
Challenges in building a diagnostic for 'sepsis'

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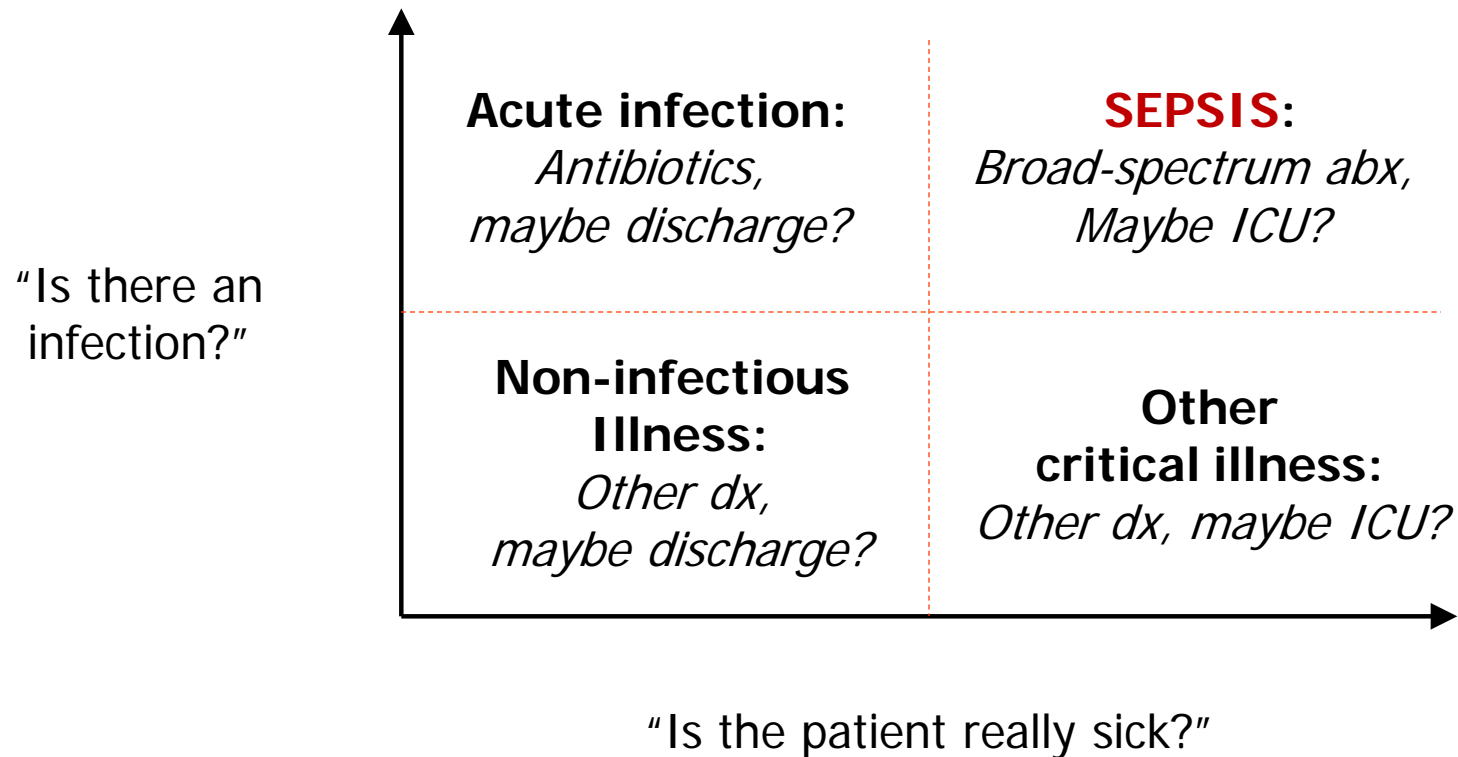
NASEM Sepsis diagnostics workshop
Aug 27, 2020

