SUPPLEMENTAL MATERIAL

An Estimate of Missed Pediatric Sepsis in the Emergency Department

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Supplement to Methods

Data Sources

The Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP) is a family of databases containing discharge data for >95% of visits to US hospitals (1). When the study was started in 2016, data were only available up to 2013 in the HCUP databases. The years 2010-2011 were the most recent years available with the highest numbers of sepsis admissions and available variables required to link inpatient and emergency department (ED) visits and determine institutional characteristics. We obtained data from four states (CA, FL, MA, NY) using both State Inpatient Databases (SID) and State Emergency Department Databases (SEDD). These states and this 2-year time frame were selected due to availability of unique patient identifiers, availability of linking variables to allow analysis of institutional characteristics, and relatively high numbers of pediatric sepsis inpatient admissions.

We were unable to link inpatient admissions with prior ED visits for 44% of pediatric patients due to missing unique identifiers. Synthetic unique identifiers, as assigned by state data organizations, are needed to track patients across clinical settings while satisfying privacy guidelines (2).

Identification of Pediatric Patients Admitted with Severe Sepsis/Septic Shock

In the SID, we used International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to identify patients 0-19 years old admitted to an inpatient unit with severe sepsis (995.92) and/or septic shock (785.52). We used these diagnoses because patients with severe sepsis and/or septic shock are at highest risk for mortality and are most likely to benefit from timely diagnosis. These diagnoses also enable comparison of results from the current study with those of previous epidemiologic studies on sepsis (3–5). This is a visit-level analysis (patients can have multiple records for separate admissions to the same or different hospitals). We only included codes that were present on admission, so as not to include cases with sepsis resulting from hospital-acquired infections. We collapsed related records for the same episode of sepsis wherein the patient was initially diagnosed and admitted at one institution and then transferred to another institution for continued management. For the analysis, we considered the characteristics of the original or diagnosing institution, since we are interested in potential associations with missed sepsis diagnosis.

Linking Sepsis Admissions with Prior Emergency Department Visits

Within our cohort of inpatient severe sepsis/septic shock admissions, we used the SEDD to identify those patients who had at least one ED treat-and-release visit in the 7 days prior to their sepsis admission. This is a visit-level analysis (patients can have multiple records for separate ED visits to the same or different hospitals). Since we were interested only in ED treat-and-

release visits, we excluded 143 visits wherein the patient was transferred to an acute hospital for inpatient admission. We also excluded 4 visits with missing ED dispositions. Finally, 30 visits with an ED ICD-9 diagnosis (in any discharge diagnosis position, i.e., not just first-listed diagnosis) of septic shock (785.52), toxic shock syndrome (040.82), or any ICD-9 diagnosis included under the HCUP Clinical Classifications Software [CCS] code septicemia (code 2 – includes sepsis [995.91] and severe sepsis [995.92]) (6) were excluded from this group and categorized as correctly diagnosed sepsis. For reasons that are not apparent in the database, these patients were documented as "released" from the ED even after being diagnosed with sepsis. Possible explanations may be mis-coding of dispositions (e.g., patients were admitted not discharged), or patients may be coded as discharged but actually transferred to another hospital for higher level of care.

We present the 20 most common diagnoses given at prior ED treat-and-release visits as categorized by the HCUP CCS. The CCS is a diagnosis and procedure categorization scheme based on ICD-9-CM. It collapses ICD-9's over 14,000 diagnosis codes and 3,900 procedure codes into a smaller number of clinically meaningful categories that are more useful for summarizing data than are individual ICD-9 codes (7). In **Supplement Table 1**, we list all CCS categories presented in our data with their associated ICD-9 codes.

Determination of Potentially Missed Sepsis Diagnosis

Within this sub-cohort of patients with an ED treat-and-release visit prior to their inpatient sepsis admission, we sought to identify cases with potentially missed sepsis diagnoses. Per the Symptom-Disease Pair Analysis of Diagnostic Error (SPADE) method, an ED diagnosis or symptom that is rarely associated with the diagnosis of interest can serve as a negative control to help discriminate between prior ED visits unrelated to the condition vs. prior ED visits related to the condition. For this study, we were unable to identify a negative control, as described, for sepsis. Thus, we employed an expert panel to rate the likelihood that each patient's ED visit was related to his/her subsequent sepsis admission. This multidisciplinary panel of 3 board-certified clinicians has >65 years of combined experience in urban and rural settings. The panel was given only the patient's age and list of ED ICD-9 diagnoses. No other clinical data were provided because users of HCUP databases are prohibited from identifying individual patients, thus precluding access to medical records. We used a Likert scale (very unlikely, unlikely, likely, or very likely) for the panel's ratings, which were later dichotomized to likely (potentially missed sepsis) and unlikely (unlikely missed sepsis). **Supplement Figure 1** illustrates the derivation of the study population and determination of potentially missed sepsis diagnosis.

