, other advantages of a uniform triage system are that: 1) it is much easier to provide a large dataset, which is necessary to gain sufficient power to study less frequently used flowcharts and discriminators with high percentages of misclassification; 2) it is possible to compare the validity of triage systems in different countries and compare indirectly the influences of health care system on patient's urgency, which might help policy makers to improve child health; 3) different settings collect different general and clinical characteristics of patients, which increases diversity of the data. This might improve the search for new discriminators in order to improve triage.

All these advantages can improve future research to triage systems and finally leading to better paediatric emergency care. Therefore we intend to conduct a multicentre prospective observational study in different European countries in which we will compare the validity of the MTS in different health care settings and in which we will search for new discriminators (e.g. a combination of vital signs) that predict urgency in children with or without a chronic illness.

Conclusions

We addressed options for improvement of the MTS for specific patients groups. It confirmed that the MTS could be improved by age specific modifications for children with fever, and suggested that there was room for improvement for children with a chronic illnesses.

In order to further improve triage at the ED, we recommend to conduct large international studies that will focus on new discriminators like health care characteristics, children with

chronic illnesses and a combination of vital signs. In those studies, it is important that we use a predefined 'silver' standard as outcome measure for patient's 'true' urgency as outcome measure, which in our opinion is a standard that combines prognostic markers (abnormal vital signs or immediate life-saving interventions), disease severity (admission, conditions in need of early treatment), and case complexity (resource use) and provides a definition for five urgency levels.

CHAPTER 12

English summary/ Nederlandse samenvatting

ENGLISH SUMMARY

The general aim of this thesis was to improve triage for paediatric patients visiting the emergency department (ED) (**Chapter 1**). The first part of this thesis described modifications of the Manchester Triage System (MTS) for paediatric emergency care. The MTS is the most commonly used triage system used in European EDs and was used to classify paediatric and adult patients.[7] Previous studies have shown that the reliability of MTS was moderate to good.[12-14] The validity of the MTS for paediatric emergency care was moderate and showed room for improvements.[16]

Before conducting a study aimed to improve the MTS, it was important to analyze if the moderate validity has severe consequences for individual patients and if adaptations were actually needed. In order to evaluate this, we studied patients with conditions that could have deteriorated in the waiting room and thus on patients that were severely undertriaged. In **chapter 2**, we conducted a case study in which the consequences of severe undertriage were evaluated by three paediatricians experienced in triage and emergency care and we searched for determinants to predict severe undertriage in the total population. Among the 17600 patients who visited the ED, 119 (0.9%) patients were severely undertriaged by the MTS. This misclassification by the MTS was mainly caused by the absence discriminators requiring the measurement of vital signs in the MTS and in half the patients it could have led to severe consequences. Determinants for severe undertriage obtained from a multivariate logistic regression analysis were allocation to the flowchart 'Unwell child' (OR 11.1, 95% CI 5.5 to 22.3) and children younger than 3 months (OR 4.2, 95% CI 2.3 to 7.7). These results suggested that systematic assessment of vital signs for these selected groups of children could prevent severe undertriage. However, only systematic assessment of the vital signs in all children could prevent clinically severe undertriage in children.

Since our study on severe undertriage suggested that very young children were more frequently undertriaged than older children, we conducted a study on triage of neonates, defined as children younger than 1 month, in **chapter 3**. In this multicentre observational study, we explored if a neonatal flowchart was needed to improve the MTS for young children. The need for a neonatal flowchart was based on three criteria: 1) a substantial number of neonates; 2) the flowcharts and discriminators available in the MTS were insufficient to allocate a triage category; and 3) the validity of the MTS in neonates was lower compared with older children. From the nearly 70000 children under the age of sixteen years, who presented to one of the four European EDs, 2.7% were neonates and these neonates were more frequently allocated to general flowcharts than older children (RR 2.6, 95%CI 2.5-2.7). To assess the validity of the MTS, a predefined reference standard and hospitalisation were used as outcome measures. Both outcome measures showed that the positive likelihood ratio of high urgency in neonates was significant higher than the positive likelihood ratio in older children, while the negative likelihood ratio and the DOR did not differ. Therefore, we concluded that despite a substantial number of neonates visiting the ED and nurses who had difficulties to triage neonates, there was no need to develop a neonatal flowchart because the validity of the MTS in neonates was acceptable.

Other suggestions for improvement of the MTS were specific for children with infectious symptoms. In **chapter 4**, the severity of illness of 2835 febrile children referred by their parents (self-referrals) and 1774 febrile children referred by their general practitioner were

compared to evaluate if self-referral could be used to downtriage these patients since half of these patients were classified as 'immediate' or 'very urgent' by the original MTS. Markers for severity of illness were extensive diagnostic tests (i.e. extensive laboratory tests or radiological examination), extensive therapeutic interventions (i.e. intravenous fluids or medication, or nebulizers), and hospitalisation. These markers were more frequently observed among patients referred by general practitioner than self-referrals. Taken together, 43% of children referred by their general practitioner needed extensive diagnostic tests or therapeutic interventions, hospitalization or a combination of these against 27% of self-referred children (OR 2.0, 95% CI 1.75-2.27). Although febrile children referred by general practitioner were more severely ill than self-referred, we concluded that a considerable number of parents properly acted on their child's severity of illness by presenting their child to the ED on their own initiative.

