



## 文献精读

# Lactate Testing in Suspected Sepsis: Trends and Predictors of Failure to Measure Levels

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2008级临床医学八年制

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# CONTENT

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# BACKGROUND

- Elevated serum lactate levels have long been known to **identify patients** with severe hypoperfusion and **predict death**.

血浆中乳酸水平的升高有助于鉴别患者严重低灌注的程度并预测死亡风险。

- Measuring lactate levels can risk stratify patients with suspected sepsis, to **prompt aggressive early treatment**, and help **monitor the impact of therapy**.

测定乳酸水平有利于将疑似脓毒症患者按危险程度分层，以做到尽早治疗和监测疗效。





# BACKGROUND

- Implementation of bedside lactate measurement in the emergency department has also been associated with **reduced time to administration of IV fluids** in patients with suspected sepsis and **decreased rates of ICU admission and mortality**.

在急诊室使用床旁乳酸检测可以减少疑似脓毒症患者静脉输液的时间和降低ICU的入院率和死亡率。





# BACKGROUND

lactate testing

识别疑似患者  
评估死亡风险

尽早开展治疗  
评估治疗疗效

减少输液时间  
入院率&死亡率



**a key component**  
of

the Surviving Sepsis Campaign (SSC) Guidelines







# BACKGROUND

- Lactate measurement is a core component of the 3-hour bundle, whereas repeat lactate measurement for patients with hyperlactatemia is part of the 6-hour bundle.

乳酸测定是3小时集束化管理的核心组成部分，6小时集束化管理中包含高乳酸血症患者重复测定乳酸的要求。





# WHAT WE DON'T KNOW

- Less is known about **how lactate use has changed** over time or **how frequently clinicians are ordering this test** in appropriate patients in hospitals that are not associated with the SSC.

几乎没人知道在这段时间里乳酸测定的情况相较于以前是否发生了变化，也不知道医生们在非SSC相关医院里针对合适病人中使用这一指标的频率。

- Little is known about **which clinical factors are associated with failure to measure a lactate** in septic patients.

没有人知道什么样的临床因素会使得脓毒症患者测定乳酸失败。





# THEY WANT TO KNOW

- Given the benefits associated with lactate testing, it is important to better understand **how this test is being used, and gaps in its use**, in order to identify potential areas for quality improvement.

如果想提升乳酸检测在潜在领域的使用价值并从中获益，那么了解这一检测的适用方法和它的局限性是什么就显得十分重要。







# WHAT THEY DID

- We evaluated 11-year trends in serum lactate testing in **patients with suspected sepsis** and **identified predictors of failure to appropriately measure lactates** at two academic medical centers that were not participating sites in the SSC.

使用两家不参加SSC的教学医院的详尽临床数据库，评估了11年内在疑似脓毒症病人血浆乳酸检测倾向，并确定了合适进行乳酸检测而未做的预测因素。





# MATERIALS & METHODS

- Aged 18 and older
- Admitted to Massachusetts General Hospital (MGH) and Brigham and Women's Hospital (BWH)
- Between January 1, 2003, and December 31, 2013
- Who had a blood culture order during hospitalization

1) 年龄 $\geq$ 18岁 ; 2) 入住MGH或者BWH ;

3) 2003.1.1至2013.12.31期间入院 ; 4) 在院期间有至少1次血培养





# CODE

- International Classification of Diseases,  
Ninth Revision,  
Clinical Modification (ICD-9-CM) codes





# SUBGROUP

- We defined **severe sepsis** using the methods of Angus et al as modified by Iwashyna et al. This widely cited claims definition uses 1,286 codes for infection and 13 codes for acute organ dysfunction; if a code from both categories is present, or an explicit code for severe sepsis (995.92) or septic shock (785.52) is present, the patient is labeled as having severe sepsis.

1. 1286个感染编码+13个急性器官功能不全编码
2. 严重脓毒症 ( 995.92 ) 或脓毒症休克 ( 785.52 )





# SUBGROUP

- In order to enable us to estimate the timing of **suspected sepsis**, we focused on the subset of patients who had at least one blood culture order with concurrent parenteral antibiotics started within  $\pm 1$  day of the blood culture, with any antibiotics continued for at least 3 days (or until death or hospital discharge if this occurred prior to 3 d).
  1. 至少进行一次血培养
  2. 并在培养的前后1天内同时胃肠外途径给予至少3天的抗生素（或在3天内死亡或出院）







# SUBGROUP

- Even though some of these patients likely ended up having noninfectious diagnoses, we reasoned that clinicians' decisions to order blood cultures and at least 3 days of new antibiotics were strong indicators that they initially **suspected a possible infection** and therefore lactate measurement was also indicated for these patients.

