Critical Care Medicine

Diagnostic Uncertainty Among Critically Ill Children Admitted to the Pediatric Intensive Care Unit: A Multi-Center Study

--Manuscript Draft--

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Abstract:	Objectives: This study aimed to identify the prevlence of and factors associated with diagnostic uncertainty when critically ill children are admitted to the pediatric intensive care unit (PICU). Understanding diagnostic uncertainty is necessary to develop effective strategies to reduce diagnostic errors in the PICU. Design: Multi-center retrospective cohort study with structured medical record review by trained clinicians using a standardized instrument to identify diagnostic uncertainty in narrative clinical notes. Diagnoses and diagnostic uncertainty were compared across time from PICU admission to hospital discharge. Generalized linear mixed models were used to determine patient, clinician, and encounter characteristics associated with diagnostic uncertainty at PICU admission. Setting: Four academic tertiary-referral PICUs. Patients: 882 randomly selected patients 0-18 years old who were non-electively admitted to participating PICUs. Interventions: None Measurements and Main Results: PICU admission notes for 228 of 882 (25.9%) patients indicated diagnostic uncertainty. Multivariable analysis showed that patients admitted during daytime weekdays were less likely to have diagnostic uncertainty at admission (OR 0.59, p=0.037), while patients who had more imaging tests (OR 1.2, p<0.001) and more differential diagnoses documented (OR 2.15, p<0.001) were more likely to have uncertainty. Diagnostic uncertainty was significantly associated with diagnostic discordance between attending intensivists and resident physicians/advanced practice providers (OR 4.78, p=0.001), diagnostic discordance between PICU admission and discharge (OR 2.69, p=0.024), and having a neurologic discharge diagnosis (OR 1.87, p=0.03). Finally, diagnostic uncertainty at PICU admission was significantly associated with the occurrence of diagnostic error (OR 5.9, p=0.026). There were no significant associations between diagnostic uncertainty and patient demographics, illness severity, attending intensivists' characteristics, length of stay, or mortality. Conclusions: Diagnostic uncertainty at PICU admission was common and was associated with increased diagnostic testing, diagnostic discordance, and diagnostic error. Better recognition and management of diagnostic uncertainty could inform interventions to improve diagnosis among critically ill children.
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Cover Letter

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HARVARD MEDICAL SCHOOL
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February 27, 2024

Timothy G. Buchman, PhD, MD, MCCM
Editor-in-Chief, *Critical Care Medicine*
Society of Critical Care Medicine
500 Midway Drive
Mount Prospect, IL 60056

Dear Dr. Buchman,

We would like to submit our manuscript, **Diagnostic Uncertainty Among Critically Ill Children Admitted to the Pediatric Intensive Care Unit: A Multi-Center Study**, for consideration for publication in *Critical Care Medicine.*

Last year, *Critical Care Medicine* published our initial paper from the same multi-center work, "Prevalence and Characteristics of Diagnostic Error in Pediatric Critical Care: A Multi-Center Study," which advanced our understanding of diagnostic error among critically ill children. One of the key findings we reported was the significant association between diagnostic uncertainty and diagnostic error. In this companion manuscript, we further describe the frequency of diagnostic uncertainty at pediatric intensive care unit (PICU) admission through to discharge. We also delineate clinical factors that are associated with diagnostic uncertainty at PICU admission. We believe that these findings are significant and will be of interest to your readers since it shows that diagnostic uncertainty at ICU admission can potentially be used for early identification of heightened diagnostic error risk in this population.

A pilot study to establish feasibility of the methods was previously published as follows. Patients included in the pilot study were not included in the main study.

> Cifra CL, Ten Eyck P, Dawson JD, Reisinger HS, Singh H, Herwaldt LA. Factors Associated with Diagnostic Error on Admission to a PICU: A Pilot Study. *Pediatr Crit Care Med.* 2020;21(5):e311-e315.

An abstract of the main study with preliminary results was presented as a platform at the American Academy of Pediatrics National Conference and Exhibition 2021, and was published as an abstract as follows.