In **chapter 5**, the performance of the MTS was compared between children with chronic illnesses and previously healthy children, who presented the ED with infectious symptoms defined as fever, shortness of breath, or diarrhoea and/or vomiting (N=8592). Chronic illnesses represented conditions that can be 'reasonably expected to last at least 12 months (unless death intervenes) and to involve either several different organ systems or 1 organ system severely enough to require specialty paediatric medical care' and were coded according to a widely used list of diagnostic codes for congenital and chronic acquired disorders. The performance of the MTS, evaluated by a reference standard based on abnormal vital, resource use, hospitalisation, and follow-up, was lower among those with a chronic illness than in those without a chronic illness ($DOR_{\text{children with a chronic illness}}$ 4.8, 95%CI 3.9-5.9 versus $DOR_{\text{previously healthy children}}$ 8.7, 95%CI 7.1-11,1 respectively). Moreover, children with a chronic illness were at higher risk to be undertriaged. The subgroup analyses revealed that the DOR of children with a cardiovascular illness (DOR 3.8, 95%CI 2.2-6.5) a respiratory illness (DOR 2.5, 95% CI 1.2-5.5), a gastrointestinal illness (DOR 2.6, 95% CI 1.3-4.9), or another congenital or genetic defect (DOR 3.3, 95%CI 2.0-5.4) was significantly lower than those of previously healthy children. Despite the identification of these subgroups, it was not feasible to propose specific modifications for children with a chronic illness due to heterogeneity of the underlying conditions. For this reason, we concluded that the MTS performs suboptimal in children with a chronic illness and that triage nurses have to take into account patient's chronic illness and if necessary use their experience to overrule the MTS.

Chapter 6 described an international external validation study of modifications which showed improvement of the MTS in earlier studies in the Netherlands. The first set of modifications (MTS version 1) tested were age-specific modifications of discriminators for infectious problems e.g. 'hot child' and 'persistent vomiting' with high percentages of misclassification and the second set of modifications (MTS version 2) were the addition of vital signs heart rate, respiratory rate and oxygen saturation to the MTS. The modifications were simulated by retrospectively applying the MTS versions 1 and 2 to more than 60000 children who were triaged with the original MTS at one of the four European EDs. Hospitalisation was used as outcome measure to observe the effect of the modifications in the total population. This resulted in improvements by MTS version 1 as the DOR improved from 4.8 (95%CI 4.6-5.1) to 6.2 (95%CI 5.9-6.6), but not in improvements by MTS version 2. The modifications suggested in MTS version 1 showed improvement of the MTS performance in internal and

external validation studies. These modifications should be implemented in the following edition of the MTS.

The validity of the MTS could be improved by moving certain discriminators to a higher or lower triage category. For this reason, in **chapter 7**, machine learning approaches were used to explore if triage could be improved for children allocated to the MTS flowcharts 'shortness of breath', 'worried parent' or 'fits' by remodelling MTS discriminators, by combining the current MTS discriminators, or by adding patients characteristics like age and sex. Machine learning approaches used were CART, RIPPER, OPUS and EXPLORE. Again, the independent reference standard was used for patients' 'true urgency' and to calculate sensitivity, specificity, and DORs. The algorithms CART and RIPPER did not significantly improve the discriminative ability of the MTS. The area under the receiver operating curves (AUC) of the original MTS flowchart 'Shortness of breath', 'worried parent' and 'fits' ranged from 0.58 to 0.60. When CART was used the AUCs were between 0.50 and 0.58 and when RIPPER was used between 0.50 and 0.53. Moreover, in all three flowcharts CART and RIPPER decreased the sensitivity and increased the specificity. The OPUS and EXPLORE algorithms were used to search for combinations of low urgency discriminators that could predict high urgency and vice versa. OPUS found four association rules for the flowchart 'Shortness of breath' that could possibly improve the MTS. However, the addition of these rules to the MTS reclassifies only 0.4% (N=144) of the total population. In conclusion, the machine learning algorithms CART, RIPPER, OPUS and EXPLORE showed no improvement of the MTS. For this reason, future studies should focus on new discriminators that can predict 'urgency', because the current MTS discriminators in combination with patients characteristics are not sufficient to improve the MTS.

