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Relationship between Time of Day of Medical Emergency Team Activations and Outcomes of Hospitalized Pediatric Patients

Joshua Feder[1] Christa Ramsay[2] Anne Tsampalieros[3] Nick Barrowman[3] Kara Richardson[2] Sara Rizakos[4] Julia Sweet[4] James Dayre McNally[2,5] Anna-Theresa Lobos[5]

[1] Department of Pediatrics, Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada
[2] Department of Respiratory Therapy, Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada
[3] Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada
[4] MD Candidate, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[5] Division of Critical Care, Children's Hospital of Eastern Ontario, Department of Pediatrics, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

Address for correspondence Anna-Theresa Lobos, MD, FRCPC, Division of Critical Care, Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa, Ontario, K1H 8L1, Canada (e-mail: alobos@cheo.on.ca).

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Abstract

This study was conducted to investigate whether outcomes of medical emergency team (MET) activations differ by time of day of in-hospitalized pediatric patients. This is a retrospective cohort study. Data were extracted from the charts of 846 patients (with one or more MET activations) over a 5-year period. It was conducted at Children's Hospital of Eastern Ontario, a tertiary pediatric hospital in Ottawa, Canada, affiliated with University of Ottawa. Patients included children <18 years, admitted to a pediatric ward, who experienced a MET activation between January 1, 2016 and December 31, 2020. We excluded patients reviewed by the MET during a routine follow-up, planned pediatric intensive care unit (PICU) admissions from the ward, and MET activation in out-patient settings, post-anesthesia care unit, and neonatal intensive care unit. There was no intervention. A total of 1,230 MET encounters were included as part of the final analysis. Daytime (08:00–15:59) MET activation was associated with increased PICU admission (25.3%, $p = 0.04$). There was some evidence of a higher proportion of critical deterioration events (CDEs) during daytime MET activation; however, this did not reach statistical significance (24%, $p = 0.09$). The highest MET dosage occurred during the evening hours, 16:00 to 23:59 (15/1,000 admissions), and it was lowest overnight, 00:00 to 07:59 (8.8/1,000 admissions, $p < 0.001$). This period of lowest MET dosage immediately preceded the highest likelihood of PICU admission (08:00, 37.5%) and CDE (09:00, 30.2%). Following the period of lowest MET activity overnight, MET activations during early daytime hours were associated with the highest likelihood of unplanned PICU admission and CDEs. This work identifies potential high-risk periods for undetected critical deterioration and targets for future quality improvement.

Keywords
- pediatric
- critical care
- medical emergency team
- rapid response system
- critical deterioration events
- PICU admission

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Introduction

Following hospital admission, children admitted to in-patient wards remain at risk of clinical deterioration.[1] Given children's propensity to compensate for physiologic derangements, timely identification of acute deterioration is essential to improving patient outcomes.[2] Studies demonstrate that delayed identification of deterioration significantly increases the likelihood of unplanned pediatric intensive care unit (PICU) admission, more severe illness at PICU admission, and higher mortality.[3–6] To help mitigate such outcomes, rapid response systems (RRSs) and medical emergency teams (METs) have been widely implemented across pediatric hospitals.

A MET is composed of critical-care–trained health care providers including a physician and a nurse who, upon activation, respond to deteriorating patients.[7–9] In North America, respiratory therapists are often an additional member of the MET, who are responsible for providing respiratory therapies (i.e., inhaled salbutamol), monitoring and managing pulmonary conditions as well as the technical aspects of respiratory support equipment. Currently, there are strong data supporting the value of pediatric METs as they have been shown to reduce PICU admission from the in-patient ward,[9,10] the duration of clinical instability prior to activation (i.e., latency),[2] in-hospital cardiopulmonary arrest,[11,12] and overall hospital mortality.[2,10–12] With the value of RRS/MET established, recent efforts have turned to understanding operations and optimizing performance with many studies focused on the RRS-afferent limb.

The afferent limb of the RRS is focused on factors that contribute to detection of clinical deterioration and the MET activation.[13] The dose–response relationship between the MET activation rate (i.e., MET dosage, # activations/1,000 admissions) and patient outcomes has been well studied and in both pediatrics and adult populations; a low MET dosage has been associated with worse patient outcomes.[9,14] Further, failure to detect or delays in identification of clinical change increase unplanned pediatric and adult intensive care unit (ICU) admission rate and lead to worse patient outcomes.[15–19] Recent adult studies have shown significant differences in activation rates and patient outcomes depending on the time of day with more frequent calls at night and worse patient outcomes following nighttime MET activation.[15,20–23] These differences may occur due to variation in staffing, physician experience, overnight monitoring policies, and MET composition. Furthermore, these nighttime MET activations have been shown to follow hours of undetected clinical changes, leading to patient deterioration and unplanned ICU admission.[24,25]

Currently the literature describing the impact of time of day on hospitalized pediatric patients is sparse.[15,20–23] The overall objective of this study is to investigate whether outcomes of MET activations differ by time of day of the activation in hospitalized pediatric patients. Our primary outcome is unplanned PICU admission. Secondary outcomes included critical deterioration events (CDEs) as well as admission-level outcomes for total hospital and PICU length of stay (LOS).

Materials and Methods

Study Design and Setting

Children's Hospital of Eastern Ontario (CHEO) Research Ethics Board approved this study (study approval number: #19/110X). This is a cohort study of hospitalized pediatric in-patients, less than 18 years old, who were admitted to an in-patient ward and received a MET activation at CHEO from January 1, 2016 to December 31, 2020. CHEO is a tertiary care pediatric hospital affiliated with the University of Ottawa, accredited for training by the Royal College of Physicians and Surgeons of Canada. CHEO has 170 inpatient beds including a 10-bed, mixed cardiac and medical-surgical PICU (500–600 admissions per year). CHEO does not have a step-down or high-dependency unit.