> Christina L. Cifra, Jason W. Custer, Craig M. Smith, Kristen A. Smith, Jodi Bloxham, Sonali Ramesh, Patrick Ten Eyck, Jeffrey D. Dawson, Heather S. Reisinger, Hardeep Singh, Loreen A. Herwaldt; Diagnostic Uncertainty Among Critically Ill Children Admitted to the Pediatric Intensive Care Unit: A Multi-center Study. *Pediatrics* February 2022; 149 (1 Meeting Abstracts February 2022): 399.

All authors named attest to have participated in the conception, design, execution, and writing of the manuscript and are accountable for all aspects of the work.

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This work and the manuscript's first author, Dr. Cifra, was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) through a K12 grant to the University of Iowa Stead Family Department of Pediatrics (#HD027748-28), Agency for Healthcare Research and Quality (AHRQ) through a K08 grant (#HS026965) and internal start-up grants from the University of Iowa Carver College of Medicine Department of Pediatrics and the Boston Children's Hospital Division of Medical Critical Care. This work was further supported by the National Center for Advancing Translational Sciences of the National Institutes of Health (#UM1TR004403) through the University of Iowa's Institute for Clinical and Translational Science. Dr. Singh is supported by the AHRQ (R01HS27363)and the Houston VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (CIN 13–413).

Dr. Landrigan has consulted with and holds equity in the I-PASS Institute, which seeks to train institutions in best handoff practices and aid in their implementation. In addition, Dr. Landrigan has received monetary awards, honoraria, and travel reimbursement from multiple academic and professional organizations for teaching and consulting on sleep deprivation, physician performance, handoffs, and safety, and has served as an expert witness in cases regarding patient safety and sleep deprivation. None of the other authors have relevant disclosures.

Thank you for your consideration.

Sincerely,

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Financial Disclosures and Conflicts of Interest:

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Key words: critical care, pediatrics, diagnostic error, patient safety, quality improvement

ABSTRACT

Objective: This study aimed to identify the prevalence of and factors associated with diagnostic uncertainty when critically ill children are admitted to the pediatric intensive care unit (PICU). Understanding diagnostic uncertainty is necessary to develop effective strategies to reduce diagnostic errors in the PICU.

Design: Multi-center retrospective cohort study with structured medical record review by trained clinicians using a standardized instrument to identify diagnostic uncertainty in narrative clinical notes. Diagnoses and diagnostic uncertainty were compared across time from PICU admission to hospital discharge. Generalized linear mixed models were used to determine patient, clinician, and encounter characteristics associated with diagnostic uncertainty at PICU admission.

Setting: Four academic tertiary-referral PICUs.

Patients: 882 randomly selected patients 0-18 years old who were non-electively admitted to participating PICUs.

Interventions: None

Measurements and Main Results: PICU admission notes for 228 of 882 (25.9%) patients indicated diagnostic uncertainty. Multivariable analysis showed that patients admitted during daytime weekdays were less likely to have diagnostic uncertainty at admission (OR 0.59, p=0.037), while patients who had more imaging tests (OR 1.2, p<0.001) and more differential diagnoses documented (OR 2.15, p<0.001) were more likely to have uncertainty. Diagnostic uncertainty was significantly associated with diagnostic discordance between attending intensivists and resident physicians/advanced practice providers (OR 4.78, p=0.001), diagnostic discordance

between PICU admission and discharge (OR 2.69, *p*=0.024), and having a neurologic discharge diagnosis (OR 1.87, *p*=0.03). Finally, diagnostic uncertainty at PICU admission was significantly associated with the occurrence of diagnostic error (OR 5.9, *p*=0.026). There were no significant associations between diagnostic uncertainty and patient demographics, illness severity, attending intensivists' characteristics, length of stay, or mortality.

Conclusions: Diagnostic uncertainty at PICU admission was common and was associated with increased diagnostic testing, diagnostic discordance, and diagnostic error. Better recognition and management of diagnostic uncertainty could inform interventions to improve diagnosis among critically ill children.

KEY POINTS

Question: What are the prevalence of and factors associated with diagnostic uncertainty among children admitted to the pediatric intensive care unit (PICU)?