The second part of this thesis focused on specific tools to assess patient's severity of illness at the ED. In **chapter 8** we studied whether we could use discriminators of the MTS as indicators of alarming signs rather than urgency classification alone, to predict hospitalisation at the moment of presentation at the ED. For this observational cohort study, we included 2455 children with fever who were all triaged with a computerized version of the MTS, in which the most appropriate flowchart and all applicable discriminators could be documented. In total, 14 discriminators or flowcharts represented alarming signs of serious infection. Since the MTS flowchart chosen influenced the maximum number of alarming signs that could be selected, the percentages of alarming signs positive were calculated for each individual patient. In the total population, 563 patients had to be hospitalized. The positive likelihood ratio of hospitalization were 5.0 (95% CI 3.9-6.5) for children with more than 20% of alarming signs positive at triage and 12.0 (95% CI 5.2-27.6) for children with more than 40% of the alarming signs positive at triage. The negative likelihood ratios were close to 1 indicating that low percentages or absence of alarming signs could not be used to predict discharge. Therefore it can be concluded that using the content of the MTS differently, the MTS can be a readily available tool to predict hospitalization at the ED.

Vital signs measurement play an important role in the assessment of patient's severity of illness. However, vital signs do not only deviate if patients are critically ill, but can also be influenced by other factors like pain. Therefore **Chapter 9** determined the relationship between the vital signs 'heart rates' and 'respiratory rates' and pain. For this multicentre prospective observational study, we included more than 85000 children younger than 16

years who attended the ED. Manchester pain scores and vital sign values were recorded at triage assessment. Univariable and multivariable linear regression analysis conducted to assess the relationship between the vital signs and Manchester pain scores, showed that pain affected heart rate and respiratory rates in a complex, non-linear way. Both heart rates and respiratory rates decreased when children had mild to moderate pain according to the Manchester pain scale, while they increased in children with severe pain. This association disappeared, when children were older than five years of age. Finally, we developed pain score appropriate centile charts (2.5th, 10th, 25th, 50th, 75th, 90th, and 97.5th) of heart rates and respiratory rates for different age groups by using Generalized Additive Models for Location, Scale, and Shape (GAMLSS) in order to improve the interpretation of vital signs at triage and had to conclude that especially in younger children, heart rates increased when patients had severe pain.

Another way to assess severity of illness by vital signs is the use of Paediatric Early Warning Scores (PEWS), which are physiology-based scoring systems based on a combination of several vital signs to identify patients at risk of clinical deterioration. Since different PEWS for both ED and in-hospital settings were developed, we compared in **chapter 10** the performance of ten different PEWS, which could be divided into six scoring systems and four triggering systems. A scoring system sums scores of different parameters to one numeric value, which determines patient's risk for clinical deterioration. A triggering system considers a patient at risk if one of the parameters is positive. The performance of the different PEWS was assessed by discriminative ability of the PEWS to predict intensive care admission or hospitalization in nearly 18000 children visiting a paediatric ED. In total, two percent (N=373) were admitted to an intensive care unit or died at the ED and 16% of patients (N=2,828) were admitted to hospital. The discriminative ability of the PEWS, expressed by area under the receiver operator curve, were moderate to good for intensive care admission (range 0.60-0.82) and poor to moderate for admission to hospital (range 0.56-0.68). Scoring systems performed better than triggering systems, although none of the cut-off levels showed both a high sensitivity and high specificity.

Finally, this thesis ends with a general discussion described in **chapter 11.** Several options to improve triage at the ED are summarized and discussed. Methodological issues and gaps on how to evaluate a triage system are highlighted in a systematic review on the use and quality of different reference standards, resulting in recommendations and requirements for such standard.
The last part of the general discussion is dedicated to future studies that should focus on international collaborating networks for prospective data collection including new discriminators (patient or setting related) in order to improve current triage methods and improve paediatric emergency care.

NEDERLANDSE SAMENVATTING

De doelstelling van dit proefschrift was het verbeteren van triage voor kinderen op de spoedeisende hulp (SEH) (**Hoofdstuk 1**). Het eerste gedeelte van dit proefschrift beschreef aanpassingen van het Manchester Triage Systeem voor kinderen. Het MTS is het meest gebruikte triage systeem op SEH's in Europa en wordt gebruikt om zowel volwassenen als kinderen te triëren.[7] Eerdere studies hebben aangetoond, dat de betrouwbaarheid van het MTS matig tot goed was.[12-14] en de validiteit matig, wat aanleiding gaf het MTS verder te verbeteren.[16]

