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Opzet artikel TriAGE

Practice variation across five European pediatric emergency departments: a prospective observational study.

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Abstract

Objectives: To compare pediatric health care practice variation among five European Emergency Departments (EDs), to analyze variability in decisions about diagnostic testing, treatment, and admission.

Design and Population: Consecutive pediatric ED visits in five European in four countries (Austria, Netherlands, Portugal, United Kingdom) were prospectively collected during a study period of 9-36 months (2012-2014).

Primary outcome measures: Practice variation was studied for the following management outcome measures: lab testing, imaging, administration of intravenous medication, and patient disposition after assessment at the ED.

Analysis: multivariable logistic regression was used to adjust for general patient characteristics and markers of disease severity. To assess whether ED was significantly associated with management, the goodness-of-fit of regression models based on all variables with and without ED as explanatory variable was compared. Management measures were analysed across different categories of presenting complaints.

Results: Data from 111,922 children were included, with a median age of 4 years (IQR 1.7-9.4). There were large differences in frequencies of MTS urgency and selected MTS presentational flow charts. ED was a significant covariate for management measures. The variability in management among EDs was fairly consistent across different presenting complaints after correction for confounders. Adjusted odds ratios (aOR) for laboratory testing were consistently higher in one hospital, for example, while aOR for imaging were consistently higher in another hospital. Iv administration of medication and fluids and admission was significantly more likely in yet two other hospitals, compared to others, for most presenting complaints.

Conclusions: Distinctive hospital-specific patterns in variability of management could be observed in these five pediatric EDs, which were consistent across different groups of clinical presentations. This could indicate fundamental differences in pediatric health care practice, influenced by differences in factors such as organization of primary care, diagnostic facilities and available beds, professional culture and patient expectations.

Article Summary

Strengths and limitations:

- Large European study on pediatric practice variation in EDs including the entire range of pediatric presentations
- Information on presenting complaint available
- Correction for important patient characteristics and markers of disease severity
- No data on differential diagnosis after assessment by ED physician or outcome
- No specific data on referral status available

Introduction

Variability in health care delivery can indicate appropriate use, over- and underuse of resources. Differences in patient characteristics, including severity and nature of presenting problems, result in differences in diagnostic and therapeutic management [1]. This resulting variation in management is warranted, because different clinical problems require different management to achieve best patient outcome [2-4].

Yet variation can also arise from other factors, like differences in practice guidelines and adherence, medical tradition, patient expectations, or healthcare organization [5-9]. In these instances, both deviations in management to the lower and higher end of the spectrum and higher and lower resource use can be associated with poorer outcomes or lower cost efficiency, depending on the underlying factors. Studying practice variation has therefore been acknowledged as an important tool to identify areas with potential for improvement of patient care.

Several studies have observed practice variation in the pediatric emergency setting, for specific presentations [10, 11], such as minor head injury or respiratory symptoms. Other studies have focused on variability in resource use in pediatric emergency departments (EDs) in low acuity presentations. These studies reported that physician training background was associated with resource use and that diagnostic testing and procedures were less frequent in the low acuity group [12, 13]. Many studies have been conducted in the North American setting and not all were able to adjust for differences in patient characteristics, such as disease severity [14]. Large scale European studies are scarce.

The aim of this large multicenter study was to compare pediatric health care practice among five European Eds. We wanted to analyze variability in decisions about diagnostic testing, treatment, and admission, after adjustment for patient characteristics, across subgroups of presenting problems covering the broad spectrum of pediatric ED presentations.

Method

Study design, data source and study population

This study is part of the TrIAGE project (Triage Improvement Across General Emergency departments for pediatric patients), a prospective observational study. The study design has been described in detail elsewhere [15]. In brief, during this project electronic health record data of all ED visits of children <16 years were prospectively collected in five different hospitals in four different countries. The five participating hospitals were: Erasmus Medical Centre, the Netherlands; Maasstad Hospital,

the Netherlands; St. Mary's hospital Imperial College Healthcare NHS Trust, United Kingdom; Hospital Prof. Dr. Fernando Fonseca, Portugal; Vienna General Hospital, Austria. In the latter ED, only low urgent trauma cases presented, because the majority of trauma patients were seen in the traumatology department.

Study sites were diverse in their catchment area and complexity of the patient population, number of visits, and organization of health care. Data were obtained by questionnaires obtained from the participating EDs **(Appendix 1)**. The enrolment period varied from 8 to 36 months between 2012 and 2015, during which 119,209 consecutive ED visits were included**.** Nurses at the participating EDs were informed about the study and encouraged to be complete in their registration of routine medical data [15]. The study was approved by the medical ethics committees of all participating institutions. The requirement for informed consent was waived.

Children with incomplete triage data were excluded from the analysis. Complex comorbidity has been linked to a higher use of diagnostics and therapeutic interventions at the ED [16]. Children with known complex comorbidity were therefore excluded if patient-level information was available. This was the case for hospitals with high proportions of comorbidity: Erasmus MC, St Mary's and General hospital Vienna (10-38% comorbidity). Maasstad Hospital and Hospital Fernando Fonseca reported an estimated total comorbidity of less than 10%, and much lower proportions of complex comorbidity, and did not provide patient-level information. Comorbidity was defined according to the Pediatric Medical Complexity Algorithm [17, 18].

Main outcome measures

We evaluated ordering of diagnostic tests (laboratory testing and imaging at the ED), administration of intravenous (iv) medication or fluids, and hospital admission. Laboratory testing included tests and cultures in blood, urine, faeces, and cerebrospinal fluid. Imaging included X-ray, ultrasound, computed tomography, and MRI. Admission was defined as admission from the ED to the general ward or PICU.

Confounders

Patient characteristics (age, gender), physiological parameters (heart rate, respiratory rate, oxygen saturation, temperature), presentational flow chart and urgency according to the Manchester triage system (MTS), and presentation during office hours or during out-of-office hours were considered as potentially confounding variables. Office hours were defined as Monday until Friday, between 08:00 am and 05:59 pm, and all other time points were defined as out-of-office hours. Vital signs and age were included as continuous variables.

In all participating hospitals, the MTS was routinely used for triage of presenting children. The MTS consists of 53 presentational flow charts that cover almost all presentations to EDs [19]. Presentational flow charts in turn consist of signs and symptoms that classify patients into 5 urgency categories, indicating the time to first contact with the treating clinician. These categories were assigned to three groups: MTS emergent or very urgent (<10 minutes waiting time), MTS urgent (< 60 minutes waiting time), and MTS standard (60-120 minutes) or non-urgent (120- 240 minutes waiting time).

To create subgroups of comparable presenting symptoms, we used MTS presentational flow charts. These were grouped into 9 categories as defined in our previous publications: cardiac, dermatologic, ear/nose/throat, gastrointestinal, neurologic/psychiatric/intoxications, respiratory, trauma/muscular, unwell and urinary/gynaecological [15, 20]. Heterogeneous presentations with low frequency were grouped together as 'other' **(Appendix 2).**

In addition to the subgroups of presenting symptoms based on MTS presentational flow charts, we defined a subgroup of infectious presentations, because suspected infection is an important reason for presentation at the ED. We defined this subgroup as children <5 years old, who had been assigned to the presentational flow chart shortness of breath or vomiting/diarrhea or had presented with fever (defined as temperature >= 38.5°C on presentation or MTS discriminator hot child).

Statistical analysis

We evaluated ordering of diagnostic tests, initiation of treatment, and hospital admission across centers, adjusting for differences in patient characteristics. Variability across EDs in laboratory testing, imaging, iv medication, and admission was analyzed using multivariable logistic regression models, adjusting for identified confounders. In this analysis, the Maasstad hospital was (randomly) selected as the reference. Differences between EDs are expressed as adjusted odds ratios (aORs), relative to practice in the Maasstad hospital, with 95% confidence intervals (CIs).

Patient characteristics and all other included variables are presented using descriptive statistics with absolute numbers, proportions, ranges and medians as appropriate. Vital signs are presented as proportion abnormal, based on the Advanced Pediatric Life Support reference values, with fever defined as a temperature>= 38.5° C [21].

To assess whether ED was significantly associated with management when adjusted for confounding factors, the fit of regression models based on all variables with and without ED as explanatory variable was compared using the generalized likelihood ratio test statistic. Patients were then

stratified according to categories of MTS presentational flow charts and separate regression analyses were performed within those strata. Because the ED of General hospital Vienna only treated a small proportion of trauma patients, this hospital was excluded from the analysis in the category trauma/muscular. Results of the presentational flow chart category 'other' are not presented, because of the inherent heterogeneity of this category.

Missing data for vital signs were imputed 25 times using the MICE algorithm in R (version 3.6.3). These missing data were assumed to be missing at random, conditional on other variables in the database. The imputation model included all predictors and outcome measures and additional descriptors of case mix: patient age and sex, date and time of arrival, and triage characteristics [15, 22]. Analyses were performed with IBM SPS statistics, version 25 (IBM corporation, Armonk, NY).

Results

Study group

Of all 119,209 ED visits of patients 16 years or younger included in the TrIAGE cohort, 5,706 were excluded because of complex comorbidity, leaving 113,503 who met the inclusion criteria. A total of 1,581 presentations had to be excluded because of missing presentational flow chart (n=1,578 presentations) or missing time of arrival (n= 3 presentations), resulting in a study group of 111,922 presentations (94%).

Across the 5 EDs, the median age at presentation ranged from 3.8 to 5.7 years, and 42-48% of children were female (**Table 1**). Most children presented with general malaise or because of parental concern, trauma or injuries, gastro-intestinal or respiratory complaints. Between 11% and 33% of children had tachypnea at presentation an, 11–18% tachycardia, and 4-9% had a recorded temperature of >= 38.5^{o}C. In concordance with differences in frequency of abnormal vital signs, the case mix of patients differed among EDs with respect to MTS urgency and presentational complaint. In Erasmus and Maasstad hospital, for example, 46-47% of patient were triaged as urgent, compared to 18-24% of patients presenting at the three other hospitals (**Table 1)**.