Findings: This retrospective cohort study involving structured medical record review found that 228 of 882 (25.9%) patients non-electively admitted to four academic tertiary-referral PICUs had diagnostic uncertainty at PICU admission. Diagnostic uncertainty was significantly associated with increased diagnostic testing, diagnostic discordance, and diagnostic error.

Meaning: Diagnostic uncertainty at PICU admission can be used to identify patients at risk for diagnostic error and can inform interventions to improve diagnosis among critically ill children.

INTRODUCTION

Diagnosing critically ill children is a complex, iterative, and multi-disciplinary process (1, 2). Because all possible outcomes of critical illness and their probabilities cannot be fully known (3), uncertainty is inherent in diagnosis. Diagnostic uncertainty has been defined as the subjective perception of clinicians of their inability to provide an accurate explanation of a patient's health problem (4). Uncertainty may arise in the pediatric intensive care unit (PICU) due to gaps in current critical care science, gaps in the PICU team's knowledge base, incomplete or inaccurate communication of a patient's health information, and patient- or situation-specific factors that make it difficult to discern relevant information (5).

Maladaptive and inappropriate responses to diagnostic uncertainty can lead to poor patient care and outcomes. Overconfidence and the failure to recognize or acknowledge uncertainty may prevent healthcare teams from further investigating alternative diagnoses (6, 7), which can lead to diagnostic error (8). On the other hand, clinicians' anxiety and intolerance to uncertainty can lead to overuse of diagnostic resources, overdiagnosis, and overtreatment with all their attendant risks and potential adverse effects (9, 10). Unsurprisingly, diagnostic uncertainty has been associated with longer lengths of hospital stay, increased morbidity/mortality for patients (11), and a higher likelihood of burnout for clinicians (12, 13).

Given that intensivists' and PICU teams' responses to diagnostic uncertainty can substantially affect patient care and outcomes, we must understand how prevalent diagnostic uncertainty is and how it affects the diagnostic process in pediatric critical care. This is an important first step in developing effective interventions to improve

diagnosis in the PICU. In this study, we aimed to identify the prevalence of and factors associated with diagnostic uncertainty when critically ill children are admitted to intensive care.

MATERIALS AND METHODS

This is a multi-center retrospective cohort study using structured medical record review among patients non-electively admitted to four PICUs. The University of Iowa Institutional Review Board (UI IRB) approved and provided oversight for the study for all sites (IRB #201812777, “Dx PICU: Multi-center Study of Diagnostic Documentation and Diagnostic Errors in the Pediatric Intensive Care Unit - Retrospective Chart Review Study,” approved January 7, 2019). Study procedures were conducted in accordance with the ethical standards of the UI IRB and with the Helsinki Declaration of 1975. We previously reported the prevalence of and factors associated with diagnostic error in the same study population in this journal (14). We report this additional work focused on diagnostic uncertainty in accordance with the STROBE guidelines (15) (see *Supplement*).

Study Setting and Population

Four tertiary referral academic PICUs located in varying urban and rural locations participated in this study. Two PICUs are medical-surgical units and two are combined cardiac and medical-surgical units. The four PICUs have a range of 19 to 40 beds/unit and admit an average of 1,300 (range 1,100-1,900) patients per unit per year, of which an average of 69% are non-elective admissions.

We included patients who were admitted from January to December 2018. Patients were randomly selected per season (stratified random sampling of admissions in January-March, April-June, July-September, October-December) using a validated online computer algorithm (Research Randomizer© (16)) and screened for inclusion. We included patients 0-18 years old who were non-electively admitted to the PICUs. We excluded scheduled admissions (e.g., post-operative patients), readmissions within 30 days of a prior PICU admission, patients who were still hospitalized at the time of screening for study inclusion, and patients for whom the site PI was the attending physician during the first seven days of admission.