Voordat wij een onderzoek naar aanpassingen van het MTS konden verrichten, was het noodzakelijk om in kaart te brengen of misclassificatie door het MTS consequenties heeft voor individuele patiënten en dus of aanpassingen aan het systeem wel noodzakelijk waren. Om dit te evalueren, moesten wij ons richten op patiënten met aandoeningen die konden verslechteren in de wachtkamer. Dit waren dus de ernstig ondergetrieerde patiënten. In **hoofdstuk 2**, hebben drie kinderartsen gespecialiseerd in triage en spoedeisende zorg casus van patiënten bestudeerd en de consequenties van ernstige ondertriage ingeschat. Daarnaast werd er gezocht naar factoren in de gehele populatie die de kans op ernstige ondertriage verhoogden. Van de 17600 kinderen die de SEH bezochten, waren er 119 (0.9%) ernstig ondergetrieerd, waarvan ongeveer de helft ernstige consequenties kon ondervinden. De onderschatting van de ernst werd met name veroorzaakt doordat er in het MTS geen discriminatoren zijn opgenomen voor het meten van vitale kenmerken. Andere factoren, verkregen uit een multivariate logistische regressie analyse, die de kans op ondertriage verhoogden waren kinderen toegewezen aan het stroomdiagram 'Onwel geworden kind' (OR 11.1, 95% CI 5.5-22.3) en kinderen jonger dan 3 maanden (OR 4.2, 95% CI 2.3 to 7.7). Deze resultaten suggereerden dat het routinematig meten van vitale kenmerken voor deze patiëntengroepen ernstige ondertriage kon doen verminderen. Echter, alleen het routinematig meten van vitale kenmerken in alle kinderen kon gevallen van ernstig ondertriage voorkomen.

Aangezien het onderzoek naar ernstige ondertriage suggereerde dat de urgentie van jonge kinderen vaker werd onderschat, hebben wij in **hoofdstuk 3** een onderzoek uitgevoerd naar het triëren van neonaten (kinderen jonger dan 1 maand). In dit observationele onderzoek op verschillende SEH's, hebben we de noodzaak voor een stroomdiagram voor neonaten onderzocht. De behoefte hieraan was gebaseerd op drie criteria. Allereerst moest het aantal neonaten substantieel zijn, daarnaast moesten de huidige stroomdiagrammen en discriminatoren beschikbaar in het MTS niet toereikend zijn om deze patiënten te triëren en als laatste moest de validiteit van het MTS voor neonaten lager zijn dan de validiteit van het MTS voor oudere kinderen. Van de bijna 70000 kinderen onder de 16 jaar, die een van de vier Europese SEH's bezochten, was 2.7% jonger dan één maand. Deze neonaten werden tevens vaker toegewezen aan een algemeen stroomdiagram dan oudere kinderen (RR 2.6, 95%CI 2.5-2.7). Voor het bepalen van de validiteit werd MTS vergeleken met een vooraf gedefinieerde referentiestandaard en ziekenhuisopname. Beide uitkomstmaten lieten een hogere positieve likelihood ratio voor hoge urgentie zien bij neonaten. Er werd geen verschil gevonden in negatieve likelihood ratios en diagnostische odds ratios. Om deze reden moesten we concluderen dat ondanks dat een substantieel aantal neonaten zich op de SEH presenteren en verpleegkundigen vaak moeilijkheden ondervinden om neonaten te triëren, er geen noodzaak was een nieuw stroomdiagram voor neonaten op de SEH te creëren.

Andere mogelijkheden voor het verbeteren van het MTS waren specifiek voor kinderen die de SEH bezochten met infectieuze symptomen. In **hoofdstuk 4** werd de ziekte-ernst van 2855 kinderen met koorts verwezen door hun ouders (zelfverwijzers) en van 1774 kinderen met koorts verwezen door hun huisarts vergeleken. Dit om te onderzoeken of zelfverwijzers toegewezen konden worden aan een lagere urgentiecategorie, aangezien de helft van de kinderen met koorts wordt toegewezen aan de urgentiecategorieën 'Acuut' en 'Zeer urgent' door het originele MTS. Indicatoren voor ziekte-ernst waren uitgebreide diagnostische testen zoals uitgebreid laboratorium onderzoek of radiologisch onderzoek, uitgebreide therapeutische interventies zoals intraveneuze toediening van vocht of medicatie of een aerosolbehandeling, of opname. Deze indicatoren werden vaker geobserveerd in patiënten die door een huisarts werden verwezen: bij 43% van de door de huisarts verwezen kinderen was een of meer van deze indicatoren aanwezig in vergelijking met 27% van de zelfverwijzers (OR 2.0, 95% CI 1.75-2.27). Ondanks dat kinderen met koorts verwezen door een huisarts zieker waren dan zelfverwijzers, concluderen we dat nog steeds een aanzienlijk aantal zelfverwijzers terecht de SEH bezoeken en dat ouders de ziekte-ernst van hun kind vaak goed inschatten.

