

A photograph of a family playing soccer in a park. An older man in a light blue long-sleeved shirt and blue jeans is in the center, looking down at a red and white soccer ball. A young boy in a light green t-shirt and blue jeans is running towards the ball. To the right, a younger man in a dark jacket and grey pants is also running. In the background, another person is visible, and the scene is set in a grassy field with trees and a stone wall under a bright sky.

Medical and Scientific Affairs: Overview of Physicians Council Report on Sepsis Pilot Study

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Sepsis WG

- Meets twice monthly beginning June 2024
- In order to assess the likely impact of changes to sepsis criteria in FDA guidance, the WG members doing donor chart review participated in a prospective data collection initiative – Sepsis Pilot Study
- The data were collected, analyzed, and a report was written to summarize the context of sepsis in the US, and the concerns of the AATB PC Sepsis WG
- The report was provided to Dr. Marks 9/20/2024

Current FDA “Sepsis Criteria”

Sepsis (includes, but is not limited to, bacteremia, septicemia, sepsis syndrome, systemic infection, systemic inflammatory response syndrome (SIRS) or septic shock):

In reference to deceased donors, **if any of these conditions is specifically diagnosed in the medical records during a hospital stay immediately preceding death, you should determine the donor to be ineligible.**

Sepsis may be described by the following clinical evidence. You should consider these signs *in light of other information obtained about the donor in making a donor eligibility determination.*

Clinical evidence of infection; and

Two or more of the following systemic responses to infection if unexplained:

- Temperature of >100.4° F (38° C);
- Heart rate >90 beats/min;
- Respiratory rate >20 breaths/min or PaCO₂ <32; or
- WBC >12,000 cells/mm³, < 4,000 cells/mm³, or >10% immature (band) forms.
- More severe signs of sepsis include unexplained hypoxemia, elevated lactate, oliguria, altered mentation, and hypotension.
- Positive (pre-mortem) blood cultures might be associated with the above signs.

Sepsis Pilot Study: Data Collected

Data Collected during Pilot (Concurrently with Donor Chart Review):

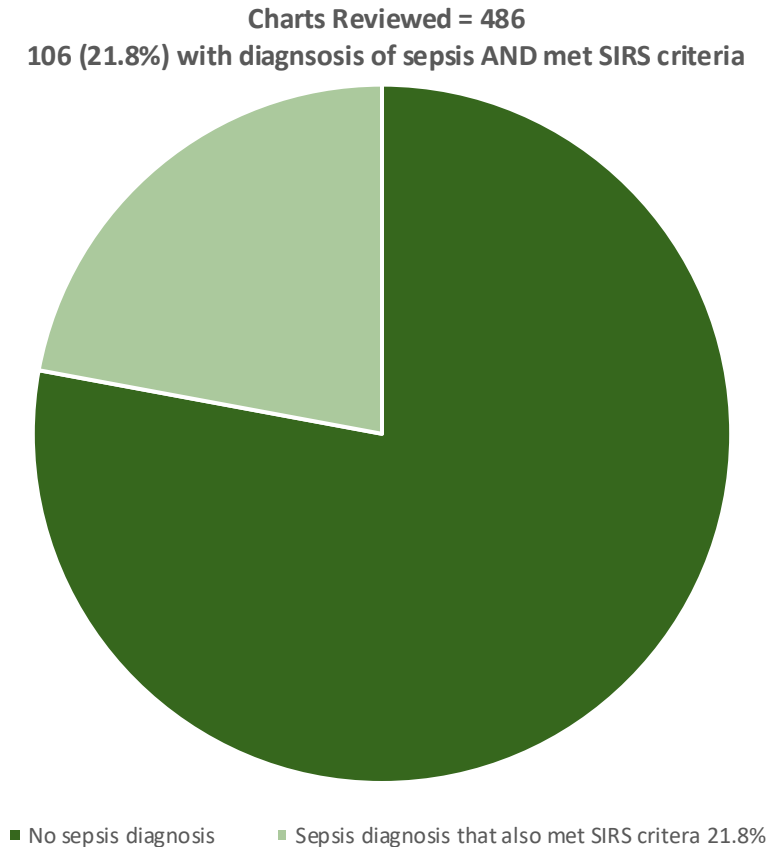
- A. Chart number
- B. Chart Review Date
- C. Donor ID (de-identified/not provided)
- D. Sepsis Diagnosed During Hospital Stay (in problem list or discharge diagnosis) [corresponds to first part of sepsis screening criteria in current DE guidance]
- E. SIRS (or SOFA) + Suspicion of Infection criteria met? [corresponds to second part of sepsis screening criteria in current DE guidance]
- F. If yes, was sepsis later “ruled out” by treating MD?
- G. Sepsis is not diagnosed in the chart, but medical director believes there is potential for transmissible infection
- H. Transmissible/ suspected infection treated appropriately and not a concern at TOD
- I. Medical director believes true risk of transmissible infection present?
- J. Cause of Death?
- K. Notes

Sepsis Pilot Study Report Highlights

- **Background:** Current screening criteria, evolution of sepsis as clinical diagnosis/ syndrome, EMR challenges, overview of careful record review before and after sent to medical director for review, acknowledgement of MTB transmission and sepsis concerns
- Frequency of sepsis diagnosis among individuals with in-hospital deaths: Literature review, providing separate data source and context for the pilot study data
 - In summary, these data indicate that a diagnosis of sepsis impacts approximately 35% of the potential in-hospital cadaveric HCT/P donor pool. More significantly, when clinical criteria such as infection coupled with organ dysfunction is added, over 50% of potential in-hospital cadaveric donors are impacted.