Description of MET

A detailed description of the CHEO RRS has been previously described.[12] Team composition at CHEO varies by time of day. During daytime hours (08:00–15:59), the team is composed of a PICU attending, PICU registered nurse (RN), and respiratory therapist. During evening (16:00–23:59) and overnight (00:00–07:59) hours, in addition to the PICU RN and respiratory therapist, the MET physician coverage is provided by an in-house PICU fellow and senior pediatric resident, with PICU attending backup (generally not in-house). The MET responds to hospitalized in-patients and outpatient clinic settings. The MET does not respond to patients in the emergency department. Our hospital MET recommends activation based on published age-specific criteria: airway threat, apnea, hypoxemia, moderate to severe respiratory distress, tachypnea, hypotension, tachycardia or bradycardia, poor peripheral perfusion, acute drop in Glasgow Coma Scale by greater than two points, seizure, or other change in neurological status.[10] Any member of the health care team and all nonmedical caregivers may activate the MET.[10]

Sources of Data

The study cohort consisted of all patients admitted to one of the pediatric wards at CHEO between January 1, 2016 and December 31, 2020. The sample was selected based on admissions during this 5-year period. A formal sample size calculation was not performed. Patients were excluded if they were >18 years old, or were never admitted to an in-patient ward. We excluded patients admitted to PICU from a routine post-PICU discharge follow-up visit, a planned MET activation (i.e., initiation of noninvasive ventilation [NIV] for home use setup in stable, chronic conditions such as sleep apnea, which do not represent unexpected clinical decompensation), outpatients, patients in the post-anesthesia care unit, or transfers from NICU.

MET Encounter

As patients may have multiple MET activations during an admission, an entity referred to as a "MET encounter" was created. A MET encounter was defined as the time from initial MET activation until the MET signs off from being

involved in patient care. The encounter duration may range from hours to days and may include a single or multiple assessments by the MET. If a subsequent activation occurs following MET sign off, a new MET encounter begins. MET encounters were classified according to the timing of the initial activation, as either daytime (08:00–15:59), evening (16:00–23:59), or overnight (00:00–07:59). These time periods were selected due to variations in MET composition, ward physician staffing, nursing and respiratory therapist workflow. Patients with multiple activations during their admission were categorized based on the timing of their initial activation, within each MET encounter.

Data Collection

Clinical data were extracted retrospectively using the hospital electronic medical records (EMRs), including but not limited to demographics, comorbidities, technology dependence, and most responsible service. Patients who had more than one MET encounter were included multiple times, and linked using an identifying key. Information related to MET activations is collected prospectively by the MET at the time of patient assessment and stored in the patient's EMR. This includes timing of activation, vital signs at the time of activation, reason for activation, and whether the patient was admitted to the PICU following the initial activation or MET follow-up. Vital sign data available from the patient chart were used to determine whether they achieved MET activation criteria as outlined by Tibballs and Kinney.[10]

Outcomes and Patient Characteristics

All outcomes were compared across three time intervals (daytime, evening, overnight). The primary outcome was the proportion of MET activations that resulted in PICU admission. Secondary outcomes were MET dosage, proportion of CDE, and PICU and total hospital LOS (from initial time of MET activation). In this study, CDE is defined as NIV, intubation, vasopressor infusions, dialysis, extracorporeal membrane oxygenation (ECMO), and antiepileptic infusions within 12 hours of PICU admission.[6] Of note, high flow nasal cannula (HFNC) therapy was not included in the definition of CDE as this therapy can be instituted on the pediatric ward and does not require PICU admission. We also reported on patient mortality, although due to very few deaths, we did not perform any statistical comparisons.

The Clinical Classifications Software (CCS) was used to present admission diagnoses using the International Classification of Diseases 10th Revision (ICD-10) coding system, which has been used in prior pediatric studies.[12,26] ICD-10 codes were also used to identify patients with complex chronic conditions using the framework established by Feudtner and colleagues.[27]

Statistical Analysis

All statistical analyses were performed using R statistical software version 4.0.2. Means with standard deviations for normally distributed continuous variables and median with interquartile range for nonnormally distributed variables were calculated. Categorical variables were described using frequencies and percentages. Holm's method was used for multiple testing. The unit of analysis was the encounter for all characteristics and outcomes, other than LOS where the unit of analysis was each patient's first admission. For patients who were admitted to the PICU on their first hospital admission, PICU LOS was calculated. A chi-squared test was performed to test for differences in proportion by encounter time category (daytime 8:00–15:59 vs. evening 16:00–23:59 vs. overnight 00:00–07:59). Where counts were small, Fisher's exact test was used. A Kruskal–Wallis test was performed to test for differences in the age at time of activation and latency time by encounter time. A Kruskal–Wallis test was performed to test for differences in a patient's LOS (hospital and PICU) by encounter time. The proportion of MET activations by hour of day was calculated, together with 95% multinomial confidence intervals (CIs).[28] A chi-square goodness-of-fit test was used to test equality of those proportions. The proportion of MET calls that resulted in a PICU admission directly from that encounter and the proportion which resulted in a CDE within 12 hours after admission were calculated. The Wilson score method was used to generate 95% CIs around these proportions. MET dosage, defined as MET activations per admission, was modeled as a Poisson random variable with log number of admissions as an offset to estimate the overall rate and rate according to time interval, with 95% CIs. Two-sided *p*-values less than 0.05 were considered statistically significant.

Results

Cohort Development and Details

Over the 5-year study period, there were 1,585 MET activations from 846 discrete patients. From the 1,585 MET activations, 1,402 MET encounters were identified. Of these, 172 encounters were removed from the analysis because they met at least one exclusion criterion, leaving 1,230 encounters for analysis. ►**Supplementary Fig. S1** (available in online version only) illustrates the flow chart. Among the final cohort, there were 422 total admissions to PICU.