Validation of Potentially Missed Sepsis Construct

To assess the validity of our potentially missed sepsis construct, we performed several analyses. First, we assessed the temporal profile of ED treat-and-release visits within the 7-day window prior to inpatient sepsis admission. We hypothesized that ED treat-and-release visits with true missed sepsis would be disproportionately high in the few days before sepsis admission, consistent with the rapid progression of disease expected in severe sepsis. In contrast, ED treat-and-release visits with unlikely missed sepsis (unrelated to subsequent sepsis admission) would be more evenly distributed throughout the 7-day period prior to hospitalization. We constructed a generalized linear model following a Poisson distribution to compare the two distributions. Second, we compared the distribution of ED diagnoses in our cohort of patients admitted with sepsis with a previous recent ED treat-and-release visit to that of

all ED treat-and-release visits drawn from all four states. We anticipated that the relative distribution of ED diagnoses would be skewed towards diagnoses such as fever (more associated with sepsis) and away from diagnoses such as sprain/strain (less associated with sepsis). Third, we instituted a structured review process for the expert panel and assessed interrater reliability across reviewers (kappa statistic).

Covariates: Patient and Institutional Characteristics

Since our goal was to determine associations with potentially missed sepsis, we needed to include variables present at the time of diagnosis. Thus, for the analysis, we considered patient characteristics documented at the time of their visit to the initial diagnosing institution and characteristics of this institution; i.e., the ED where patients with potentially missed sepsis were treated and released (most proximal visit for those with multiple visits), the institution where patients were initially seen before being transferred to final inpatient units for admission (for patients with 2 or more related records for the same sepsis episode), or the institution where patients were admitted for sepsis (for patients with only one record). Patient characteristics included age, gender, race and ethnicity, payer (insurance status), presence of any comorbid chronic medical condition, and day of ED visit (weekday vs. weekend). Institutional characteristics included location (state), type of hospital ownership, status as a dedicated children's hospital, teaching hospital status, presence of fully implemented electronic health records, availability of dedicated pediatric services (pediatric ED and pediatric intensive care unit), and the annual volume of ED visits. Previous studies have identified these factors to be associated with diagnostic errors in sepsis and other conditions (8–13).

Statistical Analysis

We hypothesized that 10% of children admitted for severe sepsis/septic shock had missed sepsis in a prior ED visit, requiring at least n=1,716 sepsis admissions to detect this proportion (+/-1.4%) with at least 80% power (α=0.05).

Missing Data and Multiple Imputation Procedures

We identified the proportion of records with missing data per variable (**Supplement Table 2**) and determined that 331 (17%) of records had missing data for at least one variable. We used multiple imputation by chained equations (MICE) procedures to impute values for missing variables (14,15). Multiple imputation is an accepted technique in epidemiological and clinical research, which uses statistical modeling accounting for uncertainty about the missing data by creating several different plausible imputed data sets and appropriately combining results obtained from each of them (14). Multiple imputation has been shown to generate less biased estimates with greater statistical efficiency compared to complete case analysis (16).

Fifty imputed data sets were separately created for patient-level data and hospital-level data. We merged these data sets together for analysis. We used Rubin's rules to combine model results across the multiply imputed data sets (15). Unless stated otherwise, all statistics and standard errors reported in this study were based upon combined results from the multiple imputed data. Imputed data sets were created using the "ICE" package for Stata, which uses MICE procedures to create imputed data sets. MICE procedures based upon Markov Chain Monte Carlo methods are desirable as they do not make assumptions about the joint probability function for the variables included in missing data model. Predictive mean matching was used to predict missing

values for all continuous variables, while appropriate versions of logistic regression models (e.g., logit, ordinal logit, multinomial logit) were used to predict categorical measures.

