Performance of a multi-disciplinary emergency department observation protocol for acetaminophen overdose.

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TOXICOLOGY INVESTIGATION

Performance of a Multi-disciplinary Emergency Department Observation Protocol for Acetaminophen Overdose

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Abstract The availability of 20-h *N*-acetylcysteine (NAC) infusion for low-risk acetaminophen (APAP) overdose enabled our center to implement an Emergency Department observation unit (OU) protocol as an alternative to hospitalization. Our objective was to evaluate our early experience with this protocol. This retrospective cohort study included all patients treated for low-risk APAP overdose in our academic hospital between 2006 and 2011. Cases were identified using OU and pharmacy records. Successful OU discharge was defined as disposition with no inpatient admission. Differences in medians with 95 % confidence intervals were used for comparisons. One hundred ninety-six patients received NAC for APAP overdose with a mean age of 35 years (SD 14); 73 % were white, and 43 % were male. Twenty (10 %) received care in the OU; 3/20(15 %) met criteria for inclusion in the OU protocol and 13/20(65 %) were discharged successfully. Out of the 196 patients, 10 met criteria for inclusion in the OU protocol but instead received care in the inpatient setting. The median total length of stay from presentation to ED discharge was 41 h for all patients treated in the OU, compared to 68 h for ten patients who met criteria for inclusion in the OU protocol but who were admitted (difference 27 h, 95 % CI 18–72 h). ED observation for APAP overdose can be a viable alternative to inpatient admission. Most patients were successfully discharged from the OU. This evaluation identified both over- and under-utilization of the OU. OU treatment resulted in shorter median length of stay than inpatient admission.

Keywords Overdose · Observation · Acetaminophen · Length of stay

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Introduction

Background and Importance

Acetaminophen (APAP) is the most commonly ingested pharmaceutical in overdose and also causes the highest morbidity and mortality after overdose [1, 2]. Treatment conventionally involved an intravenous infusion of N-acetylcysteine (IV NAC) given over 3 days, requiring inpatient stays between about 62 and 76 h [3, 4]. A 20-h course of IV NAC therapy has been shown to be effective in patients with low-risk acetaminophen ingestion [5].

It is potentially feasible to complete the 20-h IV NAC protocol in an ED observation unit (OU). However, treating overdose patients may require resources beyond those typical of an OU, including psychiatric and social services, and the selective use of restraints for patient safety [6]. These needs may provide a barrier to appropriate OU care and disposition of the APAP overdose patient in the absence of an established protocol [7].

Goals

We developed a multi-disciplinary protocol for the treatment of APAP overdose in an OU. Emergency physicians, nursing, toxicology, pharmacy and psychiatry were involved in developing the protocol, which was designed to provide 20 h of IV

NAC and psychiatric evaluation as needed during an observation period designed to determine if the patient required inpatient admission, further psychiatric treatment or if the patient could be discharged home. Physicians employed in the ED received an email and an announcement made at Grand Rounds describing the new protocol. At each subsequent monthly Morbidity and Mortality Conference, usage rates of this and other observation protocols were provided to those in attendance. At the time of this study, the observation unit was staffed by emergency physicians and mid-level providers 24 h per day and with access to psychiatric consultation in the ED at all times. Our primary goal is to report our experience during the first 5 years of protocol initiation as a critical component of the implementation process [8, 9]. Here, we report on the over- and of the OU protocol and characterize disposition and recidivism for patients for whom the OU protocol was initiated. These observations are placed in context by comparison to patients who were eligible for the OU protocol but who were admitted directly from the ED to an inpatient setting for treatment with IV NAC.

Methods

Study Design

This retrospective cohort study involved review of the medical records for patients presenting with acute, low-risk APAP overdose. The study was approved by the local Institutional Review Board.