Table 1. Baseline characteristics

		Emergency department					
		Maasstad	Erasmus	Fernando	St Marys	Wien	Total
	N	10484	13958	53175	15027	19268	111922
Patient characteristics							
	Age in yrs (median, IQR)	5.7 (1.9-11.6)	4.1	4.7 (2.0-9.5)	3.8 (1.5-8.7)	3.9 (1.6-8.3)	4.4 (1.7-9.4)
	Gender, n % female	43.3	2	47.9	44.2	47.5	46.2
Abnormal vital signs (95 th percentile APLS 2017)*							
	Tachypnea (%)	32.9	20.3	10.8	16.9	22.3	16.9
	Bradypnea (%)	1.9	5.2	7.5	1.3	4	5.3
	Tachycardia (%)	18.2	12.3	12.9	14.1	10.8	13.1
	Bradycardia (%)	4.4	7.9	6	4.3	10.3	6.6
	Oxygen saturation<94% (%)	1.9	1.8	1.5	1.4	1	1.5
	Fever (Temp >= 38.5 degrees (%))	8	9.3	4	6.4	6.6	5.8
Number of abnormal vital signs (%)	0	53.9	61.7	67	69.9	59.4	64.2
	1	33.8	30.1	27.8	23.1	33.3	28.9
	2	11.6	7.7	4.9	6.4	7	6.4
	3	0.7	0.6	0.3	0.6	0.3	0.4
MTS urgency (%)	Emergent| very urgent	15.7	14	11.9	10.6	5.4	11.2
	Urgent	47.4	45.7	20.4	24.3	18.1	26.2
	Standard| non-urgent	36.8	40.3	67.7	65.1	76.5	62.5

Time of presentation (%)	Office hours	39.8	57.3	42.3	36	43.6	42.1
	Out of office hours	60.2	42.7	57.7	64	56.4	57.9
Presentational flow chart categories							
	Cardiac	0.4	1.8	1.2	0.8	1.8	1.2
	Dermatologic	8.5	12	14.3	9.9	14	12.8
	ENT	1.6	12	14	4.4	14	10.2
	Gastrointestinal	10	24	16.2	11.5	21.1	15.4
	Neurologic/psychiatric	2.4	3.8	3.1	2.8	4	3.7
	Respiratory	12.1	8.8	11.2	11.2	16.6	11.8
	Trauma/muscular	44.3	9.5	14.7	23.2	3.3	18.6
	Unwell	16.2	20.3	19	30.9	17.1	20.1
	Urinary/gynaecological	1.2	2.8	2.3	1.5	2.3	2.1
	Other	3.4	2.9	3.9	3.9	6	4.1

*presented as percentage of measured values. Percentage of missing values of vital signs is displayed below.

Missing values	Maasstad	Erasmus	Fernando	St Marys	Wien	Total
Heart rate	60.9% (n=6380)	51.1% (n=7138)	35.9% (n=19106)	19.6% (n=2940)	61.4% (n=11830)	42.3% (n=47394)
Respiratory rate	83.1% (n=8712)	68.2% (n=9531)	35.9% (n=19106)	23.6% (n=3544)	86.8% (n=16715)	51.5% (n= 57608)
Oxygen saturation	61.2% (N=6418)	69.4% (n=9694)	34.4% (n=18279)	19.8% (n=2973)	61.2% (n=11799)	43.9% (n=49163)
Temperature	57.9% (n=6069)	47.4% (n=6626)	12.1 % (n=6431)	32.4% (n=4872)	1% (n=194)	21.6% (n= 24192)

Management differences across EDs

Management also varied among EDs, with Vienna performing lab tests in 36% of presentations against 9.2% in St Mary's. Likewise, imaging was performed in 24-37% of presentations in Maasstad, Erasmus and Fernando, while in only 7.2% of patients presenting in Vienna. Differences in therapy were less pronounced but, with regards to admission, high admission rates (20-23%) were observed in Erasmus and Maasstad, while only 4.6-9.6% of patients were admitted in the other hospitals **(Table 2).** Inclusion of ED as confounding variable in the multivariable regression model improved model fit for all management measures ($p<0.001$), indicating that management differed depending on the ED of presentation.

Table 2. Management per ED		Maasstad	Erasmus	Fernando	St Marys	Wien	Total
	N	10484	13968	53175	15027	19268	111922
Diagnostic	Lab any (%)	20	28.5	13.1	9.2	35	19.1
	Imaging any (%)	37.2	24.9	23.7	14.2	7	21
Therapy	Iv medication or fluids (%)	12.8	9.5	7.5	4.1		7.2
Admission	General admission/ ICU admission (%)	23.4	20.3	5.2	9.6	4	9.3
	ICU admission (% of total)	0.2	2.2	0.3	0.1		0.4

Table 2. Management per ED

Management differences within presentational flow chart categories

Because management will be guided by presenting complaint, we assessed differences in management across EDs in children with comparable presenting complaints. The size of presentational flow categories relative to total presentations varied per hospital. The MTS urgency within categories also differed, with higher MTS urgency in Maasstad and Erasmus, indicating differences in patient populations between EDs (**Table 1, Figure 1**).

In most presentational flow chart categories we observed, after adjusting for patient characteristics, time of presentation and markers disease severity, that patients presenting in Vienna and, for some categories, Erasmus MC, were more likely to receive lab testing. Patients presenting in Fernando were more likely to receive imaging in the majority of categories, followed by Maasstad and Erasmus MC **(Figure 1).** Iv administration of medication or fluids was more likely in Maasstad hospital and, in some categories, in Erasmus MC and Fernando, compared to other hospitals. Admission was more likely in Maasstad hospital, followed by Erasmus MC. The chance of admission was consistently lower elsewhere after adjustment for other parameters, with the exception of smaller categories with broader confidence intervals. One ED had an overall average or lower likelihood of medical interventions (St Mary's), but for other EDs, instead of overall high or low resource use, there were specific interventions that were performed more or less likely within EDs (**Figure 1, Figure 2**). The likelihood of administration of iv medication and admission seemed to vary in parallel directions.

Subanalysis in infectious children

An additional regression analysis was performed in the subgroup of young children with suspected infectious diseases. Similar patterns of variability in management across EDS were observed (**Table 3)**. Lab testing was more likely in Vienna and in Erasmus MC, imaging more likely in Fernando, iv medication and admission more likely in Maasstad hospital, followed by Erasmus MC. This means that, in this more homogeneous group of children, there was no apparent lower variability in management among different EDs.

Table 3. aOR for management in infectious children (n=23695)	Any Lab tests		Any Imaging		Iv medication or fluids		Admission (ICU&general)	
	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
Maasstad	Reference		Reference		Reference		Reference	
Erasmus	2.64	(2.33-2.99)	3.66	(2.93-4.56)	0.63	(0.53-0.73)	0.75	(0.65-0.85)
Fernando	0.89	(0.79-1.00)	6.91	(5.63-8.48)	0.43	(0.38-0.50)	0.19	(0.17-0.22)
St Marys	0.36	(0.30-0.41)	1.99	(1.57-2.52)	0.25	(0.20-0.30)	0.33	(0.29-0.38)
Wien	2.88	(2.54-3.27)	2.85	(2.28-3.57)	0.36	(0.30-0.43)	0.17	(0.15-0.20)

Table 3. aOR for infectious children <5 yrs.

Based on MTS flow chart ' diarrhea and vomiting'– or ' shortness of breath', or based on presence of fever (MTS discriminator hot child/adult or temp>=38°C)). OR are adjusted for age, gender, MTS urgency category, heart rate, respiratory rate, oxygen saturation, temperature, and time of presentation.

Discussion

In this large observational study of pediatric practice variation across five European EDs, management was associated with ED of presentation. We observed ED-related patterns of variability in the likelihood of diagnostic testing, iv medication and admission, which remained stable across groups of clinical presentations, after correcting for several general patient characteristics and markers of disease severity known to be associated with management. Though one ED had overall low resource use, there were large differences across other EDs in likelihood for imaging or laboratory testing, after correcting for the differences in disease severity and presenting symptoms that were observed between hospitals.

Other unmeasured medical and non-medical factors are likely to play a role in hospital-specific patterns of variability. The proportion of self-referred patients differed greatly among hospitals (**Appendix 1**). Reasons for primary care physicians to refer to an ED include available diagnostic facilities, request for professional opinion, or expected need for in-hospital treatment[6]. This means that disease characteristics of referred and non-referred presentations are likely to differ. These factors could partly be corrected for by the measures of disease severity and presenting symptoms.

Prior out-of-hospital diagnostics and treatment will also influence management at the ED. The higher rate of referrals by primary care physicians in Maasstad hospital and Erasmus MC could account for the higher likelihood of admission to these hospitals, as has been reported previously [7, 23]. Parent and patient expectations regarding management differ between self-referred and referred patients. Presentation at ED without prior consultation of the primary care physician can be triggered by parental perceptions of disease severity and the expectation that specific diagnostic facilities or treatment available at the ED are required [6, 24-27]. This can also stimulate health care providers to perform additional testing or influence their treatment decisions [28]. However, referral status only cannot explain the variability in management that was observed in the three hospitals with comparably low referral rates.

A myriad of other factors has been linked to clinical management. Financial incentives embedded in the organization of healthcare systems could differ across EDs. National or local professional culture, standard of care and facilities might partly account for the observed variability, such as preferences for lab testing, imaging, and the availability thereof [29-31]. Differences in practice guidelines, reflecting these differences in professional culture and diagnostic options, could also be of influence. These are neither harmonized across European countries, nor is adherence likely to be comparable

across EDs. Holding varying guideline recommendations regarding lab tests and imaging partly responsible for the observed patterns would reflect international differences in the general value placed on specific diagnostic tests, regardless of disease presentation, as the differences in additional testing were rather consistent and apparently independent of presenting complaint.

Parent and patient expectations and preferences regarding healthcare are affected by cultural and socio-economic factors. These, in turn, influence management decisions and could represent another non-medical factor contributing to the observed variability [28, 32]. Professional education and training have been reported to be associated with management, where pediatric specialty training was linked to a lower amount of diagnostic testing [5, 33]). However, in our study there was no difference in respect to those factors among hospitals with higher and lower likelihood of testing.

Strengths/limitations:

A major strength of this study is that we could adjust for several relevant patient characteristics and markers of disease severity, due to the availability of triage urgency data, presentational flow chart, vital signs and basic patient characteristics. We could include a large sample of patients from different European countries. This is an advantage, because these differences can help in identifying relevant factors responsible for practice variation, but also represents a limitation, since individual effects could not be disentangled. Hospitals differed in multiple characteristics, such as the availability of primary care physicians, rate of self-referrals, and patient case mix. Patient-specific data on referral were not available for all hospitals, and referral status could therefore not be included in the regression analyses. In addition, availability of resources, including staffing and beds, could vary during the project, but exact data were missing for our analysis.

We used the selected MTS presentational flow chart as a proxy for presenting symptoms. In the course of the evaluation at the ED, the initial impression will have changed in a proportion of children, due to the elucidation of other signs and symptoms, which could lead to adjustments to the differential diagnosis and changes in subsequent management steps. Because we had no data on differential diagnosis and final diagnosis, we could only stratify according to presenting symptom. The remaining heterogeneity of patients within categories and between EDs will have contributed to the observed variability in management. We did not have patient outcome measures available, therefore appropriateness of deviations, compared to the benchmark, could not be assessed in terms of effects on outcomes.