Multivariable Models

We constructed generalized linear mixed models (GLMM) with random effects at the hospital level to examine the odds of potentially missed sepsis in the ED among pediatric patients admitted with severe sepsis/septic shock controlling for patient and institutional characteristics. We built the model in four steps, achieving better model fit with each iteration (Model 0: intercepts as outcomes with no covariates, Model 1: patient demographics, Model 2: patient demographics + individual level covariates, Model 3: hospital-level covariates, Model 4: patient demographics + individual level covariates + hospital-level covariates). We did not categorize continuous variables in the models. No variables were removed because of non-significance in bivariable analyses. We created a correlation matrix which showed no evidence of collinearity across independent variables (highest correlation was 0.55 and standard errors were stable throughout the model-building process; calculated variance inflation factors were all <4).

Supplement to Results

Supplement Table 3 shows the 20 most common diagnoses given at prior ED treat-and-release visits.

There were 20 patients with multiple ED treat-and-release visits within 7 days prior to their inpatient sepsis admission; 19 patients had two visits and 1 patient had three visits. Of these, 13 patients had at least 2 consecutive ED visits during which sepsis was potentially missed before inpatient sepsis admission. In this subgroup, the most common diagnoses were fever (60%), pneumonia (20%), and other unknown and unspecified cause of morbidity and mortality (20%).

Validation of Potentially Missed Sepsis Construct

Temporal profile analysis showed that ED treat-and-release visits with potentially missed sepsis were clustered in the few days prior to inpatient sepsis admission; more than 50% were admitted for sepsis 0-1 day after their ED visit. The mean number of days between ED presentation and sepsis admission for patients with potentially missed sepsis was significantly less than for patients with unlikely missed sepsis (1.9 vs. 2.6 days, p=0.008), consistent with the expected rapid progression of the disease (**Supplement Figure 2**). We also found that the distribution of the top 20 most common ED diagnoses in our cohort were over-represented compared to the overall pediatric ED population. As expected, diagnoses such as fever and lower respiratory disease (17), both common presenting symptoms in sepsis, were more common than other diagnoses. Diagnoses such as paralysis, deficiencies and other anemia, and other nutritional/endocrine/metabolic disorders (chronic conditions) were also more common in the study cohort relative to the general ED population (**Supplement Table 4**).

References for Supplemental Material

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Supplement Table 1. Healthcare Cost and Utilization Project Clinical Classification Software Single-Level Codes and ICD-9-CM Codes Used in Analyses

