Diagnostic Errors in the Pediatric and Neonatal ICU: A Systematic Review*

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Objective: Diagnostic errors lead to preventable hospital morbidity and mortality. ICU patients may be at particularly high risk for misdiagnosis. Little is known about misdiagnosis in pediatrics, including PICU and neonatal ICU. We sought to assess diagnostic errors in PICU and neonatal ICU settings by systematic review.

Data Sources: We searched PubMed, Embase, CINAHL, and Cochrane.

Study Selection: We identified observational studies reporting autopsy-confirmed diagnostic errors in PICU or neonatal ICU using standard Goldman criteria.

Data Extraction: We abstracted patient characteristics, diagnostic error description, rates and error classes using standard Goldman criteria for autopsy misdiagnoses and calculated descriptive statistics.

Data Synthesis: We screened 329 citations, examined 79 full-text articles, and included 13 studies (seven PICU; six neonatal ICU). The PICU studies examined a total of 1,063 deaths and 498 autopsies. Neonatal ICU studies examined a total of 2,124 neonatal deaths and 1,259 autopsies. Major diagnostic errors were found in 19.6% of autopsied PICU and neonatal ICU deaths (class I, 4.5%; class II, 15.1%). Class I (potentially lethal) misdiagnoses in the PICU (43% infections, 37% vascular) and neonatal ICU (62% infections, 21% congenital/metabolic) differed slightly. Although missed infections were most common in both settings, missed vascular events were more common in the PICU and missed congenital conditions in the neonatal ICU.

Conclusion: Diagnostic errors in PICU/neonatal ICU populations are most commonly due to infection. Further research is needed to better quantify pediatric intensive care–related misdiagnosis and to define potential strategies to reduce their frequency or mitigate misdiagnosis-related harm. (*Pediatr Crit Care Med* 2015; 16:29–36)

Key Words: autopsy; diagnostic errors; intensive care units; meta-analysis; neonatal; pediatric intensive care units

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Diagnostic errors in medicine represent a large source of preventable morbidity and mortality in hospitalized patients. It has been estimated that diagnostic error results in 40–80,000 deaths annually in the United States (1). ICU patients may be at significantly higher risk for diagnostic errors and thus are a population that deserves special focus (2–4).

Diagnostic errors are defined as diagnoses that are missed, wrong, or delayed, as detected by some subsequent definitive test or finding (5). Patient harm may result from unrecognized disease, unnecessary diagnostic testing, or inappropriate therapy. Misdiagnosis-related harm is preventable harm suffered from treatment provided for a condition not actually present, or the

delay or failure to treat a condition actually present when the working diagnosis was wrong or unknown (1). Not all diagnostic errors result in direct harm to the patient, but may, nevertheless, result in unnecessary resource and healthcare costs (6).

Diagnostic errors are likely underreported and underrecognized. The majority of studies reporting diagnostic error use autopsy data as the gold standard compared with clinical data to identify missed diagnosis and diagnostic error. Autopsy-based studies typically use a Goldman classification system (**Table 1**) (7). Class I errors are those that, if recognized, have the potential for direct impact on both therapy and outcome (7).

Although there is an emerging literature and investigations into diagnostic error in adult ICU medicine (4, 8, 9), relatively little is known about diagnostic error in pediatrics (10, 11) and even less is known about diagnostic error in the neonatal ICU (NICU) and PICU. It has been reported that diagnostic errors occur more frequently in patients who die in the ICU when compared with patients who die in the emergency department or in the general ward (3). Autopsy rates in pediatric patients have also been reported to be higher than in adult patients (3).

To begin to understand the burden and scope of diagnostic error in PICU and NICU patients, we performed a comprehensive search of the available literature on diagnostic error to identify studies reporting rates for PICU or NICU patients. The goal of this study was to estimate the prevalence and distribution of autopsy-confirmed diagnostic errors in PICU and NICU populations. We hypothesized that there would be limited available applicable literature. Based on a prior study of adult ICU patients (4), we hypothesized that most errors would be related to infection and vascular events; however, we expected a significant contribution of undiagnosed congenital and genetic-metabolic conditions in the pediatric population.

TABLE 1. Goldman Classification System for Diagnostic Error

Error Class	Type	Description
Major misdiagnosis	I	Missed major diagnosis with potential adverse impact on survival and that would have changed management
	II	Missed major diagnosis with no potential impact on survival and that would not have changed therapy
Minor misdiagnosis	III	Missed minor diagnosis related to terminal disease but not related to the cause of death
	IV	Other missed minor discrepancy

METHODS

A related study from our group on adult ICU patients used the same general methods described below (4).