MET Encounters and MET Dosage

►**Fig. 1(A)** depicts the proportion of MET calls by time of encounter at each hour interval. There were 434 total MET encounters during daytime (08:00–15:59), 502 during evening (16:00–23:59), and 294 overnight (00:00–07:59) (35.3% vs. 40.8% vs. 23.9% respectively, $p < 0.001$). An increasing trend was observed in the MET activations during the daytime, a plateau in the evening, and a decreasing trend during the overnight period. When evaluated by hour interval, the lowest number of calls was between 07:00 and 07:59 (26, 2.1%), with the highest between 18:00 and 18:59 (78, 6.3%). The overall MET activation rate or "dose" during the study period was 38.8 MET activations per 1,000 admissions. ►**Fig. 1B** illustrates the average MET dosage (# of MET activations per 1,000 admissions) across the three time periods. MET dosage was 8.8 overnight, 13.0 in the daytime, and 15.0 in the evening ($p < 0.001$).

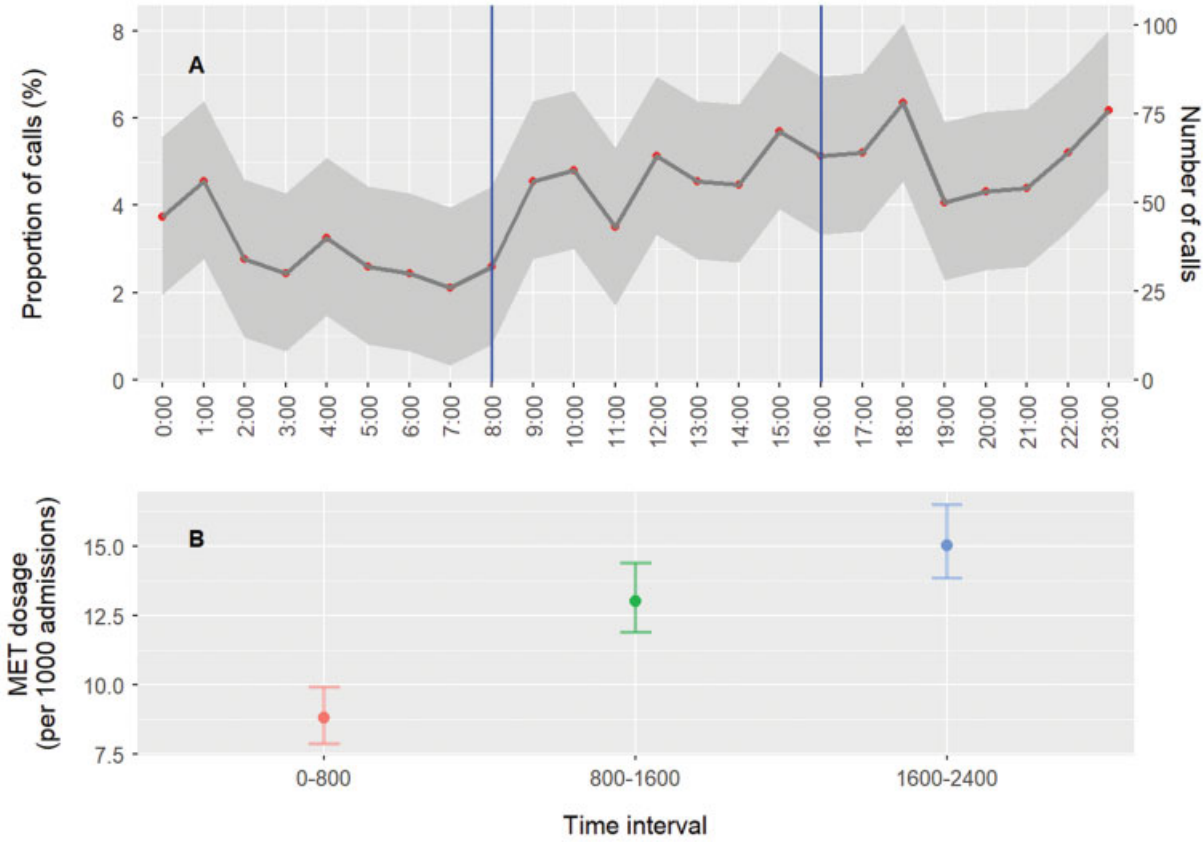

Fig. 1 (A) Percentage of medical emergency team (MET) calls by time of encounter and (B) dosage by encounter time interval. (A) The vertical axis on the left is the percent of MET call by time of encounter and the vertical axis on the right is the absolute number of calls by time of encounter. The gray shading illustrates the 95% confidence interval (CI) bands around each proportion. Please note that for each time listed, it implies that hour (i.e., 7:00 = 07:00–07:59). (B) There were 1,229 encounters and 33,376 admissions overall. The overall MET dosage is 36.8 per 1,000 admissions (95% CI: 34.8–38.9). MET dosage by 8-hour intervals. There were 294 encounters between 00:00 and 08:00 and the MET dosage is 8.8 per 1,000 admissions (95% CI: 7.8–9.9). There were 434 encounters between 08:00 and 16:00 and the MET dosage is 13.0 per 1,000 admissions (95% CI: 11.8–14.3). There were 501 encounters between 16:00 and 00:00 and the MET dosage is 15.0 per 1,000 admissions (95% CI: 13.7–16.4).

►**Table 1** illustrates the characteristics of the study patients as well as between-group differences between daytime, evening, and overnight activations. After correcting for multiple testing, no *p*-values were less than 0.05.

Patient Outcomes

Differences between daytime, evening, and overnight MET activations leading to unplanned PICU admission, CDEs, and differences in LOS (PICU and total hospital LOS) are reported in ►**Table 2**. Patients were more likely to be admitted to the PICU following daytime MET activation compared with other time periods; however, this did not reach statistical significance (38.7% vs. 32.1% vs. 31.6%, $p = 0.06$). There difference was statistically significant when only considering PICU admission following the initial MET activation within the MET encounter (25.3% vs. 21.1% vs. 17.7% respectively, $p = 0.04$). ►**Fig. 2A** graphically depicts the proportion of MET activations by time of day that result in PICU admission. The highest likelihood of PICU admission occurred between 08:00 and 09:00 (20, 37.5%), with the lowest at 07:00 (3, 11.5%). The most prominent change in proportion needing admission to the PICU occurred between the 07:00 and 08:00 hours followed by a slight downward slope during the remainder of daytime hours.