1. 有血培养
2. 使用新的抗生素至少3天





# SUBGROUP

- We defined “**suspected septic shock**” as a blood culture order and both vasopressors (norepinephrine, epinephrine, dopamine, vasopressin, or phenylephrine) and at least 3 days of antibiotics started within  $\pm 1$  day of blood culture order.

1. 一次血培养结果
2. 使用升压药物
3. 在血培养的前后1天内给予至少3天的抗生素





# RESULTS

**TABLE 1. Clinical Characteristics of Hospitalized Patients With Suspected Infection, Severe Sepsis, and Suspected Septic Shock, 2003–2013**

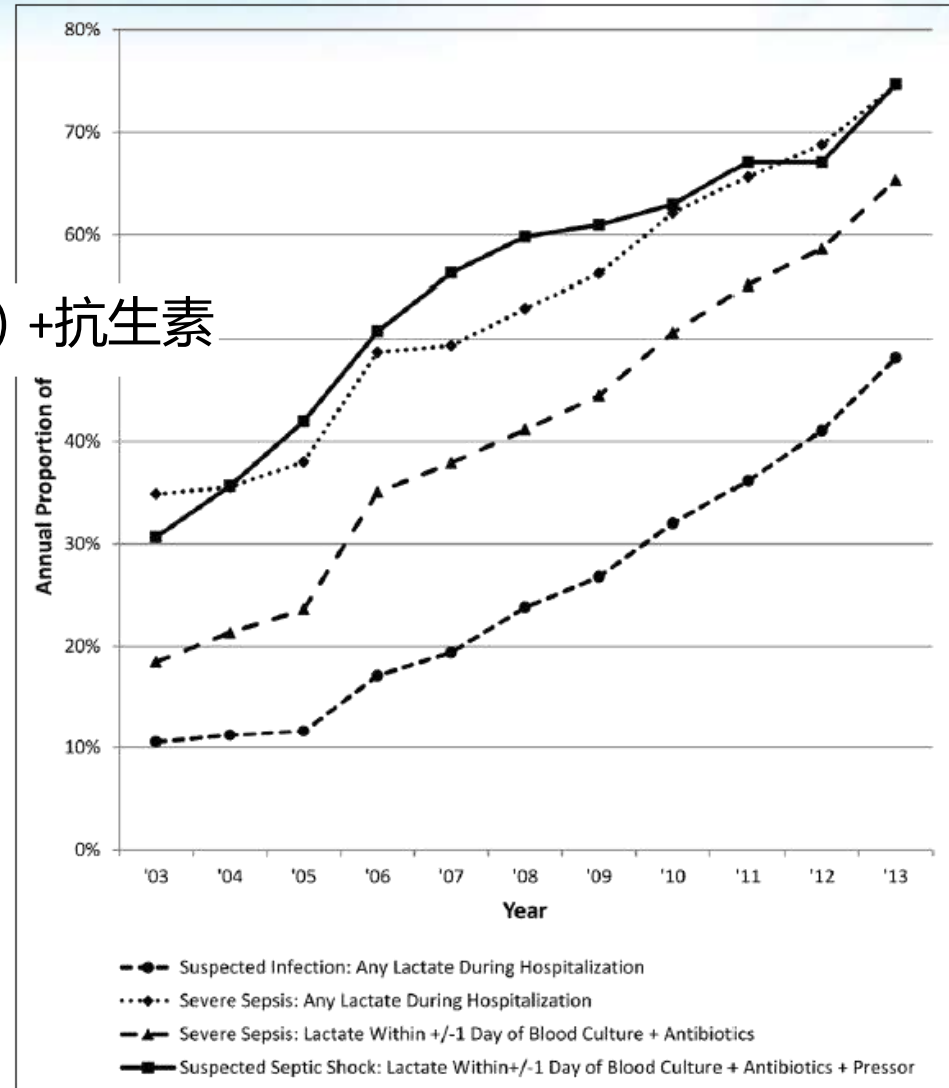
Clinical Characteristic	Suspected Infection <sup>a</sup> ( <i>n</i> = 230,620)	Severe Sepsis <sup>b</sup> ( <i>n</i> = 41,275)	Suspected Septic Shock <sup>c</sup> ( <i>n</i> = 24,330)
Median age (IQR)	61 (47–73)	65 (53–76)	63 (51–74)
Male sex, <i>n</i> (%)	119,892 (52.0)	23,453 (56.8)	14,073 (57.8)
White race, <i>n</i> (%)	177,398 (76.9)	32,761 (79.4)	19,120 (78.6)