Data Collection

Clinician Reviewers and Training

Four to five trained clinician reviewers (pediatric intensivists or advanced practice providers [APPs]) who had been practicing full-time in the PICU for at least one year reviewed patients' electronic health records (EHRs) in each PICU. To standardize the review process, the lead site provided in-person or online training sessions for each participating PICU. Clinician reviewers were trained on data abstraction and the use of standardized instruments to identify evidence of diagnostic uncertainty, diagnostic discordance, and diagnostic error in clinical notes (17). More than one clinician reviewer reviewed 37% of included patient records, informing the calculation of inter-rater reliability (IRR) in the determination of diagnostic uncertainty. Clinician reviewers did not review records of patients they directly cared for at PICU admission.

Determination of Diagnostic Uncertainty, Diagnostic Discordance, and Diagnostic Error

Diagnostic uncertainty. The primary outcome for this study was the presence of diagnostic uncertainty as determined from clinicians' narrative diagnosis documentation at various timepoints during PICU admission. We defined diagnostic uncertainty as clinicians' subjective perception of their inability to accurately explain a patient's health problem (4). Reviewers used a standard instrument (**Box 1**) (17) to identify evidence of diagnostic uncertainty in attending physicians' diagnosis narratives and other documentation in the PICU admission note, the last progress note before PICU discharge, and the hospital discharge summary. They reviewed the resident physician's or APP's note if the attending physician did not write a narrative note. Reviewers were trained to use the instrument to determine both direct and indirect indicators of diagnostic uncertainty. Direct indicators included the use of specific words and question marks to refer to the diagnosis, documentation of differential diagnoses, and the use of symptoms as diagnoses. Indirect indicators included subspecialty consultation, diagnostic testing, and test-of-treatment strategies, all of which were only considered if performed specifically to resolve diagnostic uncertainty. Using both direct and indirect indicators as a guide, reviewers then made an overall assessment as to the presence of diagnostic uncertainty at that particular point in time.

Diagnostic discordance. Similarly, we used a standard rubric (*Supplement Box A*) (18) to determine if the attending physician's and resident physician's/APP's primary diagnoses were discordant at PICU admission and if the primary diagnosis at PICU admission and at PICU discharge were discordant. This rubric classifies the diagnoses being compared as either identical, different in terms of specificity, hierarchically different, or diagnostically different. Additionally, it may classify the diagnoses as

different due to a complication that arose during admission for comparisons made between admission and discharge.

Diagnostic error. Clinician reviewers were also trained to identify diagnostic error from chart documentation using the validated Revised Safer Dx instrument (*Supplement Box B*) (14, 19), which we described in detail in our prior work to determine the prevalence of and factors associated with diagnostic error in the same population (14). Clinicians reviewed charts for possible diagnostic error occurring between admission and transfer out of the PICU or up to 7 days after PICU admission, whichever came first. The Revised Safer Dx instrument defines diagnostic error as missed opportunities to make a correct or timely diagnosis within the context of an evolving diagnostic process, considering information available to PICU clinicians at particular time points. The opportunity could have been missed by the provider, care team, system, and/or the patient/family (20). Consistent with prior chart review studies on diagnostic error (21, 22), in performing reviews for diagnostic error, we considered the final diagnosis at hospital discharge as the "correct" diagnosis explaining the patient's clinical presentation on admission. Each case with a potential diagnostic error (Revised Safer Dx item #13 scored $\geq$ 4) was presented at a consensus meeting wherein the lead principal investigator (PI) and three site PIs made the final determination of whether a diagnostic error occurred.

Clinical Characteristics

Finally, we collected data on patients' demographic and clinical/encounter characteristics from the EHR. Attending physicians' characteristics were determined from surveys of site PIs. On the basis of their expertise as PICU clinicians, reviewers

also determined whether the patient's initial presentation at PICU admission was typical of their primary diagnosis at hospital discharge.

Statistical Analysis

We used generalized linear mixed models (GLMMs) to perform: 1) bivariable (unadjusted) analyses comparing characteristics between patients with and without evidence of diagnostic uncertainty and 2) multivariable analysis to estimate the odds of identifying evidence of diagnostic uncertainty (dependent variable) given specific patient, clinician, and encounter characteristics (independent variables). GLMMs were constructed treating the institution (PICU) as a random effect to control for positively-correlated error variance arising from clustering of clinical characteristics by site. We evaluated models for all possible combinations of covariates predicting diagnostic uncertainty and selected the model with the lowest Akaike Information Criterion (AIC).