Search Strategy

We searched published literature through November 11, 2013, for observational studies that examined the prevalence of diagnostic errors in the PICU and NICU, as diagnosed by the reference standard of autopsy. Databases searched included PubMed, Embase, Cumulative Index to Nursing and Allied Health Literature, and the Cochrane Database of Systematic Reviews. There were no language limitations. The search strategies were designed by expert searchers (K.A.R., V.G.) together with clinical investigators (J.W.C., B.D.W., D.E.N.-T.). Search terms included ICU, critical care, intensive care, pediatric, neonatal; AND diagnostic error, misdiagnosis, diagnostic delay, diagnostic error; AND necropsy, autopsy. All of the clinical investigators who served as reviewers have expertise in critical care medicine or evaluation of diagnostic errors. Two reviewers (J.W.C., B.D.W.) independently screened each abstract. All studies considered eligible by either reviewer were subjected to a full article review to determine inclusion in the final analysis. Disagreements between the two primary reviewers were resolved by discussion and group consensus with a third author (D.E.N.-T.). Bibliographies from retrieved articles were screened for other relevant studies. We did not attempt to contact authors or identify meeting abstracts, unpublished studies, or other gray literature.

Inclusion Criteria

Studies of 10 or more patients who died in PICUs or NICUs with diagnostic errors confirmed by autopsy were included.

Exclusion Criteria

Studies that lacked original data, PICU or NICU specific data, or examined only a single patient condition (e.g., diaphragmatic hernia) were excluded.

Data Abstraction

Three authors (J.W.C., B.D.W., D.E.N.-T.) abstracted the data for pooled analysis. These data included number of deaths, autopsies, error class, underlying diagnoses, country, and ICU type. We did not assess the quality of included studies. We grouped errors for analysis using the Goldman classification scheme (Table 1). Data were tabulated using Microsoft Excel 2008 for Mac (Microsoft, Redmond, WA).

Descriptive statistics were calculated using Stata V.11 (Stata, College Station, TX). A p value of less than 0.05 was considered statistically significant. Because error rate estimates are influenced by the overall autopsy rate (fraction of deaths undergoing autopsy) (12), we developed a statistical model to estimate the "true" projected error rate under a hypothetical 100% autopsy rate. A random intercept logistic regression model was fit to the