Table 1 Characteristics of the study population. Data are given in mean and standard deviation or frequency and percent

		Total		Enrolled (n=20)		Eligible and not enrolled (n=10)		Not eligible (n=166)	
Age		35	(14)	29	(10)	29	(11)	36	(14)
Race									
	Caucasian	144	73.5 %	14	70.0 %	9	90.0 %	121	72.9 %
	African American	50	25.5 %	5	25.0 %	1	10.0 %	44	26.5 %
	Other	1	0.5 %	0	0.0 %	0	0.0 %	1	0.6 %
	Hispanic	1	0.5 %	1	5.0 %	0	0.0 %	0	0.0 %
Sex									
	Female	111	56.6 %	13	65.0 %	7	70.0 %	91	54.8 %
	Male	85	43.4 %	7	35.0 %	3	30.0 %	75	45.2 %
Payer status									
	Medicare or Medicaid	78	39.8 %	2	10.0 %	4	40.0 %	72	43.4 %
	Self-pay	66	33.7 %	11	55.0 %	4	40.0 %	51	30.7 %
	Private insurance	52	26.5 %	7	35.0 %	2	20.0 %	43	25.9 %
Adverse reaction to NAC		6	3.1 %	0	0.0 %	0	0.0 %	6	3.6 %
Disposition									
	Admit—Step Down	67	34.2 %	0	0.0 %	3	30.0 %	64	38.6 %
	Admit—Medicine Floor	55	28.1 %	0	0.0 %	6	60.0 %	49	29.5 %
	Admit—MICU	44	22.4 %	0	0.0 %	1	10.0 %	43	25.9 %
	Admit—Observation Protocol	20	10.2 %	20	100.0 %	0	0.0 %	0	0.0 %
	PES—Home	6	3.1 %	0	0.0 %	0	0.0 %	6	3.6 %
	PES—Admit	3	1.5 %	0	0.0 %	0	0.0 %	3	1.8 %
	Home	1	0.5 %	0	0.0 %	0	0.0 %	1	0.6 %
Psych hold signed									
	Yes	177	90.3 %	17	85.0 %	10	100.0 %	150	90.4 %
	No	1	0.5 %	0	0.0 %	0	0.0 %	1	0.6 %
	NA	18	9.2 %	3	15.0 %	0	0.0 %	15	9.0 %
Acetaminophen use for pain (other)		10	55.6 %	2	66.7 %	0	0.0 %	8	53.3 %
Acetaminophen use for pain (dental)		6	33.3 %	0	0.0 %	0	0.0 %	6	40.0 %
Other acetaminophen use		2	11.1 %	1	33.3 %	0	0.0 %	1	6.7 %

Other acetaminophen use refers to use as an ingredient in a sleep aid

NAC N-acetylcysteine, the intravenous antidote used for acetaminophen overdose, *MICU* medical intensive care unit, *OU* observation unit at our institution, *PES* psychiatric emergency services, *NA* not applicable

Subjects and Setting

The protocol was implemented on September 5, 2006 at an urban, academic ED that has a volume of about 90,000 visits annually. Patients presenting between protocol implementation and July 1, 2011 were screened for inclusion if the hospital pharmacy generated a bill for IV NAC. Patients aged 18 years or older who initially presented to the ED and who received IV NAC for acetaminophen overdose were included. Patients presenting to the ED for acetaminophen exposure who did not require treatment with IV NAC were excluded from the study. Characteristics of the study population are listed in Table 1.

Observation Protocol

The full OU protocol is given in the Online Resource. Briefly, patients known to be presenting within 20 h of an acute APAP ingestion with normal liver enzymes who are plotted above the Rumack–Matthew nomogram treatment line but deemed low risk (<10 %) based on actual or predicted time of IV NAC infusion [5, 10] are eligible for treatment in the OU; full eligibility criteria are listed in Table 2. Physician discretion may also be used to enroll a patient in the OU protocol. Treatment in the protocol includes 20 h of IV NAC and a psychiatric evaluation if the APAP ingestion occurred in the setting of a suicide attempt. The protocol also includes repeat transaminase levels (aspartate aminotransferase or AST, and alanine aminotransferase or ALT) and renal function testing, coagulation studies and acetaminophen level performed at 20 h post-ingestion to ensure normalcy before disposition from the observation period. As needed anti-emetics and symptom control for anaphylactoid reaction to NAC are also included in the order set used in the protocol.