Implications

Our analysis revealed substantial variability in management, even after adjustment for relevant patient characteristics and markers of disease severity. We acknowledge that not all practice variation is unwarranted or problematic, because contextual and patient-related factors such as those described above can cause variation that is not associated with lower quality care [34].

However, we believe that our findings of consistently higher likelihood of lab testing or imaging in some hospitals, compared to others, are sufficient reason to further study underlying reasons for these patterns. This evaluation should involve patient important outcomes and prior out-of-hospital management, to assess the entire trajectory of care and to produce suggestions for improvements in patient care.

Conclusion

In this analysis of pediatric health care practice among five European Emergency Departments distinctive hospital-specific patterns in variability of management could be observed, which were consistent over different groups of clinical presentations. This pattern in variability could indicate fundamental differences in pediatric health care practice across countries, influenced by factors such as organization of primary care, diagnostic facilities and available beds, professional culture and patient expectations.

Author contributions:

I.M., F.S., C.A. S.G, H.M. and J.Z. substantially contributed to the conception and design of the TrIAGE study and data acquisition. F.R., H.M., P.B. and J.Z., conceived the study idea. F.R. performed the analysis and F.R., P.B., H.M. and J.Z. interpreted the results. F.R. wrote the first draft of the manuscript. All authors revised it critically for important intellectual content and gave their approval of the final version. All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. J.Z. is guarantor.

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Ethical approval statement:

The study was approved by the participating institutions' medical ethical committees: Medical Ethics Committee Erasmus MC (MEC-2013-567), Maasstad Ziekenhuis Board of Directors (Protocol L2013-103), Imperial College London Joint Research Compliance Office (Reference number: 14SM2164; Ethics reference number 14/WA/1051), Comissão de Ética para a Saúde do Hospital Prof. Dr. Fernando Fonseca EPE (Reunião de 06 de Dezembro de 2017), Ethik Kommission Medizinische der Medizinischen Unversität Wien (EK Nr: 1405/2014). All waived the requirement for informed consent.

Figure legends

Figure 1. aOR for management according to presentational flow chart categories

Figure 2. Radar charts presenting aOR for management outcome measures in the 5 largest presentational flow chart categories

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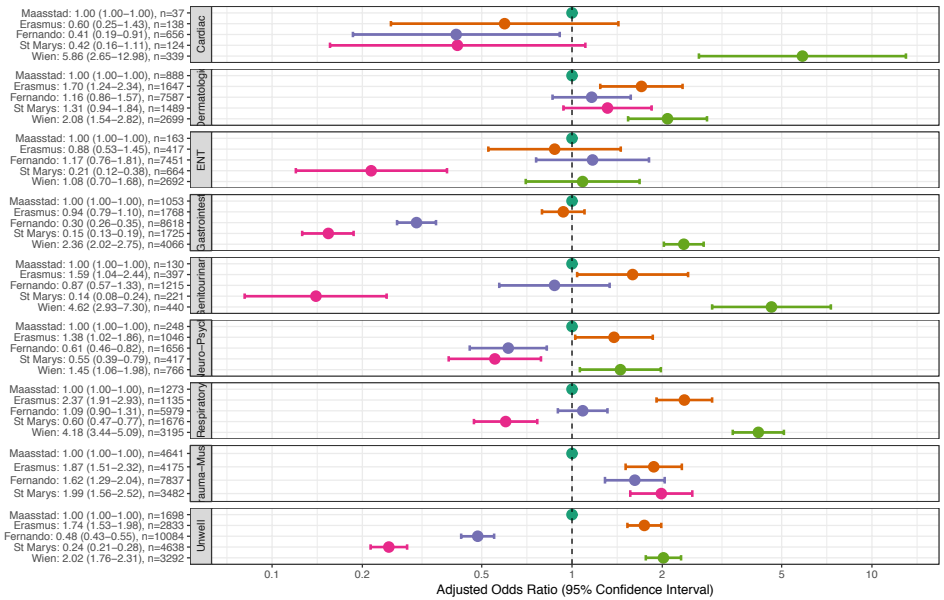
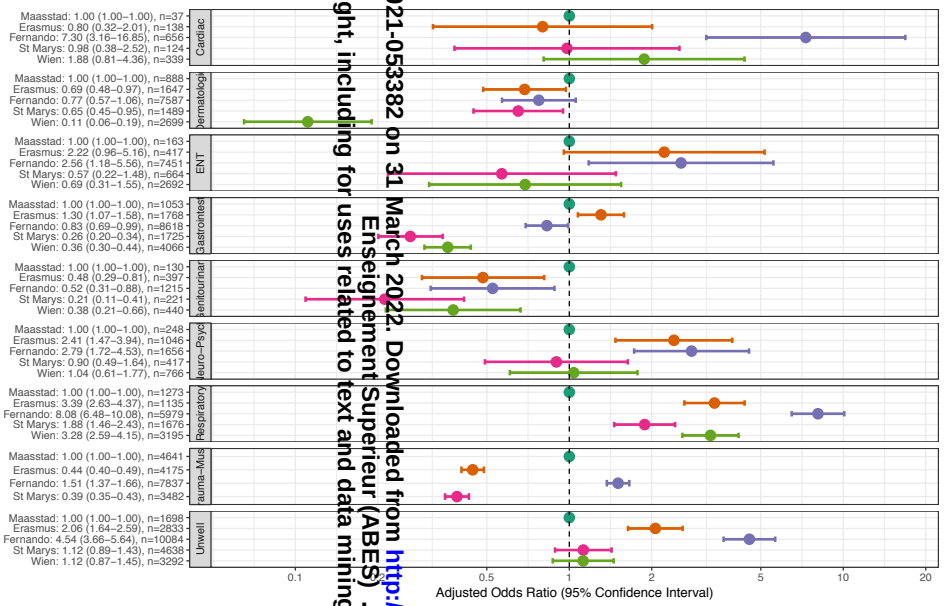
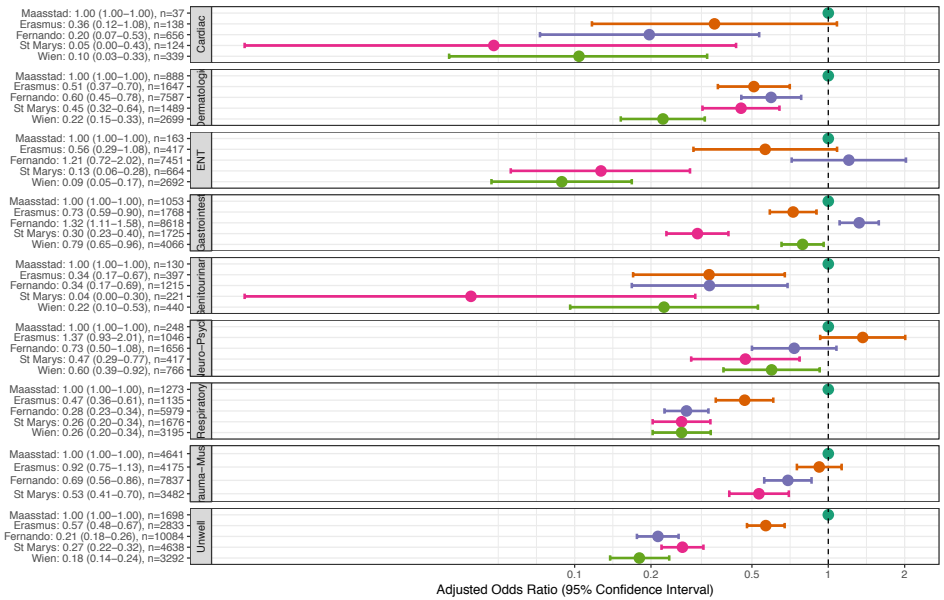
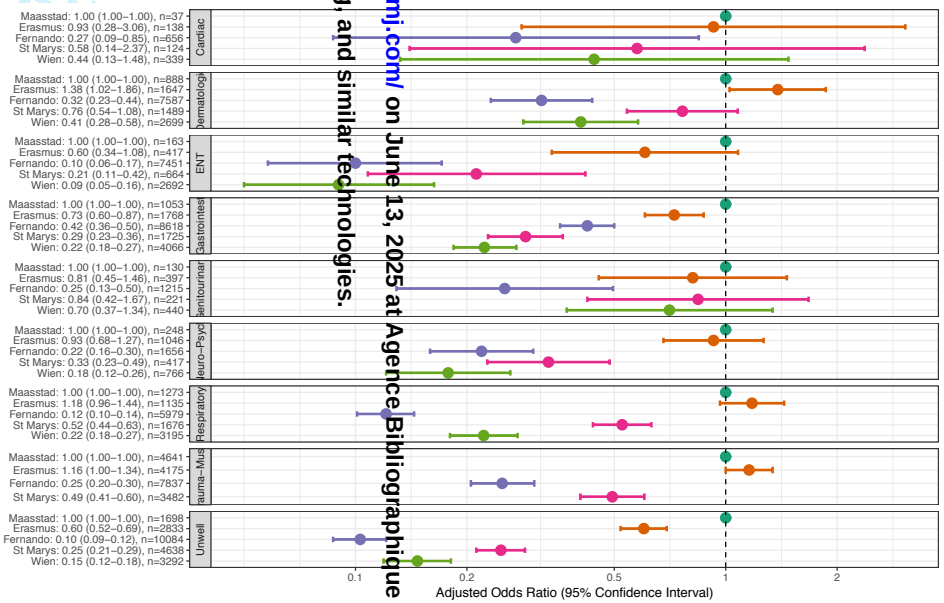


