Table 2
Primary and secondary endpoints.

Sepsis management bundle	Intervention	Comparator	p-Value
	Median [IQR] or n (%)		
	$n = 22$	$n = 58$	
3-hour bundle completion	20 (91)	49 (85)	0.72
Time to completion (minutes)	59 [34.5–64.3]	70.5 [49–121.5]	0.013
	$n = 13$	$n = 37$	
6-hour bundle completion	11 (84.6)	29 (78.4)	1.0
Time to completion (minutes)	181 [91–208]	183 [126–211]	0.58
Time to completion of individual bundle components (minutes)	$n = 22$	$n = 58$	
Fluids	13 [12–24.3]	35 [20.8–61.8]	0.002
Blood cultures	22 [12–29]	25.5 [17–53]	0.09
Antibiotics	46 [31–61.5]	68 [49–96]	0.009
Antibiotics within 60 min	16 (72.7)	19 (32.8)	0.002

We found no difference between groups for the primary endpoint of 3-hour or 6-hour bundle compliance, but the time to completion of the 3-hour bundle and several individual components were significantly shorter when a pharmacist was present, which is consistent with a previous study [8]. Rapid antibiotic administration and completion of the 3-h bundle has been associated with lower risk-adjusted in-hospital mortality [9]. In 2018, the Surviving Sepsis Campaign published a special article advocating the combination of the 3- and 6-hour bundles into a single "hour-1 bundle." This is intended to promote more rapid initiation of treatment and prevent the extension of resuscitation measures over a long period of time [10].

There are multiple limitations of this study. First, a single center study may have less external validity and generalizability to other institutions. There may have been missed opportunities as daily activities do not always allow for prompt pharmacist response to sepsis alerts. Finally, the definitions used for sepsis, severe sepsis, and septic shock are based on current CMS definitions and criteria that differ from those used by guidelines updated after the initiation of this study [11].

Early identification and appropriate management of sepsis and septic shock is critical for improving patient outcomes. The results of this study suggest that the incorporation of pharmacists as a standard part of the multidisciplinary sepsis response team may significantly decrease time to treatment in patients presenting to the ED with sepsis.

Conflicts of interest

None.

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Platelet indices may not be associated with diagnosis and prognosis of gastrointestinal bleeding

Dear Editor,

I read with a great interest the article of Senel et al. about the diagnostic and prognostic value of platelet indices in the gastrointestinal system bleeding [1]. The authors reported that platelet indices might be used in diagnosis and prognosis of gastrointestinal bleeding. I would like to comment about this paper.

Firstly, the data of this study were obtained retrospectively. Pre-analytical and analytic factors are important sources of variations or errors in clinical laboratory measurements. Several factors like as partially clotting of specimen with activation and aggregation of platelets during venipuncture, ethylenediaminetetraacetic acid (EDTA)-induced platelet aggregation, severe microcytosis, fragmentation of red cells or presence of cryoglobulinemia may affect the correct measurement platelet count and indices. If there is any suspicion about occurrence of the measurement error, the complete blood count should be repeated with a second sample. Reliability of tests cannot provide completely in retrospective

Abbreviations: EDTA, ethylenediaminetetraacetic acid, MPV, mean platelet volume, PCT, plateletcrit.

studies due to pre-analytical and analytical factors. Harrison and Goodall emphasized categorically importance of that all blood samples should be collected, handled and processed in the same way so that the effect of pre-analytical variables in mean platelet volume (MPV) studies [2].

Secondly, although the platelet indices include platelet count, plateletcrit (PCT), MPV, and platelet distribution width may be routinely reported with complete blood count, their measurements have not standardized yet. Noris et al. reviewed the clinical importance of MPV measurement in recent years and they notified that because the wide variability of MPV as well as the very poor standardization of the methodologies used for MPV measurement, it has presently no role in making diagnosis and defining prognosis in any acquired illness in real life [3]. The MPV is dependent on time of analysis after sampling, method of analysis, anticoagulant used and specimen storage temperature [4]. The authors reported that blood platelets were measured usage with Sysmex XE 2100 hematology analyzer, but the measurement times after blood sampling were not standardized as specified in discussion. MPV increases progressively by exposure to EDTA. This increment in MPV occurs up to 30% within 5 min and then gains extra 10–15% over the subsequent 2 h [4]. The MPV measurements by the MPV measurement times varied up to 12.5% in a meta-analysis study and this difference was notified as 2–50% by the review of Jackson and Carter [4,5]. Because the measurement times after blood sampling were not standardized in this study, the accuracy of data was questionable.