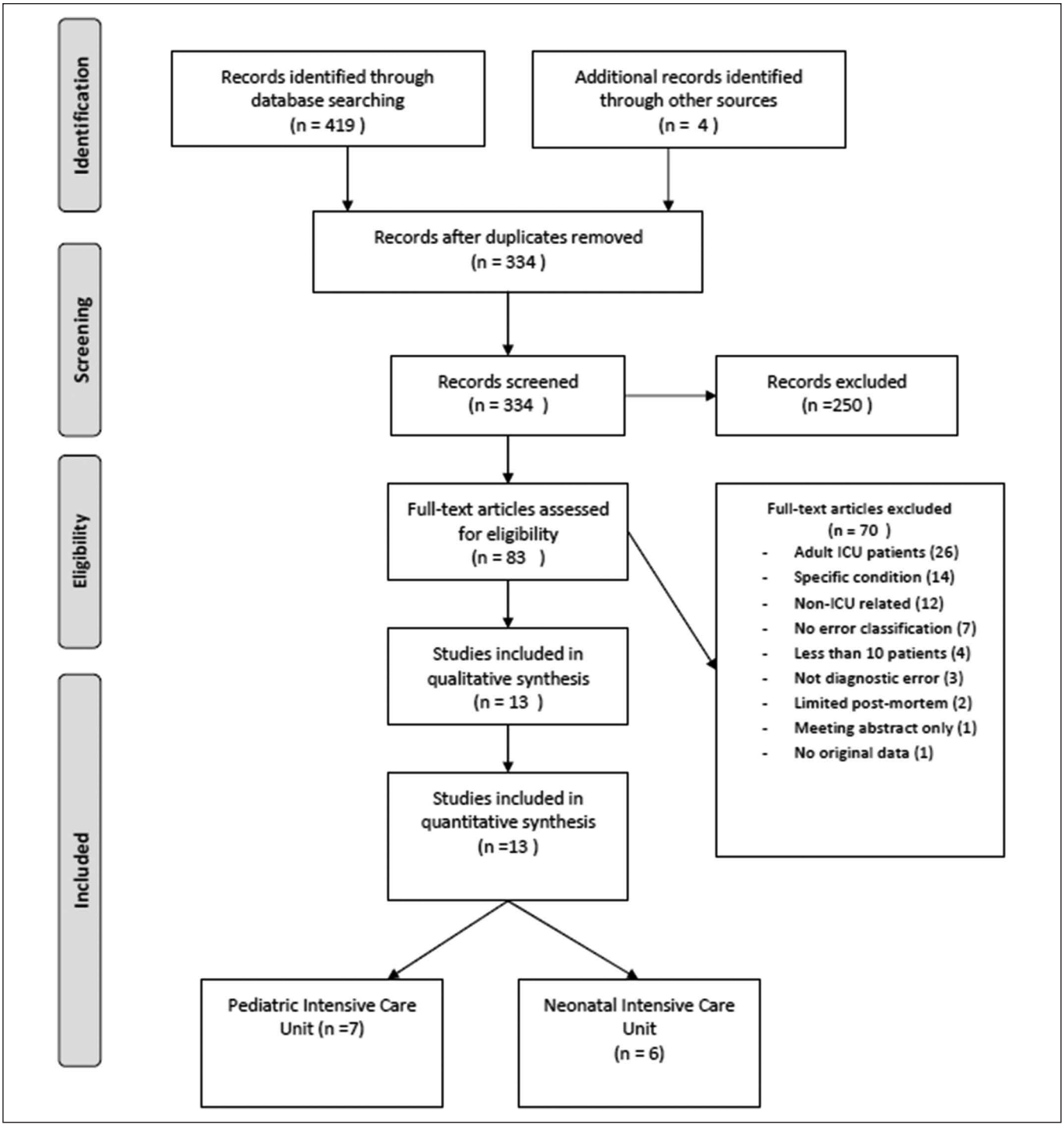

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for study identification, screening, eligibility, and inclusion.

class I misdiagnosis rate (number of class I errors vs number of autopsies performed) as a nonlinear function of the percent of autopsies performed (natural spline with 2 *df*). A likelihood ratio test was performed with R V.2.11.1 (R Foundation for Statistical Computing, Vienna, Austria) to determine if the nonlinear function was justified over a linear fit. The random intercept was included to account for natural variation across studies as is standard in meta-analysis. We controlled for size of study (number of autopsies) and the study time period in this model.

This review was prepared in accordance with the Meta-analysis of Observational Studies in Epidemiology (13) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (14) guidelines for systematic reviews of observational studies.

RESULTS

We identified 329 citations and screened 79 full-text articles for study inclusion (**Fig. 1**). Seven studies with PICU data were

TABLE 2. Summary of Studies Included in Analysis

Author	Year	Country	Type of Study	Length of Study Period (Mo)	Total No. of Deaths	No. of Autopsies Used for Analysis	Class I Errors	Class II Errors	Class III Errors	Class IV Errors
PICU studies										
Cardosos et al (15)	2006	Brazil	Prospective	28	206	102	12	21	33	7
Goldstein et al (3)	1996	United States	Prospective	56	121	88	2	5	5	NR
Pons et al (17)	1996	Spain	Retrospective	42	110	44	2	11	2	3
Ortega et al (16)	1997	Spain	Retrospective	144	93	56	3	14	10	9
Stambouly et al (18)	1993	United States	Retrospective	89	193	50	5	9	54	22
ten Berge et al (19)	2006	The Netherlands	Retrospective	54	87	19	5	NR	NR	NR
Von Dessauer et al (20)	2011	Chile	Prospective	60	253	139	3	9	10	NR
Neonatal ICU studies										
Barr and Hunt (22)	1999	Australia	Retrospective	72	229	91	5	15	NR	NR
Brodlie et al (26)	2002	United Kingdom	Retrospective	120	314	209	6	14	20	NR
Dahr et al (24)	1998	Canada	Prospective	72	545	338	7	57	251	NR
Delgado et al (23)	2008	Spain	Retrospective	72	309	128	4	23	36	65
Kabra and Udani (21)	2001	India	Prospective	13	240	197	24	53	57	7
Kumar et al (25)	2000	United States	Retrospective	120	487	296	1	34	70	25

NR = not reported.

included (3, 15–20) and six studies reporting data for NICU patients (21–26). (**Table 2**) Principal reasons for exclusion were studies of adult ICU patients and studies restricted to a single, specific condition (Fig. 1). In total, major errors occurred in 19.6% (class I, 4.5%; class II, 15.1%). Individual class I and II misdiagnoses are listed in **Table 3** (PICU) and **Table 4** (NICU). The most common class I/II errors were infections (30.8%; PICU, 44.5%; NICU, 25.1%), vascular events (18.3%; PICU, 28.7%; NICU, 14.0%), and congenital disorders (malformations, genetic/metabolic) (16.2%; PICU, 16.8%; NICU, 16.0%).

PICU

PICU studies were conducted in Brazil, Chile, the Netherlands, Spain (2), and the United States (2) (Table 2). Four of the studies were retrospective and three prospective. All used the Goldman classification scheme for reporting diagnostic errors; however, not all studies report on class III and IV errors. Two of the studies included data from patients admitted after the year 2000 (19, 20). Data collection ranged from 28 to 144 months (mean, 67.6 mo). Autopsy rates ranged from 22% to 72% (weighted mean, 46%; median, 48%).

