Peer Review File
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Reviewer Comments

Reviewer A

Comment 1: Abstract, Line 28- Need clarification of the statement "Because there is a perception that cTn is only a marker for AMI, education of medical teams will be essential to promote the concept that troponin is a sensitive marker of myocardial injury." While this statement is likely correct, the authors need to expand the discussion on the difference between myocardial infarction and injury as it relates to hsTn's. I agree this is a major concept that providers need education on when hsTn's are instituted.
Reply 1: Changed to: "While cTn is the standard biomarker for detection of myocardial injury caused by AMI, education of medical teams will be essential to promote the concept that troponin is a sensitive marker of myocardial injury irrespective of the underlying etiology."

Comment 2: Abstract, line 30- correct to "Point of care testing devices promise
Reply 2: Promises has been changed to promise.

Comment 3: Abstract, line 31- POC testing "must have equivalent sensitivity as central lab tests." While true, I think a better statement would state that POC assays require sensitivity and specificity equivalent to central lab tests in order to be acceptable.
Reply 3: changed to the following: "…but require analytical sensitivity and specificity that is equivalent to central lab tests in order to be acceptable."

Comment 4: Page 4, line 74- "The group that initiates the changes can originate from either of these groups." Would change to "The implementation plan can be driven by any of these groups" or some similar
Reply 4: agreed that this better wording and have changed this sentence to read exactly as recommended.

Comment 5: Page 5, line 91- I would eliminate the statement "An earlier time to rule out AMI enables fast treatment decision, eg initiation of thrombolytic therapy…". Use of thrombolytics should never to based on troponin results, as they are only used in contemporary cardiology in the case of STEMI, which is a clinical and ECG diagnosis, not a serologic diagnosis.
Reply 5: This line has been eliminated.

Comment 6: Page 6, line 109- "cardiac troponin is one of the clinical chemistry tests where high analytical sensitivity is required…."
Reply 6: Changed "were" to "where"

Reviewer B

Comment 1: This is a very well written and comprehensive overview. I have two minor suggestions.

-suggestion related to parapraph on page 5: "Implementation of an accelerated of an accelerated diagnostic pathway requires that laboratory to consistently report testing results within one hour from the time of specimen collection (not the test order). This is a challenge today for many central laboratories. Ideally, results of the first cTn test should be available before the collection of the second sample." I think it is important to mention that even when a lab cannot report within one hour from the time of specimen collection, one can still implement accelerated diagnostic protocols. What is most important (even critical) is the standardized 1 hour window between blood draws, but when the reporting time exceeds 1 hour, one can still benefit from implementing an accelerated protocol.

Reply 1: added, "The accelerated diagnostic protocol can still be implemented even if the result of the first sample is not completed when the second sample needs to be collected. Cutoff concentrations for serial testing are specifically linked to the time interval between collections. Therefore it is important to adhere to the schedule of draws as inaccurate interpretations could occur if the timing is not aligned."

Comment 2: -suggestion related to parapraph on page 8:

"If after the initial lecture, the medical staff is still uncertain or hesitant to adopt hs-cTn assays, the sponsor could arrange for a small clinical trial where aggregate troponin test results on patients from the facility could be made available to the medical staff."

I would suggest to remove this sentence. This reviewer feels professionals should be able to implement international guidelines, without the need of additional small local replication studies, which are often poorly performed and underpowered, and could therefore even be counterproductive.

Reply 2: this sentence has been removed.