<b>Comorbidities</b>			
Cancer, <i>n</i> (%)	50,532 (21.9)	8,215 (19.9)	4,095 (16.8)
Diabetes mellitus, <i>n</i> (%)	42,484 (18.4)	6,229 (15.1)	3,081 (12.7)
Heart failure, <i>n</i> (%)	35,346 (15.3)	9,183 (22.3)	5,685 (23.4)
Liver disease, <i>n</i> (%)	13,667 (5.9)	2,682 (6.5)	1,446 (5.9)
Lung disease, <i>n</i> (%)	36,925 (16.0)	6,115 (14.8)	3,391 (13.9)
Renal disease, <i>n</i> (%)	27,829 (12.1)	588 (14.3)	2,694 (11.1)
Median Elixhauser score (IQR)	6 (0–12)	9 (5–14)	8 (4–13)
Positive blood cultures, <i>n</i> (%)	22,389 (9.7)	9,637 (23.4)	5,381 (22.1)
Nonmedical service, <i>n</i> (%)	77,269 (33.5)	11,563 (28.0)	10,748 (44.2)
Required ICU care, <i>n</i> (%)	65,218 (28.3)	24,761 (60.0)	20,178 (82.9)
Median hospital length of stay (IQR)	7 (4–13)	13 (7–24)	15 (8–26)
Hospital mortality, <i>n</i> (%)	14,687 (6.4)	7,502 (18.2)	6,300 (25.9)