►**Fig. 2B** graphically depicts the proportion of MET calls by time of day, resulting in CDEs. The proportion of CDEs by time of day differed, particularly between daytime (24%) and overnight (17.7%) activations; however, this did not reach statistical significance ($p = 0.09$). The lowest likelihood of CDE occurred at 00:00 (3, 6.8%), which was followed by a gradual increasing trend during the overnight period, reaching a peak at 09:00 (18, 30.2%).

Median total hospital LOS was longer for patients requiring daytime activations compared with evening and overnight activations (9.9 vs. 7.7 vs. 6.5 days, respectively, $p = 0.01$). In addition, patients with daytime activation had longer PICU LOS as well; however, this did not reach statistical significance ($p = 0.06$).

There were 14 deaths over the entire study period. Of the 14 children who died, 7 had daytime MET activations, 4 had evening, and 3 had overnight. None of the patients died at the time of MET activation or as part of a CDE (i.e., within 12 hours of admission to PICU).

Table 1 Characteristics of patients at the time of encounter at the encounter level

Overall $n = 1{,}230$ encounters				
Characteristic	**Daytime encounters (8:00–15:59), $n = 434$**	**Evening encounters (16:00–23:59), $n = 502$**	**Overnight encounters (0:00–7:59), $n = 294$**	***p*-Value**
Age (y), median (IQR)	2.0 (0.4–9.2)	2.3 (0.4–12.6)	2.7 (0.4–10.1)	0.38
Sex, male *n* (%)	243 (56.0%)	280 (55.8%)	171 (58.2%)	0.79
Airway disease	42 (9.7%)	61 (12.2%)	28 (9.5%)	0.36
Respiratory disease	90 (20.7%)	99 (19.8%)	58 (19.8%)	0.93
Cardiac disease	105 (24.2%)	101 (20.2%)	50 (17.0%)	0.06
GI disease	103 (23.8%)	126 (25.2%)	56 (19.0%)	0.13
Neurologic disease	129 (29.8%)	107 (21.4%)	69 (23.5%)	0.01
Endocrine disease	38 (8.8%)	32 (6.4%)	16 (5.4%)	0.18
Renal disease	49 (11.3%)	30 (6.0%)	16 (5.4%)	0.003
Heme disease	26 (6.0%)	18 (3.6%)	9 (3.1%)	0.10
Oncological disease	37 (8.5%)	43 (8.6%)	17 (5.8%)	0.30
Rheumatological disease	6 (1.4%)	6 (1.2%)	3 (1.0%)	0.95
Infectious disease[a]	7 (1.6%)	2 (0.4%)	4 (1.4%)	0.15
Congenital disease	104 (24.0%)	101 (20.2%)	65 (22.2%)	0.38
Born premature	67 (15.5%)	64 (12.9%)	31 (10.6%)	0.15
Comorbidities				0.05
None	135 (31.1%)	177 (35.3%)	112 (38.1%)	
1	98 (22.6%)	134 (26.7%)	74 (25.2%)	
2+	201 (46.3%)	191 (38.0%)	108 (36.7%)	
Technology dependence				
Tracheostomy or tracheostomy and ventilated	9 (2.1%)	16 (3.2%)	6 (2.0%)	0.46
NIPPV	17 (3.9%)	11 (2.2%)	12 (4.1%)	0.22
Service admitted				0.003
General pediatrics	289 (66.6%)	308 (61.4%)	213 (72.4%)	
Subspecialty pediatrics	91 (21.0%)	111 (22.1%)	46 (15.6%)	
General or subspecialty surgery	52 (12.0%)	60 (12.0%)	28 (9.5%)	
Psychiatry/adolescent medicine	1 (0.2%)	22 (4.4%)	6 (2.0%)	
Other	1 (0.2%)	1 (0.2%)	1 (0.3%)	

Abbreviations: GI, gastrointestinal; IQR, interquartile range; NIPPV, noninvasive positive-pressure ventilation.
Note: Proportions were compared using chi-squared tests or Fisher's exact test, as appropriate. A Kruskal–Wallis test was performed to test for differences in the age at the time of activation and latency time by encounter time.
[a]After correcting for multiple tests there is little evidence for difference between groups, with the exception of service admitted and renal disease ($p = 0.057$ for both).

Characteristics of Initial MET Activation within Each MET Encounter

►**Table 3** depicts between-group differences (daytime, evening, and overnight) in characteristics of initial MET activation. There was evidence for between-group differences in the reason for activation ($p = 0.01$, after correcting for multiple tests). Concerns regarding a patient's "breathing" were the most reported activation reason in all three time periods.

Post-hoc Exploration of Observations

We observed a significant decline in MET dosage overnight (00:00–07:59) immediately followed by a sharp rise in the likelihood of PICU admission at 08:00 and CDE at 09:00.