In **hoofdstuk 5** werd de werking van het MTS vergeleken in kinderen met en zonder een chronische ziekte. Dit onderzoek werd verricht onder 8592 kinderen die de SEH bezochten met infectieuze symptomen zoals koorts, benauwdheid of braken en/of diarree. Chronische ziekten werden gedefinieerd als aandoeningen waarvan verwacht kan worden dat ze tenminste 12 maanden aanhouden tenzij de conditie tot de dood leidt en dat de aandoening meerdere orgaansystemen betreft of één enkel orgaan systeem maar dan wel zodanig ernstig dat specialistische zorg vereist is. Deze chronische ziekten werden gecodeerd volgens een algemene lijst voor congenitale en verworven ziekten. De werking van het MTS werd vergeleken met een referentiestandaard gebaseerd op afwijkende vitale kenmerken, verrichte diagnostiek en therapie, opname en follow-up. Het MTS bleek kinderen met een chronische ziekte minder goed te triëren dan voormalig gezonde kinderen ($DOR_{\text{chronisch zieke kinderen}}$ 4.8, 95%CI 3.9-5.9 en $DOR_{\text{voormalig gezonde kinderen}}$ 8.7, 95%CI 7.1-11). Bovendien werd de urgentie van kinderen met een chronische ziekte vaker onderschat. Wanneer we verschillende subgroepen onderzochten, zagen we dat de DOR van kinderen met een cardiovasculaire aandoening (DOR 3.8, 95%CI 2.2-6.5), een respiratoire aandoening (DOR 2.5, 95% CI 1.2-5.5), een gastro-intestinale aandoening (DOR 2.6, 95% CI 1.3-4.9), of een congenitale dan wel genetische aandoening (DOR 3.3, 95%CI 2.0-5.4) significant lager was dan de DOR van voormalig gezonde kinderen. Ondanks dat het MTS minder goed was in het triëren van bepaalde subgroepen, was het niet mogelijk om aanpassingen van het MTS voor deze specifieke kinderen te genereren. Dit omdat de diversiteit binnen deze patiëntengroepen te groot bleek om de urgentie van deze kinderen te bepalen aan de hand van slechts enkele discriminatoren. Daarom moesten we concluderen dat het MTS suboptimaal presteerde voor kinderen met een chronische conditie en dat triage verpleegkundigen eventueel hun ervaring moeten gebruiken om de toegekende urgentie te overrulen in het geval van een chronische ziekte.

Hoofdstuk 6 beschreef een internationaal onderzoek naar de externe validiteit van aanpassingen aan het MTS die in eerdere onderzoeken verbetering van triage liet zien. De eerste reeks van aanpassingen (MTS versie 1) waren leeftijd specifieke aanpassingen aan discriminatoren van het MTS met een hoog percentage misclassificatie, die infectieuze

symptomen zoals 'koorts' en 'aanhoudend braken' beschrijven. De tweede reeks aanpassingen (MTS versie 2) betrof de toevoeging van de vitale kenmerken hartslag, ademhalingsfrequentie en zuurstofsaturatie aan het MTS. De aanpassingen werden voor dit onderzoek gesimuleerd door MTS versie 1 en 2 retrospectief toe te passen op een database waarin meer dan 60000 kinderen werden opgenomen die getrieerd werden met het originele MTS tijdens bezoek aan een van de vier Europese SEH's.
Opname werd gebruikt als uitkomstmaat om het effect van de aanpassingen te meten. MTS versie 1 zorgde voor een stijging van de DOR van 4.8 (95%CI 4.6- 5.1) naar 6.2 (95%CI 5.9-6.6) Echter MTS versie 2 zorgde niet voor verbeteringen. MTS versie 1 liet in interne en externe validatie studies verbeteringen zien. Deze aanpassingen moeten daarom opgenomen worden in een nieuwe versie van het MTS.

Het MTS kon mogelijk verbeterd worden door discriminatoren in combinatie met andere patiëntkarakteristieken zoals leeftijd te verplaatsen naar een hogere of lagere urgentiecategorie. Om deze reden, werd er in **hoofdstuk 7**, gekeken of triage verbeterd kon worden door het modelleren van stroomdiagrammen, het combineren van discriminatoren of het toevoegen van patiëntkarakteristieken. Dit werd gedaan door de machine learning algoritmen CART, RIPPER, OPUS en EXPLORE toe te passen op de stroomdiagrammen 'Kortademigheid', 'Bezorgde ouders' en 'Insult'. Wederom werd de onafhankelijke referentiestandaard als proxy voor de werkelijke urgente van patiënten gebruikt om de sensitiviteit, specificiteit en oppervlakte onder de receiver operator curve (AUC) te berekenen De algoritmes CART and RIPPER lieten geen verbeteringen van de stroomdiagrammen zien. De AUC's van de originele stroomdiagrammen varieerden tussen de 0.58 en 0.60. Door het gebruik van CART werden deze tussen de 0.50 en 0.58 en door het gebruik van RIPPER tussen de 0.50 en 0.53. Vervolgens werden de OPUS en EXPLORE algoritmen toegepast om combinaties van discriminatoren te zoeken die in het MTS leiden tot ondertriage of overtriage. OPUS vond 4 combinaties van discriminatoren die mogelijk het stroomdiagram 'Kortademigheid' kon verbeteren. Echter de toevoeging van deze combinaties aan het MTS zal slechts aan 0.4% (N=144) kinderen een hogere urgentie toekennen. Om deze reden concludeerden wij dat de machine learning algoritmes CART, RIPPER OPUS en EXPLORE het huidige MTS niet konden verbeteren en dat nieuwe studies zich moeten richten op nieuwe discriminatoren.