# Lactate Measurements During Hospitalization and at the Time of Suspected Sepsis

- Suspected infection
- ...◆... Severe sepsis
- ▲— Severe sepsis+血培养 ( ±1d ) +抗生素
- Suspected septic shock

Rising annual proportion of patients with suspected and diagnosed sepsis that had serum lactates measured during hospitalization or at the time of suspected sepsis, 2003–2013.



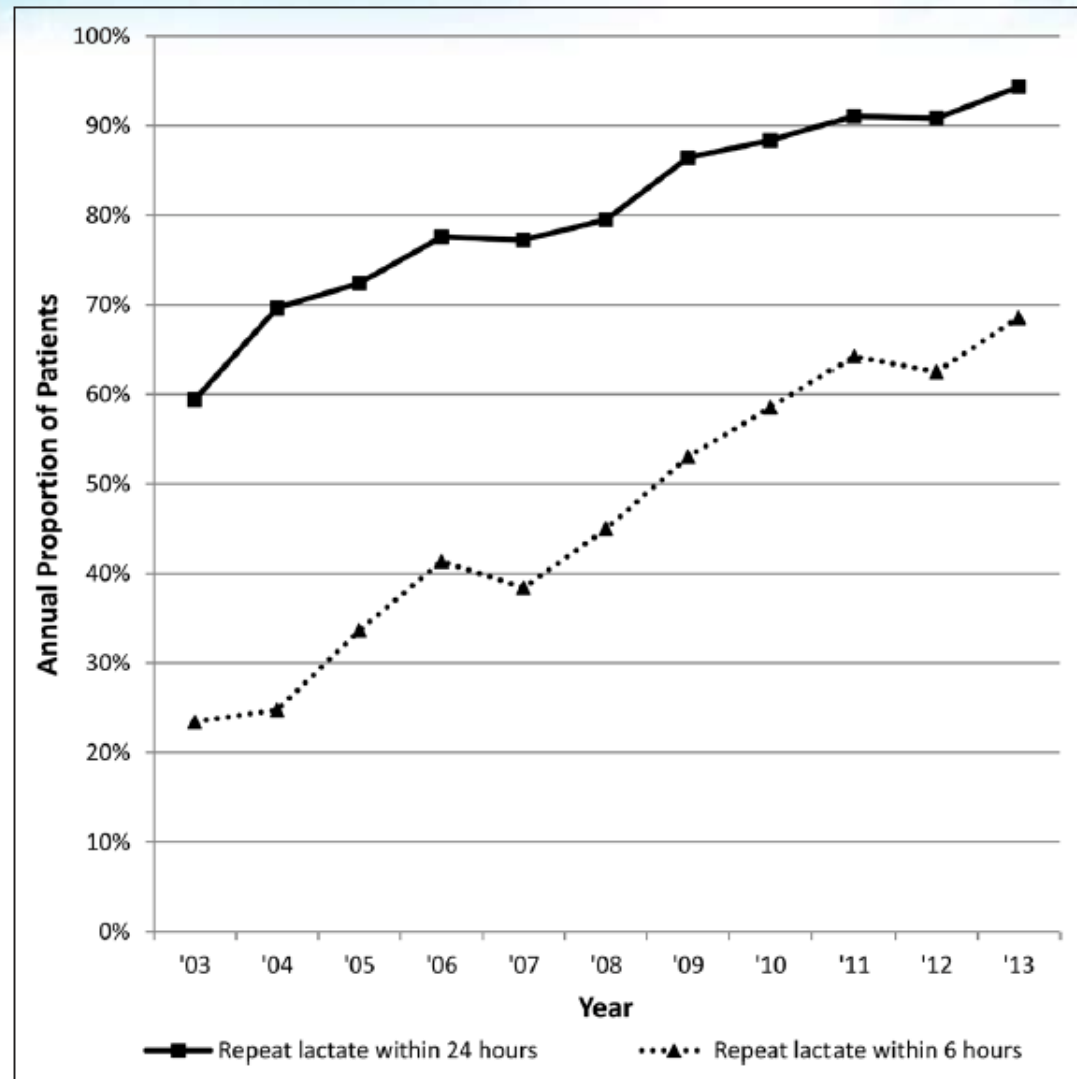




# Serial Lactate Testing

- 2003:
  - 6h: 23%
  - 24h: 59%
- 2013:
  - 6h: 69%
  - 24h: 94%

Rising annual rates of repeat lactate measurements within 6 and 24 hours after documented lactate levels  $\geq 4.0$  mmol/L in patients with suspected infection, 2003–2013.







# DISCUSSION

- This suggests that the use of **lactate clearance** as a resuscitation target and the SSC recommendations of **serial lactate testing** for patients with hyperlactatemia have not become fully ingrained in clinicians yet.