Disclosures

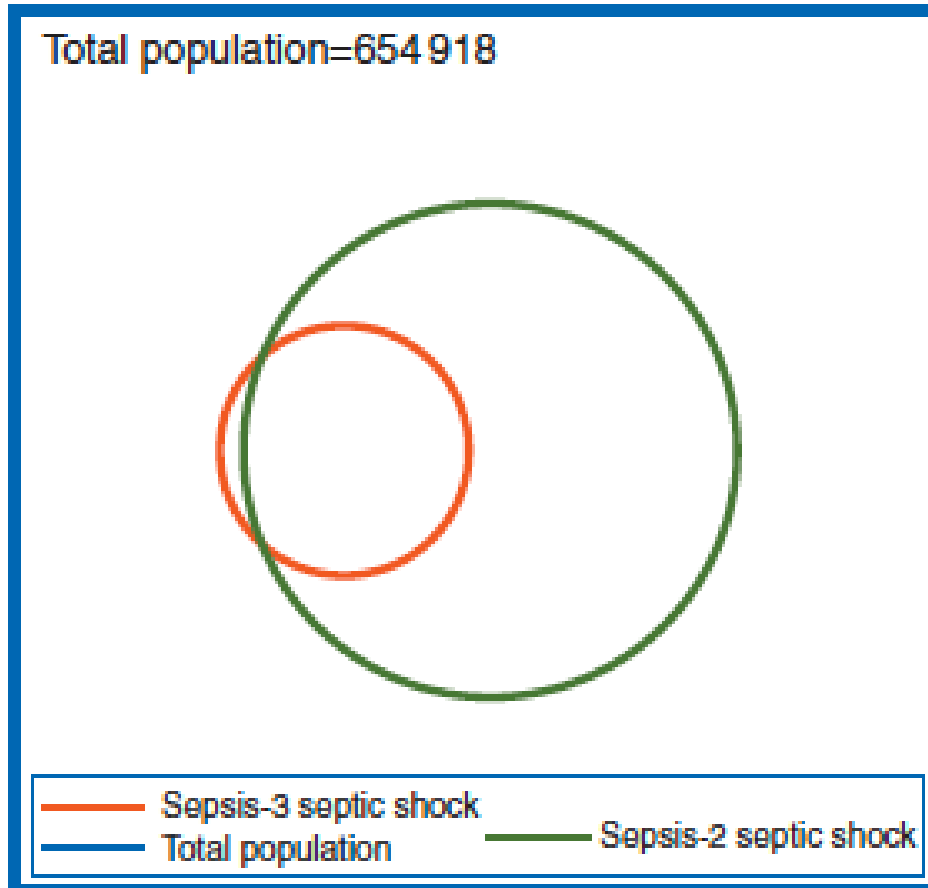
Employee of and stockholder in Inflammatrix, Inc.

Sepsis has two 'axes'

Sepsis-3 (*Singer et al. JAMA 2016*): Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.



Who has 'organ dysfunction'?