Het tweede gedeelte van dit proefschrift richtte zich op specifieke hulpmiddelen om ziekte-ernst van patiënten die de SEH bezoeken in te schatten. In **hoofdstuk 8** onderzochten we of discriminatoren in het MTS gebruikt konden worden als alarmsymptomen om opname te voorspellen. Voor dit observationele cohort onderzoek, includeerden we 2455 kinderen met koorts die allen getrieerd werden met een digitale versie van het MTS. Hierin werden het toegewezen stroomdiagram en de aan- of afwezigheid van alle discriminatoren in de betreffende stroomdiagram vastgelegd. In totaal vertegenwoordigden 14 discriminatoren en stroomdiagrammen alarmerende symptomen voor ernstige infecties. Aangezien het toegewezen stroomdiagram de maximale hoeveelheid te selecteren alarmerende symptomen beïnvloedt, werd voor iedere patiënt het percentage positieve alarmerende symptomen berekend. In totaal werden 563 patiënten opgenomen. De positieve likelihood ratio's voor opname was 5.0 (95% CI 3.9-6.5) voor kinderen met waarbij meer dan 20% van de alarmsymptomen aanwezig waren bij triage and 12.0 (95% CI 5.2-27.6) voor kinderen met waarbij meer dan 40% van de alarmsymptomen aanwezig waren bij triage. De negatieve likelihood ratio's lagen rond de 1, wat betekent dat lage percentages of afwezigheid van

alarmsymptomen de kans op opname niet uitsluit. Daarom kan geconcludeerd worden dat door het MTS op een andere manier te gebruiken, het als een nuttig instrument toegepast kan worden om opname te voorspellen bij binnenkomst op de SEH.

Vitale kenmerken spelen een cruciale rol bij het inschatten van de ziekte-ernst van de patiënt. Echter, vitale kenmerken zijn niet enkel afwijkend door ernstige ziekte maar worden ook beïnvloed door andere factoren zoals pijn. Daarom werd in **hoofdstuk 9** de relatie tussen de vitale kenmerken hartslag en ademhalingsfrequentie en pijn geobserveerd. Voor deze prospectieve observationele studie, uitgevoerd op meerdere SEH's, includeerden we meer dan 85000 kinderen jonger dan 16 jaar die de SEH bezochten. Op het moment van triage werden Manchester pijnscores en vitale kenmerken gemeten en geregistreerd. Univariable and multivariable lineaire regressie analyses werden verricht om de relatie tussen de vitale kenmerken en de pijnscores te bestuderen en lieten zien dat pijn de vitale kenmerken op een complexe, niet lineaire manier beïnvloedde. Zowel de hartslag als de ademhalingsfrequentie werden lager als een kind milde tot matige pijn ondervond, maar werden hoger zodra de pijn ernstig was. De relatie tussen pijn en vitale kenmerken verdween zodra kinderen ouder waren dan 5 jaar. Uiteindelijk, ontwikkelden we pijn en leeftijd specifieke referentiecurven met daarin de 2.5^{e}, 10^{e}, 25^{e}, 50^{e}, 75^{e}, 90^{e}, and 97.5^{e} percentielen voor de hartslag en ademhalingsfrequentie met behulp van Generalized Additive Models for Location, Scale, and Shape (GAMLSS) zodat de interpretatie van vitale kenmerken bij triage verbeterd kon worden.

Een andere manier om de ziekte-ernst te bepalen aan de hand van vitale kenmerken is door het gebruik van Paediatric Early Warning Scores (PEWS). Dit zijn systemen die fysiologische parameters, in de vorm van een combinatie van verscheidene vitale kenmerken, gebruiken om patiënten met het verhoogd risico op een verslechtering van de klinische conditie te detecteren. Aangezien er verscheidene PEWS voor zowel SEH patiënten als opgenomen patiënten zijn ontwikkeld, vergeleken we in **hoofdstuk 10** tien verschillende PEWS, waarbij een onderscheid werd gemaakt tussen zogenoemde numerieke en activerende systemen. Een numeriek systeem telt de scores toegekend aan verschillende parameters bij elkaar op tot een numerieke waarde, die het risico op verslechtering bepaalt. Bij een activerend systeem daarentegen, is het risico op verslechtering verhoogd indien één van de parameters positief wordt bevonden. De verschillende PEWS werden geëvalueerd door het discriminerend vermogen tussen wel en geen opname op de intensive care afdeling of een reguliere afdeling te voorspellen in een cohort bestaande uit bijna 18000 kinderen die de SEH bezochten. In totaal werd 2% (N=373) van de patiënten opgenomen op de intensive care afdeling of overleed op de SEH en werd 16% van de patiënten (N=2,828) opgenomen op een reguliere afdeling. Het discriminerend vermogen van de verschillende PEWS, uitgedrukt door de oppervlakte onder de receiver operator curve, was matig tot goed voor opname op de intensive care afdeling (namelijk tussen de 0.60-0.82) and slecht tot matig voor opname op een reguliere afdeling (namelijk tussen de 0.56-0.68). Het discriminerend vermogen van numerieke systemen bleek beter dan dat van activerende systemen. Echter geen van de afkappunten voor de numerieke systemen lieten zowel een hoge sensitiviteit als specificiteit zien.