The PICU studies examined a total of 1,063 PICU deaths and 498 autopsies (Table 4). Major errors occurred in 20.2% (class I, 6.4%; class II, 13.8%). Class I and II errors are detailed in Table 3. A total of 32 Goldman Class I errors were identified with the most frequent related to missed infection (43.8%) and vascular events (37.5%). Class II errors were identified in 69 cases with the most frequent again related to infection (44.9%) and vascular events (24.6%). Congenital malformations and heritable genetic/metabolic disorders together accounted for another 23.2%. Class III and IV errors were identified in 109 and 41 autopsies, respectively. Some autopsies were associated with multiple errors in one or more class.

TABLE 3. Breakdown of Misdiagnoses Class I and Class II by Final Diagnosis Reported for PICU Studies

Class I (32; 6.4% of Autopsies)	Class II (69; 13.8% of Autopsies)
Infection (14)	**Infection (31)**
Bacterial (3)	Bacterial (6)
Viral (3)	Viral (7)
Fungal (3)	Other (18)
Not specified (5)	**Vascular events (17)**
Vascular events (12)	Thrombosis (3)
Hemorrhage (6)	Hemorrhage (6)
Thrombosis (4)	Other (8)
Ischemic bowel (2)	**Congenital malformations (10)**
Genetic/metabolic	Congenital heart disease (6)
Cystic fibrosis	Coronary dysplasia
Other (5)	Biliary atresia
CNS tumor	Valvular dysplasia
Other malignancy (2)	Thalamic angioma
Not specified	**Genetic/metabolic (6)**
	Chronic granulomatous disease
	Glycogen storage disease
	Bruton agammaglobulinemia
	Severe combined immunodeficiency
	Tyrosinemia
	α-1 antitrypsin deficiency
	Abdominal pathology (5)
	Adrenal necrosis (4)
	Hepatic necrosis (1)

Unless otherwise stated in parenthesis only one patient had the diagnosis.

TABLE 4. Breakdown of Misdiagnoses Class I and Class II by Final Diagnosis Reported for Neonatal ICU Studies

Class I (47; 3.7% of Autopsies)	Class II (196; 15.5% of Autopsies)
Infection (29)	**Infection (32)**
Bacterial (6)	Bacterial (18)
Viral (0)	Viral (6)
Fungal (23)	Not specified (8)
Vascular events (3)	**Vascular events (31)**
IVC thrombosis with pulmonary embolism	Intraventricular hemorrhage (11)
Hemopericardium	Venous thromboembolism (6)
Adrenal hemorrhage	Adrenal hemorrhage (2)
Congenital malformations (4)	Myocardial infarction (3)
Coarctation of aorta	Pulmonary embolism (2)
Interrupted aortic arch	Cerebral arteriovenous malformation
Congenital diaphragmatic hernia	Pulmonary hemorrhage
Tracheal atresia	Not specified (5)
Genetic/metabolic (6)	**Congenital malformations (27)**
Congenital adrenal hypoplasia	Polycystic kidney (2)
Smith-Lemli-Opitz	Renal dysplasia
Cornelia De Lange	Ureteral stenosis
OTC deficiency	Total anomalous pulmonary venous return
DiGeorge syndrome	Colonic atresia
Gangliosidosis	Not specified (21)
Abdominal pathology (4)	**Genetic/metabolic (2)**
Necrotizing enterocolitis	Lymphangiectasia
Small bowel perforation	**Central nervous system (28)**
Intussusception	Global pathology (22)
Sigmoid volvulus	Kernicterus (4)
Other	Hypoxic ischemic encephalopathy (2)
Pericardial effusion	**Abdominal pathology (14)**
	Necrotizing enterocolitis (3)
	Hepatic necrosis (9)
	Visceral laceration (2)
	Other (18)
	Meconium aspiration (12)
	Trauma (3)
	Necrosis of respiratory tract (3)
	Diagnosis not specified (44)

Unless otherwise stated in parenthesis only one patient had the diagnosis.

Neonatal ICU

NICU studies were conducted in Australia, Canada, India, Spain, the United Kingdom, and the United States (Table 2). Four of the studies were retrospective and two prospective. All used the Goldman classification scheme for reporting diagnostic errors; however, not all studies report on class III and IV errors. The studies reported a specific diagnosis for class II errors in 78% of the cases. One of the studies included data from patients admitted after the year 2000 (23). Data collection ranged from 14 to 120 months (mean, 78.3 mo). Autopsy rates ranged from 39% to 82% (weighted mean, 59%; median, 61%).