Discussion

This study investigates the relationship between time of day of MET activations and outcomes in hospitalized pediatric

Table 2 Outcomes of interest by time of encounter

Outcome of interest				*p*-Value
n = 1,230 encounters	Daytime encounters (8:00–15:59), *n* = 434	Evening encounters (16:00–23:59), *n* = 502	Overnight encounters (0:00–7:59), *n* = 294	
Admitted to PICU at the time of initial activation (within the encounter)	110/434 (25.3%)	106/502 (21.1%)	52/294 (17.7%)	0.04
Admitted to PICU on MET follow-up[a]	58/324 (17.9%)	55/398 (13.8%)	42/246 (17.1%)	0.32
Any admission to PICU from MET encounter (activation + follow-up)	168/434 (38.7%)	161/502 (32.1%)	93/294 (31.6%)	0.06
Critical deterioration event within 12 hours of any subsequent PICU admission[b]	104/433 (24.0)	99/501 (19.8)	52/294 (17.7)	0.09
n = 846 patients	*n* = 273 patients	*n* = 353 patients	*n* = 220 patients	
LOS in hospital for first admission[c] (d), median (IQR)	9.9 (4.3–21.2)	7.7 (3.8–17.9)	6.5 (3.4–16.4)	0.01
n = 277 patients with at least one PICU admission during their first hospital admission	*n* = 100	*n* = 109	*n* = 68	
LOS of first PICU admission (d), median (IQR)	3.9 (1.9–9.0)	3.5 (1.7–6.0)	3.6 (2.1–8.3)	0.04

Abbreviations: IQR, interquartile range; LOS, length of stay; MET, medical emergency team; PICU, pediatric intensive care unit.
Note: Proportions were compared using chi-squared tests or Fisher's exact test, as appropriate. A Kruskal–Wallis test was performed to test for differences in the age at the time of activation and latency time by encounter time.
[a]Includes those who did not get admitted to the PICU at initial encounter.
[b]Includes noninvasive ventilation, intubation, ventilation via tracheostomy, ECMO, inotropes/pressors, dialysis, antiepileptic infusion within 12 hours of admission among those who had available information.
[c]Time of initial activation to time of d/c.

patients. Our study found that MET activations during daytime hours (08:00–15:59) were associated with an increased proportion of unplanned PICU admission compared with evening (16:00–23:59) and overnight (00:00–07:59) activations. The time period associated with the highest risk of unplanned PICU admission (08:00–08:59) immediately follows the period with the lowest MET activation rate, i.e., MET dosage (00:00–07:59). Furthermore, results of this study suggest that patients who required early daytime MET activation appeared to suffer worse outcomes, as shown by the increased likelihood of CDEs at 09:00 to 09:59, and prolonged PICU and total hospital LOS.

Our findings are consistent with a large pediatric study out of Cincinnati Children's (a 634-bed quaternary care hospital with a 35-bed PICU) that reviewed 3,115 MET activations and also described a low MET activation rate in the overnight hours with a peak in the early daytime period.[29] We build on their findings by proving that the MET dosage is significantly lower in the overnight period. More so, we add important clinical knowledge by examining key patient outcomes and their relationship to time of day. Specifically, we describe novel findings of higher rates of unplanned PICU admission and CDE immediately following this period of low MET dosage overnight. Additionally, our finding of higher rates of unplanned PICU admission in the daytime is consistent with a study of 542 MET activations from Nicklaus Children's Hospital in Miami (a 289-bed pediatric hospital with a 40-bed PICU).[30] We add to their results by having examined outcomes by 1-hour intervals, which allowed us to make more specific conclusions regarding the impact of time of day. We are the first pediatric study to examine the impact of time of day on both MET dosage and patient outcomes following MET activation, while describing key relationships between the two.

Our study demonstrates differences in patient outcomes depending on the timing of MET activation. We report a higher rate of unplanned PICU admission following daytime MET activation and a significant increase in the likelihood of unplanned PICU admission at 08:00, immediately following the period of lowest MET dosage overnight (00:00–07:59).[20,29–31] Our results suggest that important clinical deterioration may go undetected overnight in hospitalized pediatric patients leading to sicker patients by morning and consequently higher likelihood of unplanned PICU admission in the daytime. This may occur for several reasons. First most Canadian pediatric inpatient wards have reduced nursing-to-patient ratios during the evening and are less likely to have attending pediatricians in-house, as well as fewer