We calculated inter-rater reliability for identifying evidence for diagnostic uncertainty and diagnostic error using Fleiss, et al.'s method (23) to calculate the *kappa* (k) coefficient taking into consideration that each record had a varying number of raters (24). We used R version 4.1.2 and Stata version 14.2 for statistical analyses.

RESULTS

Prevalence of Diagnostic Uncertainty

PICU admission notes for 228 of 882 patients (25.9%) were indicative of diagnostic uncertainty, which was consistent across all sites (range 22%-29%). Inter-rater reliability of the determination of diagnostic uncertainty was moderate (kappa=0.50, p <0.001). Diagnostic uncertainty in clinical notes remained present in 101 of 671 patients (15.1%)

at PICU discharge (included only patients transferred to another inpatient unit after at least 24 hours in the PICU) and 58 of 882 (6.6%) of patients at hospital discharge. Indirect, rather than direct indicators of diagnostic uncertainty, were more evident in clinical documentation, most commonly signified by clinicians' use of diagnostic tests or subspecialty consultation to help resolve uncertainty. Most diagnoses were documented as clinical narratives in the PICU notes (97.8% of PICU admission notes and 96.4% of progress notes prior to PICU discharge); however, at discharge, a substantial proportion of diagnoses were documented only as problem lists/billing codes (43.3%) (**Table 1**).

Clinical Characteristics Associated with Diagnostic Uncertainty at PICU admission

Bivariable (unadjusted) GLMMs with a random intercept for each PICU did not show a significant difference among patients with vs. without diagnostic uncertainty at PICU admission with regards to patients' age, gender, race/ethnicity, illness severity, presence of complex chronic conditions, time/day of PICU admission, PICU census at the time of admission, and attending physician characteristics. However, compared with patients without diagnostic uncertainty, more patients with diagnostic uncertainty had an atypical presentation on admission (6.6% vs. 2.9%, OR 2.35, p=0.016) and had a neurologic diagnosis at discharge (26.3% vs. 15%, OR 2.03, p<0.001), while fewer patients had a respiratory (44.7% vs. 56.6%, OR 0.62, p=0.002) or trauma-related discharge diagnosis (0.9% vs. 6.6%, OR 0.13, p=0.004). In addition, patients with diagnostic uncertainty had higher utilization of diagnostic resources with more imaging tests ordered (OR 1.18, p<0.001) and more subspecialties consulted (OR 1.34, p<0.001) within the first 24 hours of admission. Although PICU/hospital length of stay

and mortality were not significantly different between patients with vs. without diagnostic uncertainty, those with uncertainty had more diagnostic discordance between clinicians at PICU admission (8.8% vs. 2.6%, OR 3.60, $p<0.001$) and between PICU admission and PICU discharge (12.8% vs. 2.9%, OR 4.90, $p<0.001$) and had more diagnostic errors up to the first 7 days of their PICU stay (4.4% vs. 0.5%, OR 9.95, $p=0.001$) (*Supplement Table A*).

Multivariable analysis using a GLMM specifying site (PICU) as a random effect found that patients admitted during daytime weekdays were less likely to have diagnostic uncertainty at admission (OR 0.59, $p=0.037$), while patients who had more imaging tests ordered (OR 1.2, $p<0.001$) and more differential diagnoses documented (OR 2.15, $p<0.001$), were more likely to have uncertainty. Diagnostic discordance between clinicians (OR 4.78, $p=0.001$), diagnostic discordance between PICU admission and PICU discharge (OR 2.69, $p=0.024$), and having a neurologic discharge diagnosis (OR 1.87, $p=0.03$) were also significantly associated with diagnostic uncertainty. Finally, the occurrence of diagnostic error was significantly associated with diagnostic uncertainty at PICU admission (OR 5.9, $p=0.026$). There were no significant associations between diagnostic uncertainty and patient demographics, illness severity, attending intensivist characteristics, length of stay, or mortality (**Table 2**).

