

Using NHSN's Antimicrobial Use Option to Monitor and Improve Antibiotic Stewardship in Neonates

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BACKGROUND: The Antimicrobial Use (AU) Option of the Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN) is a surveillance resource that can provide actionable data for antibiotic stewardship programs. Such data are used to enable measurements of AU across hospitals and before, during, and after stewardship interventions.

METHODS: We used monthly AU data and annual facility survey data submitted to the NHSN to describe hospitals and neonatal patient care locations reporting to the AU Option in 2017, examine frequencies of most commonly reported agents, and analyze variability in AU rates across hospitals and levels of care. We used results from these analyses in a collaborative project with Vermont Oxford Network to develop neonatal-specific Standardized Antimicrobial Administration Ratio (SAAR) agent categories and neonatal-specific NHSN Annual Hospital Survey questions.

RESULTS: As of April 1, 2018, 351 US hospitals had submitted data to the AU Option from at least 1 neonatal unit. In 2017, ampicillin and gentamicin were the most frequently reported antimicrobial agents. On average, total rates of AU were highest in level III NICUs, followed by special care nurseries, level II-III NICUs, and well newborn nurseries. Seven antimicrobial categories for neonatal SAARs were created, and 6 annual hospital survey questions were developed.

CONCLUSIONS: A small but growing percentage of US hospitals have submitted AU data from neonatal patient care locations to NHSN, enabling the use of AU data aggregated by NHSN as benchmarks for neonatal antimicrobial stewardship programs and further development of the SAAR summary measure for neonatal AU.

ABSTRACT



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Neonates represent a challenging but high-priority population for targeted hospital antibiotic stewardship efforts. Maternal and infant risk factors for neonatal sepsis are common.^{1,2} These risks, coupled with the diagnostic difficulties that confront neonatal practitioners, often lead to initiation and continuation of antibiotics in the absence of a clear indication.^{1,3} Because mortality associated with neonatal sepsis is high, especially among preterm and very low birth weight infants,^{3–5} it is difficult to delay or avoid antibiotic use when documented risk factors are present. However, neonatal antibiotic exposure is associated with increased risk of various adverse events, including disruption to the developing microbiome, bronchopulmonary dysplasia, necrotizing enterocolitis, late-onset sepsis, invasive candidiasis, and mortality.^{1,6,7} Despite this challenge of weighing infection risk against adverse antibiotic effects, opportunities exist for reducing the number of unnecessary antibiotic starts, decreasing duration of therapy, and improving overall judiciousness of antimicrobial use (AU) in neonates.

Antibiotic stewardship programs (ASPs) aim to improve patient outcomes while minimizing unintended consequences associated with AU.⁸ To achieve these goals, ASPs are focused on decreasing inappropriate use, and the Centers for Disease Control and Prevention (CDC) developed the Core Elements of Hospital ASPs for facilities to implement to aid in this process.^{9,10} Determining antibiotic appropriateness is challenging in any patient population, even more so in neonates, whose signs and symptoms of infection are often subtle and nonspecific.³ Adding further complexity, rates of AU in NICUs are highly variable and often unexplained by burden of proven infection.^{6,11} In situations in which appropriate AU is not clearly defined, “an initial first step could be to educate the NICU team on their own prescribing practices to engender a discussion on best practices.”¹² Electronic AU surveillance systems can contribute substantially to ASP efforts, because they enable hospitals to streamline data collection and reporting, provide timely, comparative AU benchmarks, and

make available additional data and analytic options that can help guide medication use evaluations and prompt changes in prescribing practices when those changes are indicated.

The CDC’s National Healthcare Safety Network (NHSN) is a public health surveillance system used to collect, analyze, report, and make available data for monitoring, measuring, and responding to health care–associated infections, AU and antimicrobial resistance, blood transfusion safety events, and adherence to infection prevention practices and antibiotic stewardship. The NHSN’s Antimicrobial Use and Resistance (AUR) Module provides the infrastructure and support necessary for hospitals to electronically submit and monitor their AUR. The AU Option of the AUR Module enables hospitals to report, track, compare, and interpret AU to improve ASP decision-making. Here, we describe hospitals and units reporting neonatal data to the NHSN’s AU Option, summarize AU data reported in 2017, present plans to develop neonatal AU benchmark metrics through collaboration with the Vermont Oxford Network (VON), and discuss the integral role electronic surveillance plays in neonatal antimicrobial stewardship.