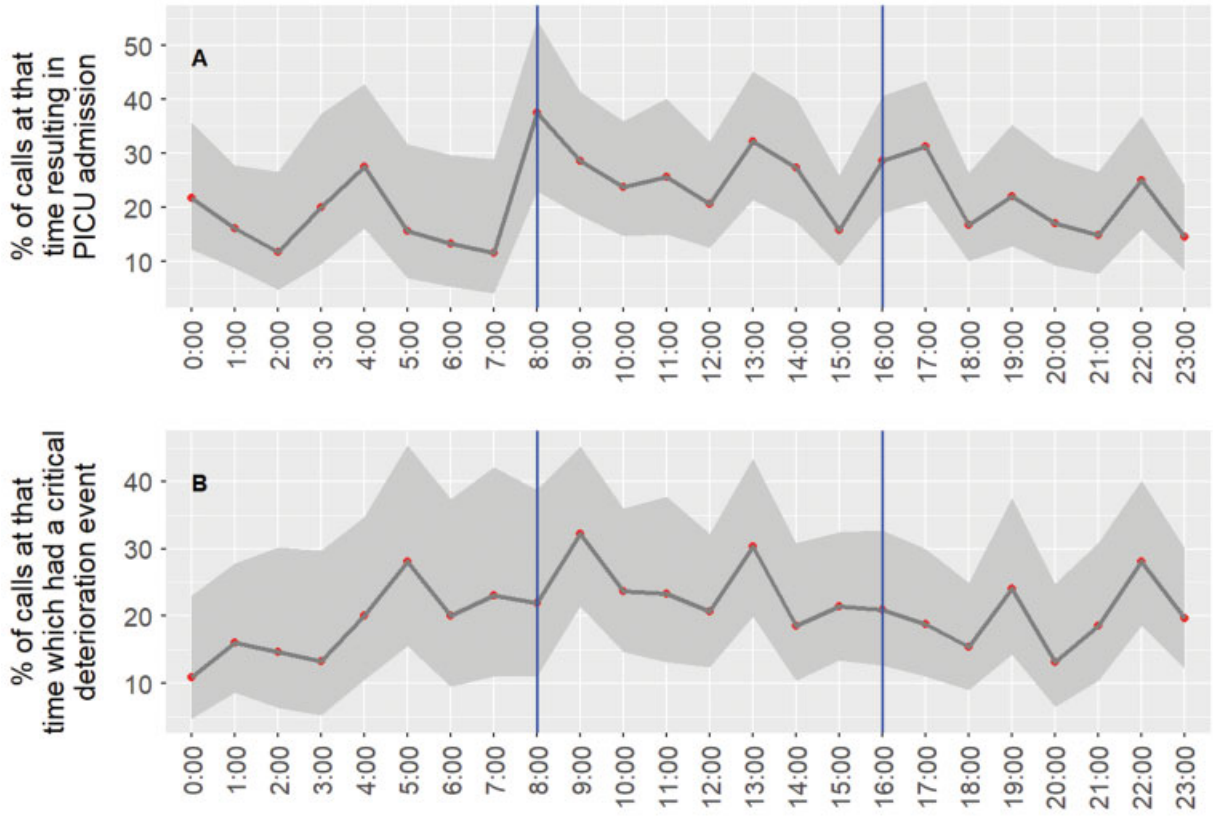

Fig. 2 Percentage of MET calls leading to (**A**) PICU admission and (**B**) critical deterioration event. The vertical axis on the left is the percent of MET calls by time of encounter that had a (A) PICU admission or (B) a critical deterioration event within 12 hours from the initial encounter. The gray shading represents 95% confidence interval bands around each proportion of calls with the outcome. Panel A: The lowest proportion of PICU admissions was between 7 and 759 a.m., $n = 3$ (11.5%), and the highest proportion between 8 and 859 a.m., $n = 20$ (37.5%). Panel B: The lowest proportion of critical deterioration events was between 0 and 0:59 a.m., $n = 4$ (10.9%), and the highest proportion between 9 and 959 a.m., $n = 18$ (32.1%). PICU, pediatric intensive care unit.

medical trainees.[15,32–34] Studies suggest that overnight understaffing of nurses and physicians is associated with poor patient outcomes, increased individual nursing responsibility, and therefore less frequent patient monitoring and impaired detection of patient decompensation.[20,32,35] Second, in academic hospitals, inpatient wards are often covered overnight by trainees with less experience than attending staff. Furthermore, nighttime trainees are often also tasked with managing competing priorities such as admissions from the emergency department or consultations on off-service (i.e., general surgery patient admitted on the geographical oncology ward) patients, further reducing physician availability to assess ward patients.[15,33] Lastly, sleep deprivation is common among health care workers and can result in impaired cognitive performance and clinical judgment.[15,34,36,37] Cumulatively, these conditions may lead to infrequent monitoring and a higher likelihood of undetected clinical changes in hospitalized patients overnight, which are then discovered by daytime staff early in their shift.[31] In addition to the reasons above, another potential explanation for the differences observed between nighttime and daytime is the difference in physician presence. The PICU attending is present at each daytime MET activation bringing significant expertise and the added ability to advocate for immediate patient transfer.

Our study is the first to investigate the impact of diurnal variation on the rate of CDEs in pediatric patients. CDEs were originally described by Bonafide et al as a more relevant metric to evaluate pediatric MET performance given that cardiopulmonary arrest and mortality rates are extremely low in children.[6] Of further importance, CDEs are reported to be independently associated with a fivefold increase in in-hospital pediatric mortality and their frequency to be significantly reduced by MET implementation.[6] While Bonafide et al included NIV, intubation, and vasoactive infusion initiation within 12 hours of admission, we expanded our definition of CDE to include the initiation of dialysis, ECMO, and antiepileptic infusions, given that these interventions require PICU admission at our institution.[6] We found some evidence that patients admitted following daytime activation were more likely to experience a CDE than other time periods.[20,31,38] Although we were unable to extract whether the specific patients who were missed overnight were those who experienced a CDE, we hypothesize our finding may be due to undetected clinical deterioration overnight, resulting in more unstable patients by morning, thus requiring rapid

Table 3 Characteristics of initial medical emergency team activation by time of encounter

Overall, $n = 1{,}230$ encounters				
Characteristic	**Daytime encounters (8:00–15:59), $n = 434$**	**Evening encounters (16:00–23:59), $n = 502$**	**Overnight encounters (0:00–7:59), $n = 294$**	***p*-Value**
MET dosage: MET activations/ 1,000 admissions	13.0	15.0	8.8	<0.001
Reason for call				0.002
Airway threat	20 (4.6%)	23 (4.6%)	12 (4.1%)	
Breathing	226 (52.1%)	215 (42.8%)	135 (45.9%)	
Circulation	61 (14.1%)	74 (14.7%)	70 (23.8%)	
Neurologic	51 (11.8%)	69 (13.7%)	29 (9.9%)	
Caregiver worried	10 (2.3%)	25 (5.0%)	4 (1.4%)	
Health care provider worried	37 (8.5%)	57 (11.4%)	24 (8.2%)	
Other	29 (6.7%)	39 (7.8%)	20 (6.8%)	
Vital signs meeting activation criteria				
Heart rate	101/432 (23.4%)	130/500 (26.0%)	80/293 (27.3%)	0.45
Blood pressure	8/417 (1.9%)	10/475 (2.1%)	13/275 (4.7%)	0.05
Respiratory rate	194/433 (44.8%)	193/497 (38.8%)	111/292 (38.0%)	0.10
Oxygen saturation <90%	28/434 (6.5%)	29/502 (5.8%)	19/294 (6.5%)	0.89
Met any of above criteria[a]	242/415 (58.3)	255/470 (54.3%)	159/274 (58.0%)	0.41
Latency				0.56
< 1 h	187/350 (53.4%)	260/423 (61.5%)	145/264 (54.9%)	
1–4 h	126/350 (36.0%)	137/423 (32.4%)	95/264 (36.0%)	
5–8 h	23/350 (6.6%)	16/423 (3.8%)	17/264 (6.4%)	
> 9 h	14/350 (4.0%)	10/423 (2.4%)	7/264 (2.7%)	