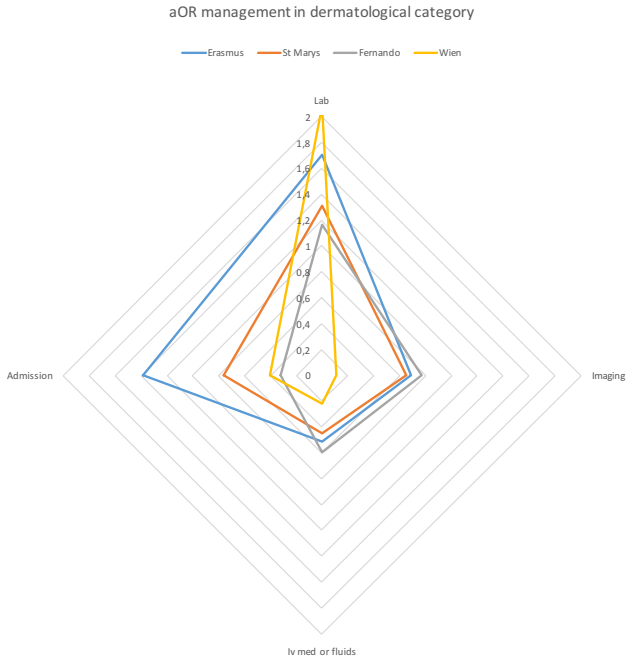


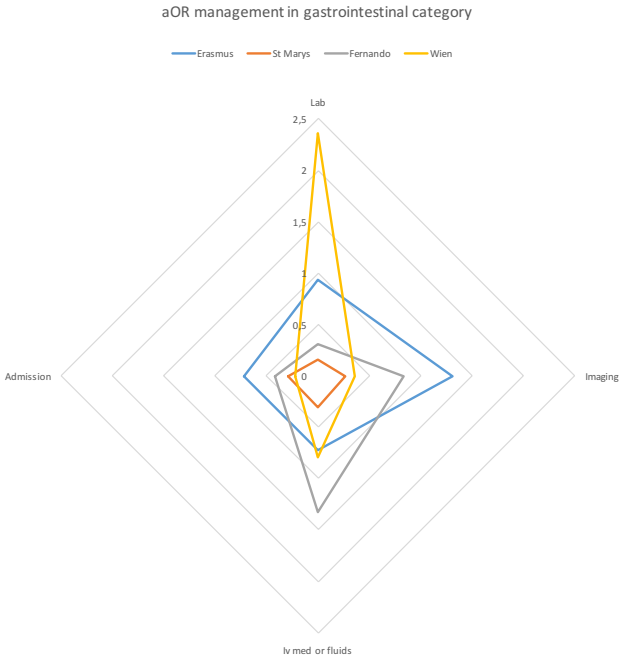


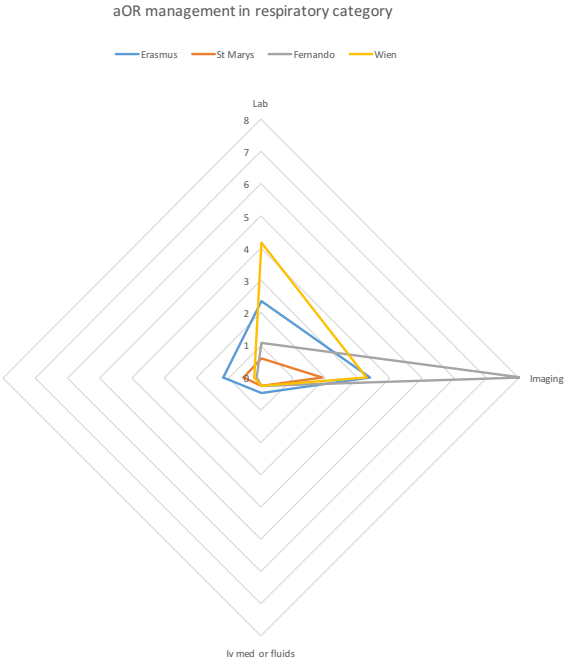


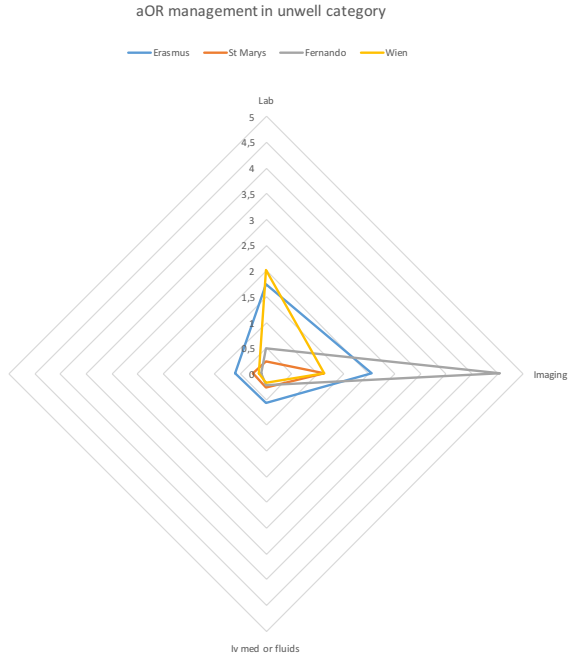
OR are adjusted for age, gender, MTS urgency category, heart rate, respiratory rate, oxygen saturation, temperature and time of presentation

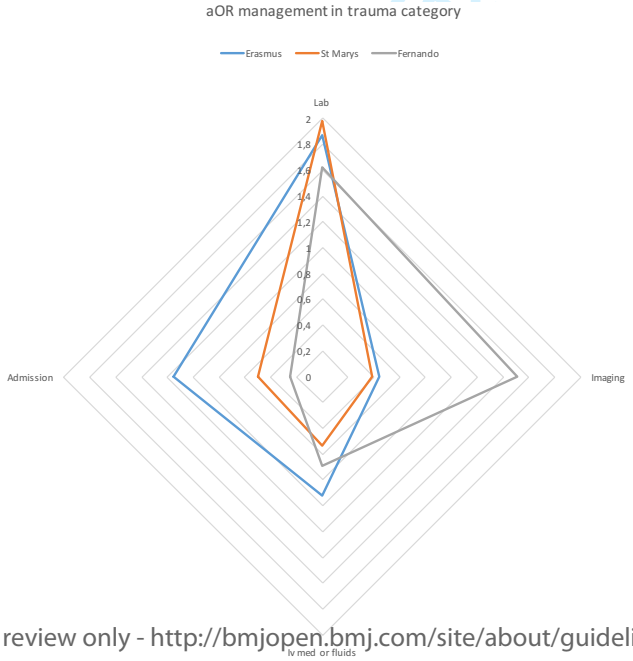
Figure 2











Appendix 1. ED Characteristics

	Maasstad Hospital, Rotterdam, the Netherlands	**Erasmus MC, Rotterdam, the Netherlands**	**Hospital Fernando da Fonseca, Lisbon, Portugal**	**St Mary's Hospital, London, United Kingdom**	**General Hospital, Vienna, Austria**
Hospital characteristics	Teaching hospital 59 pediatric beds	University hospital 60 pediatric beds	Community hospital 91 pediatric beds	University hospital 46 pediatric beds	University hospital 74 pediatric beds
Catchment area	Urban Generally low socio-economic status	Urban Mixed high and low socio-economic status	Mixed urban and rural Generally low socio-economic status	Urban Mixed high and low socio-economic status	Urban Mixed high and low socio-economic status
Emergency department characteristics	Mixed adult-pediatric 9500 children/year	Pediatric only till October 2014, from then on mixed 6500 children/year	Pediatric only 60,000 children/year	Pediatric only 27,000 children/year	Pediatric only 22,000 children/year
Supervising physician	Pediatrician	Pediatrician	Pediatrician	Pediatric emergency physician	Pediatrician
Inclusion period	01-05-2014 to 31-10-2015	01-01-2012 to 31-12-2014	01-03-2014 to 28-02-2015	01-07-2014 to 28-02-2015	01-01-2014 to 31-12-2014
Number of patients included	10,484	13,968	53,175	15,027	19,268
Primary care availability	24/7	24/7	Daytime and evenings	Daytime and evenings	Daytime
Referral by emergency service	4.5%	8.9%	4.0%	5.6%	Not available
Self-referral	17%	27%	96%	82%	>90%*
Comorbidity in all children	<10%*	38%	<10%*	11%	10%

Appendix 2. MTS presentational flow charts reclassified into 10 presentational flow chart categories

Category	MTS presentational flow charts[15]
Cardiac	Chest pain, palpitations
Dermatologic	Abscesses and local infections, bites and stings, burns and scalds, rashes, Wounds
Ear Nose Throat	Ear problems, facial problems, sore throat
Gastrointestinal	Abdominal pain in adults, abdominal pain in children, diarrhoea and vomiting, gastrointestinal bleeding
Neurologic, psychiatric and intoxications	Apparently drunk, behaving strangely, collapsed adult, fits, Headache, mental illness, overdose and poisoning, self-harm
Respiratory	Asthma, shortness of breath in adults, shortness of breath in children
Trauma/Muscular	Assault, back pain, falls, head injury, limping child, limb problems, major trauma, neck pain, torso injury
Unwell	Crying baby, irritable child, unwell adult, unwell child, worried parent
Urinary/gynaecological	Pregnancy, per vaginum bleeding, sexually acquired infection, testicular pain, urinary problems
Other	Allergy, dental problems, diabetes, eye problems, exposure to chemicals, foreign body, major incidents

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and time period within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title Database: Method Title Not applicable
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			Present
Objectives	3	State specific objectives, including any prespecified hypotheses			Present
Methods					
Study Design	4	Present key elements of study design early in the paper			Present
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			Present

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Method Method Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Methods
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			Methods

Bias	9	Describe any efforts to address potential sources of bias			Methods
Study size	10	Explain how the study size was arrived at			Methods
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			Methods
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			Methods
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	Methods

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	Not applicable
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Methods/results
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure			

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			
Discussion					
Key results	18	Summarise key results with reference to study objectives			
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion/limitation.
Interpretation	20	Give a cautious overall interpretation of results considering objectives,			

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results			
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Statement

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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Practice variation across five European pediatric emergency departments: a prospective observational study.

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Keywords: practice variation, emergency department, pediatrics, resource use

Abstract

Objectives: To compare pediatric health care practice variation among five European Emergency Departments (EDs) by analyzing variability in decisions about diagnostic testing, treatment, and admission.

Design and Population: Consecutive pediatric visits in five European EDs in four countries (Austria, Netherlands, Portugal, United Kingdom) were prospectively collected during a study period of 9-36 months (2012-2015).

Primary outcome measures: Practice variation was studied for the following management measures: lab testing, imaging, administration of intravenous medication, and patient disposition after assessment at the ED.

Analysis: multivariable logistic regression was used to adjust for general patient characteristics and markers of disease severity. To assess whether ED was significantly associated with management, the goodness-of-fit of regression models based on all variables with and without ED as explanatory variable was compared. Management measures were analysed across different categories of presenting complaints.

Results: Data from 111,922 children were included, with a median age of 4 years (IQR 1.7-9.4). There were large differences in frequencies of Manchester Triage System (MTS) urgency and selected MTS presentational flow charts. ED was a significant covariate for management measures. The variability in management among EDs was fairly consistent across different presenting complaints after adjustment for confounders. Adjusted odds ratios (aOR) for laboratory testing were consistently higher in one hospital while aOR for imaging were consistently higher in another hospital. Iv administration of medication and fluids and admission was significantly more likely in two other hospitals, compared to others, for most presenting complaints.