METHODS

Data Sources

We aggregated monthly hospital AU data for our analyses of AU in neonatal units. The AU Option enables hospitals to submit data from 4 NHSN-defined neonatal location types: level I well newborn nurseries, level II special care nurseries, level II-III NICUs, and level III NICUs.¹³ In the NHSN, levels I and II are defined in accordance with the American Academy of Pediatrics.¹⁴ The NHSN defines level II-III units as those housing both level II and level III newborns and infants, analogous to a mixed acuity unit for neonatal critical care patients.¹³ Level III and IV NICUs, as defined by the Academy of Pediatrics, are both considered level III in the NHSN.

Hospitals submit AU as days of therapy (DOTs) for 90 antimicrobial agents across 4 routes of administration: digestive, intramuscular, intravenous, and respiratory.

Electronic medication administration (eMAR) and/or barcoded medication administration (BCMA) systems serve as data sources for DOTs. Admission discharge transfer systems, used by hospitals to track patients throughout their hospital stays, serve as data sources for days present, the denominator in rate calculations.¹⁵ Days present are defined as the time period during which a patient is at risk for antimicrobial exposure for a given patient care location, calculated as the number of patients present in a particular location for any portion of a calendar day.¹⁵ DOTs and days present are aggregated monthly to the patient care location-level before submission; no patient-level information is reported. Participation is voluntary, and all reporting is electronic, with no manual data entry.¹⁵

AU Option Participation

We used neonatal AU data and hospital characteristics self-reported in the 2017 NHSN Annual Hospital Survey for a descriptive analysis of hospitals reporting neonatal data to the AU Option (2011–2018). We used 2017 NHSN central line–associated bloodstream infection data, a reporting requirement for hospitals participating in Centers for Medicare and Medicaid Services’ Hospital Inpatient Quality Reporting program, to estimate the number of hospitals in each state providing neonatal intensive care. With hospitals reporting central line–associated bloodstream infection data to the NHSN from an NICU as our denominator, we estimated the proportion of eligible facilities reporting NICU data to the AU Option in 2017, by state. We approximated the number of US hospitals providing well newborn care using an American Hospital Association report of hospitals with at least 1 birth in 2015.¹⁶ Using this estimate as our denominator, we calculated the proportion of eligible US hospitals reporting well newborn data to the AU Option in 2017.

AU Data Validation and Analyses

We reviewed all 2017 neonatal AU data submitted to NHSN and excluded records from analyses if days present were reported to be 0 or if large changes in location-level DOTs or days present (>70%

change in value, where 1 value was >100) were observed from 1 month to the next. Using validated data pooled across months and facilities, we identified the 5 antimicrobial agents in each level of patient care with the greatest number of DOTs. Next, for each level of patient care within a facility, we calculated drug-specific pooled rates by dividing pooled DOTs by pooled days present and multiplying by 1000. SAS version 9.3 software (SAS Institute, Inc, Cary, NC) was used for all analyses.

Preparation for Development of Neonatal AU Benchmark Metrics

The AU Option offers numerous analysis tools to help in the interpretation and tracking of AU by ASPs. One option provides Standardized Antimicrobial Administration Ratios (SAARs) for select groups of antimicrobial agents and select locations. The SAAR is a National Quality Forum–endorsed metric used to compare observed AU (ie, DOTs reported by a hospital for a specified set of patient care locations and a defined time period) to predicted AU (ie, predicted DOTs, calculated by using nationally aggregated data that are risk adjusted for location and hospital characteristics).¹⁷ Because neonatal AU differs substantially from adult and pediatric AU in terms of clinical indications and choice of agents, the Division of Healthcare Quality Promotion at the CDC is collaborating with the VON to develop neonatal-specific SAARs.

The VON is a nonprofit organization with a global reach that works collaboratively with health care professionals to improve the quality and safety of health care for newborn infants. With VON's guidance, the Division of Healthcare Quality Promotion organized a group of US subject matter experts to create materials necessary for the development of neonatal SAARs. This group, known as the Antibiotic Stewardship Program Special Interest Group (ASP-SIG), met monthly from 2017 to 2018. Through these meetings, neonatal-specific NHSN Annual Hospital Survey questions were developed to gather hospital-level patient care and admission information associated with neonatal AU for inclusion in predictive models. In addition, neonatal ASP targets

were identified, and SAAR agent categories were created.