Table 2 Proportions of patients meeting inclusion and exclusion criteria for the OU protocol

	Total		Enrolled (n=20)		Eligible and not enrolled (n=10)		Not eligible (n=166)	
Inclusion criteria								
Single overdose	157	80.1 %	18	90.0 %	10	100.0 %	129	77.7 %
Time of ingestion able to be estimated	133	67.9 %	18	90.0 %	10	100.0 %	105	63.3 %
Acetaminophen level drawn between 4–20 h	128	65.3 %	17	85.0 %	10	100.0 %	101	60.8 %
Patient above nomogram treatment line								
Yes	53	27.0 %	8	40.0 %	10	100.0 %	35	21.1 %
N risk>10 %	10	5.1 %	1	5.0 %	0	0.0 %	9	5.4 %
N below treatment line	62	31.6 %	8	40.0 %	0	0.0 %	54	32.5 %
NA	71	36.2 %	3	15.0 %	0	0.0 %	68	41.0 %
Initial LFTs normal	149	76.0 %	16	80.0 %	10	100.0 %	123	74.1 %
Exclusion criteria								
Abnormal vital signs	111	56.6 %	3	15.0 %	0	0.0 %	108	65.1 %
Abnormal								
Systolic blood pressure	58	52.3 %	1	33.3 %	0	0.0 %	57	52.8 %
Diastolic blood pressure	42	37.8 %	0	0.0 %	0	0.0 %	42	38.9 %
Heart rate	71	64.0 %	3	100.0 %	0	0.0 %	68	63.0 %
Oxygen saturation	9	8.1 %	0	0.0 %	0	0.0 %	9	8.3 %
Temperature	1	0.9 %	0	0.0 %	0	0.0 %	1	0.9 %
Severe systemic illness in ED	11	5.6 %	0	0.0 %	0	0.0 %	11	6.6 %
Altered mental status in ED	62	31.6 %	2	10.0 %	0	0.0 %	60	36.1 %
Known allergy to NAC	0	0.0 %	0	0.0 %	0	0.0 %	0	0.0 %
Delayed absorption	53	27.0 %	4	20.0 %	0	0.0 %	49	29.5 %
Co-ingestions	69	35.2 %	0	0.0 %	0	0.0 %	69	41.6 %
Multiple doses of acetaminophen taken	31	15.8 %	2	10.0 %	0	0.0 %	29	17.5 %
Time of ingestion cannot be estimated	65	33.2 %	2	10.0 %	0	0.0 %	63	38.0 %
History of alcoholism	25	12.8 %	2	10.0 %	0	0.0 %	23	13.9 %
Significant co-morbidities	12	6.1 %	0	0.0 %	0	0.0 %	12	7.2 %

Note: Patients enrolled in the observation protocol who did not meet inclusion or exclusion criteria were enrolled at physician discretion

ED emergency department, *NAC N*-acetylcysteine, *LFTs* liver function tests

Data Collection

Data were abstracted from the hospital's electronic medical record system by a single investigator and recorded on a paper case report form using a pre-specified data dictionary. Abstracted data were patient demographics, specifics of the APAP ingestion, laboratory results, treatments, disposition, length of stay (LOS) and return visits to the ED within 3 days and 1 year from discharge.

Outcomes

Outcomes were successful discharge from the OU, over- and under-use of the OU protocol for APAP overdose, LOS and recidivism. Overuse was defined as enrollment in the protocol despite not being eligible while underuse was defined as admission to an inpatient setting despite being eligible for treatment in the OU protocol. Successful discharge from the OU protocol was defined as the disposition of the patient