Conclusions: Distinctive hospital-specific patterns in variability of management could be observed in these five pediatric EDs, which were consistent across different groups of clinical presentations. This could indicate fundamental differences in pediatric health care practice, influenced by differences in factors such as organization of primary care, diagnostic facilities and available beds, professional culture and patient expectations.

Article Summary

Strengths and limitations:

- Large European study on pediatric practice variation in EDs including the entire range of pediatric presentations
- Information on presenting complaint available
- Adjustment for important patient characteristics and markers of disease severity
- No data on differential diagnosis after assessment by ED physician or outcome
- No specific data on referral status available

Introduction

Variability in health care delivery can indicate appropriate use, over- and underuse of resources. Differences in patient characteristics, including severity and nature of presenting problems, result in differences in diagnostic and therapeutic management [1]. This resulting variation in management is warranted, because different clinical problems require different management to achieve the best patient outcome [2-4].

Yet variation can also arise from other factors, like differences in practice guidelines and adherence, medical tradition, patient expectations, or healthcare organization [5-9]. In these instances, both deviations in management to the lower and higher end of the spectrum and higher and lower resource use can be associated with poorer outcomes or lower cost efficiency, depending on the underlying factors. Studying practice variation has therefore been acknowledged as an important tool to identify areas with potential for improvement of patient care.

Several studies have observed practice variation in the pediatric emergency setting, for specific presentations [10, 11], such as minor head injury or respiratory symptoms. Other studies have focused on variability in resource use in pediatric emergency departments (EDs) in low acuity presentations. These studies reported that physician training background was associated with resource use and that diagnostic testing and procedures were less frequent in the low acuity group [12, 13]. Many studies have been conducted in the North American setting and not all were able to adjust for differences in patient characteristics, such as disease severity [14]. Large scale European studies are scarce.

This large multicenter study aimed to compare pediatric health care practice among five European Eds. We wanted to analyze variability in decisions about diagnostic testing, treatment, and admission, after adjustment for patient characteristics, across subgroups of presenting problems covering the broad spectrum of pediatric ED presentations.

Method

Study design, data source and study population

This study was embedded in the TrIAGE project (Triage Improvement Across General Emergency departments for pediatric patients), a prospective observational study and followed from observations in previous analyses. The study design has been described in detail elsewhere [15]. In brief, during this project electronic health record data of all ED visits of children <16 years were prospectively collected in five different hospitals in four different countries. The five participating

hospitals were: Erasmus Medical Centre, the Netherlands; Maasstad Hospital, the Netherlands; St. Mary's hospital Imperial College Healthcare NHS Trust, United Kingdom; Hospital Prof. Dr. Fernando Fonseca, Portugal; Vienna General Hospital, Austria. In the latter ED, only low urgent trauma cases presented, because the majority of trauma patients were seen in the traumatology department.

Study sites were diverse in their catchment area and complexity of the patient population, number of visits, and organization of health care. Data were obtained by questionnaires obtained from the participating EDs **(Appendix 1)**. Four EDs were pediatric EDs, and one was mixed adult-pediatric. The supervising physician was a pediatrician in all EDs, and in one site a pediatric emergency physician. The enrolment period varied from 8 to 36 months between 2012 and 2015, during which 119,209 consecutive ED visits were included**.** The differences in patient load account for differences in enrollment time to include sufficient patients. Also practical reasons, such as availability of staff to help in high quality data collection, played a role.

Nurses at the participating EDs were informed about the study and encouraged to be complete in their registration of routine medical data [15]. The study was approved by the medical ethics committees of all participating institutions. The requirement for informed consent was waived.

Children with incomplete triage data were excluded from the analysis. Complex comorbidity has been linked to a higher use of diagnostics and therapeutic interventions at the ED [16]. Children with known complex comorbidity were therefore excluded if patient-level information was available. This was the case for hospitals with high proportions of comorbidity: Erasmus MC, St Mary's and General hospital Vienna (10-38% comorbidity). Maasstad Hospital and Hospital Fernando Fonseca reported an estimated total comorbidity of less than 10%, and much lower proportions of complex comorbidity, and did not provide patient-level information. Comorbidity was defined according to the Pediatric Medical Complexity Algorithm [17, 18].

Main outcome measures

We evaluated ordering of diagnostic tests (laboratory testing and imaging at the ED), administration of intravenous (iv) medication or fluids, and hospital admission. Laboratory testing included tests and cultures in blood, urine, faeces, and cerebrospinal fluid. Imaging included X-ray, ultrasound, computed tomography, and magnetic resonance imaging (MRI). Admission was defined as admission from the ED to the general ward or pediatric intensive care unit (PICU).

Confounders

Patient characteristics (age, gender), physiological parameters (heart rate, respiratory rate, oxygen saturation, temperature), presentational flow chart and urgency according to the Manchester triage

system (MTS), and presentation during office hours or during out-of-office hours were considered as potential confounding variables. Office hours were defined as Monday until Friday, between 08:00 am and 05:59 pm, and all other time points were defined as out-of-office hours. Vital signs and age were included as continuous variables.

In all participating hospitals, the MTS was routinely used for triage of presenting children. The MTS consists of 53 presentational flow charts that cover almost all presentations to EDs [19].
The triage nurses are trained to select the most specific presentational flow chart. Only if there is no defining symptom at presentation the nurse will select an aspecific flow chart, like unwell child or crying baby. To ensure sufficient standardization of triage, triage nurses using the Manchester Triage System are well-trained.

Presentational flow charts in turn consist of signs and symptoms that classify patients into 5 urgency categories, indicating the time to first contact with the treating clinician. These categories were assigned to three groups: MTS emergent or very urgent (<10 minutes waiting time), MTS urgent (< 60 minutes waiting time), and MTS standard (60-120 minutes) or non-urgent (120- 240 minutes waiting time).

To create subgroups of comparable presenting symptoms, we used MTS presentational flow charts. These were grouped into 9 categories as defined in our previous publications: cardiac, dermatologic, ear/nose/throat, gastrointestinal, neurologic/psychiatric/intoxications, respiratory, trauma/muscular, unwell and urinary/gynaecological [15, 20]. Heterogeneous presentations with low frequency were grouped together as 'other' **(Appendix 2).**

In addition to the subgroups of presenting symptoms based on MTS presentational flow charts, we defined a subgroup of infectious presentations, because a suspected infection is an important reason for presentation at the ED. We defined this subgroup as children <5 years old, who had been assigned to the presentational flow chart shortness of breath or vomiting/diarrhea or had presented with fever (defined as temperature >= 38.5°C on presentation or MTS discriminator hot child).

Statistical analysis

We evaluated ordering of diagnostic tests, initiation of treatment, and hospital admission across centers, adjusting for differences in patient characteristics. Variability across EDs in laboratory testing, imaging, iv medication, and admission was analyzed using multivariable logistic regression models, adjusting for identified confounders. In this analysis, the Maasstad hospital was (randomly)

selected as the reference. Differences between EDs are expressed as adjusted odds ratios (aORs), relative to practice in the Maasstad hospital, with 95% confidence intervals (CIs).

Patient characteristics and all other included variables are presented using descriptive statistics with absolute numbers, proportions, ranges and medians as appropriate. Vital signs are presented as proportion abnormal, based on the Advanced Pediatric Life Support reference values, with fever defined as a temperature>= 38.5° C [21].

To assess whether ED was significantly associated with management when adjusted for confounding factors, the fit of regression models based on all variables with and without ED as explanatory variable was compared using the generalized likelihood ratio test statistic. Patients were then stratified according to categories of MTS presentational flow charts and separate regression analyses were performed within those strata. Because the ED of General hospital Vienna only treated a small proportion of trauma patients, this hospital was excluded from the analysis in the category trauma/muscular. Results of the presentational flow chart category 'other' are not presented, because of the inherent heterogeneity of this category.

Missing data for vital signs were imputed 25 times using the MICE algorithm in R (version 3.6.3). These missing data were assumed to be missing at random, conditional on other variables in the database. The imputation model included all predictors and outcome measures and additional descriptors of case mix: patient age and sex, date and time of arrival, and triage characteristics [15, 22]. Analyses were performed with IBM SPS statistics, version 25 (IBM corporation, Armonk, NY).

Patient and public involvement: Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Results

Study group

Of all 119,209 ED visits of patients 16 years or younger included in the TrIAGE cohort, 5,706 were excluded because of complex comorbidity, leaving 113,503 who met the inclusion criteria. A total of 1,581 presentations had to be excluded because of missing presentational flow chart (n=1,578 presentations) or missing time of arrival (n= 3 presentations), resulting in a study group of 111,922 presentations (94%).

Across the 5 EDs, the median age at presentation ranged from 3.8 to 5.7 years, and 42-48% of children were female (**Table 1**). Most children presented with general malaise or because of parental concern, trauma or injuries, gastro-intestinal or respiratory complaints. Between 11% and 33% of children had tachypnea at presentation an, 11–18% tachycardia, and 4-9% had a recorded temperature of >= 38.5^{o}C. In concordance with differences in frequency of abnormal vital signs, the case mix of patients differed among EDs with respect to MTS urgency and presentational complaint. In Erasmus and Maasstad hospital, for example, 46-47% of patient were triaged as urgent, compared to 18-24% of patients presenting at the three other hospitals (**Table 1)**.

Table 1. Baseline characteristics

		Emergency department					
		Maasstad	Erasmus	Fernando	St Marys	Wien	Total
	N	10484	13958	53175	15027	19268	111922
Patient characteristics							
	Age in yrs (median, IQR)	5.7 (1.9-11.6)	4.1 (1.8-8.8)	4.7 (2.0-9.5)	3.8 (1.5-8.7)	3.9 (1.6-8.3)	4.4 (1.7-9.4)
	Gender, n % female	43.3	42.2	47.9	44.2	47.5	46.2
Abnormal vital signs (95 th percentile APLS 2017)*							
	Tachypnea (%)	32.9	30.3	10.8	16.9	22.3	16.9
	Bradypnea (%)	1.9	5.2	7.5	1.3	4	5.3
	Tachycardia (%)	18.2	12.3	12.9	14.1	10.8	13.1
	Bradycardia (%)	4.4	7.9	6	4.3	10.3	6.6
	Oxygen saturation<94% (%)	1.9	1.8	1.5	1.4	1	1.5
	Fever (Temp >= 38.5 degrees (%))	8	9.3	4	6.4	6.6	5.8
Number of abnormal vital signs (%)	0	53.9	51.7	67	69.9	59.4	64.2
	1	33.8	30.1	27.8	23.1	33.3	28.9
	2	11.6	7.7	4.9	6.4	7	6.4
	3	0.7	0.6	0.3	0.6	0.3	0.4
MTS urgency (%)	Emergent| very urgent	15.7	14	11.9	10.6	5.4	11.2
	Urgent	47.4	45.7	20.4	24.3	18.1	26.2
	Standard| non-urgent	36.8	40.3	67.7	65.1	76.5	62.5

Time of presentation (%)	Office hours	39.8	57.3	42.3	36	43.6	42.1
	Out of office hours	60.2	42.7	57.7	64	56.4	57.9
Presentational flow chart categories							
	Cardiac	0.4	1.2	1.2	0.8	1.8	1.2
	Dermatologic	8.5	12	14.3	9.9	14	12.8
	ENT	1.6	14	14	4.4	14	10.2
	Gastrointestinal	10	12	16.2	11.5	21.1	15.4
	Neurologic/psychiatric	2.4	3.1	3.1	2.8	4	3.7
	Respiratory	12.1	8.8	11.2	11.2	16.6	11.8
	Trauma/muscular	44.3	9.5	14.7	23.2	3.3	18.6
	Unwell	16.2	20.3	19	30.9	17.1	20.1
	Urinary/gynaecological	1.2	2.8	2.3	1.5	2.3	2.1
	Other	3.4	2.9	3.9	3.9	6	4.1

*presented as percentage of measured values. Percentage of missing values of vital signs is displayed below.