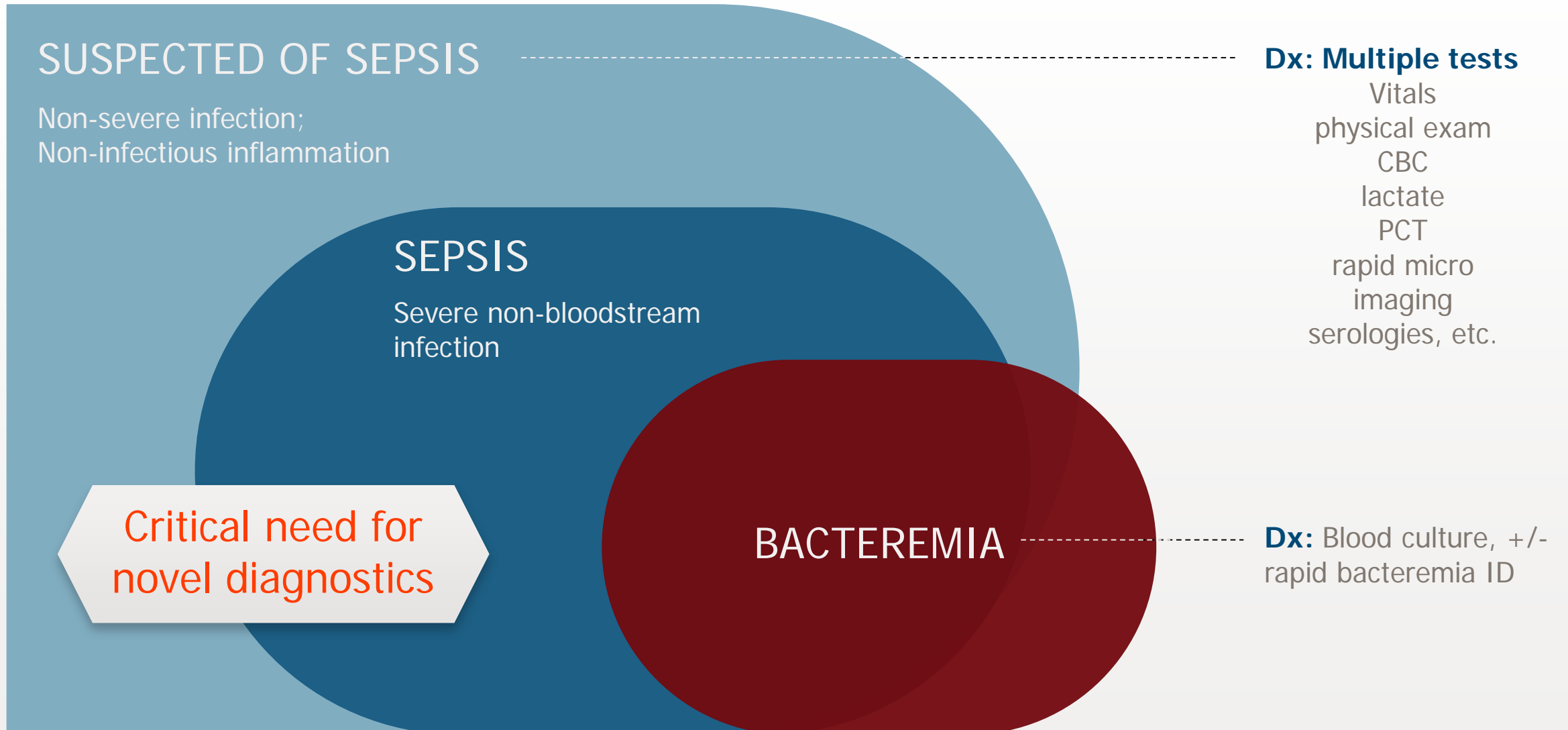
In a cohort of 654k ICU patients:

Green = sepsis-2 + shock

Orange = sepsis-3 + shock

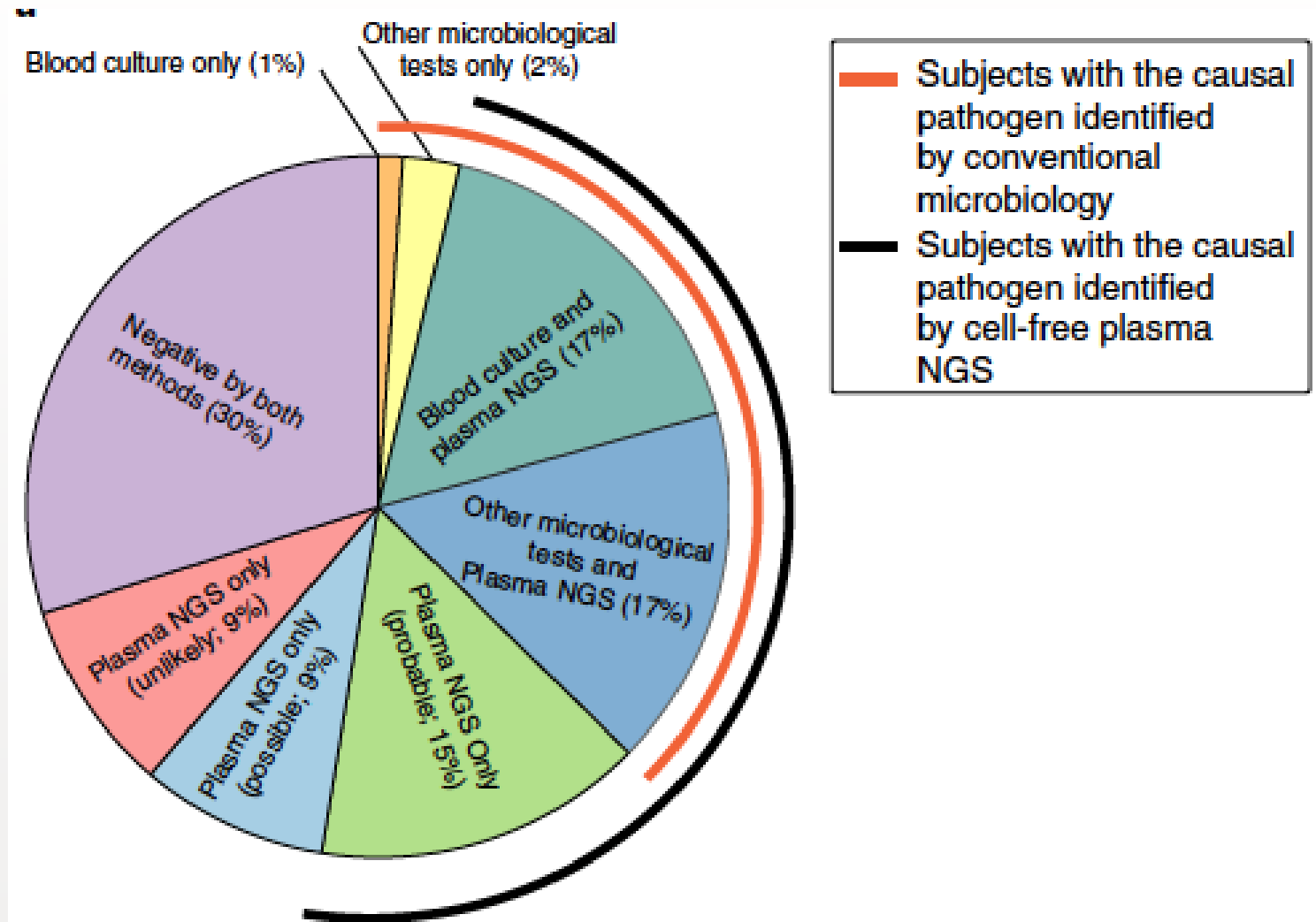
Which one is 'right'?