Sepsis Pilot Study Report: Results

- Total number of donor charts reviewed were 486
- Total number of donor charts with sepsis diagnosis 112
- Total number of donor charts with sepsis diagnosis AND meets SIRS Criteria 106
- 95% of donors diagnosed with sepsis (112) also met SIRS criteria ($106/112=95\%$) and as percentage of total chart reviewed were 21.8%.

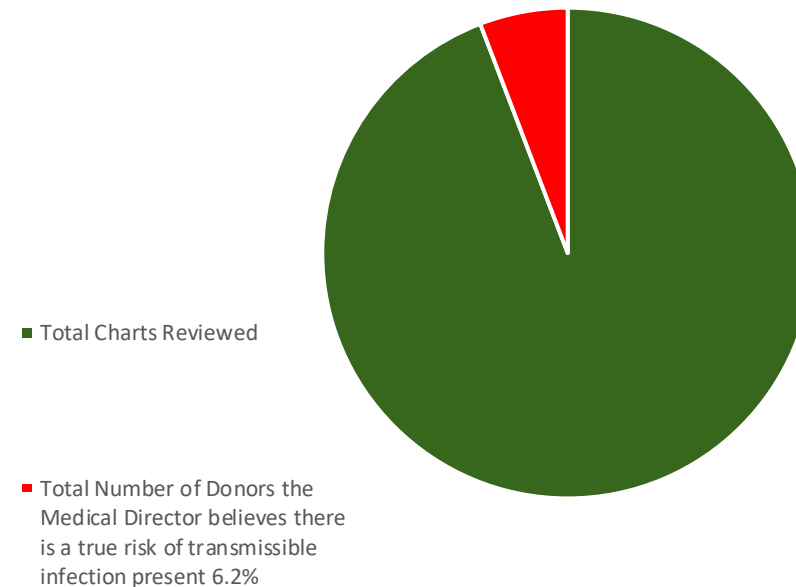


Sepsis Pilot Study Report: Results

Total Number of Donors diagnosed with Sepsis for which the Medical Director believes the suspected infection was treated appropriately and therefore is not a concern at the time of death were 64 donors.

- As a percentage of charts with diagnosis of Sepsis ($64/112$) = 57%
- As a percentage of donor charts meeting Sepsis + SIRS ($64/106$) = 60%
- As a percentage of all donor charts reviewed ($64/486$) = 13%

Total Number of Donors the Medical Director believed there is a true risk of transmissible infection present (30/486)



Sepsis Pilot Study Report: Results

Table 1. Donor charts where transmissible infection is suspected by medical director, in relation to various criteria

Criterion (total number of donor charts with the listed criterion):	Number (and %) with Transmissible Infection suspected
Sepsis Diagnosis AND SIRS + suspected infection (106)	19 (17.9%)
SIRS + Suspected infection but no explicit sepsis diagnosis documentation (73)	8 (10.95%)
Sepsis later ruled out (40)	2 (5%)
Infection treated appropriately (78)	3 (3.8%)
Total Charts (486)	30 (6.2%)

Sepsis Pilot Study Report: Discussion

- The study did not evaluate those donors who were excluded by pre-screeners due to infection/sepsis concerns, due to those charts never making it to review by medical directors, suggesting that the percentage of sepsis diagnosis in overall deceased donors is at least larger than 23%.
- Literature review indicated that a diagnosis of sepsis impacts approximately 35% (at least one third of donors) of the potential in-hospital cadaveric HCT/P donor pool (see details above).
- The pilot study shows that the total percentage of donors who had either a sepsis diagnosis or met SIRS criteria constituted about 38% of charts reviewed.
- Discussed strengths and limitations of the data

Sepsis Pilot Study Report: Discussion

Table 2: Percentage of Donor Charts that would be found ineligible if exclusionary criteria during the hospital stay immediately preceding death include:

Sepsis Diagnosis Present	Sepsis AND SIRS Criteria Met	SIRS Criteria Met	Sepsis OR SIRS Criteria Met
23%	21.8%	36.8%	38%

Sepsis Pilot Study Report: Conclusions

- The AATB Physicians Council Sepsis Working Group (PC Sepsis WG) believes the donor screening criteria for “sepsis” would best be aligned with the presence of a true systemic infection transmissible by tissues given that is what produces the actual risk to recipients, not the physiologic response to an infection (i.e., with sepsis being a dysregulated physiologic response to a suspected infection, which is in itself is not transmissible).
- Currently, the donor eligibility guidance permits medical directors to accept donors meeting SIRS/ SOFA criteria if they believe the symptoms are explained by an alternative diagnosis.
- Currently medical directors feel comfortable accepting donors when
 - there was a clinical diagnosis of sepsis during the hospital stay when a source of infection was identified that was adequately treated prior to death
 - the clinical record indicates that sepsis is resolved (albeit that does not occur frequently)

Sepsis Pilot Study Report: Conclusions

- The AATB Physicians Council Sepsis WG believes that prevention of tuberculosis transmission is best done from the standpoint of improved epidemiologic and risk factor screening and stratification, which has since been implemented through the updated DRAI and eligibility Standards. As tuberculosis lesions can “hide” in tissues without causing Sepsis syndrome, a more robust and specific analysis tool was needed and created.
- The AATB PC Sepsis WG is working to formulate criteria for screening for tissue transmissible systemic infections, and plan to then develop algorithm/flow chart to aid in making the donor eligibility determination.
- We can foresee that consideration of having stricter sepsis criteria for donors of tissues containing viable cells than donors of highly processed tissues (like AATB developed for MTB donor screening) could be very helpful in balancing safety and availability.