RESULTS

As of April 1, 2018, 351 acute care hospitals reported at least 1 month of neonatal AU data to the AU Option. Hospitals were primarily composed of large (interquartile range [IQR]: 170–395 beds) general acute care (90%) academic teaching hospitals (72%) (Table 1). More hospitals reported from a special care nursery or NICU but not a well newborn nursery (42%) than from a well newborn nursery alone (17%). These 351 hospitals reported from 544 unique neonatal units: 224 well newborn nurseries, 64 special care nurseries, 154 combined level II-III NICUs, and 102 level III NICUs. The majority of participating hospitals reported from 1 (56%) or 2 (38%) unique neonatal units (range: 1–8).

In 2017, 311 facilities reported at least 1 month of data to the AU Option, 76%

reported ≥6 months, and 57% reported ≥11 months. In 2017, 1041 hospitals reported to NHSN from any level II-III or level III NICU, 213 (20.5%) of which submitted to the AU Option from an NICU. Submission of neonatal data to the AU Option varied greatly by state, as did the number of hospitals with NICUs eligible for participation (Fig 1). At least half of eligible hospitals in Vermont, Utah, Colorado, Missouri, and Oregon reported 2017 NICU data to the AU Option. Eligible hospitals in 10 states, Washington, District of Columbia, and Puerto Rico have not yet reported. Approximately 3062 US hospitals reported at least 1 birth in 2015. In 2017, 177 (5.8%) hospitals reported data to the AU Option from a well newborn nursery.

Internal validation of 2017 neonatal AU data submitted to the NHSN led to the exclusion of 1.7% of records. Validated 2017 data included 309 hospitals reporting from 456 unique neonatal units. Among these

TABLE 1 Characteristics of Hospitals Submitting At Least 1 Month of Data to the NHSN AU Option From 1 or More Neonatal Units, 2011–2018 (*n* = 351)

Characteristic	Facilities, <i>n</i> (%)
Facility type	
General acute care	316 (90.0)
Military	13 (3.7)
Children's	10 (2.8)
Critical access	6 (1.7)
Women's	3 (0.9)
Women's and children's	3 (0.9)
Teaching status ^a	
Nonteaching	97 (27.6)
Undergraduate teaching	54 (15.4)
Graduate teaching	79 (22.5)
Major teaching	121 (34.5)
Bed size	
>200 beds	241 (68.7)
51–200 beds	91 (25.9)
≤50 beds	19 (5.4)
Location types reported	
Special care nursery or NICU only	147 (41.9)
Well newborn nursery only	59 (16.8)
Both special care nursery or NICU and well newborn nursery	145 (41.3)

^a Teaching status as defined in and reported through the NHSN Patient Safety Component Annual Hospital Survey. Undergraduate teaching refers to a facility that has a program for medical or nursing students only. Graduate teaching refers to a facility that has a program for postgraduate medical training (ie, residency and/or fellowships). Major teaching refers to a facility that has a program for medical students and postgraduate medical training.