Dit proefschrift werd afgesloten met een algemene discussie beschreven in **hoofdstuk 11**. De beschreven opties om triage op de SEH te verbeteren werden hierin samengevat

en bediscussieerd. Methodologische uitdagingen en beperkingen van onderzoek dat de werking van triage systemen evalueert, worden aangestipt in een systematische review over het gebruik en de kwaliteit van verschillende referentiestandaarden. Tevens werden er aanbevelingen gedaan en minimale vereisten gesteld voor een referentiestandaard voor toekomstig onderzoek. Het laatste deel van de algemene discussie werd gewijd aan het belang van een internationale samenwerking bij het opzetten van een groot prospectief observationeel onderzoek naar verbeteringen gericht op nieuwe (instelling- als patiënt specifieke) discriminatoren en dus naar verbetering van de spoedeisende zorg voor kinderen.

Appendices

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II LIST OF ABBREVIATIONS

ALTE	Apparently Life Threatening Event
ATS	Australasian Triage Scale
AUC	Area Under the receiver operator Curve
CART	Classification And Regression Tree
CI	Confidence Interval
DOR	Diagnostic Odds Ratio
ED	Emergency Department
ESI	Emergency Severity Index
EXPLORE	EXhaustive Procedure for Logic-Rule Extraction
GAMLSS	Generalized Additive Models for Location, Scale, and Shape
GP	General Practitioner
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
IQR	Interquartile Range
IV	Intravenous
MTS	Manchester Triage System
NA	Not Applicable
NNT	Number Needed to Treat
OPUS	Optimized Pruning for Unordered Search
OR	Odds Ratio
PedCTAS	Paediatric Canadian Triage and Acuity Scale
PEWS	Paediatric Early Warning Scores
PRISM	Paediatric RiSK of Mortality score
RIPPER	Repeated Incremental Pruning to Procedure Error Reduction
ROC	Receiver Operating Characteristic
SBC	Schwartz Bayesian Information Criteria
SD	Standard Deviation
SE	Standard Error
SPSS	Statistical Packages for Social Sciences

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IV ABOUT THE AUTHOR

Nienke Seiger was born on the 9th of July 1983 in Oldenzaal, the Netherlands. She passed secondary school (Gymnasium) at the 'Twents Carmel Lyceum' in Oldenzaal in 2001. In the same year she moved to Rotterdam where she started her medical training at the Erasmus University of Rotterdam. During her study she participated in several study and student-related associations. In her final year she participated in a research project to evaluate undertriage of children by the Manchester Triage System and she became interested in paediatrics and scientific research.

After obtaining her medical degree in 2010, she enrolled in the research project 'Improvement of paediatric triage at the emergency department' under supervision of Prof. dr. H.A. Moll at the department of general paediatrics of the Erasmus MC – Sophia Children's Hospital in Rotterdam. The general aim of this research project was to improve triage for paediatric emergency care. The project was performed in close collaboration with the departments of medical informatics (Prof. dr. J. van der Lei) and centre for medical decision making (Prof. dr. E.W. Steyerberg) of the Erasmus MC in Rotterdam, the paediatric department of Fernando Fonseca Hospital in Lisbon, the paediatric department of Haga Hospital – Juliana Children's Hospital in The Hague, and the paediatric accident and emergency department of St. Mary's Hospital in London.

During her PhD-period, Nienke obtained her Master of Science degree in Clinical Epidemiology at the Netherlands Institute for Health Sciences in Rotterdam (2011). In May 2013 she started as a resident in paediatrics (AGNIO) at the Maasstad Hospital in Rotterdam and in January 2014 she started her paediatric training at the Maasstad Hospital (Dr. M. Groeneweg) and the Erasmus MC– Sophia Children's Hospital in Rotterdam (Prof. Dr. M. de Hoog).

In her spare time, Nienke likes to sail, cook, read, play sports, and spend time with family and friends. She is married to Martijn Barmen 't Loo, who works as a process engineer at Kuwait Petroleum Europoort. Together with their daughter Pleun they live in Rotterdam.