Missing values	Maasstad	Erasmus	Fernando	St Marys	Wien	Total
Heart rate	60.9% (n=6380)	51.1% (n=7138)	35.9% (n=19106)	19.6% (n=2940)	61.4% (n=11830)	42.3% (n=47394)
Respiratory rate	83.1% (n=8712)	68.2% (n=9531)	35.9% (n=19106)	23.6% (n=3544)	86.8% (n=16715)	51.5% (n= 57608)
Oxygen saturation	61.2% (N=6418)	69.4% (n=9694)	34.4% (n=18279)	19.8% (n=2973)	61.2% (n=11799)	43.9% (n=49163)
Temperature	57.9% (n=6069)	47.4% (n=6626)	12.1 % (n=6431)	32.4% (n=4872)	1% (n=194)	21.6% (n= 24192)

Management differences across EDs

Management also varied among EDs, with Vienna performing lab tests in 36% of presentations against 9.2% in St Mary's. Likewise, imaging was performed in 24-37% of presentations in Maasstad, Erasmus and Fernando, while in only 7.2% of patients presenting in Vienna. Differences in therapy were less pronounced but, with regards to admission, high admission rates (20-23%) were observed in Erasmus and Maasstad, while only 4.6-9.6% of patients were admitted in the other hospitals **(Table 2).** Inclusion of ED as confounding variable in the multivariable regression model improved model fit for all management measures ($p<0.001$), indicating that management differed depending on the ED of presentation.

Table 2. Management per ED		Maasstad	Erasmus	Fernando	St Marys	Wien	Total
	N	10484	13968	53175	15027	19268	111922
Diagnostic	Lab any (%)	20	28.5	13.1	9.2	35	19.1
	Imaging any (%)	37.2	24.9	23.7	14.2	7	21
Therapy	Iv medication or fluids (%)	12.8	9.5	7.5	4.1		7.2
Admission	General admission/ ICU admission (%)	23.4	20.3	5.2	9.6	4	9.3
	ICU admission (% of total)	0.2	2.2	0.3	0.1		0.4

Table 2. Management per ED

Management differences within presentational flow chart categories

Because management will be guided by presenting complaint, we assessed differences in management across EDs in children with comparable presenting complaints. The size of presentational flow categories relative to total presentations varied per hospital. The MTS urgency within categories also differed, with higher MTS urgency in Maasstad and Erasmus, indicating differences in patient populations between EDs (**Table 1, Figure 1**).

In most presentational flow chart categories we observed, after adjusting for patient characteristics, time of presentation and markers disease severity, that patients presenting in Vienna and, for some categories, Erasmus MC, were more likely to receive lab testing. Patients presenting in Fernando were more likely to receive imaging in the majority of categories, followed by Maasstad and Erasmus MC **(Figure 1).** Iv administration of medication or fluids was more likely in Maasstad hospital and, in some categories, in Erasmus MC and Fernando, compared to other hospitals. Admission was more likely in Maasstad hospital, followed by Erasmus MC. The chance of admission was consistently lower elsewhere after adjustment for other parameters, with the exception of smaller categories with broader confidence intervals. One ED had an overall average or lower likelihood of medical interventions (St Mary's), but for other EDs, instead of overall high or low resource use, there were specific interventions that were performed more or less likely within EDs (**Figure 1, Figure 2**). The likelihood of administration of iv medication and admission seemed to vary in parallel directions.

Subanalysis in infectious children

An additional regression analysis was performed in the subgroup of young children with suspected infectious diseases. Similar patterns of variability in management across EDs were observed (**Table 3)**. Lab testing was more likely in Vienna and in Erasmus MC, imaging more likely in Fernando, iv medication and admission more likely in Maasstad hospital, followed by Erasmus MC. This means that, in this more homogeneous group of children, there was no apparent lower variability in management among different EDs.

Table 3. aOR for management in infectious children (n=23695)	Any Lab tests		Any Imaging		Iv medication or fluids		Admission (ICU&general)	
	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
Maasstad	Reference		Reference		Reference		Reference	
Erasmus	2.64	(2.33-2.99)	3.66	(2.93-4.56)	0.63	(0.53-0.73)	0.75	(0.65-0.85)
Fernando	0.89	(0.79-1.00)	6.91	(5.63-8.48)	0.43	(0.38-0.50)	0.19	(0.17-0.22)
St Marys	0.36	(0.30-0.41)	1.99	(1.57-2.52)	0.25	(0.20-0.30)	0.33	(0.29-0.38)
Wien	2.88	(2.54-3.27)	2.85	(2.28-3.57)	0.36	(0.30-0.43)	0.17	(0.15-0.20)

Table 3. aOR for infectious children <5 yrs.

Based on MTS flow chart ' diarrhea and vomiting' or ' shortness of breath', or based on presence of fever (MTS discriminator hot child/adult or temp>=38°C)). OR are adjusted for age, gender, MTS urgency category, heart rate, respiratory rate, oxygen saturation, temperature, and time of presentation.

Discussion

In this large observational study of pediatric practice variation across five European EDs, management was associated with ED of presentation. We observed ED-related patterns of variability in the likelihood of diagnostic testing, iv medication and admission, which remained stable across groups of clinical presentations, after correcting for several general patient characteristics and markers of disease severity known to be associated with management. Though one ED had overall low resource use, there were large differences across other EDs in likelihood for imaging or laboratory testing, after adjusting for the differences in disease severity and presenting symptoms that were observed between hospitals.

Other unmeasured medical and non-medical factors are likely to play a role in hospital-specific patterns of variability. The proportion of self-referred patients differed greatly among hospitals (**Appendix 1**). Reasons for primary care physicians to refer to an ED include available diagnostic facilities, request for a professional opinion, or expected need for in-hospital treatment[6]. This means that disease characteristics of referred and non-referred presentations are likely to differ. These factors could partly be adjusted for by the measures of disease severity and presenting symptoms.

Prior out-of-hospital diagnostics and treatment will also influence management at the ED. The higher rate of referrals by primary care physicians in Maasstad hospital and Erasmus MC could account for the higher likelihood of admission to these hospitals, as has been reported previously [7, 23]. Parent and patient expectations regarding management differ between self-referred and referred patients. Presentation at ED without prior consultation of the primary care physician can be triggered by parental perceptions of disease severity and the expectation that specific diagnostic facilities or treatment available at the ED are required [6, 24-27]. This can also stimulate health care providers to perform additional testing or influence their treatment decisions [28]. However, referral status only cannot explain the variability in management that was observed in the three hospitals with comparably low referral rates.

A myriad of other factors has been linked to clinical management. Financial incentives embedded in the organization of healthcare systems could differ across EDs. National or local professional culture, standard of care and facilities might partly account for the observed variability, such as preferences for lab testing, imaging, and the availability thereof [29-31]. Differences in practice guidelines, reflecting these differences in professional culture and diagnostic options, could also be of influence.

These are neither harmonized across European countries, nor is adherence likely to be comparable across EDs. Holding varying guideline recommendations regarding lab tests and imaging partly responsible for the observed patterns would reflect international differences in the general value placed on specific diagnostic tests, regardless of disease presentation, as the differences in additional testing were rather consistent and independent of presenting complaint.

Parent and patient expectations and preferences regarding healthcare are affected by cultural and socio-economic factors. These, in turn, influence management decisions and could represent another non-medical factor contributing to the observed variability [28, 32]. Professional education and training have been reported to be associated with management, where pediatric specialty training was linked to a lower amount of diagnostic testing [5, 33, 34]). However, in our study there was no difference in respect to those factors among hospitals with higher and lower likelihood of testing.

Strengths/limitations:

A major strength of this study is that we could adjust for several relevant patient characteristics and markers of disease severity, due to the availability of triage urgency data, presentational flow chart, vital signs and basic patient characteristics. We could include a large sample of patients from different European countries. This is an advantage, because these differences can help in identifying relevant factors responsible for practice variation, but also represents a limitation, since individual effects could not be disentangled. Hospitals differed in multiple characteristics, such as the availability of primary care physicians, rate of self-referrals, and patient case mix. Patient-specific data on referral were not available for all hospitals, and referral status could therefore not be included in the regression analyses. In addition, the availability of resources, including staffing and beds, could vary during the project, but exact data were missing for our analysis.

We used the selected MTS presentational flow chart as a proxy for presenting symptoms. In the course of the evaluation at the ED, the initial impression will have changed in a proportion of children, due to the elucidation of other signs and symptoms, which could lead to adjustments to the differential diagnosis and changes in subsequent management steps. Because we had no data on differential diagnosis and final diagnosis, we could only stratify according to presenting symptoms. The remaining heterogeneity of patients within categories and between EDs will have contributed to the observed variability in management. We did not have patient outcome measures available, therefore the consequences of deviations, compared to the benchmark, could not be assessed in terms of effects on outcomes.

Implications

Our analysis revealed substantial variability in management, even after adjustment for relevant patient characteristics and markers of disease severity. We acknowledge that not all practice variation is unwarranted or problematic, because contextual and patient-related factors such as those described above can cause variation that is not associated with lower quality care [35].