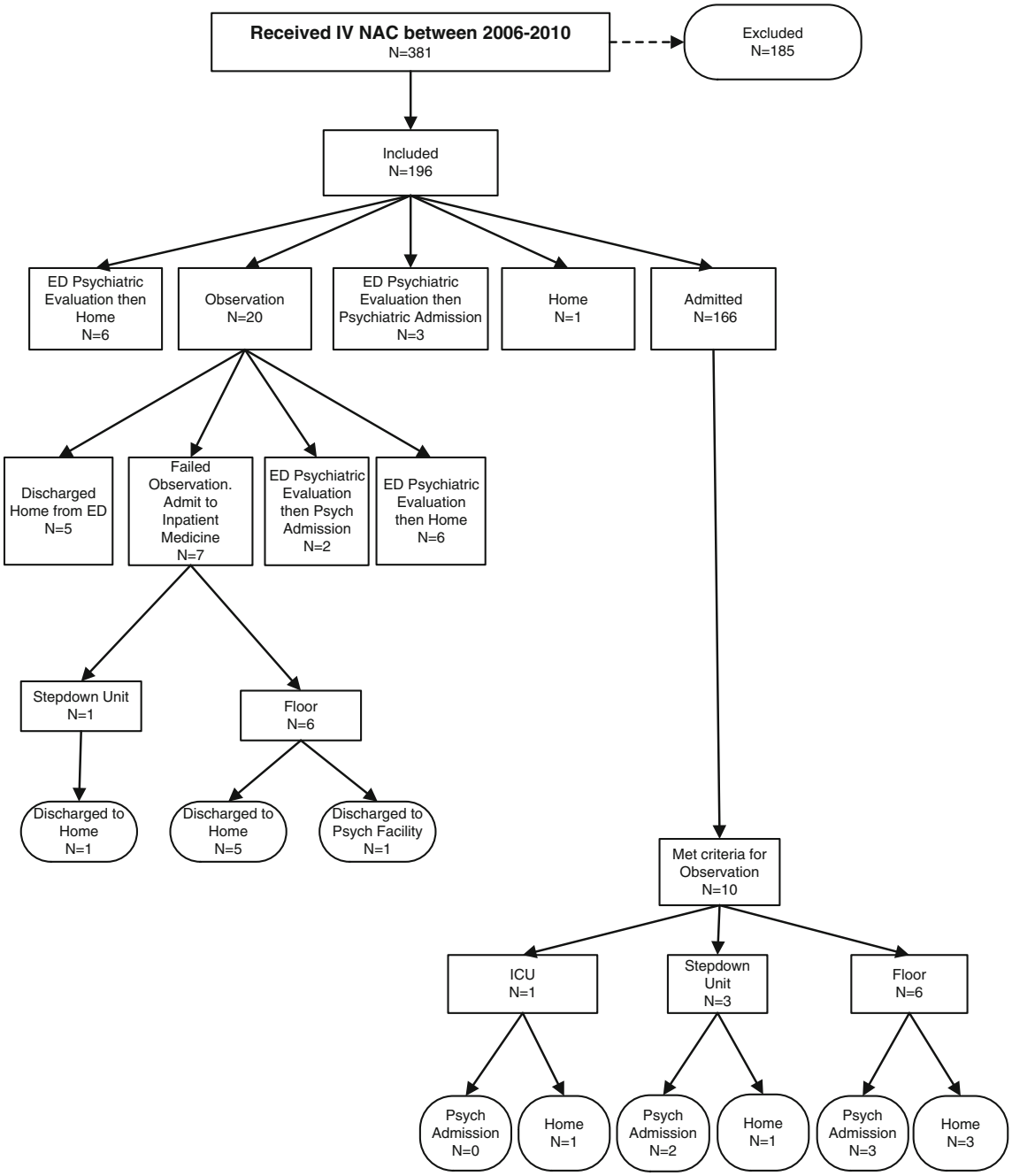

Fig. 1 Flow diagram showing initial disposition, disposition from the observation unit and disposition from the hospital for patients treated with IV NAC for acetaminophen overdose. *IV NAC* intravenous *N*-acetylcysteine, the antidote to acetaminophen overdose; *N* number of patients; *ED* emergency department; *ICU* intensive care unit. *Numbers* of patients in each category are shown in brackets: (*X*)

either to home or to an inpatient psychiatric admission as needed. LOS was defined as the time from presentation to the ED to discharge home after completing inpatient and psychiatric treatment. Three-day and 1-year recidivism rates were considered.