CCS Label	Description	ICD-9-CM Codes
2	Septicemia	0031 0202 0223 0362 0380 0381 03810 03811 03812 03819 0382 0383 03840 03841 03842 03843 03844 03849 0388 0389 0545 449 77181 7907 99591 99592
246	Fever of unknown origin	7806 78060 78061
7	Viral infection	0500 0501 0502 0509 0510 05101 05102 0511 0512 0519 0522 0527 0528 0529 05310 05311 05312 05313 05314 05319 05371 05379 0538 0539 0540 05410 05411 05412 05413 05419 0542 0546 05471 05473 05474 05479 0548 0549 05579 0558 0559 05600 05609 05679 0568 0569 0570 0578 0579 05810 05811 05812 05881 05882 05889 05900 05901 05909 05910 05911 05912 05919 05920 05921 05922 0598 0599 0600 0601 0609 061 0650 0651 0652 0653 0654 0658 0659 0660 0661 0663 0664 06640 06642 06649 0668 0669 071 0720 0723 07272 07279 0728 0729 0737 0738 0739 0740 0741 0743 0748 075 0780 0781 07810 07811 07812 07819 0782 0783 0784 0785 0786 0787 07881 07882 07888 07889 0790 0791 0792 0793 0794 07950 07951 07952 07959 0796 0798 07981 07982 07983 07988 07989 0799 07998 07999 7908
133	Other lower respiratory disease	5131 514 515 5160 5161 5162 5163 51630 51631 51632 51633 51634 51635 51636 51637 5164 5165 51661 51662 51663 51664 51669 5168 5169 5172 5178 5183 5184 51889 5194 5198 5199 7825 78600 78601 78602 78603 78604 78605 78606 78607 78609 7862 7863 78630 78631 78639 7864 78652 7866 7867 7868 7869 7931 79311 79319 7942 V126 V1260 V1261 V1269 V426
126	Other upper respiratory infections	0320 0321 0322 0323 0340 460 4610 4611 4612 4613 4618 4619 462 4640 46400 46401 46410 46411 46420 46421 46430 46431 4644 46450 46451 4650 4658 4659 4730 4731 4732 4733 4738 4739 78491
155	Other gastrointestinal disorders	538 5581 5582 5640 56400 56401 56402 56409 5641 5645 5647 5648 56481 56489 5649 5680 56881 56882 56889 5689 56981 56982 56983 56984 56985 56986 56987 56989 5699 5790 5791 5792 5798 5799 7871 7872 78720 78721 78722 78723 78724 78729 7873 7874 7875 7876 78760 78761 78762 78763 7877 7879 78791 78799 7892 7893 78930 78931 78932 78933 78934 78935 78936 78937 78939 7894 78940 78941 78942 78943 78944 78945 78946 78947 78949 7899 7921 7934 7936 V127 V1270 V1279 V416 V441 V442 V443 V444 V453 V473 V535 V5350 V5351 V5359 V551 V552 V553 V554
251	Abdominal pain	7890 78900 78901 78902 78903 78904 78905 78906 78907 78909 78960 78961 78962 78963 78964 78965 78966 78967 78969
122	Pneumonia (except that caused by tuberculosis or sexually transmitted disease)	00322 0203 0204 0205 0212 0221 0310 0391 0521 0551 0730 0830 1124 1140 1144 1145 11505 11515 11595 1304 1363 4800 4801 4802 4803 4808 4809 481 4820 4821 4822 4823 48230 48231 48232 48239 4824 48240 48241 48242 48249 4828 48281 48282 48283 48284 48289 4829 483 4830 4831 4838 4841 4843 4845 4846 4847 4848 485 486 5130 5171
55	Fluid and electrolyte disorders	2760 2761 2762 2763 2764 2765 27650 27651 27652 2766 27669 2767 2768 2769 9951

250	Nausea and vomiting	7870 78701 78702 78703 78704
83	Epilepsy; convulsions	3450 34500 34501 3451 34510 34511 3452 3453 3454 34540 34541 3455 34550 34551 3456 34560 34561 3457 34570 34571 3458 34580 34581 3459 34590 34591 7803 78031 78032 78033 78039
159	Urinary tract infections	03284 59000 59001 59010 59011 5902 5903 59080 59081 5909 5950 5951 5952 5953 5954 59581 59582 59589 5959 5970 59780 59781 59789 59800 59801 5990
253	Allergic reactions	4771 5186 5583 6910 6918 6920 6921 6922 6923 6924 6925 6926 69270 69271 69272 69273 69274 69279 69281 69282 69283 69284 69289 6929 6930 6931 6938 6939 7080 7081 7082 7083 7084 7085 7088 7089 9950 9953 99560 99561 99562 99563 99564 99565 99566 99567 99568 99569 9957 V071 V1381 V140 V141 V142 V143 V144 V145 V146 V147 V148 V149 V150 V1501 V1502 V1503 V1504 V1505 V1506 V1507 V1508 V1509 V727
259	Residual codes; unclassified	3020 32700 32701 32709 32710 32711 32712 32713 32714 32719 32720 32721 32722 32723 32724 32725 32726 32727 32729 32740 32741 32742 32743 32744 32749 32751 32759 3278 78002 7801 78050 78051 78052 78053 78054 78055 78056 78057 78058 78059 78064 78065 7809 78093 78094 78095 78096 78097 78099 7815 7816 7823 78261 78262 7828 7829 7830 7836 7842 7901 7906 7909 79091 79092 79093 79094 79095 79099 7932 7939 79399 7949 79581 79582 79589 7963 7964 7965 7966 7969 7980 7981 7982 7989 7992 79921 79922 79923 79924 79925 79929 7993 7998 79981 79982 79989 7999 V070 V072 V073 V0731 V0739 V0751 V0752 V0759 V078 V079 V131 V138 V1389 V139 V152 V1521 V1522 V1529 V153 V1581 V1584 V1585 V1586 V1587 V1589 V159 V160 V161 V162 V163 V164 V1640 V1641 V1642 V1643 V1649 V165 V1651 V1652 V1659 V166 V167 V168 V169 V170 V171 V172 V173 V174 V1741 V1749 V175 V176 V177 V178 V1781 V1789 V180 V181 V1811 V1819 V182 V183 V184 V185 V1851 V1859 V186 V1861 V1869 V187 V188 V189 V190 V191 V1911 V1919 V192 V193 V194 V195 V196 V197 V198 V210 V211 V212 V218 V219 V418 V419 V428 V4281 V4282 V4283 V4284 V4289 V429 V438 V4381 V4382 V4383 V4389 V447 V448 V449 V4571 V4572 V4573 V4574 V4575 V4576 V4577 V4578 V4579 V4583 V4584 V4586 V4587 V4588 V4589 V460 V463 V468 V469 V470 V471 V472 V479 V480 V488 V489 V498 V4981 V4982 V4983 V4984 V4986 V4987 V4989 V499 V500 V501 V503 V5041 V5042 V5049 V508 V509 V590 V5901 V5902 V5909 V591 V592 V593 V594 V595 V596 V5970 V5971 V5972 V5973 V5974 V598 V599 V640 V6400 V6401 V6402 V6403 V6404 V6405 V6406 V6407 V6408 V6409 V641 V642 V643 V644 V6441 V6442 V6443 V690 V691 V692 V693 V694 V695 V698 V699 V8301 V8302 V8381 V8389 V8401 V8402 V8403 V8404 V8409 V848 V8481 V8489 V851 V8552 V860 V861 V8701 V8702 V8709 V8711 V8712 V8719 V872 V8731 V8732 V8739 V8741 V8742 V8743 V8744 V8745 V8746 V8749 V8801 V8802 V8803 V8811 V8812 V8901 V8902 V8903 V8904 V8905 V8909
82	Paralysis	3420 34200 34201 34202 3421 34210 34211 34212 34280 34281 34282 3429 34290 34291 34292 3430 3431 3432 3433 3434 3438 3439 3440 34400 34401 34402 34403 34404 34409 3441 3442 3443 34430 34431 34432 3444 34440 34441 34442 3445 34460 3448 34481 34489 3449 78072 7814