The NICU studies examined a total of 2,124 neonatal deaths and 1,259 autopsies (Table 4). Major errors occurred in 19.2%

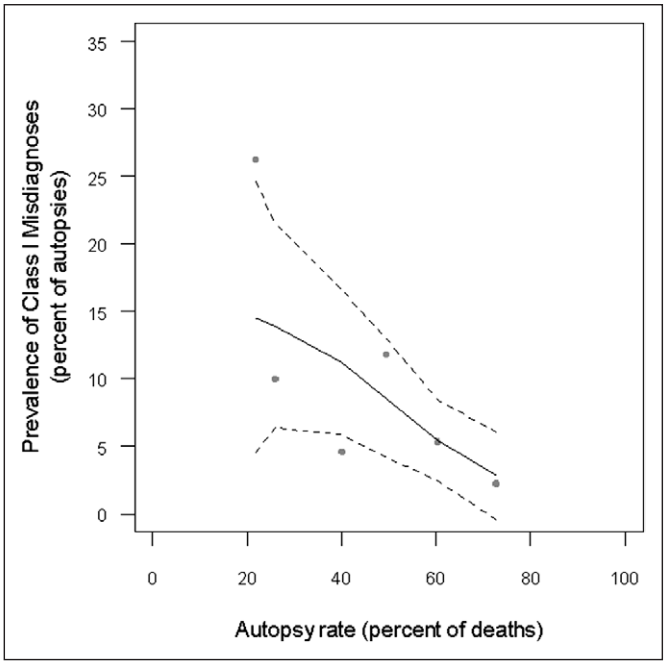

Figure 2. Prevalence of class I misdiagnosis as a function of autopsy rate for PICU patients.

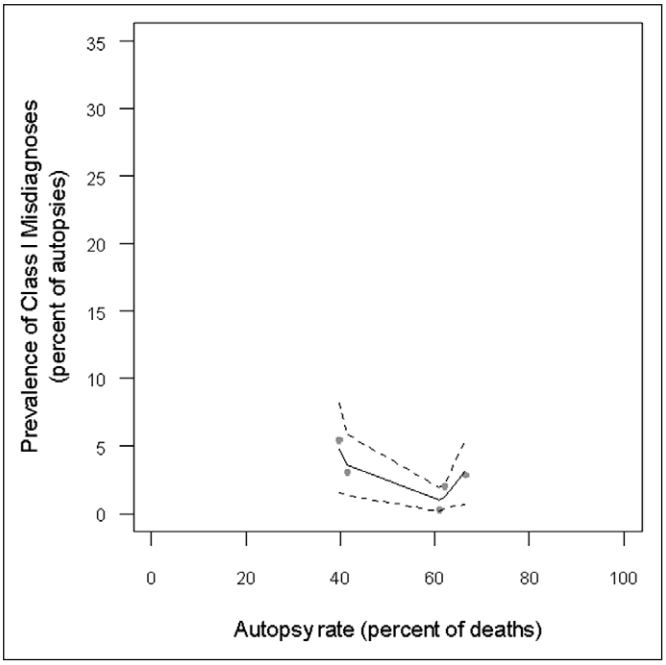

Figure 3. Prevalence of class I misdiagnosis as a function of autopsy rate for neonatal ICU patients.

(class I, 3.7%; class II, 15.5%). Class I and II errors are detailed in Table 4. A total of 47 Goldman class I errors were identified with the most frequent related to missed infection (61.7%). Congenital malformations and heritable genetic/metabolic conditions together accounted for another 21.3%. Class II errors were identified in 196 cases with the most frequent of reported diagnoses again related to infection (16.3%). Vascular events (15.8%) and congenital/metabolic disorders (14.7%) were also frequently missed. Class III and IV errors were identified in 434 and 97 autopsies, respectively. Some autopsies were associated with multiple errors in one or more class.

Impact of Autopsy Rate

The prevalence of class I misdiagnosis went down with increasing autopsy rates in the PICU (**Fig. 2**) and to a lesser extent in the NICU (**Fig. 3**). We attempted to predict the prevalence of class I misdiagnoses, if every patient who died in the PICU or NICU had an autopsy (a hypothetical "perfect" 100% autopsy rate); however, due to the paucity of data in these pediatric populations, we could not calculate a statistically valid result.

Error Risk Factors and Causes

Some studies reported on cognitive, systems, or clinical factors associated with diagnostic errors. Dahr et al (24) found a strong correlation between diagnostic uncertainty and missed diagnosis. Several PICU studies concluded that there was no correlation between PICU length of stay and missed diagnosis (15, 17–19). Kabra and Udani (21) concluded that there was no correlation between gestational age in the NICU population and missed diagnosis. None of these factors, however, were reported in a sufficient number of studies to pool results.