使用乳酸清除率作为复苏目标和ssc提出的对于高乳酸血症的患者使用连续乳酸测定这样的理念并未在临床上深入人心。

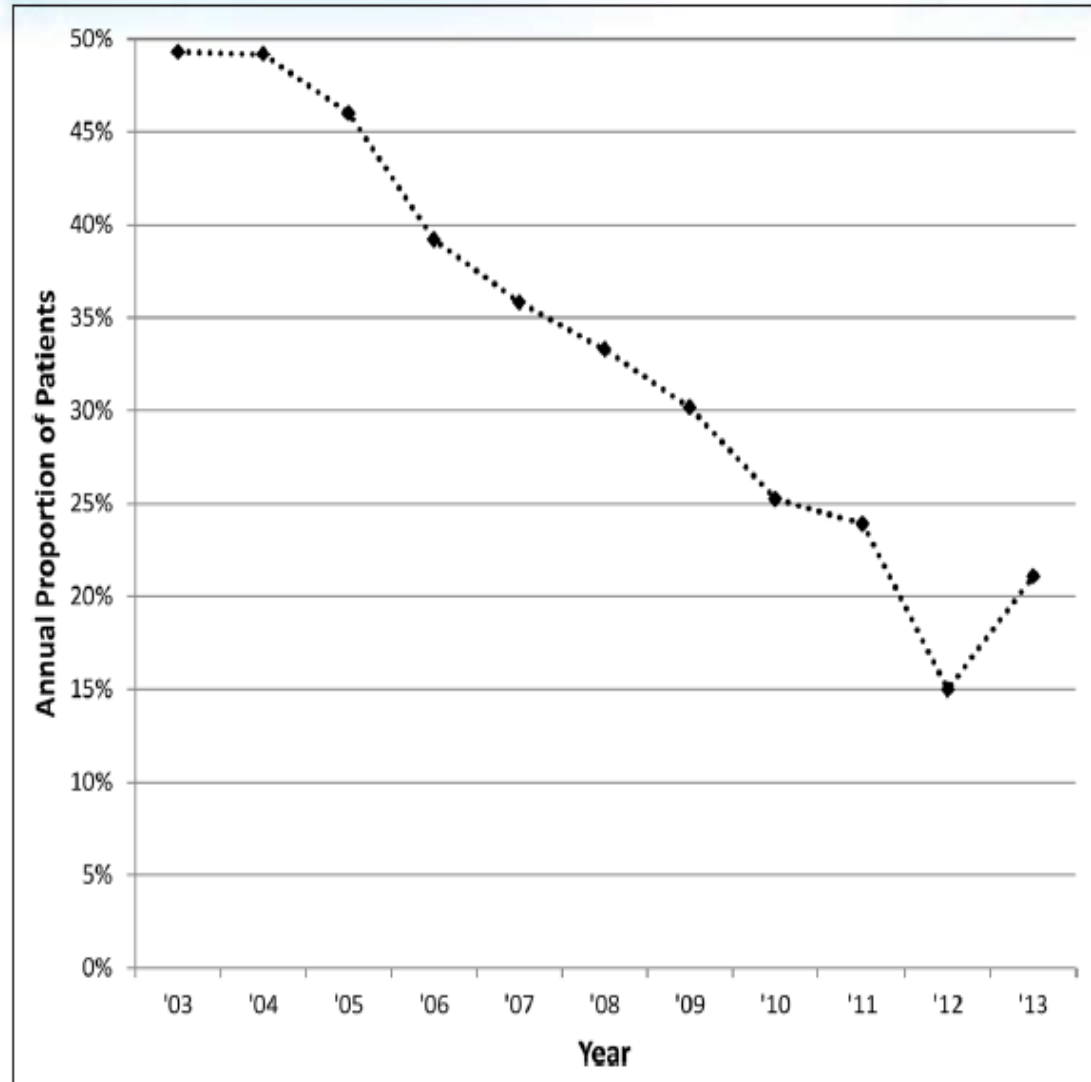




# Clinical Threshold for Measuring Lactates

In patients with suspected infection, 998 out of 2,024 cases (49%) received vasopressors prior to or on the day of lactate measurement in 2003 compared with 2,139 of 10,153 cases (21%) in 2013.

Decreasing proportion of patients with suspected infection who required vasopressors before or on the day of first lactate measurement, 2003–2013.





# DISCUSSION

- Lactates were increasingly measured in patients who were not on vasopressors, suggesting that clinicians have lowered their thresholds for obtaining lactate levels by extending testing to patients without overt hypotension.

在未使用血管活性药物的患者中乳酸测定率的增加说明临床医生对于没有明显低血压的患者变得更愿意获得他们的乳酸水平。





- Documenting the prognostic utility of lactate, its use as **a therapeutic target for resuscitation**, its ability to **alter provider behavior**, and the potential for rapid testing to **improve patient outcomes**.

预先测定乳酸：

1. 作为复苏的治疗目标
2. 改变提供医疗的人员的行为
3. 通过快速乳酸测定提升患者疾病结局





- Studies demonstrating the use of lactate as a severity marker **in hemodynamically stable patients** with suspected infection could also explain why clinicians are extending the test to patients who are not on vasopressors.

有研究表明，在血流动力学稳定的疑似感染患者中使用乳酸作为疾病严重程度的标志，这就可以解释为什么对于未使用血管活性药物的患者医生们更广泛的使用了乳酸测定。







- Reflects the increasing success and penetration of the SSC, which has emphasized the importance of spot and serial lactate testing, to clinicians and hospitals around world.

乳酸测定率的增加反映了ssc提出的乳酸单次测定和序贯测定的重要性传递给了世界各地的医院和医生们。





# Lactate Testing in 2013 in Patients With Severe Sepsis

- Of the 5,071 patients with severe sepsis in 2013, 1,758 (35%) did not have a lactate measured at the time of suspected sepsis, and 1,288 (25%) did not have a lactate measured at any point during hospitalization.