Bacteremia diagnostics are not necessarily sepsis diagnostics



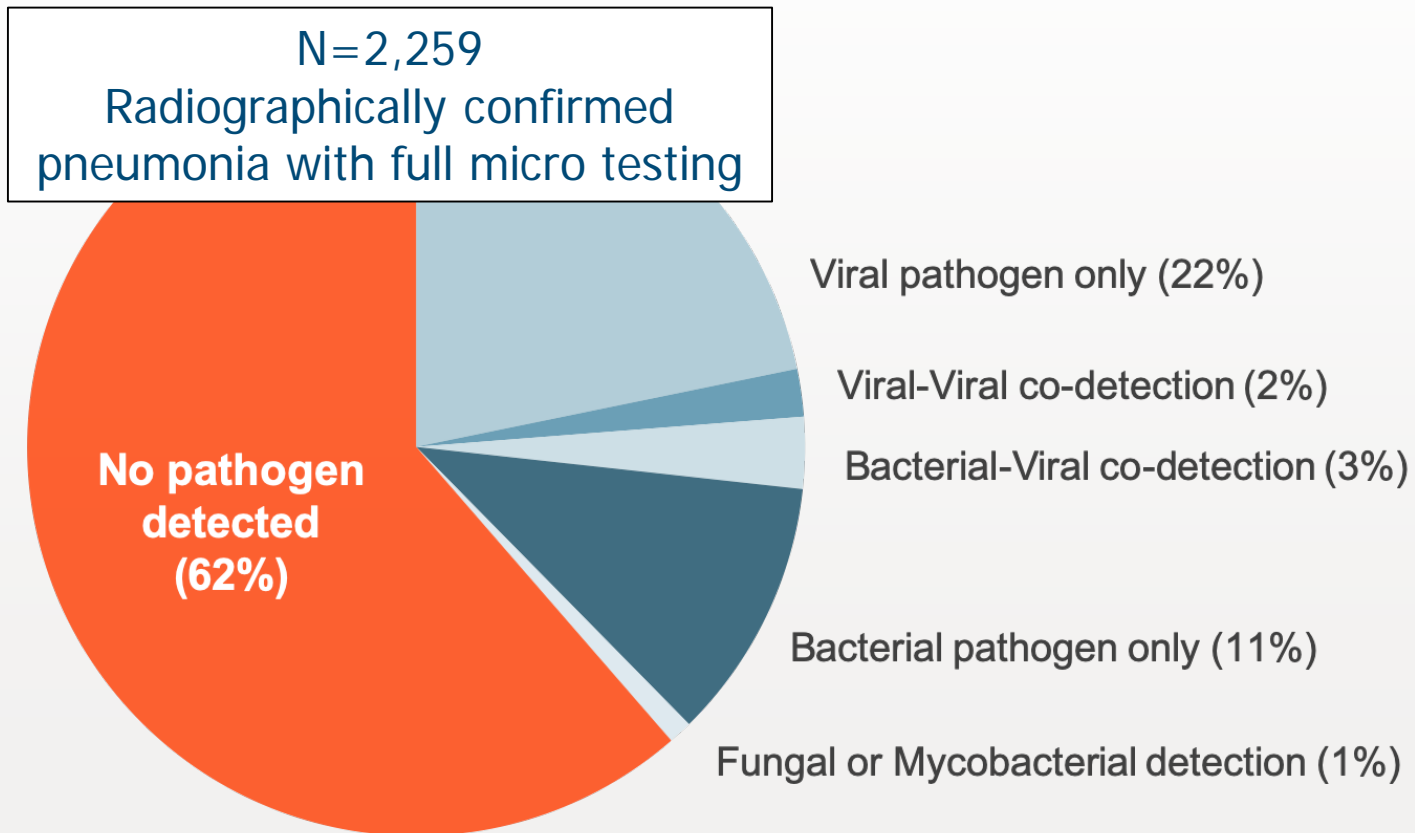
Is a microorganism a pathogen?

Pushing the bounds with NGS is only a marginal benefit



Who has a non-bloodstream infection?