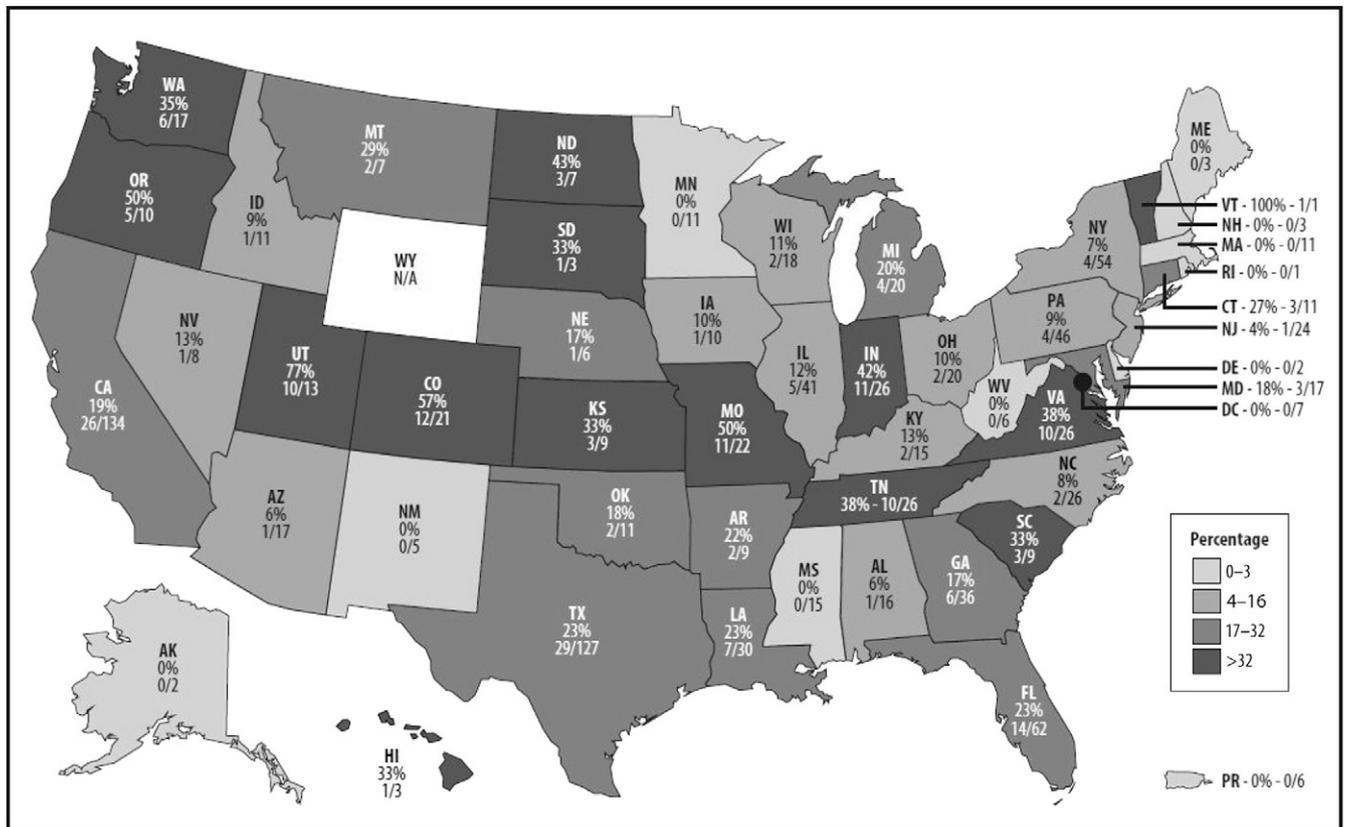


FIGURE 1 Number and percentage of US general acute care hospitals with a level II-III or level III NICU reporting to the NHSN AU Option in 2017, by state.

309 hospitals, ampicillin and gentamicin were the 2 most commonly used antimicrobial agents in all 4 levels of neonatal care, and the majority of total AU in each level of care (71%–97%) was composed of 4 agents (Fig 2). A larger variety of antimicrobial drugs was used in NICUs compared to special care and well newborn nurseries, with 50 different antimicrobial agents used at least once in a level III NICU, 45 in a level II-III NICU, 31 in a special care nursery, and 22 in a well newborn nursery. Among hospitals reporting ≥ 4 months of 2017 neonatal AU data, the median number of unique antimicrobial agents used was 10 (IQR: 6–18) among hospitals reporting only from a special care nursery or NICU and 3 (IQR: 2–4) among hospitals reporting only from a well newborn nursery.

Although special care nurseries reported the highest median rates of ampicillin and gentamicin, total AU was highest in level III NICUs, followed by special care nurseries,

level II-III NICUs, and well newborn nurseries (Table 2). On average, level III NICUs had more days present per month (IQR: 327–1233) compared to level II-III NICUs (IQR: 168–533), well newborn nurseries (IQR: 152–523), and special care nurseries (IQR: 51–215).

We identified and prioritized 5 neonatal ASP targets and developed 7 SAAR antimicrobial categories to help hospitals monitor their AU to meet stewardship goals (Table 3). Once developed, neonatal SAARs will be submitted for National Quality Forum endorsement as a tool for public health surveillance and quality improvement; SAARs are not intended for public reporting and/or payment at this time.