V LIST OF PUBLICATIONS

1. **Seiger N,** van Veen M, Almeida H, Steyerberg EW, van Meurs AH, Carneiro R, Alves CF, Maconochie I, van der Lei J, Moll HA. Improving the Manchester Triage System for pediatric emergency care: an international multicentre study. PLoS One. 2014 Jan 15;9(1):e83267. doi: 10.1371/journal.pone.0083267.

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VII PHD PORTFOLIO

Erasmus MC Department: General Paediatrics
Research School: Netherlands Institute for Health Sciences (NIHES)
PhD period: July 2009 – September 2011
Promotor: Prof. dr. Henriëtte A. Moll

1. PHD TRAINING	YEAR	WORKLOAD (ECTS)
General academic skills		
Biomedical English writing and communication	2010	4.0
Workshop 'How to apply for grants'	2010	0.5
Good clinical practice	2012	1.0
Research skills		
Master of science clinical epidemiology	2009-2011	40.0
Core curriculum		
Classical methods for data-analysis	2009	5.7
Clinical epidemiology	2009	5.7
Study design	2010	4.3
Methodological topics in epidemiologic research	2010	1.4
Modern statistical methods	2010	1.4
In-depth courses		
Courses for the qualitative researcher	2010	1.4
Missing values in clinical research	2011	0.7
Advanced analysis of prognostic research	2011	0.9
Repeated measurements	2011	1.4
Bayesian statistics	2011	1.4
Summer programme		
Principles of research in medicine	2009	0.7
Methods of clinical research	2009	0.7
Introduction to decision-making medicine	2009	0.7
Clinical decision analysis	2009	0.7
Clinical trials	2009	0.7
Pharmaco-epidemiology	2009	0.7
Conceptual foundation of epidemiologic study design	2010	0.7
Case-control studies	2010	0.7
Markers and prognostic research	2010	0.7
Health economics	2010	0.7
Introduction to public health	2010	0.7
Primary and secondary prevention research	2010	0.7
Advances in epidemiologic study design	2010	0.4
Seminars and workshops		
Annual PhD-day Sophia Children's Hospital, Rotterdam	2009-2011	2.7
National study day 'More efficiency at emergency departments', Amsterdam	2010	0.4
Research Masterclass, 28th Annual meeting of the European society of paediatric infectious diseases, Nice, France	2010	0.9
Annual meeting of the Manchester Triage System international reference group, Manchester, United Kingdom	2010	0.9
Research Masterclass, 29th Annual meeting of the European society of paediatric infectious diseases, The Hague	2011	0.9
Annual meeting of the Manchester Triage System international reference group, Graz, Austria	2011	0.9

Young investigators day, congress of the Dutch Society for paediatrics, Veldhoven	2012	0.9
Annual meeting of the Manchester Triage System international reference group, Oslo, Norway	2012	0.9
Annual meeting of the Manchester Triage System international reference group, Rotterdam	2013	0.9
National conferences - presentations		
ZonMW 10 years of research, Utrecht [Poster presentation]	2009	0.4
Congress of the Dutch society for paediatrics, Veldhoven [Oral presentation]	2010	0.9
Congress of the Dutch society for emergency department nurses, Ede [Oral presentation]	2011	0.9
Sophia scientific research organization (SSWO), Rotterdam [poster presentation]	2010	0.9
International conferences - presentations		
28th Annual meeting of the European society of paediatrics infectious diseases, Nice, France [poster presentation]	2010	0.4
Research masterclass, 28th annual meeting of the European society of paediatrics infectious diseases, Nice, France [oral presentation]	2010	0.9
6th European congress on emergency medicine, Stockholm, Sweden [oral presentation]	2010	0.9
Annual meeting of the Manchester Triage System international reference group, Graz, Austria [oral presentation]	2011	0.9
29th Annual meeting of the European society of paediatric infectious diseases, The Hague [poster presentation]	2011	0.4
5th Europaediatrics congress, Vienna, Austria [poster presentation]	2011	0.4
30th Annual meeting of the European society of paediatric infectious diseases, Thessaloniki [poster presentation]	2012	0.4
Annual meeting of the Manchester Triage System international reference group, Oslo, Norway [oral presentation]	2012	0.9
7th European congress on emergency medicine, Antalya, Turkey [2 oral presentations]	2012	1.8
4th Congress of European academy of paediatric societies, Istanbul, Turkey [poster presentation]	2012	0.4
Annual meeting of the Manchester Triage System international reference group, Rotterdam [oral presentation]	2013	0.9

2. TEACHING	YEAR	WORKLOAD (ECTS)
Supervising Master's thesis		
A. Aown Aldeen, medical student, Erasmus University, Rotterdam	2011	3.0
D. Matena, medical student, Erasmus University, Rotterdam	2011	0.4
S. Tajjiou , medical student, Erasmus University, Rotterdam	2011-2012	1.5
Other		
Supervising data-entry students (Z. Grocmen, B. Salar, F. Suddle, E. Kakar, S. Aammari)	2012-2013	1.5
Peer review of articles for international scientific journals	2012-2013	1.0