Most patients with infections
don't have positive microbiology

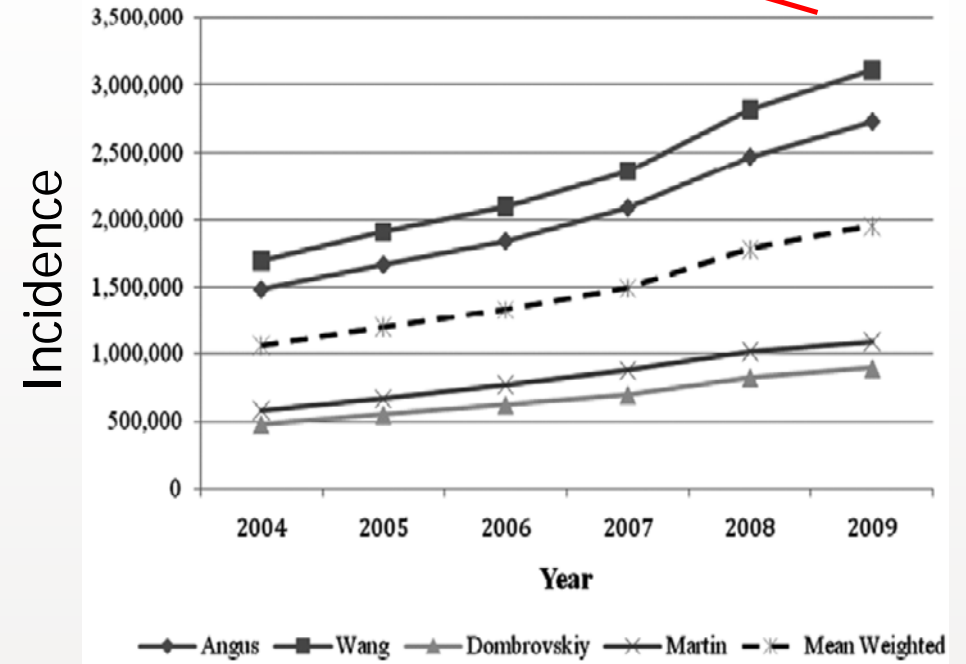
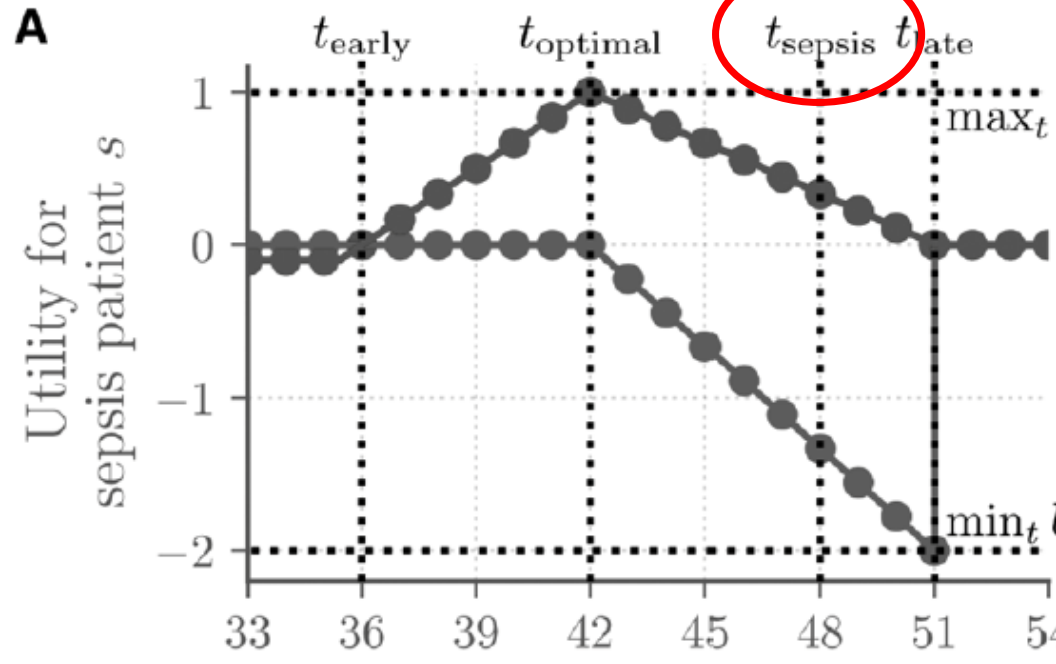


Physicians can't agree on
the rest:

Free kappa 0.24(!) – 0.7 in
adjudicating who has a
bacterial infection

*Lopansri, J Intens Care,
2019*

EHR 'sniffers': what is 'sepsis' in the record?