DISCUSSION

This systematic review builds on recent data describing diagnostic errors in the adult ICU (4) and is the first to aggregate available data on PICU and NICU misdiagnosis. We found that 6.4% of autopsied PICU patients and 3.7% of autopsied NICU patients had a class I diagnostic error. We also found that 13.8% of autopsied PICU patients and 15.5% of autopsied NICU patients had a class II diagnostic error. Error rates in the PICU population are similar to recently published data on adult ICU patients (4), but the reported NICU data show a slightly lower overall error rate.

These results must be interpreted in the context of knowing that not all patients who died underwent autopsy. There is likely bias in selecting which patients undergo an autopsy (i.e., autopsies are thought to be more aggressively pursued when the cause of death is clinically uncertain), so measured error rates vary as a function of the autopsy rate and may differ from the "true" error rate where all patients were autopsied (4, 12, 27). We attempted to create a model-based estimate of the "true" class I error rate, but the data were too limited to make an accurate assessment. It would be difficult to estimate the burden of misdiagnosis on pediatric mortality with the available data. Adult data suggest that as many as 40,500 adult ICU patients per year die as a result of diagnostic error (4). Since our data show similar error rates to adults, the pediatric impact is likely to be significant. Autopsy-based studies cannot assess morbidity attributable to diagnostic error in patients who survive their ICU stay, but the impact on patients and the healthcare system is likely substantial. Diagnostic error is known to contribute to reoperations and increased length of stay in ICUs (28, 29). Studies based on closed malpractice claims suggest that misdiagnosis results in serious morbidity as often as death (30).

Major errors (class I/II) most often involved missed infections (30.8%) and vascular events (18.3%). Overall, this is similar to adult ICU patients, but in adults, vascular events outnumber infections (4), whereas the reverse is true for children and neonates. Undiagnosed congenital malformations and heritable genetic/metabolic conditions also contributed to major diagnostic errors (16.2%). These were more often seen in NICU patients than in PICU patients and were much more likely to be considered lethal (i.e., class I). This is not surprising since PICUs typically treat older children in whom congenital disorders have a tendency to have been previously diagnosed.

There are limited data to determine the root cause of misdiagnosis and possible solutions. We were unable to draw broad inferences across studies because risk factors were inconsistently reported. The diagnostic process is complex and cognitive or system errors may occur at any step (31, 32). One of the studies suggested that teams were at least aware of diagnostic uncertainty (24), contrary to what has been reported for adults (33). Information overload and poor data management have been suggested as possible reasons to explain why ICUs may have a higher prevalence of misdiagnosis than the general hospital population. Information technology that allows for more efficient retrieval and organization of patient data (34) may help reduce ICU diagnostic error (1).

Pediatric hospitalized patients present special cognitive challenges because of the wide range of ages, developmental stages, and diagnoses cared for simultaneously (35). Unlike adults, age-specific diseases with variable presentations add to the diagnostic complexity. This is especially so for congenital malformations and genetic/metabolic disease. Advances in genetic testing may improve future diagnostic accuracy (36). Antemortem testing should be considered, although costs may also factor into the equation (6). Postmortem genetic and metabolic testing is becoming more frequent and may also be appropriate for pediatric patients where the cause of death is in question. Studies have shown that genetic and metabolic postmortem testing can identify a previously missed diagnosis approximately 18% of the time (37). Findings from postmortem genetic studies may have a significant impact on other family members as well as future offspring of the decedent's parents.

Numerous strategies to improve diagnostic accuracy have been proposed, but none has been tested for their impact on hard clinical outcomes (38). A targeted approach to diagnostic education in medical training may improve diagnostic reasoning skills (39). Enhanced training in the cognitive aspects of diagnosis and awareness of potential biases might help reduce cognitive error (40). Systems-oriented solutions to reduce diagnostic errors may hold special promise (32). Maintaining adequate staffing models, appropriate physician to patient ratios, and 24/7 presence of or access to expert clinicians in ICUs may reduce error rates (41, 42). Computer-based diagnostic decision support tools are expected to transform medical diagnosis in the future and have been shown to be effective in some limited settings (43). Few tools, however, have been created for or tested in the complex PICU or NICU environments (44, 45).

LIMITATIONS

There are several limitations of this review. The majority of included studies were retrospective, and there is potential for selection bias in those autopsied. The autopsy-based design did not permit assessment of nonlethal misdiagnosis-related morbidity, which could be substantial. Our review yielded small sample sizes at single centers, and it is unclear from the reports if there was similar access to diagnostic tests across the different institutions. It is very possible that variation in the availability of diagnostic tests may have influenced the rates of misdiagnosis. Error causes or contributory factors were generally not studied or only studied inconsistently. There were no comparative data on staffing models, attending oversight, or other systems factors. The majority of these studies are older, with only four of 13 studies published after 2002. With the changing landscape of healthcare and healthcare technology, these studies may not be an accurate reflection of current diagnostic error rates. We did not restrict the quality of included studies, and there is a risk that the original authors could have misclassified the diagnostic errors. Despite these weaknesses, coherence of our study's findings with the more robust data available from adult ICU populations (4) speaks to the likely validity of our overall estimates and breakdown of most frequently missed disorders.