2013年，有35%的患者在疑诊脓毒症时没有进行乳酸测定，有25%的患者在住院期间没有进行过乳酸测定。



Clinical Characteristic	Lactate Measured ( <i>n</i> = 3,313)	No Lactate Measured ( <i>n</i> = 1,758)	<i>p</i> <sup>a</sup>
Median age (IQR)	67 (55–77)	65 (54–76)	0.012 <sup>b</sup>
Male sex, <i>n</i> (%)	1,913 (57.7)	1,015 (57.7)	0.997
White race, <i>n</i> (%)	2,636 (79.6)	1,442 (82.0)	0.036 <sup>b</sup>
Median Elixhauser score (IQR)	9 (5–14)	8 (4–13)	< 0.001 <sup>b</sup>
Vasopressor before or at the time of suspected sepsis, <i>n</i> (%)	1,411 (42.6)	375 (21.3)	< 0.001 <sup>b</sup>
Mechanical ventilation at the time of suspected sepsis, <i>n</i> (%)	921 (27.8)	264 (15.0)	< 0.001 <sup>b</sup>
ICU care before or at the time of suspected sepsis, <i>n</i> (%)	2,171 (65.5)	589 (33.5)	< 0.001 <sup>b</sup>
Positive blood cultures before or at the time of suspected sepsis, <i>n</i> (%)	510 (15.4)	177 (10.1)	< 0.001 <sup>b</sup>
Laboratory derangements (at the time of suspected sepsis)			
Albumin < 2.5 g/dL, <i>n</i> (%)	567 (17.1)	179 (10.2)	< 0.001 <sup>b</sup>
Anion gap > 16 mEq/L, <i>n</i> (%)	678 (20.5)	80 (4.6)	< 0.001 <sup>b</sup>
Bands ≥ 5%, <i>n</i> (%)	617 (18.6)	140 (8.0)	< 0.001 <sup>b</sup>
Creatinine ≥ 2.0 mg/dL, <i>n</i> (%)	861 (26.0)	268 (15.2)	< 0.001 <sup>b</sup>
Hematocrit < 21%, <i>n</i> (%)	390 (11.8)	175 (10.0)	0.050
International normalized ratio > 1.5, <i>n</i> (%)	731 (22.1)	231 (13.1)	< 0.001 <sup>b</sup>
Platelets < 100/μL, <i>n</i> (%)	905 (27.3)	494 (28.1)	0.553
Total bilirubin ≥ 2.0 mg/dL, <i>n</i> (%)	414 (12.5)	112 (6.4)	< 0.001 <sup>b</sup>
WBC > 12,000/μL, <i>n</i> (%)	1,724 (52.0)	624 (35.5)	< 0.001 <sup>b</sup>
WBC < 4,000/μL, <i>n</i> (%)	556 (16.8)	356 (20.3)	0.002 <sup>b</sup>
Hospital-onset sepsis, <i>n</i> (%)	436 (13.2)	704 (40.1)	< 0.001 <sup>b</sup>
Nonmedical service, <i>n</i> (%)	781 (23.6)	613 (34.9)	< 0.001 <sup>b</sup>
Hospital (Brigham and Women's Hospital vs Massachusetts General Hospital), <i>n</i> (%)	1,252 (37.8)	754 (42.9)	< 0.001 <sup>b</sup>



# Lactate Testing in 2013 in Patients With Severe Sepsis

- Patients who **did not have a lactate measured at the time of suspected sepsis** were more likely to be younger, have a lower burden of comorbidities, not require vasopressors or mechanical ventilation or ICU care, have hospital-onset sepsis, be admitted to a nonmedical service, and have fewer signs of organ dysfunction or infection compared with those who did have lactates measured.

年轻，合并症轻，不需要血管活性药物、机械通气或ICU监护，有院内感染的脓毒症，接受非医疗服务，器官功能不全或感染体征少







# Lactate Testing in 2013 in Patients With Severe Sepsis

- Hospital-onset sepsis :
  - the first blood culture order associated with initiation of parenteral antibiotics occurring **on or after the 3rd calendar day of admission**, with day of admission being day 1.

第一次的血培养和肠外抗生素使用发生在入院后的第三天及以后，其中入院当天为第一天。







# Lactate Testing in 2013 in Patients With Severe Sepsis

- **Median hospital length of stay** was longer in the no-lactate group (14 d vs 11 d;  $p < 0.001$ ), although the hospital mortality rate was lower (10% vs 17%;  $p < 0.001$ ).