DISCUSSION

We found that diagnostic uncertainty was common in the pediatric critical care setting given that we observed evidence of diagnostic uncertainty in the medical records of about one of every four children at PICU admission. The prevalence of uncertainty

was remarkably similar across the four PICUs in our study despite their varying size, patient population, and geographic location. To our knowledge, this is the first study to report the frequency of diagnostic uncertainty in the PICU, thus contributing to the sparse literature describing diagnostic uncertainty in medicine. Many practicing pediatric intensivists will not be surprised by the high frequency of diagnostic uncertainty given the challenges of critical care diagnosis. Diagnosing critically ill children can be difficult because of patients' complex and variable pathophysiology, the high cognitive load of balancing recognition of life-threatening conditions with thoughtful investigations for underlying etiologies of disease, the need to communicate effectively within and across healthcare teams, and the low signal-to-noise ratio within the PICU environment (1, 25).

Our estimate of the prevalence of diagnostic uncertainty at PICU admission is similar to that of a study of adult dyspneic patients presenting to the emergency department, where clinicians indicated uncertainty for 31% of patients in the cohort (11). In contrast, in a study conducted within a pediatric hospital medicine service, clinicians indicated diagnostic uncertainty only for 5% to 10% of patients (26), likely because they were asked to identify uncertainty at any point in the hospitalization. This is consistent with our study's findings that evidence of diagnostic uncertainty decreases over time, as is expected if the diagnostic process proceeds as intended and the etiology of critical illness becomes more clearly defined. However, even at hospital discharge, diagnostic uncertainty was not completely resolved for all patients. Patients with lingering diagnostic uncertainty at transitions of care likely represent a vulnerable cohort (27) whose diagnostic trajectories and outcomes should be studied further.

Our study also found that clinicians more commonly implied rather than explicitly described their diagnostic uncertainty in their notes. This finding is aligned with prior work showing that intensivists do not communicate diagnostic uncertainty well, either in verbal handoffs (28) or in clinical documentation, which was also demonstrated in our previous study describing diagnosis narratives in the PICU (29). This finding is important since explicitly acknowledging and communicating diagnostic uncertainty helps the multi-disciplinary PICU team establish a more accurate shared mental model, which, if it includes an understanding of existing uncertainty, can enable team members to identify opportunities to refine the diagnosis (30).

Of note, evidence of diagnostic uncertainty was associated with a 6-fold increase in the odds of diagnostic error up to the first 7 days of PICU admission, which may partly be related to suboptimal management of uncertainty that can lead clinicians astray. Some authors have questioned whether medicine's overreliance on standard protocols and pathways obscures uncertainty in practice (31), leading to diagnostic error due to premature closure and anchoring. On the other hand, consistent with our findings that diagnostic uncertainty was associated with increased testing, overzealous attempts to resolve uncertainty can result in overuse of resources, imposing financial and logistic tolls on the healthcare system (9, 10, 32), and increasing clinicians' cognitive burden, since potentially irrelevant information adds to the "noise" of PICU care which can also result in misdiagnosis. The finding of a strong association between diagnostic uncertainty and error is also relevant since it provides a new opportunity to determine diagnostic error risk. Diagnostic errors have historically been difficult to address since their discovery and consequences are usually delayed and only recognized long after

the error has occurred (33). Unlike other patient safety problems such as hospital-acquired infections or medication errors (34, 35), we lacked sufficient knowledge about factors that increase patients' risk for misdiagnosis. Our findings now suggest that diagnostic uncertainty on admission can serve as a marker of diagnostic error risk early in the diagnostic process when decision-making may be more amenable to intervention. Therefore, these findings lay the foundation for a targeted surveillance system to identify patients at risk for diagnostic error, akin to early warning systems for acute clinical deterioration, that could be coupled with interventions to prevent misdiagnosis in the PICU (36).