However, we believe that our findings of consistently higher likelihood of lab testing or imaging in some hospitals, compared to others, are sufficient reason to further study underlying reasons for these patterns. In that sense, ours can serve as a pilot study. As a starting point, deviations from the benchmark should prompt a general exploration of potential explanations, and how these deviations might affect patient outcome. In a second step, a review of recent guidelines and review syntheses, combined with an assessment of adherence to guidelines, could provide further insights. An accessible and feasible approach could be to increase awareness of practice guidelines during handover and rounds on a case level. Both by following recommendations with a strong evidence base for a well-defined population in favour of providing healthcare actions, and by following recommendations against certain practices because of insufficient added value, quality of care will be improved and variation will be reduced.

A related study focusing on febrile children found that admission varied across European EDs, after adjusting for explanatory variables comparable to the ones in our study but also for management at the ED, pointing to other factors than disease characteristics [36]. Factors related to organization of healthcare and local culture of care will likely play an important role. Though more difficult to influence, comparing and learning from differences in organization and medical culture can be a first step to long term changes, to ensure an sustainable healthcare system. The number of EDs required for a study searching to assess the importance of these factors depends on the heterogeneity of the EDs and healthcare systems, and on the research question. Such evaluation should preferentially involve patient important outcomes and prior out-of-hospital management, to assess the entire trajectory of care and to produce suggestions for improvements.

Conclusion

In this analysis of pediatric health care practice among five European Emergency Departments distinctive hospital-specific patterns in variability of management could be observed, which were consistent over different groups of clinical presentations. This pattern in variability could indicate fundamental differences in pediatric health care practice across countries, influenced by factors such as organization of primary care, diagnostic facilities and available beds, professional culture and patient expectations.

Author contributions:

I.M., F.S., C.A. S.G, H.M. and J.Z. substantially contributed to the conception and design of the TrIAGE study and data acquisition. F.R., H.M., P.B. and J.Z., conceived the study idea. F.R. performed the analysis and F.R., P.B., H.M. and J.Z. interpreted the results. F.R. wrote the first draft of the manuscript. All authors revised it critically for important intellectual content and gave their approval of the final version. All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. J.Z. is guarantor.

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Competing interests: non declared.

Patient consent for publication: Not required

Data sharing statement: No additional data are available.

Ethical approval statement: The study was approved by the participating institutions' medical ethical committees: Medical Ethics Committee Erasmus MC (MEC-2013-567), Maasstad Ziekenhuis Board of Directors (Protocol L2013-103), Imperial College London Joint Research Compliance Office (Reference number: 14SM2164; Ethics reference number 14/WA/1051), Comissão de Ética para a Saúde do Hospital Prof. Dr. Fernando Fonseca EPE (Reunião de 06 de Dezembro de 2017), Ethik Kommission Medizinische der Medizinischen Universität Wien (EK Nr: 1405/2014). All waived the requirement for informed consent.

Figure legends

Figure 1. aOR for management according to presentational flow chart categories

Figure 2. Radar charts presenting aOR for management outcome measures in the 5 largest presentational flow chart categories

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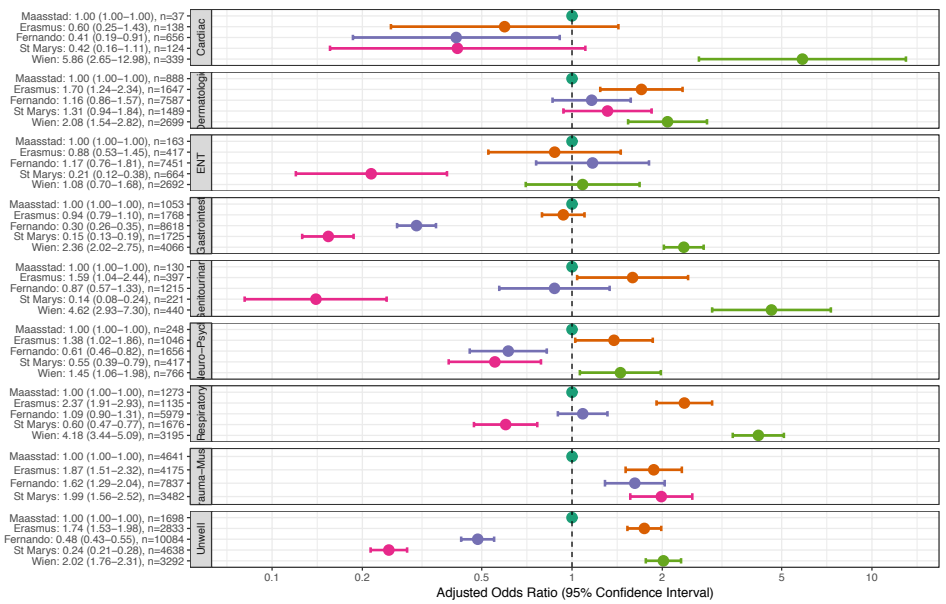
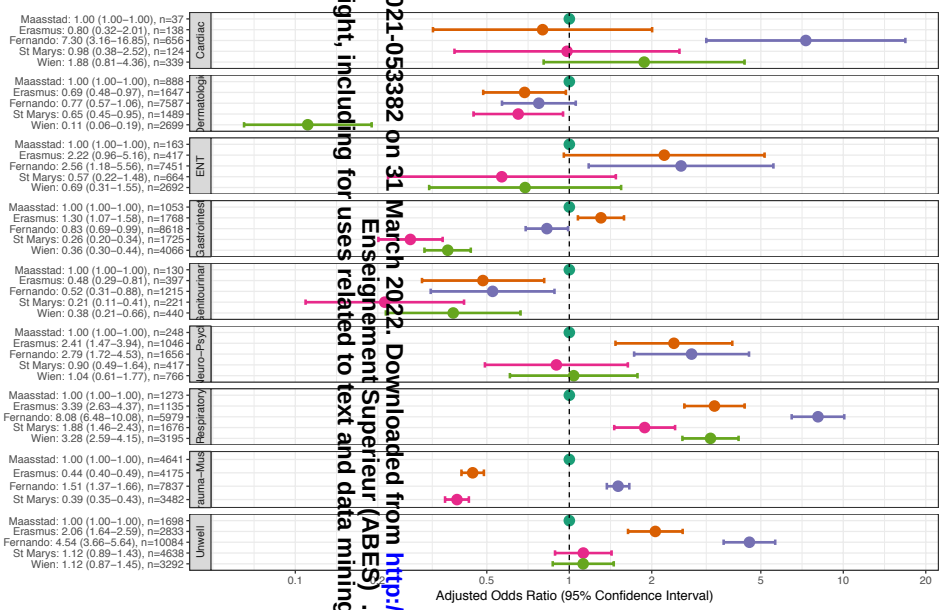
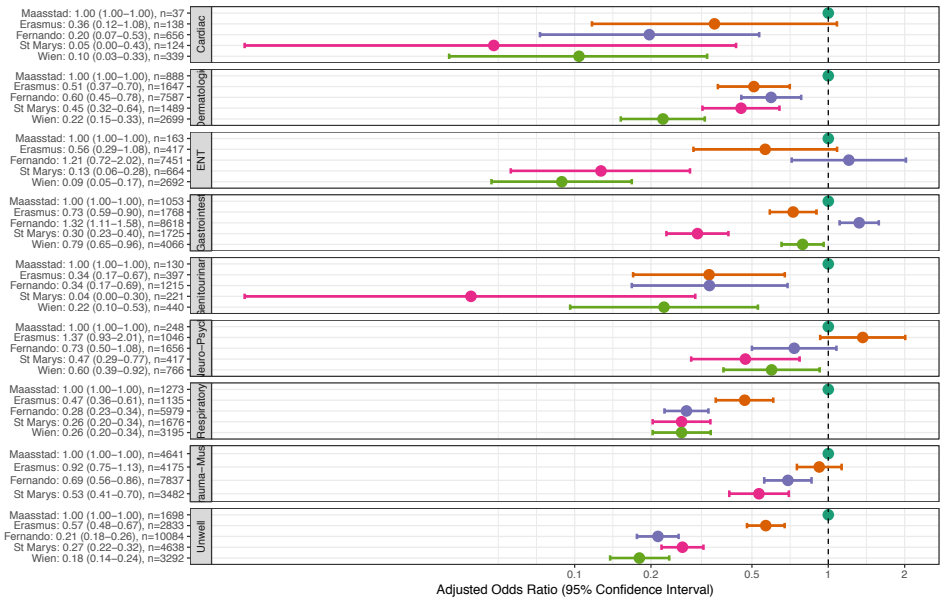
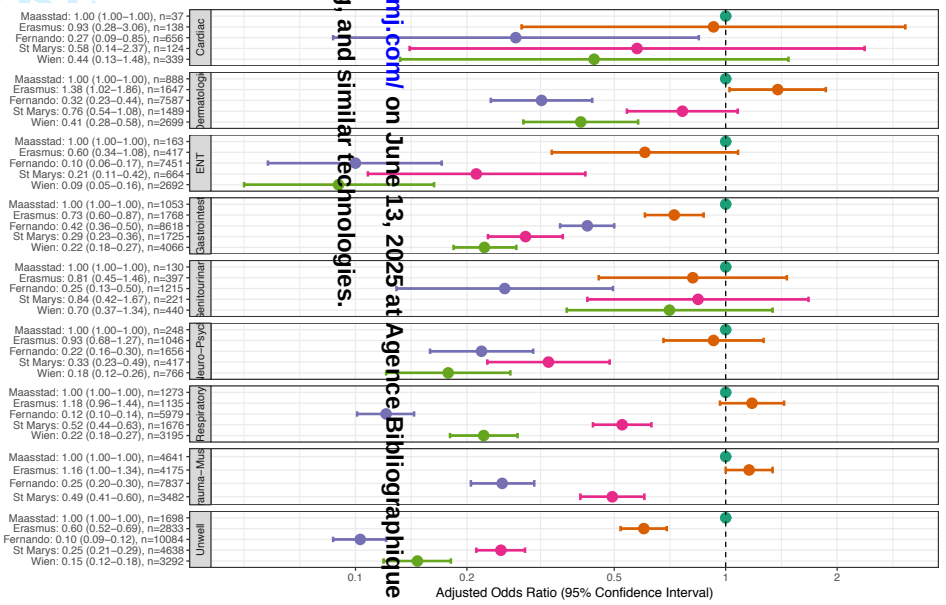
Figure 1