Abbreviation: MET, medical emergency team.
Note: Proportions were compared using chi-squared tests or Fisher's exact test, as appropriate, except for latency, which is presented categorically, but was analyzed using a Kruskal–Wallis test. After correcting for multiple tests, there is little evidence for difference between groups, with the exception reason for call ($p = 0.01$).
[a]Limited to those who had complete set of vital signs ($n = 1{,}159$).

institution of critical therapy upon admission to PICU. This suggests that health care providers may be missing a critical period of patient deterioration overnight and delaying essential critical care interventions.[29] Consistent with other studies, we found that CDEs most frequently occurred in patients needing respiratory support, specifically, NIV across all time periods.[6] Of interest, our reported rates of invasive mechanical ventilation during CDEs are lower than previous studies, which is likely due to widespread use of NIV at our institution.[6]

Overall, our results suggest that the detection of deteriorating patients and subsequent MET activation (afferent limb) are inefficient in the overnight period, with consequently sicker patients and worse outcomes in the early daytime hours. Although a recent adult study in Australia did not find a difference in afferent limb failure (ALF) between daytime and nighttime hours, this has not been specifically investigated in the pediatric MET literature to date.[39] Our finding of a significantly lower MET dosage in the overnight period indicates possible failure to detect deterioration and/or activate the MET. Pediatric studies from our center show that a dose–response relationship between MET dosage and patient outcomes exists, where a lower MET dosage is associated with worse outcomes.[9] Together, these data suggest that deteriorating patients may be undetected overnight leading to worse day-time outcomes. We can support this hypothesis by showing that patients activated in the early daytime hours appear to suffer worse clinical outcomes as 08:00 activations are most likely to result in PICU admission and 09:00 activations are most likely to result in CDEs. Our findings are supported by adult studies that show that ALF is associated with worse outcomes.[20,23] More so, our findings are supported by a large multicenter study that showed worse patient outcomes (i.e., mortality) following daytime PICU admission, particularly early morning admission (06:00–09:59).[40] This is significant because unplanned PICU admission and CDE have been shown to be independent predictors of mortality in hospitalized pediatric patients.[4–6] Possible future initiatives to optimize the afferent limb overnight that have been previously reported may include changes to physician overnight staffing and nursing monitoring policies, implementation of the previously validated Pediatric Early Warning Score, or a formal "Watcher System," both with mandatory activation criteria.[9,25,29]

This article does have a few notable limitations. First, the observational and retrospective nature of the data allows for detection of associations while causality cannot be concluded. Second, our study took place over a 5-year period, which included variability in the acceptable acuity on the in-patient ward (i.e., after September 2018, HFNC no longer required MET activation prior to application on the ward), which may have influenced our primary outcome. In addition, our study described MET activity in one tertiary care pediatric hospital, which may limit generalizability of the results. However, our findings are similar to major adult studies and the only prior small pediatric studies.[20,29–31]

Conclusions

We found that patients requiring early daytime MET activation had overall worse clinical outcomes. We identified a critical period of lowest MET dosage during the overnight hours. We found that immediately following this period of lowest MET activity, patients had the highest likelihood of PICU admission, the highest likelihood of CDE, and increased morbidity (i.e., prolonged PICU and total hospital LOS). Our findings highlight potential high-risk periods for undetected critical deterioration. Our findings also identify targets for future quality improvement aimed at preventing ALF: optimizing the overnight identification of deteriorating pediatric inpatients and reducing preventable acute patient events.

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Conflict of Interest
None declared.