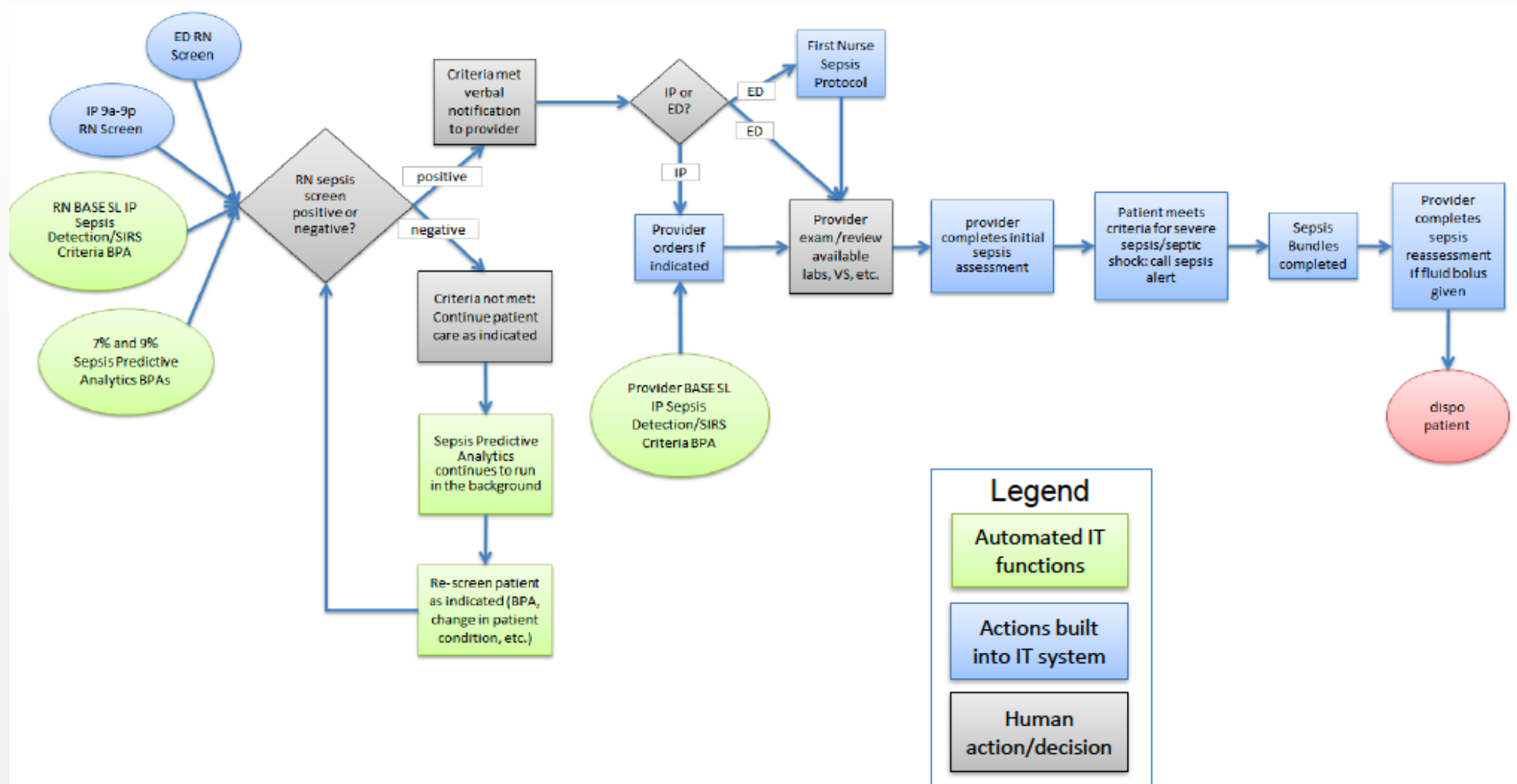


All EHR models rely on 'time of sepsis'...

...but 'sepsis' has a ~5-fold range using different criteria!

Workflow: Early - POC? Late - clinical lab?

The right answer doesn't help if given at the wrong time



Prior 'sepsis' diagnostics have been major market failures

Must make an economic difference / must cause physician practice change

Sepsis: the LightCycler SeptiFast Test MGRADE®, SepsiTTM and IRIDICA BAC BSI assay for rapidly identifying bloodstream bacteria and fungi – a systematic review and economic evaluation

Stevenson M, Pandor A, Martyn-St James M, Rafia R, Uttley L, Stevens J, *et al*. Sepsis: the LightCycler SeptiFast Test MGRADE®, SepsiTTM and IRIDICA BAC BSI assay for rapidly identifying bloodstream bacteria and fungi – a systematic review and economic evaluation. *Health Technol Assess* 2016;**20**(46).

What does the future hold?