尽管未测定乳酸组患者的院内死亡率更低，但他们的中位住院天数更长。





# DISCUSSION

- Closer examination of these patients showed a lower degree of organ dysfunction and proportion of patients in the ICU in the no-lactate group, indicating that clinicians are preferentially **drawing lactates in more severely ill patients.**

器官功能不全程度轻的ICU患者未行乳酸测定，说明临床医生对于更倾向于对更为严重的患者行乳酸测定。





- However, the hospital length of stay and mortality rate in severe sepsis patients without lactates measured were high, suggesting that clinicians may underappreciate the utility of lactate testing to identify patients with occult hypoperfusion who are at increased risk for adverse outcomes.

然而未测定乳酸的严重脓毒症患者有更长的住院天数和死亡率，提示临床医生可能低估了在隐匿性低灌注导致不良结局危险增加的患者中乳酸测定的作用。





- Interestingly, **even overt hypotension is not always triggering lactate tests**, as a quarter of patients in 2013 who required vasopressors and had concurrent blood culture orders and antibiotics never had a lactate measured at the time of suspected infection.

明显的低血压不一定会让临床医生进行乳酸测定，所以在2013年，有1/4的患者使用了血管活性药物，有血培养结果并且使用了抗生素却没有在怀疑感染时测定乳酸。





# Lactate Testing in 2013 in Patients With Severe Sepsis

- On multivariate analysis, **risk factors for failure to measure a lactate at the time of suspected sepsis** included **hospital-onset sepsis** versus community-onset sepsis (adjusted odds ratio, 7.56; 95% CI, 6.31–9.06;  $p < 0.001$ ) and **admission to a nonmedical service** (adjusted odds ratio, 2.08; 95% CI, 1.76–2.46;  $p < 0.001$ ).

未在疑似脓毒症诊断时测定乳酸的危险因素包括：院内感染的脓毒症和入住非医疗服务机构。





**TABLE 3. Multivariate Analysis of Risk Factors for Failure to Measure Serum Lactates at the Time of Suspected Sepsis in Patients With Severe Sepsis in 2013**

Potential Predictor	Adjusted OR (95% CI)	Laboratory derangements (at the time of suspected sepsis)	
Age (yr)	0.99 (0.99–1.00)	Albumin < 2.5 g/dL	0.83 (0.66–1.04) 0.104
White race	1.22 (1.03–1.46)	Anion gap > 16 mEq/L	0.32 (0.24–0.42) < 0.001 <sup>a</sup>
Elixhauser comorbidity score	0.99 (0.98–1.00)	Bands ≥ 5%	0.52 (0.41–0.66) < 0.001 <sup>a</sup>
Vasopressor before or at the time of suspected sepsis	0.42 (0.34–0.52)	Creatinine ≥ 2.0 mg/dL	0.90 (0.74–1.09) 0.270
Mechanical ventilation at the time of suspected sepsis	0.98 (0.79–1.23)	International normalized ratio > 1.5	0.86 (0.71–1.05) 0.136
ICU care before or at the time of suspected sepsis	0.28 (0.23–0.33)	Total bilirubin ≥ 2.0 mg/dL	0.60 (0.47–0.79) < 0.001 <sup>a</sup>
Positive blood cultures before or on the day of suspected infection	0.68 (0.54–0.84)	WBC > 12,000/μL	0.62 (0.53–0.72) < 0.001 <sup>a</sup>
		WBC < 4,000/μL	0.69 (0.57–0.84) < 0.001 <sup>a</sup>
		Hospital-onset sepsis	7.56 (6.31–9.06) < 0.001 <sup>a</sup>
		Nonmedical service	2.08 (1.76–2.46) < 0.001 <sup>a</sup>
		Hospital (Brigham and Women's Hospital vs Massachusetts General Hospital)	1.10 (0.95–1.26) 0.201





# DISCUSSION

- Other studies have shown that **sepsis that occurs on hospital ward units** is associated with **worse outcomes** and that this may be due to **delays in appropriate recognition and timely administration of fluids, vasoactive agents, and transfer to the ICU.**

1. 发现及诊断不及时
2. 治疗措施不及时（液体治疗和血管活性药物）
3. 转入ICU过迟





# LIMITATIONS

- **First:** only from two academic hospitals in one city.
- **Second:** the population of patients with possible sepsis may have been incomplete.
- **Third:** limited to data we could glean from electronic sources.
- **Fourth:** some degree of inaccuracy is possible when estimating the timing of suspected sepsis onset using the time stamps of blood culture orders.
- **Lastly:** some patients who did not have lactates measured might have been so overtly in shock and multiple organ failure.







**THANK YOU**