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References

1 Krmpotic K, Lobos AT, Chan J, et al. A retrospective case-control study to identify predictors of unplanned admission to pediatric intensive care within 24 hours of hospitalization. Pediatr Crit Care Med 2019;20(07):e293–e300
2 Hanson CC, Randolph GD, Erickson JA, et al. A reduction in cardiac arrests and duration of clinical instability after implementation of a paediatric rapid response system. Postgrad Med J 2010;86 (1015):314–318
3 Kause J, Smith G, Prytherch D, Parr M, Flabouris A, Hillman KIntensive Care Society (UK) Australian and New Zealand Intensive Care Society Clinical Trials Group. A comparison of antecedents to cardiac arrests, deaths and emergency intensive care admissions in Australia and New Zealand, and the United Kingdom–the ACADEMIA study. Resuscitation 2004;62(03):275–282
4 El Halal MGDS, Barbieri E, Filho RM, Trotta Ede A, Carvalho PRA. Admission source and mortality in a pediatric intensive care unit. Indian J Crit Care Med 2012;16(02):81–86
5 Odetola FO, Rosenberg AL, Davis MM, Clark SJ, Dechert RE, Shanley TP. Do outcomes vary according to the source of admission to the pediatric intensive care unit? Pediatr Crit Care Med 2008;9(01):20–25
6 Bonafide CP, Localio AR, Roberts KE, Nadkarni VM, Weirich CM, Keren R. Impact of rapid response system implementation on critical deterioration events in children. JAMA Pediatr 2014;168 (01):25–33
7 Jones DA, DeVita MA, Bellomo R. Rapid-response teams. N Engl J Med 2011;365(02):139–146
8 Jones D, Lippert A, DeVita M, Hillman K. What's new with rapid response systems? Intensive Care Med 2015;41(02):315–317
9 Kotsakis A, Lobos AT, Parshuram C, et al; Ontario Pediatric Critical Care Response Team Collaborative. Implementation of a multicenter rapid response system in pediatric academic hospitals is effective. Pediatrics 2011;128(01):72–78
10 Tibballs J, Kinney S. Reduction of hospital mortality and of preventable cardiac arrest and death on introduction of a pediatric medical emergency team. Pediatr Crit Care Med 2009;10(03): 306–312
11 Brilli RJ, Gibson R, Luria JW, et al. Implementation of a medical emergency team in a large pediatric teaching hospital prevents respiratory and cardiopulmonary arrests outside the intensive care unit. Pediatr Crit Care Med 2007;8(03):236–246, quiz 247
12 McKelvie B, McNally JD, Chan J, Momoli F, Ramsay C, Lobos AT. Increased mortality and length of stay associated with medical emergency team review in hospitalized pediatric patients: a retrospective cohort study. Pediatr Crit Care Med 2017;18(06): 571–579
13 DeVita MA, Braithwaite RS, Mahidhara R, Stuart S, Foraida M, Simmons RLMedical Emergency Response Improvement Team (MERIT) Use of medical emergency team responses to reduce hospital cardiopulmonary arrests. Qual Saf Health Care 2004;13 (04):251–254
14 Jones D, Bellomo R, DeVita MA. Effectiveness of the medical emergency team: the importance of dose. Crit Care 2009;13 (05):313
15 Sundararajan K, Flabouris A, Thompson C. Diurnal variation in the performance of rapid response systems: the role of critical care services-a review article. J Intensive Care 2016;4:15
16 Taenzer AH, Spence BC. The afferent limb of rapid response systems: continuous monitoring on general care units. Crit Care Clin 2018;34(02):189–198
17 Difonzo M. Performance of the afferent limb of rapid response systems in managing deteriorating patients: a systematic review. Crit Care Res Pract 2019;2019:6902420
18 Trinkle RM, Flabouris A. Documenting rapid response system afferent limb failure and associated patient outcomes. Resuscitation 2011;82(07):810–814
19 Barbosa V, Gomes E, Vaz S, et al. Failure to activate the in-hospital emergency team: causes and outcomes. Rev Bras Ter Intensiva 2016;28(04):420–426
20 Fernando SM, Reardon PM, Bagshaw SM, et al. Impact of nighttime rapid response team activation on outcomes of hospitalized patients with acute deterioration. Crit Care 2018;22(01):67
21 Molloy J, Pratt N, Tiruvoipati R, Green C, Plummer V. Relationship between diurnal patterns in rapid response call activation and patient outcome. Aust Crit Care 2018;31(01):42–46
22 Galhotra S, DeVita MA, Simmons RL, Schmid Amembers of the Medical Emergency Response Improvement Team (MERIT) Committee. Impact of patient monitoring on the diurnal pattern of medical emergency team activation. Crit Care Med 2006;34(06): 1700–1706
23 Barwise A, Thongprayoon C, Gajic O, Jensen J, Herasevich V, Pickering BW. Delayed rapid response team activation is associated with increased hospital mortality, morbidity, and length of stay in a tertiary care institution. Crit Care Med 2016;44(01): 54–63
24 Sax FL, Charlson ME. Medical patients at high risk for catastrophic deterioration. Crit Care Med 1987;15(05):510–515

25 Parshuram CS, Duncan HP, Joffe AR, et al. Multicentre validation of the bedside paediatric early warning system score: a severity of illness score to detect evolving critical illness in hospitalised children. Crit Care 2011;15(04):R184
26 Valiani V, Gao S, Chen Z, et al. In-hospital mobility variations across primary diagnoses among older adults. J Am Med Dir Assoc 2016;17(05):465.e1–465.e8
27 Feudtner C, Christakis DA, Connell FA. Pediatric deaths attributable to complex chronic conditions: a population-based study of Washington State, 1980-1997. Pediatrics 2000;106(1, Pt 2):205–209
28 Sison CP, Glaz J. Simultaneous confidence intervals and sample size determination for multinomial proportions. J Am Stat Assoc 1995;90(429):366–369
29 Conway SR, Tegtmeyer K, Wheeler DS, Loechtenfeldt A, Stalets EL, Brady PW. Diurnal variation in medical emergency team calls at a tertiary care children's hospital. Pediatr Qual Saf 2020;5(05):e341
30 Humphreys S, Totapally BR. Rapid response team calls and unplanned transfers to the pediatric intensive care unit in a pediatric hospital. Am J Crit Care 2016;25(01):e9–e13
31 Churpek MM, Edelson DP, Lee JY, Carey K, Snyder AAmerican Heart Association's Get With The Guidelines-Resuscitation Investigators. Association between survival and time of day for rapid response team calls in a national registry. Crit Care Med 2017;45 (10):1677–1682
32 Needleman J, Buerhaus P, Pankratz VS, Leibson CL, Stevens SR, Harris M. Nurse staffing and inpatient hospital mortality. N Engl J Med 2011;364(11):1037–1045
33 Wallace DJ, Angus DC, Barnato AE, Kramer AA, Kahn JM. Nighttime intensivist staffing and mortality among critically ill patients. N Engl J Med 2012;366(22):2093–2101
34 Bonafide CP, Localio AR, Song L, et al. Cost-benefit analysis of a medical emergency team in a children's hospital. Pediatrics 2014; 134(02):235–241
35 Neuraz A, Guérin C, Payet C, et al. Patient mortality is associated with staff resources and workload in the ICU: a multicenter observational study. Crit Care Med 2015;43(08):1587–1594
36 Sharpe R, Koval V, Ronco JJ, et al. The impact of prolonged continuous wakefulness on resident clinical performance in the intensive care unit: a patient simulator study. Crit Care Med 2010;38(03):766–770
37 Amirian I, Andersen LT, Rosenberg J, Gögenur I. Working night shifts affects surgeons' biological rhythm. Am J Surg 2015;210(02):389–395
38 Bisbal M, Pauly V, Gainnier M, et al. Does admission during morning rounds increase the mortality of patients in the medical ICU? Chest 2012;142(05):1179–1184
39 Sundararajan K, O'Connell A, Flabouris A, Thompson C. Responding to clinical deterioration: diurnal variation in afferent limb failure. Resuscitation 2021;160:14–15
40 McCrory MC, Spaeder MC, Gower EW, et al. Time of admission to the PICU and mortality. Pediatr Crit Care Med 2017;18(10):915–923