Data Management and Analysis

Study data were managed with REDCap (Vanderbilt University, Nashville, TN) and statistical analyses used SPSS 20.0 (IBM Corporation, Armonk, NY). Proportions and associated 95 % confidence intervals and medians and ranges are used to describe the data. Differences in medians with 95 % confidence intervals and differences in proportions with 95 % confidence intervals are used for comparisons. Missing data were minimal and left as missing.

Results

Characteristics of Study Subjects

Of 381 patients receiving IV NAC during the study period, 185 were excluded because IV NAC was used for contrast nephropathy or other kidney disease (n=18), hepatic failure not from APAP overdose (n=72), pulmonary disease (n=4), ingestion NOS or undifferentiated ingestion (n=12), the NAC order was discontinued before treatment was started (n=4), or because the patient was admitted directly to the hospital and was not seen in the ED (n=74). One patient chart was excluded because the initial presentation was to a different hospital. The 196 patients included in this study are described in a disposition flow diagram in Fig. 1 and by patient characteristics in Table 1.

Main Results

Figure 1 and Table 2 illustrate inclusion and exclusion of patients in the OU protocol. Twenty patients were enrolled in the observation protocol, and 13/20 (65 %, 95 % CI 43–83 %) had a successful discharge from the protocol. Of enrolled patients, only 3/20 (15 %) met objective eligibility criteria and all 3/3 (100 %) had a successful discharge. The remaining 17/20 (85 %, 95 % CI 59–93 %) were enrolled at physician discretion and 10/17 (59 %) had a successful discharge with normal vital signs and repeat laboratory testing prior to disposition. Patients enrolled at physician discretion and who were subsequently successfully dispositioned after completing the observation protocol included patients who failed to meet observation criteria due to history of alcoholism (2), ingestion concerning for delayed absorption (4) and abnormal vital signs at triage (4). Of the patients who failed the observation protocol and were subsequently admitted, at the time of disposition to the protocol 2/10 (20 %) had abnormal transaminase levels alone, 3/10 (30 %) had abnormal transaminase levels with either co-ingestions or multiple ingestions of acetaminophen, 1/10 (10 %) had co-ingestions and unknown time of ingestion, and 1/10 (10 %) had co-ingestion.

There were 13 patients presenting to the emergency department during this time period who met objective eligibility criteria for the observation protocol, and of these 10/13 (77 %, 95 % CI 50 to 93 %) were not enrolled in the protocol, representing possible underuse of the protocol. Documentation of reason for not admitting patients to the observation protocol was missing in every case. Of the 183 patients who did not meet eligibility criteria for observation, 17/183 (9.3 %), (95 % CI 6–15 %) were enrolled, representing possible overuse of the protocol.

The median total LOS was 41 h (IQR 31–73) (included time in observation unit+time in inpatient setting) for patients enrolled in the protocol compared to 68 (IQR 51–89) hours for patients who were eligible for observation, but not enrolled (see Fig. 2). The difference in medians was 27 h (95%CI 18–72 h, p=0.13). Median length of stay in the observation unit was 25 h (range 3–39 h). For patients treated in the observation protocol, recidivism (return visits to same ED) within 3 days was seen in one patient (5 %) for a reason unrelated to overdose or suicidal ideation and within 1 year after discharge in 12 patients (60 %), only three of which were visits related to overdose or suicidal ideation. For the ten patients eligible for observation but who were admitted

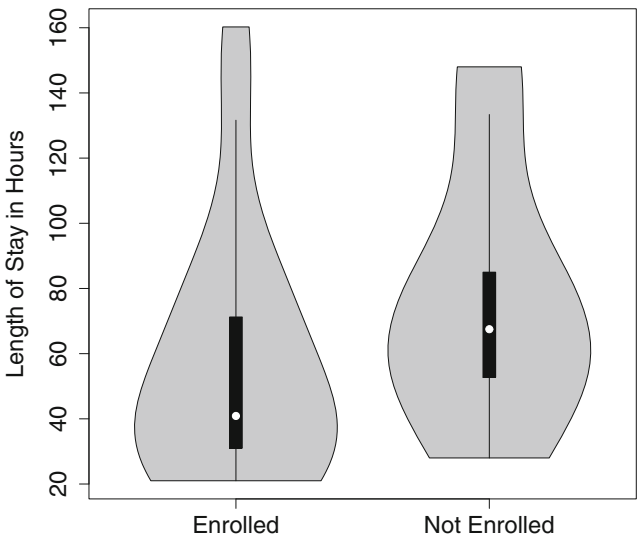

Fig. 2 Violin plot of length of stay in days. The *boxes* represent the interquartile range; the *dot within the boxes* represents the median value. The *lines* represent the limit for outliers