DISCUSSION

Only a small percentage of hospitals providing neonatal care in the United States reported AU data from neonatal patient care locations to the NHSN in 2017. However, the amount of data they submitted enabled this

first-ever report of neonatal AU using data collected by hospitals from their point-of-care, antimicrobial administration record systems and submitted electronically to a national surveillance system. These data, in turn, enabled the VON, the CDC, and a group of neonatal AU experts to begin developmental work on new metrics for benchmarking neonatal AU.

The AU Option, which the NHSN launched with the primary goal of providing actionable data for hospital ASPs, is a work in progress, and the need for greater participation by neonatal units in AU surveillance is suggested from this study's findings. Feedback from AU Option users emphasizes the utility of the SAAR in stewardship efforts and the desire for additional patient care locations in SAAR models.^{18,19} Many hospitals do not yet report neonatal data to the AU Option, and the CDC is working with the VON and other partner organizations to close that reporting gap. Some success has been achieved recently,

TABLE 2 Distribution of Data Reported to the AU Option (2017) by Level of Neonatal Care (Monthly Days Present and Pooled Rates) for the 5 Antimicrobial Agents With the Highest Mean Rates and for All Antimicrobial Agents Combined

	5%	10%	25%	50%	Mean	75%	90%	95%
Level III NICUs (n = 89)								
Days present	126	173	327	606	815	1233	1751	1988
Rate (DOTs per 1000 d present)								
Ampicillin	16	33	75	100	107	148	174	184
Gentamicin	0.3	30	51	81	80	106	136	146
Vancomycin	0.0	2.2	8.3	19	24	34	51	59
Piperacillin/tazobactam	0.0	0.0	0.0	2.2	14	12	34	70
Fluconazole	0.0	0.0	0.0	7.8	13	21	31	41
All antimicrobial agents ^a	74	115	200	285	294	376	456	505
Level II and III NICUs (n = 130)								
Days present	33	87	168	302	437	533	891	1110
Rate (DOTs per 1000 d present)								
Ampicillin	8.3	38	67	112	132	175	247	299
Gentamicin	6.0	20	45	83	95	124	169	222
Vancomycin	0.0	0.0	0.7	7.8	14	21	33	52
Ceftazidime	0.0	0.0	0.0	0.0	6.0	2.2	9.8	42
Fluconazole	0.0	0.0	0.0	0.3	5.6	6.7	21	27
All antimicrobial agents	43	85	161	249	278	369	474	588
Special care nurseries (n = 50)								
Days present	6	18	51	111	157	215	369	488
Rate (DOTs per 1000 d present)								
Ampicillin	0.0	22	66	132	153	227	316	371
Gentamicin	0.0	7.9	42	99	115	173	244	258
Cefotaxime	0.0	0.0	0.0	0.0	3.8	0.0	11	24
Penicillin G	0.0	0.0	0.0	0.0	3.6	0.0	5.5	18
Ceftazidime	0.0	0.0	0.0	0.0	2.7	0.0	1.5	21
All antimicrobial agents	0.0	38	131	263	289	406	605	657
Well Newborn nurseries (n = 174)								
Days present	31	73	152	303	399	523	808	1017
Rate (DOTs per 1000 d present)								
Ampicillin	0.0	0.0	0.3	3.8	14	16	30	73
Gentamicin	0.0	0.0	0.0	2.4	10	12	23	58
Amoxicillin	0.0	0.0	0.0	0.0	0.3	0.2	1.0	1.7
Penicillin G	0.0	0.0	0.0	0.0	0.3	0.0	0.7	1.3
Cefotaxime	0.0	0.0	0.0	0.0	0.3	0.0	0.3	1.2
All antimicrobial agents	0.0	0.0	1.5	7.8	25	29	61	133

The rate was calculated by DOTs per 1000 days present. *N* is the number of hospitals reporting at least 1 month of data from specified level of care in 2017.

^a All antimicrobial agents for which data are reported to the AU Option.

neonatal component in the NHSN to provide hospitals with a platform to report patient-level neonatal late-onset sepsis and meningitis data. Once fully implemented, AU data can be analyzed in the presence of infection data, further informing us of factors important for improved risk adjustment in future SAAR models.