CONCLUSIONS

This systematic review demonstrated that there is a paucity of literature related to diagnostic error in PICUs and NICUs. Available data suggest that diagnostic errors are potentially lethal in 6.4% of PICU and 3.7% of NICU deaths, likely causing the preventable deaths in a significant number of children. These results do not consider the impact of nonlethal morbidity. Thus far, diagnostic errors have received relatively little attention and research funding, leaving the methods to measure them underdeveloped (1). A prospective study examining the process and workflow of ICU diagnosis, diagnostic reasoning, and the impact of diagnostic error on patients is the logical next step in tackling this important issue. Policymakers and other stakeholders should consider diagnostic errors a top priority for further patient safety research.

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REFERENCES

1. Newman-Toker DE, Pronovost PJ: Diagnostic errors—The next frontier for patient safety. *JAMA* 2009; 301:1060–1062
2. Shojania KG, Burton EC, McDonald KM, et al: Changes in rates of autopsy-detected diagnostic errors over time: A systematic review. *JAMA* 2003; 289:2849–2856
3. Goldstein B, Metlay L, Cox C, et al: Association of pre mortem diagnosis and autopsy findings in pediatric intensive care unit versus emergency department versus ward patients. *Crit Care Med* 1996; 24:683–686

4. Winters B, Custer J, Galvagno SM Jr, et al: Diagnostic errors in the intensive care unit: A systematic review of autopsy studies. *BMJ Qual Saf* 2012; 21:894–902
5. Graber ML, Franklin N, Gordon R: Diagnostic error in internal medicine. *Arch Intern Med* 2005; 165:1493–1499
6. Newman-Toker DE, McDonald KM, Meltzer DO: How much diagnostic safety can we afford, and how should we decide? A health economics perspective. *BMJ Qual Saf* 2013; 22(Suppl 2):ii11–ii20
7. Goldman L, Sayson R, Robbins S, et al: The value of the autopsy in three medical eras. *N Engl J Med* 1983; 308:1000–1005
8. Newman-Toker DE, Pham JC, Winters BD, et al: Diagnostic errors in critical care settings–Managing information overload. *ICU Management* 2009; 9:6–11
9. Frohlich S, Ryan O, Murphy N, et al: Are autopsy findings still relevant to the management of critically ill patients in the modern era? *Crit Care Med* 2013; 42:1–8
10. Singh H, Thomas EJ, Wilson L, et al: Errors of diagnosis in pediatric practice: A multisite survey. *Pediatrics* 2010; 126:70–79
11. Thammasitboon S, Thammasitboon S, Singhal G: Diagnosing diagnostic error. *Curr Probl Pediatr Adolesc Health Care* 2013; 43:227–231
12. Shojania KG, Burton EC, McDonald KM, et al: Overestimation of clinical diagnostic performance caused by low necropsy rates. *Qual Saf Health Care* 2005; 14:408–413
13. Stroup DF, Berlin JA, Morton SC, et al: Meta-analysis of observational studies in epidemiology: A proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283:2008–2012
14. Moher D, Liberati A, Tetzlaff J, et al; PRISMA Group: Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med* 1990; 6:1–6
15. Cardoso MP, Bourguignon DC, Gomes MM, et al: Comparison between clinical diagnoses and autopsy findings in a pediatric intensive care unit in São Paulo, Brazil. *Pediatr Crit Care Med* 2006; 7:423–427
16. Ortega AC, Meoln FO, Fuentes MG, et al: Utility of autopsy in a pediatric intensive care unit. *An Esp Pediatr* 1997; 46:224–228
17. Pons M, Luaces C, Lobera E, et al: A study regarding correlation between clinical diagnosis and autopsy findings in a pediatric intensive care unit. *Med Intensiva* 1997; 21:9–12
18. Stambouly JJ, Kahn E, Boxer RA: Correlation between clinical diagnoses and autopsy findings in critically ill children. *Pediatrics* 1993; 92:248–251
19. ten Berge J, de Gast-Bakker DA, Plötz FB: Circumstances surrounding dying in the paediatric intensive care unit. *BMC Pediatr* 2006; 6:22–28
20. von Dessauer B, Velozo L, Benavente C, et al: Postmortem studies in the contemporary pediatric intensive care unit. *Pediatr Crit Care Med* 2011; 12:617–621