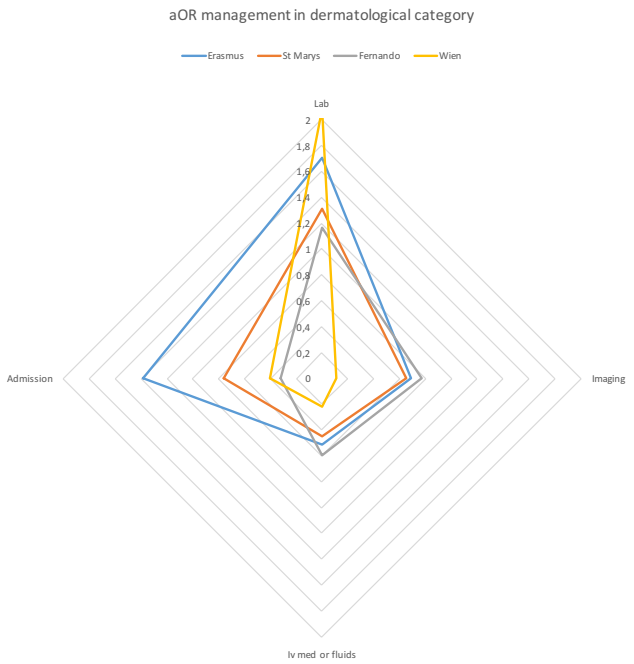


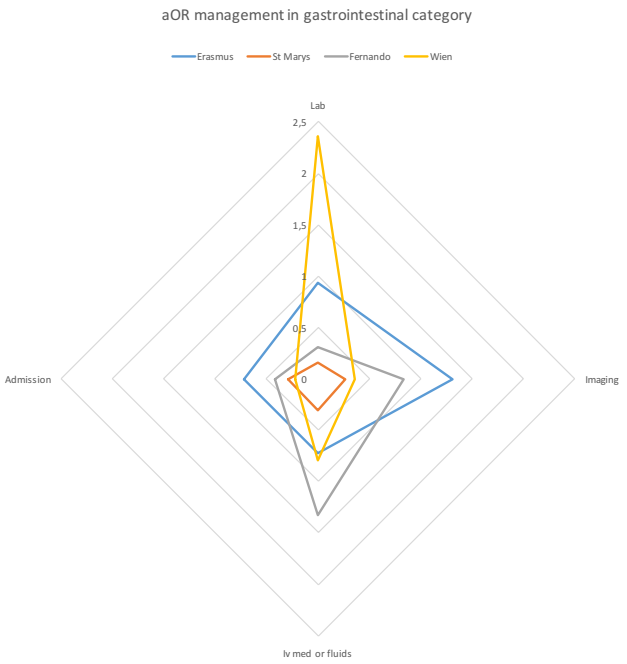


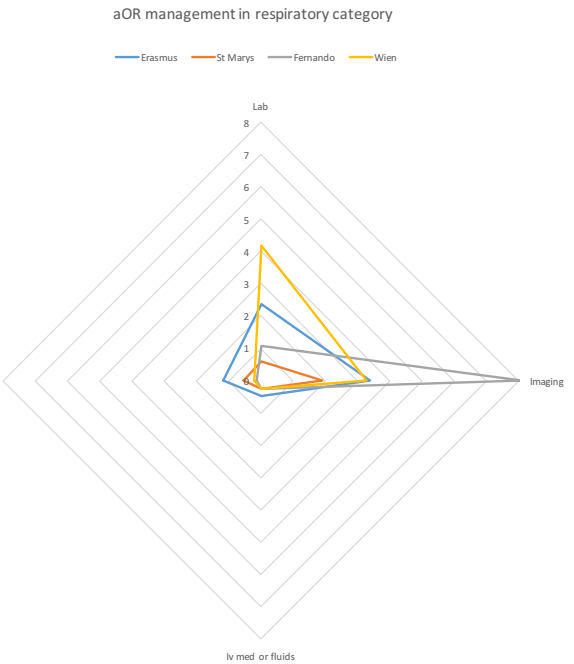


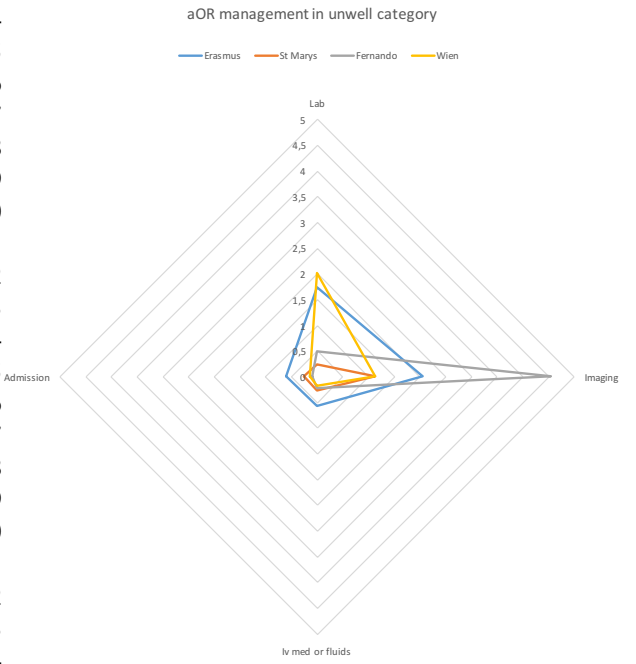
OR are adjusted for age, gender, MTS urgency category, heart rate, respiratory rate, oxygen saturation, temperature and time of presentation

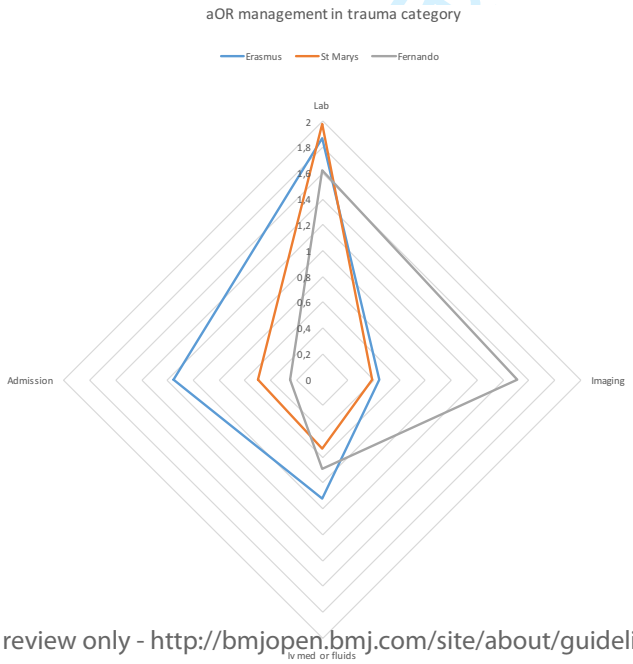
Figure 2











Appendix 1. ED Characteristics

	Maasstad Hospital, Rotterdam, the Netherlands	Erasmus MC, Rotterdam, the Netherlands	Hospital Fernando da Fonseca, Lisbon, Portugal	St Mary's Hospital, London, United Kingdom	General Hospital, Vienna, Austria
Hospital characteristics	Teaching hospital 59 pediatric beds	University hospital 60 pediatric beds	Community hospital 91 pediatric beds	University hospital 46 pediatric beds	University hospital 74 pediatric beds
Catchment area	Urban Generally low socio-economic status	Urban Mixed high and low socio-economic status	Mixed urban and rural Generally low socio-economic status	Urban Mixed high and low socio-economic status	Urban Mixed high and low socio-economic status
Emergency department characteristics	Mixed adult-pediatric 9500 children/year	Pediatric only till October 2014, from then on mixed 6500 children/year	Pediatric only 60,000 children/year	Pediatric only 27,000 children/year	Pediatric only 22,000 children/year
Supervising physician	Pediatrician	Pediatrician	Pediatrician	Pediatric emergency physician	Pediatrician
Inclusion period	01-05-2014 to 31-10-2015	01-01-2012 to 31-12-2014	01-03-2014 to 28-02-2015	01-07-2014 to 28-02-2015	01-01-2014 to 31-12-2014
Number of patients included	10,484	13,968	53,175	15,027	19,268
Primary care availability	24/7	24/7	Daytime and evenings	Daytime and evenings	Daytime
Referral by emergency service	4.5%	8.9%	4.0%	5.6%	Not available
Self-referral	17%	27%	96%	82%	>90%*
Comorbidity in all children	<10%*	38%	<10%*	11%	10%

Appendix 2. MTS presentational flow charts reclassified into 10 presentational flow chart categories

Category	MTS presentational flow charts[15]
Cardiac	Chest pain, palpitations
Dermatologic	Abscesses and local infections, bites and stings, burns and scalds, rashes, Wounds
Ear Nose Throat	Ear problems, facial problems, sore throat
Gastrointestinal	Abdominal pain in adults, abdominal pain in children, diarrhoea and vomiting, gastrointestinal bleeding
Neurologic, psychiatric and intoxications	Apparently drunk, behaving strangely, collapsed adult, fits, Headache, mental illness, overdose and poisoning, self-harm
Respiratory	Asthma, shortness of breath in adults, shortness of breath in children
Trauma/Muscular	Assault, back pain, falls, head injury, limping child, limb problems, major trauma, neck pain, torso injury
Unwell	Crying baby, irritable child, unwell adult, unwell child, worried parent
Urinary/gynaecological	Pregnancy, per vaginum bleeding, sexually acquired infection, testicular pain, urinary problems
Other	Allergy, dental problems, diabetes, eye problems, exposure to chemicals, foreign body, major incidents

The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found		RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and time period within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Title Database: Method Title Not applicable
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported			Present
Objectives	3	State specific objectives, including any prespecified hypotheses			Present
Methods					
Study Design	4	Present key elements of study design early in the paper			Present
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			Present

Participants	6	*(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed *Case-control study* - For matched studies, give matching criteria and the number of controls per case		RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	Method Method Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.		RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Methods
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group			Methods

Bias	9	Describe any efforts to address potential sources of bias			Methods
Study size	10	Explain how the study size was arrived at			Methods
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why			Methods
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed *Case-control study* - If applicable, explain how matching of cases and controls was addressed *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses			Methods
Data access and cleaning methods		..		RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.	Methods

				RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	
Linkage		..		RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	Not applicable
Results					
Participants	13	(a) Report the numbers of individuals at each stage of the study (*e.g.*, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram		RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	Methods/results
Descriptive data	14	(a) Give characteristics of study participants (*e.g.*, demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest (c) *Cohort study* - summarise follow-up time (*e.g.*, average and total amount)			
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time *Case-control study* - Report numbers in each exposure			

		category, or summary measures of exposure *Cross-sectional study* - Report numbers of outcome events or summary measures			
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period			
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses			
Discussion					
Key results	18	Summarise key results with reference to study objectives			
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Discussion/limitation.
Interpretation	20	Give a cautious overall interpretation of results considering objectives,			

		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence			
Generalisability	21	Discuss the generalisability (external validity) of the study results			
Other Information					
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based			
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	Statement

*Reference: Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.