Despite these limitations, the AU Option has served as a valuable resource for hospitals seeking to better understand their AU and for the CDC to monitor AU across facilities, states, and throughout the nation. When looking at national rates of neonatal AU among hospitals reporting to the AU Option, significant variations across facilities and units are evident. Schulman et al⁶ found that among California NICUs, rates of AU were highly variable and independent of proven infection, necrotizing enterocolitis, surgical volume, and mortality and recommends working to identify warranted ranges of AU for each level of care. Data reported to the AU Option will continue to enable tracking of interfacility variation in neonatal AU.

As new stewardship interventions are introduced, AU data will enable the assessment of their impact. For example, rates of ampicillin and gentamicin can be compared before and after introduction of the early-onset sepsis calculator²⁰ to determine if this tool is associated with decreased rates of antibiotics used empirically for early-onset sepsis. Or, as another example, many experts recommend oxacillin and gentamicin for suspected late-onset sepsis rather than vancomycin and gentamicin, unless infants are colonized with methicillin-resistant *Staphylococcus aureus*. According to data submitted to the AU Option, rates of oxacillin are low, and vancomycin remains the third most commonly used agent in NICUs, suggesting perhaps clinicians are unaware of current practice recommendations or hospitals have high rates of methicillin-resistant *Staphylococcus aureus* colonization.

These types of analyses will become even more meaningful as reporting to the AU Option increases. Hospitals interested in participating can learn more about system requirements and the implementation process on NHSN's AUR Module Web site.^{21,22}

inadvertently map infants in the NHSN to their mothers' rooms rather than to a level I nursery.

The CDC works to mitigate these limitations in various ways. New survey questions are aimed to identify potential differences in

patient population within facilities and are used to clarify how well newborns receiving antimicrobial agents are mapped in the NHSN. All survey responses will be considered as adjustments in SAAR models. In addition, the CDC plans to launch a

TABLE 3 Neonatal Antimicrobial Stewardship Targets and Proposed SAAR Antimicrobial Agent Categories

Neonatal ASP Target	SAAR Agent Category	Antimicrobials Included	Routes of Administration	NHSN Units Included
Empiric treatment of late-onset sepsis	Vancomycin	Vancomycin	IV	II, II-III, III
Broad spectrum treatment of bacterial infections	Broad spectrum antibacterial agents	Piperacillin and/or tazobactam Cefepime Ertapenem Meropenem Imipenem and/or cilastatin	IV	II, II-III, III
Prophylaxis and treatment of invasive candidiasis	Fluconazole	Fluconazole	IV, oral	II, II-III, III
Global or total antibiotic use	All antibacterial agents	All antibacterial agents in AU option	IV, IM, oral, respiratory	II, II-III, III
Empiric treatment of early-onset sepsis	Ampicillin	Ampicillin	IV	All
	Cefotaxime, Ceftazidime	Cefotaxime Ceftazidime	IV	All
Empiric treatment of early-onset and late-onset sepsis	Aminoglycosides	Gentamicin Tobramycin Amikacin	IV	All

IM, intramuscular; IV, intravenous.

Participation in the AU Option requires that facilities have either eMAR or BCMA systems in place for inpatient locations and that data are properly packaged using a standard Health Level Seven format. In a VON survey of 141 hospitals with NICUs, it was found that 92% of hospitals have an eMAR system and 94% have a BCMA system. The CDC provides current and prospective AU Option participants with resources and assistance to help guide implementation, submission, and validation efforts.^{13,15,21–23}

As we look ahead to neonatal SAAR development, information provided here can serve as encouragement for hospitals not

yet enrolled in NHSN's AU Option to become involved and for current participants to ensure data submitted is complete and valid. While we plan to provide risk-adjusted AU benchmark metrics using patient-level information in the future, in the near term, SAARs adjusted for hospital- and location-level factors can serve as a starting place for hospitals to investigate at which points their neonatal AU may deviate from what is predicted.

CONCLUSIONS

Accurately monitoring AU in a timely manner is an important part of neonatal antimicrobial stewardship and patient care.

The NHSN's AU Option provides hospitals with the surveillance tools necessary to electronically track and efficiently interpret neonatal AU, identify opportunities for improvement, and assess the effectiveness of interventions.

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