21. Kabra NS, Udani RH: Correlation between clinical diagnoses at the time of death and autopsy findings in critically sick neonates at a regional neonatal intensive care unit in India. *J Trop Pediatr* 2001; 47:295–300
22. Barr P, Hunt R: An evaluation of the autopsy following death in a level IV neonatal intensive care unit. *J Paediatr Child Health* 1999; 35:185–189
23. Delgado AP, Martin MV, Martinez A, et al: Value of autopsy in a neonatal intensive care unit. *An Pediatr (Bar)* 2008; 69:124–128
24. Dhar V, Perlman M, Vilela MI, et al: Autopsy in a neonatal intensive care unit: Utilization patterns and associations of clinicopathologic discordances. *J Pediatr* 1998; 132:75–79
25. Kumar P, Angst DB, Taxy J, et al: Neonatal autopsies: A 10-year experience. *Arch Pediatr Adolesc Med* 2000; 154:38–42
26. Brodlie M, Laing IA, Keeling JW, et al: Ten years of neonatal autopsies in tertiary referral centre: Retrospective study. *BMJ* 2002; 324:761–763
27. Podbregar M, Voga G, Krivec B, et al: Should we confirm our clinical diagnostic certainty by autopsies? *Intensive Care Med* 2001; 27:1750–1755
28. Janjua KJ, Sugrue M, Deane SA: Prospective evaluation of early missed injuries and the role of tertiary trauma survey. *J Trauma* 1998; 44:1000–1006
29. Kollef MH: Risk factors for the misdiagnosis of pneumothorax in the intensive care unit. *Crit Care Med* 1991; 19:906–910
30. Saber Tehrani AS, Lee H, Matthews SC, et al: 25-year summary of US malpractice claims for diagnostic error 1986–2010: An analysis from the National Practitioner Data Bank. *BMJ Qual Saf* 2013; 22:672–680
31. Schiff GD, Hasan O, Kim S, et al: Diagnostic error in medicine: Analysis of 583 physician-reported errors. *Arch Intern Med* 2009; 169:1881–1887
32. Thammasitboon S, Thammasitboon S, Singhal G: System-related factors contributing to diagnostic errors. *Curr Probl Pediatr Adolesc Health Care* 2013; 43:242–247
33. Podbregar M, Voga G, Krivec B, et al: Should we confirm our clinical diagnostic certainty by autopsies? *Intensive Care Med* 2001; 27:1750–1755
34. Horn W, Popow C, Unterasinger L: Support for fast comprehension of ICU data: Visualization using metaphor graphics. *Methods Inf Med* 2001; 40:421–424
35. Fackler JC, Wetzel RC: Critical care for rare diseases. *Pediatr Crit Care Med* 2002; 3:89–90
36. Saunders CJ, Miller NA, Soden SE, et al: Rapid whole-genome sequencing for genetic disease diagnosis in neonatal intensive care units. *Sci Transl Med* 2012; 4:1–13
37. Ernst LM, Sondheimer N, Deardorff MA, et al: The value of the metabolic autopsy in the pediatric hospital setting. *J Pediatr* 2006; 148:779–783
38. McDonald KM, Matesic B, Contopoulos-Ioannidis DG, et al: Patient safety strategies targeted at diagnostic errors: A systematic review. *Ann Intern Med* 2013; 158:381–389
39. Cutrer WB, Sullivan WM, Fleming AE: Educational strategies for improving clinical reasoning. *Curr Probl Pediatr Adolesc Health Care* 2013; 43:248–257
40. Thammasitboon S, Cutrer WB: Diagnostic decision-making and strategies to improve diagnosis. *Curr Probl Pediatr Adolesc Health Care* 2013; 43:232–241
41. Pronovost PJ, Angus DC, Dorman T, et al: Physician staffing patterns and clinical outcomes in critically ill patients: A systematic review. *JAMA* 2002; 288:2151–2162
42. Ward NS, Afessa B, Kleinpell R, et al; Members of Society of Critical Care Medicine Taskforce on ICU Staffing: Intensivist/patient ratios in closed ICUs: A statement from the Society of Critical Care Medicine Taskforce on ICU Staffing. *Crit Care Med* 2013; 41:638–645
43. El-Kareh R, Hasan O, Schiff GD: Use of health information technology to reduce diagnostic errors. *BMJ Qual Saf* 2013; 22(Suppl 2):ii40–ii51
44. Mani S, Ozdas A, Aliferis C, et al: Medical decision support using machine learning for early detection of late-onset neonatal sepsis. *J Am Med Inform Assoc* 2014; 21:326–336
45. Stubbs B, Kale DC, Das A: Sim•TwentyFive: An interactive visualization system for data-driven decision support. *AMIA Annu Symp Proc* 2012; 2012:891–900