232	Sprains and strains	8400 8401 8402 8403 8404 8405 8406 8407 8408 8409 8410 8411 8412 8413 8418 8419 84200 84201 84202 84209 84210 84211 84212 84213 84219 8430 8431 8438 8439 8440 8441 8442 8443 8448 8449 84500 84501 84502 84503 84509 84510 84511 84512 84513 84519 8460 8461 8462 8463 8468 8469 8470 8471 8472 8473 8474 8479 8480 8481 8482 8483 84840 84841 84842 84849 8485 8488 8489 9057
58	Other nutritional; endocrine; and metabolic disorders	2700 2701 2702 2703 2704 2705 2706 2707 2708 2709 2710 2711 2712 2713 2714 2718 2719 2725 2726 2727 2728 2729 2730 2731 2732 2733 2734 2738 2739 2750 27501 27502 27503 27509 2751 2752 2753 2754 27540 27541 27542 27549 2755 2758 2759 2771 2772 2773 27730 27731 27739 2774 2775 2776 2777 2778 27781 27782 27784 27785 27786 27787 27789 2779 2780 27800 27801 27802 27803 2781 2782 2783 2784 2788 7831 7832 78321 78322 7833 7834 78340 78341 78342 78343 7835 7837 7839 79391 7947 7957 V122 V1221 V1229 V850 V8521 V8522 V8523 V8524 V8525 V8530 V8531 V8532 V8533 V8534 V8535 V8536 V8537 V8538 V8539 V854 V8541 V8542 V8543 V8544 V8545 V8551 V8553 V8554
128	Asthma	49300 49301 49302 49310 49311 49312 49320 49321 49322 49381 49382 49390 49391 49392
134	Other upper respiratory disease	470 4710 4711 4718 4719 4720 4721 4722 4760 4761 4770 4772 4778 4779 4780 4781 47811 47819 47820 47821 47822 47824 47825 47826 47829 47830 47831 47832 47833 47834 4784 4785 4786 47870 47871 47874 47875 47879 4788 4789 5191 51911 51919 5192 5193 7841 78440 78441 78442 78443 78444 78449 7847 7848 7849 78499 7861 V414 V440 V550
59	Deficiency and other anemia	2800 2801 2808 2809 2810 2811 2812 2813 2814 2818 2819 2820 2821 2822 2823 2824 28240 28243 28244 28245 28246 28247 28249 2827 2828 2829 2830 2831 28310 28311 28319 2832 2839 2840 28401 28409 2841 28411 28412 284 2842 2848 28481 28489 2849 2850 28521 28522 28529 2858 2859
154	Noninfectious gastroenteritis	55841 55842 5589