Finally, we found that diagnostic uncertainty was statistically associated with certain characteristics of clinical documentation including naming multiple possible diagnoses, discordance between the attending intensivists' and resident physicians'/APPs' diagnoses, and diagnostic discordance between admitting and discharge diagnoses. While these findings seem obvious, they may help us identify a population of patients with evidence of diagnostic uncertainty in documentation both for research purposes and for clinical surveillance to identify those that may benefit from enhanced diagnostic support. Prior work has shown that both the characteristics of ICD-10 diagnosis codes (26) and narrative clinical notes (37) can be leveraged to identify these patients.

Our study has strengths and limitations. Participating sites were all academic tertiary referral PICUs, thus our findings regarding diagnostic uncertainty may be less applicable to smaller, non-academic units. Given the retrospective nature of our study, we determined the presence of diagnostic uncertainty only through clinical notes and did not ask clinicians about uncertainty when they were caring for patients (though

doing so is also limited by self-report bias). Thus, our observations were limited by documentation quality, especially since clinicians' documentation of diagnostic reasoning vary substantially. Our estimate of diagnostic uncertainty prevalence may also have been affected by heterogeneity in review. We previously discussed in detail the limitations of diagnostic error measurement (14) using the methods we used. Our study mitigated these limitations by including a random sample of patients across PICUs with varying sizes and geographic locations. We implemented a standard review process using trained PICU clinician reviewers and used a structured rubric designed specifically to identify evidence of diagnostic uncertainty in clinical narratives. Moreover, PICU clinician reviewers demonstrated moderate inter-rater reliability in the determination of diagnostic uncertainty.

CONCLUSIONS

Diagnostic uncertainty at PICU admission was common and was associated with increased diagnostic testing, diagnostic discordance, and diagnostic error. Diagnostic uncertainty may identify patients at risk for diagnostic error and should be considered in interventions to improve diagnosis among critically ill children. Future directions include the development and testing of programs focused on helping the PICU team better recognize, communicate, and address diagnostic uncertainty.

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FIGURE LEGENDS

Box 1. Standard Rubric for Determination of Diagnostic Uncertainty

Box 1. Standard Rubric for Determination of Diagnostic Uncertainty

Direct Expressions of Uncertainty

The clinician - (Yes/No)

- Used expressions such as "unclear" or "unknown" while referring to the diagnosis
- Used expressions such as "maybe," "probably," "likely," "possibly," "could be," "concern for," etc. while referring to the diagnosis
- Used differential diagnoses while referring to the diagnosis
- Used question marks or indicated "questionable" diagnosis
- Used symptomatic diagnoses (e.g., fever, abdominal pain, etc.)
- Used rule-out diagnoses

Indirect Expressions of Uncertainty

The clinician - (6-point Likert scale: strongly disagree to strongly agree)

- Initiated at least one subspecialty consult to resolve diagnostic uncertainty
- Ordered at least one additional diagnostic test to resolve diagnostic uncertainty
- Used the "test-of-treatment" strategy to resolve or manage diagnostic uncertainty

Overall Determination of Diagnostic Uncertainty

(6-point Likert scale: strongly disagree to strongly agree)

- The clinician experienced diagnostic uncertainty during the time of writing of the note under review