PCT is the volume occupied by platelets in the blood as a percentage and calculated according to the formula; PCT = platelet count × MPV / 10,000 [6]. Therefore, the standardization problems related with MPV values affect the calculated PCT values. Thus, the accuracy of PCT data was questionable, too.

In conclusion, MPV and PCT values may not be associated with diagnosis and prognosis of gastrointestinal bleeding.

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Assessing the methodological quality of retrospective research protocols

Medical records are informal collections of impressions and observations that contain both objective and subjective information attained during the patient care process. They are not designed or created for research but frequently are used for this secondary purpose. While chart review studies tend to be inexpensive, relatively easily performed, and do not generally require specialized equipment, there are limitations to this type of study [1]. Information in medical charts is usually at least two steps removed from the patient with clinicians recording patient information, often with an intermediate transcription, followed by the chart abstractor recording data [2]. This can lead to recording errors, misinformation, and incomplete data. Understanding potential pitfalls in these studies allows the investigator to attempt to address them in the research design phase. Although there are no universally accepted criteria for a "well-conducted" chart review, there are recommended strategies to enhance the validity, reproducibility, and overall quality of data collected from clinical records [3,4]. The aim of our study is to review research proposals submitted to the Institutional Review Board (IRB) at one academic medical center to 1) determine the proportion of research protocols that use data exclusively from chart reviews; and 2) assess and quantify the quality of these protocols using published methodologic criteria.

We conducted a retrospective cross-sectional analysis using research proposals submitted to the IRB at one academic-affiliated medical center during a one-year study period. Inclusion criteria included any original research proposals that relied solely on data from medical records to answer the questions posed by the study. Exclusion criteria included research proposals relying on death certificates, coroners' reports, or other public records, and all studies based on animal or laboratory investigations. Additional exclusion criteria included retrospective studies based on aggregate patient data and computerized databases, case reports and case series, systematic reviews, studies withdrawn by investigator, and those studies categorized as not human subjects research (NHSR).

Experienced IRB analysts evaluated the quality of protocols using a checklist of methodological criteria adapted from the published literature in collaboration from the Department of Epidemiology at Michigan State University [3-5]. For each criterion, a rating of "Yes" or "No" was assigned. Credit was given if the investigators mentioned the methodologic standard, whether or not details were provided. In order to ensure the accuracy of data abstraction, all of the investigators assessed several mock research proposals to evaluate the consistency of coding and to clarify the coding system. One investigator met frequently with abstractors to resolve questions and ensure consistency of abstraction and coding. Any proposals that were questionable were evaluated by all investigators and discussed to reach consensus and assign a code. A blinded critical review of a random sample of 10% of the charts was done to determine interrater reliability. The interrater agreement for this sample of charts was determined using kappa statistics. Descriptive statistics (mean, SD) and frequency tables were used to describe the key quantitative and qualitative variables.

During the study period, 265 studies were submitted to the IRB; 100 studies were excluded from analysis because they were categorized as NHSR (60%), exempt (19%), withdrawn by investigator (18%), or were evaluated primarily by another IRB (3%). A total of 165 protocols were included in our analysis. This represented 76% of all the eligible protocols submitted in 2015. These retrospective protocols represented 28 medical specialties, including orthopedics (15%), pediatrics (11%), surgery (10%), pharmacy (9%), cardiovascular (8%), and emergency medicine (6%). Faculty physicians were generally the principal investigators (PI) (72%), followed by residents (15%), pharmacy staff (8%), nursing staff (2%) and medical students (2%). There was wide variability (3.6%