CCS - Clinical Classification Software, ICD-9-CM - International Classification of Diseases, 9th Revision, Clinical Modification

Supplement Table 2. Proportions of Missing Data (n=1945)

Variables	Cases with Missing Data n (%)
Patient Characteristics	
Sex	12 (0.6%)
Age	0
Race/ethnicity	0
Payer	
Number of comorbid chronic conditions	0
Weekend admission	0
Hospital Characteristics	
State	0
Type of hospital ownership	23 (1.2%)
Children's hospital	135 (6.9%)
Teaching hospital	23 (1.2%)
Has fully implemented electronic records	270 (13.9%)
Has a pediatric ED	135 (6.9%)
Has a pediatric intensive care unit	135 (6.9%)
Total number of ED visits in a year	23 (1.2%)

ED - emergency department

Supplement Table 3. Twenty most common diagnoses given at emergency department treat-and-release visits followed by a sepsis admission within 7 days (n=219)[a]

CCS Label	Description	Frequency n (%)
246	Fever of unknown origin	67 (30.6)
7	Viral infection	30 (13.7)
133	Other lower respiratory disease	29 (13.2)
126	Other upper respiratory infections	24 (11.0)
155	Other gastrointestinal disorders	22 (10.0)
251	Abdominal pain	22 (10.0)
122	Pneumonia (except that caused by tuberculosis or sexually transmitted disease)	21 (9.6)
55	Fluid and electrolyte disorders	18 (8.2)
250	Nausea and vomiting	16 (7.3)
83	Epilepsy; convulsions	15 (6.8)
159	Urinary tract infections	13 (5.9)
253	Allergic reactions	11 (5.0)
259	Residual codes; unclassified	11 (5.0)
82	Paralysis	10 (4.6)
232	Sprains and strains	10 (4.6)
58	Other nutritional; endocrine; and metabolic disorders	9 (4.1)
128	Asthma	9 (4.1)
134	Other upper respiratory disease	9 (4.1)
59	Deficiency and other anemia	8 (3.7)
154	Noninfectious gastroenteritis	8 (3.7)

CCS - Clinical Classification Software

[a] This is a visit-level analysis, which includes multiple visits by a single patient. Multiple diagnoses may also be given at a single visit. All documented diagnoses were included (in any discharge diagnosis position, i.e., not just first-listed diagnosis). Diagnoses are presented in order of frequency.

Supplement Table 4. Observed frequency of most common emergency department (ED) diagnoses of patients subsequently admitted for sepsis within 7 days (n=219) compared to expected frequencies of the same diagnoses in all pediatric emergency department treat-and-release visits[a]