Table 1. Characteristics of Critically Ill Children's Diagnoses Across Time

Characteristics	PICU Admission n=882	PICU Discharge[a] n=671	Hospital Discharge n=882
Presence of diagnostic uncertainty overall[b], n (%)	228 (25.9)	101 (15.1)	58 (6.6)
Direct indicators of uncertainty			
Words/expressions indicating uncertainty used, n (%)	323 (36.6)	160 (23.9)	84 (9.5)
A symptomatic diagnosis only was documented, n (%)	116 (13.2)	56 (8.4)	36 (4.1)
Differential diagnoses documented, n (%)	189 (21.4)	68 (10.1)	31 (3.5)
Indirect indicators of uncertainty			
Subspecialty services consulted to help resolve uncertainty, n (%)	293 (33.3)	107 (15.9)	96 (10.9)
Diagnostic tests ordered to help resolve uncertainty, n (%)	391 (44.4)	110 (16.4)	100 (11.3)
"Test-of-treatment" applied to help resolve uncertainty, n (%)	177 (20.1)	83 (12.4)	94 (10.7)
Comparison of primary diagnosis[c] at PICU admission between attending and resident physician/advanced practice provider[d,e], n (%)			
Identical	368 (58.5)	N/A	N/A
Difference in specificity	221 (35.1)		
Hierarchically different	14 (2.2)		
Diagnostically different	23 (3.7)		
Comparison of the attending physician's primary diagnosis[c] at PICU/hospital discharge with diagnosis at PICU admission[e], n (%)			
Identical		416 (62.0)	509 (57.7)
Difference in specificity		207 (30.9)	270 (30.6)
Different due to complication	N/A	10 (1.5)	35 (4.0)
Hierarchically different		17 (2.5)	35 (4.0)
Diagnostically different		21 (3.1)	33 (3.7)
Days since PICU admission when the specificity of the primary diagnosis changed, median (IQR)	N/A	1 (1, 2)	2 (1, 4)
Days since PICU admission when primary diagnosis became hierarchically different or diagnostically different, median (IQR)	N/A	1 (1, 2)	2 (1, 4)
Manner of diagnosis documentation in clinical notes, n (%)			
Narrative	862 (97.8)	646 (96.4)	496 (56.3)
Problem list or billing codes	18 (2.0)	21 (3.1)	381 (43.3)
Copy-pasted documentation[f] of the primary diagnosis[c], n (%)	34 (4.0)	214 (33.3)	141 (28.5)

PICU - pediatric intensive care unit, IQR - inter-quartile range

[a]Excludes patients who were directly discharged from the PICU to home or to another institution and patients admitted and discharged/transferred from the PICU on the same day.

[b]Rubric adapted from Bhise, et al. (4).

[c]The primary diagnosis is the explanation given by the PICU clinician for the patient's acute health problem requiring PICU admission.

[d]Includes only records where both the attending physician and resident/advanced practice provider documented the primary diagnosis at PICU admission.

[e]Identical - the two diagnoses are either verbatim or medically identical; Difference in specificity - the latter diagnosis is more specific than the admission diagnosis, but otherwise identical; Different due to complication – one or more diagnoses were not foreseeable at the time of admission but became the most prominent during the patient's admission; Hierarchically different - the admission diagnosis is listed among the latter diagnoses, but is not the primary listed diagnosis; Diagnostically different - the admission diagnosis is not listed among the latter diagnoses or the two diagnoses are medically different. Rubric adapted from Hautz, et al. (18).

[f]Includes only narrative documentation. Diagnosis documentation was considered copy-pasted if copied from another clinician's previous note.

Table 2

Table 2. Logistic regression model of clinical characteristics associated with diagnostic uncertainty on pediatric intensive care unit admission[a]

Characteristic (n=864)	Odds Ratio	95% CI		*p* value
		LCL	UCL	
PICU admission during office hours (daytime weekday)	0.59	0.36	0.96	0.037
Number of imaging tests ordered in the first 24 hours of PICU admission	1.20	1.08	1.34	<0.001
Number of differential diagnoses provided at PICU admission	2.15	1.81	2.60	<0.001
Respiratory discharge diagnosis	0.66	0.42	1.05	0.079
Neurologic discharge diagnosis	1.87	1.06	3.30	0.030
Trauma discharge diagnosis	0.02	0.00	0.17	0.008
Discordance in primary diagnosis at PICU admission between attending physician and resident physician/advanced practice provider	4.78	1.88	12.60	0.001
Discordance in primary diagnosis of attending physician between PICU admission and PICU discharge	2.69	1.14	6.42	0.024
Occurrence of diagnostic error up to the first 7 days after PICU admission	5.90	1.30	32.40	0.026

CI - confidence interval, LCL - lower confidence limit, UCL - upper confidence limit, PICU - pediatric intensive care unit

[a]A generalized linear mixed model was used with site (institution) as a random effect. All possible models were evaluated and the model with lowest Akaike information criterion (AIC) was selected.