Stuff for podcast with Scott Weingart

1. Definition vs Clinical Criteria – Meaning and derivation
    a. Definitions were designed to encompass the "essence" of sepsis – what sepsis "is"
        i. Include the latest understanding of pathobiology
        ii. Probably not useful clinically at this time
    b. So we need something that is clinically helpful – and that led us to SOFA/qSOFA
    c. Why is that important ?
        i. Because there is no way a clinician can know with virtual certainty that a patient has sepsis
        ii. There isn't a hard outcome variable, something we can measure and say "Aha ! Sepsis!"
            1. No x-ray
            2. No lab test
            3. No biopsy
        iii. And that means that we can't specifically test the ability of anything we can actually measure clinically to identify patients with "sepsis" at any time – all we can say is "this sure looks like sepsis" or "its really likely that this patient has sepsis"
            1. Context – suppose you have a patient in an ICU with a documented infection, on a ventilator, requiring vasopressors and renal replacement therapy
            2. We would all feel pretty safe saying that that patient has sepsis, but there is no "gold standard" we can use to prove it
                a. If you had a patient with a stroke or an MI, you could do a biopsy, show infarcted tissue and be virtually 100% certain of the diagnosis
                b. But you can't do that for sepsis
            3. And this issue becomes really important when you are looking for something that's going to prompt you to consider sepsis when you're in the ED and you are evaluating someone you think has an infection and you're concerned – but you don't have anything as telling as a need for organ support
        iv. You need some other outcome variable – a PROXY
    d. Proxies
        i. A criticism of the papers is that we haven't identified patients with sepsis
            1. Rather we have identified patients with infection who end up doing badly – we used death and/or a significant ICU stay as a "stand-in" sepsis
                a. A patient most likely has sepsis
            2. Outcomes validity

        a. But that's the best we can do !
    3. Are there better proxies ?
        a. Maybe – we didn't find one, but maybe someone else will
        b. Likely in populations we didn't examine, for example, children
2. Delta-SOFA/qSOFA
    a. Work well to predict "badness" or "likely sepsis" in the data sets we examined
    b. Delta-SOFA (change of 2 or more points)
        i. Has predictive value at 72 hrs
        ii. But never really prospectively evaluated before Chris' analysis
        iii. Many of the indices are out of date and need revising
            1. Cardiac/pulmonary dysfunction in part based on intervention
            2. Renal based on
                a. creatinine,
                    i. which changes late
                b. UOP
                    i. Which may not reflect renal function
            3. Liver based on bilirubin
                a. Not specific
                b. Not strictly hepatic
            4. Coag based on plt count
                a. Not specific for coag
                    i. Might be bone marrow – more in common with WBC count
            5. CNS
                a. Uses GCS
                b. SOFA and qSOFA are equivalent
                    i. Get a point for less GCS < 15
    c. qSOFA
        i. Importance of identified variables
            SBP < 100
            RR < 22
            Change in MS
        ii. Are there better ones ? Do they need to change for other environments ?
3. Use of qSOFA
    a. Works especially well in EDs and on wards
        i. Where patients are in their "native state", w/o treatments that may modify qSOFA elements
        ii. Less well in ICUs, where RR, LOC, BP are often modified by intervention

1. So someone in an ICU might be deteriorating but qSOFA wont become + because they are being sedated and ventilated

b. Comparison to SIRS
   i. Only data-based analysis of SIRS is the one in Chris' paper
   ii. qSOFA has similar sensitivity to SIRS
   iii. qSOFA has much better specificity
      1. doesn't identify every post-op patient or patients with a bad cold
   iv. doesn't require any lab data – no WBC count – purely bedside an therefore should be easier to use

c. Cause and effect
   i. The analysis used retrospective data
      1. Therefore, we can't say that a + qSOFA score implies that the patient will deteriorate
      2. And we can't really talk about prediction – because we didn't study the time course
         a. All we can talk about is an association
   ii. So a prospective evaluation is important

d. Does it apply to small and medium size hospitals ?
   i. More than half the hospitals in the UPMC, the derivation dataset, have < 150 beds, 2 have < 100 beds
   ii. KPNC includes 23 hospitals, most of which have < 200 beds

e. Does it apply to resource-limited environments ?
   i. We don't know !
   ii. So let's find out
      1. There are databases that have been collected in these areas
         a. Paper by Ranzini et al examining the Latin American Sepsis Institute (LASI) data base
            i. Ranzini OT et al, Rev Bras Ter Intesiva 2013. 25:270-8, doi 10.5935/0103-507X.20130047
         b. Can qSOFA be tested in this database ?

4. Delay of treatment waiting for SOFA/qSOFA to become positive
   a. No more true with qSOFA/SOFA than it is with SIRS
      i. If a patient looks "sick" to the practitioner, treatment should be started – whatever your clinical criteria are
         1. e.g., if your gestalt is that a patient is really sick or about to become really sick, you wouldn't delay treatment waiting for hypotension or a white count

5. Septic Shock
   a. Interesting that this seems to resonate better than our approach to sepsis
   b. Because we had long discussions about what septic shock is, including why/if we needed to identify it as an entity distinct from sepsis

c. What is it ?
    i. Cardiovascular dysfunction ?
    ii. A cellular or biochemical/metabolic abnormality ?
    iii. We elected to say it was both
d. Why do we need it ? Why do we need to distinguish septic shock from sepsis ?
    i. Treatment is the same
    ii. We don't know enough about the underlying pathobiology to say that there is something unique about septic shock, something that clearly differentiates it from sepsis
    iii. So, the reasons really are epidemiologic
        Something we can count
        Or prognostic
        Something you can use to tell people that the patient isn't just “sick” but rather is “really really sick”
e. And that’s why our “definition” contains a statement about outcome –
    i. Really high mortality
    ii. And why we derived the clinical criteria on the basis of a significant mortality difference

6. What should clinicans do moving forward ?
    a. Test qSOFA and deltaSOFA prospectively
    b. Look for other variables to test
    c. Apply qSOFA and delta-SOFA to untested patient populations
        i. Children
        ii. Underserved areas
        iii. Infections that aren’t represented in the populations that were examined
            1. For example, malaria