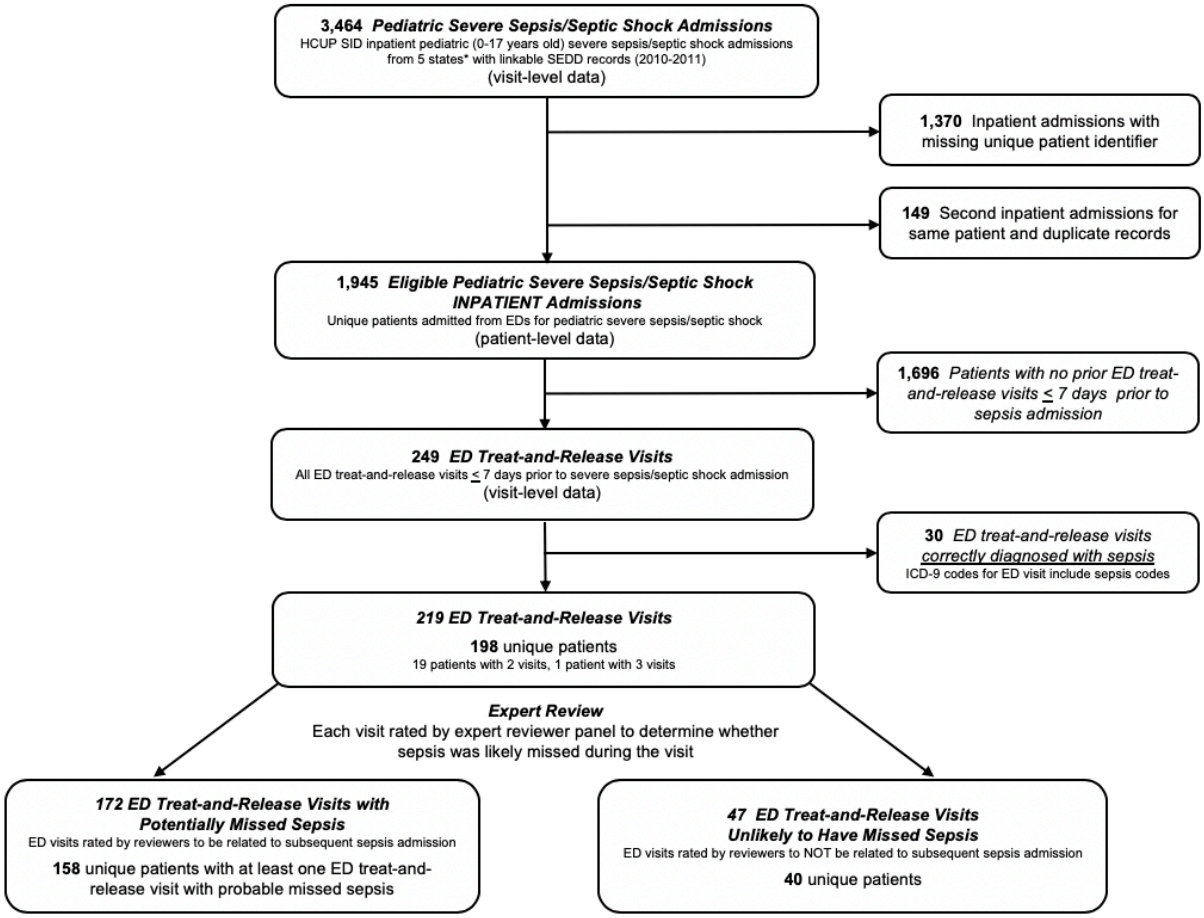
CCS Label	Description	Observed (%)	Expected (%)[b]	Observed to Expected Ratio[c]
246	Fever of unknown origin	30.6	0.75	41.1
7	Viral infection	13.7	0.32	42.2
133	Other lower respiratory disease	13.2	0.50	26.7
126	Other upper respiratory infections	11	0.89	12.3
155	Other gastrointestinal disorders	10	0.32	31.8
251	Abdominal pain	10	0.39	25.9
122	Pneumonia (except that caused by tuberculosis or sexually transmitted disease)	9.6	0.12	81.0
55	Fluid and electrolyte disorders	8.2	0.13	65.6
250	Nausea and vomiting	7.3	0.50	14.5
83	Epilepsy; convulsions	6.8	0.09	72.2
159	Urinary tract infections	5.9	0.10	58.9
253	Allergic reactions	5	0.25	20.2
259	Residual codes; unclassified	5	0.15	34.6
82	Paralysis	4.6	0.01	454.0
232	Sprains and strains	4.6	0.43	10.6
58	Other nutritional; endocrine; and metabolic disorders	4.1	0.02	179.6
128	Asthma	4.1	0.38	10.7
134	Other upper respiratory disease	4.1	0.18	22.8
59	Deficiency and other anemia	3.7	0.01	353.3
154	Noninfectious gastroenteritis	3.7	0.13	28.7

CCS - Clinical Classification Software, ED - emergency department

[a] This is a visit-level analysis, which includes multiple visits by a single patient. Multiple diagnoses may also be given at a single visit. All documented diagnoses were included (in any discharge diagnosis position, i.e., not just first-listed diagnosis). Diagnoses are presented in order of frequency found in sepsis cohort.

[b] Proportion of all ED treat-and-release visits (2010-2011 in all included states) that have the identified diagnoses.