for treatment, three (30 %) had return visits to the ED within 1 year of discharge, all for intentional overdose. There were no return visits to this hospital by any patients for acetaminophen overdose.

Limitations

This report provides important initial insight into the use of ED-based OUs for the treatment of low-risk APAP overdose. The results of this preliminary study should be considered in light of several significant limitations. First, the small sample size provided insufficient information for validating the OU protocol inclusion and exclusion criteria. Second, all of the limitations inherent to retrospective chart review studies apply. In particular, charts included in this study were abstracted by a single study investigator, which could potentially lead to bias. Since this was not a hypothesis-driven study and data points collected were predefined and objective in nature, bias is unlikely. This study shows increased median length of stay for a group of patients who met criteria to be treated in the observation protocol, but who were instead admitted to the inpatient setting. The strength of the finding is limited by small sample size and the possibility that patients placed in the inpatient setting at physician discretion may have been more ill than those placed in the observation setting. In addition, length of stay was assessed for all patients treated in the observation protocol, including patients who did not meet criteria for treatment in the protocol, which limits our ability to assess if the observation protocol itself has an effect on length of stay. Finally, we were unable to access information regarding recidivism involving other medical institutions. It is possible we have underestimated the recidivism associated with APAP overdose.

Discussion

Monitoring the use of and adherence to treatment protocols is a critical component of evidence-based clinical practice [8, 9]. Fidelity to the inclusion and exclusion criteria for the protocol was minimal and indicate the potential need for further education of our ED providers regarding the availability of the protocol. Although the inclusion and exclusion criteria for the OU protocol have not been validated, every patient that failed the observation protocol also failed to meet objective eligibility criteria for inclusion in the protocol at the time of their disposition. Conversely, the fact that so many ineligible patients were successfully treated in the protocol suggests that the objective inclusion criteria may be insufficient to differentiate those patients that can be successfully treated in the protocol. Physician discretion appeared to play a significant role in the disposition of patients, both in the decision to treat patients in the observation protocol despite patient not fully meeting criteria and in the decision to admit patients to the inpatient setting despite meeting observation criteria; however, this medical decision making was not found to be clearly described in any of the patient charts. Utilization of the observation protocol may have been affected by lack of knowledge of the availability of observation services for acetaminophen overdose. Further work is needed to guide the observation protocol inclusion and exclusion criteria for this low-risk patient population and to educate providers at our institution regarding the availability and criteria for this protocol.

Overall, despite the small sample size, the precision of our estimates is sufficient to suggest there is both over- and under-use of the protocol, and that despite lack of fidelity to inclusion and exclusion criteria, use of the protocol is associated with a reduced LOS that is sufficient to suggest resource savings without resulting in increased recidivism for overdose. A national survey of observation units utilized for multiple diagnoses in the Unites States found an average length of stay of 15.3 h and 22.3 % hospital admission rate [11]. While our study demonstrates a longer length of stay and higher admission rate than in this survey, our data suggests that it is possible to include acetaminophen overdose among the conditions eligible for ED observation.

In summary, a multi-disciplinary protocol for the treatment of low-risk APAP overdose in an ED-based OU is a viable alternative to inpatient admission. While most observed patients were successfully dispositioned from the protocol, over- and under-use was noted. Despite this noted over- and under-use, all patients treated in the observation protocol were discharged to home, or transferred to psychiatric care or to the inpatient setting as appropriate after an observation time period during which providers in both emergency medicine and psychiatry were able to take the time to determine an appropriate disposition. Patients cared for in the OU setting showed a reduced median length of stay compared with similar patients who were admitted.

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