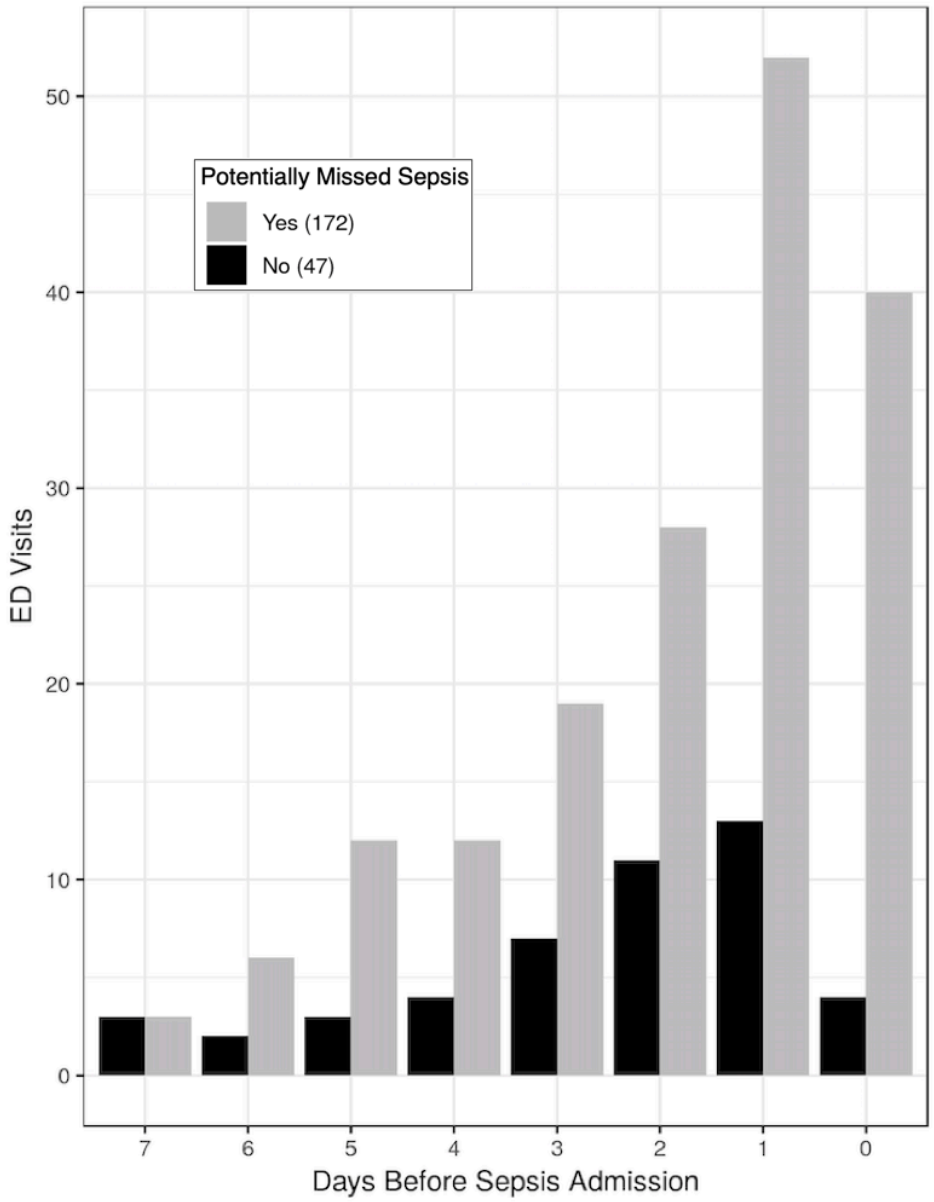
[c] Values >1 reflect disproportionate over-representation of that diagnosis compared to overall ED population.



Supplement Figure 1. Derivation of study population and determination of potentially missed sepsis diagnosis

Identification of index population of pediatric patients admitted inpatient for severe sepsis/septic shock, linking of inpatient sepsis admissions with prior emergency department treat-and-release visits, and determination of potentially missed sepsis.

ED – emergency department; HCUP – Healthcare Utilization Project; ICD-9 – International Classification of Diseases, 9th Revision; SEDD – State Emergency Department Database; SID – State Inpatient Database



Supplement Figure 2. Temporal Profile Analysis

Emergency department pediatric treat-and-release visits with potentially missed sepsis diagnoses vs. unlikely missed sepsis diagnoses (as determined by expert reviewers) in the 7 days prior to inpatient admission for severe sepsis/septic shock.

ED – emergency department