Infectious Diseases and Cardiac Events

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- No conflict of interests
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Infectious Diseases and Cardiac Events

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My job is to set the stage for a presentation of data from the DiNardo lab on increased risk of death after apparent cure of tuberculosis

Two kinds of association between acute infections and cardiac events

Short term effects:

- Heart attacks (myocardial infarction)
- Increased congestive heart failure
- Atrial fibrillation

Long term effects:

- Shortened life span

Association between pneumonia, acute MI

Clinical review of 105 cases pneumococcal pneumonia. 7 patients had an acute myocardial infarction at the time of admission. Attributed to stress resulting from infection Musher Medicine 79:210-221, 2000.

Only 1 previous study Feldman et al, Q J Med 1993

Prospective study, association between pneumococcal pneumonia and acute cardiac events. Musher, Clin Infect. Dis 45:158-65, 2007 **8% of patients have acute MI, 6% new onset AF, 14% worsening CHF. 19% have acute cardiac event(s).**

Similar findings in *Haemophilus* pneumonia, all cause community-acquired pneumonia Corrales-Medina, Musher et al. Medicine, 88:154-9, 2009 ; Circulation. 125:773-81, 2012

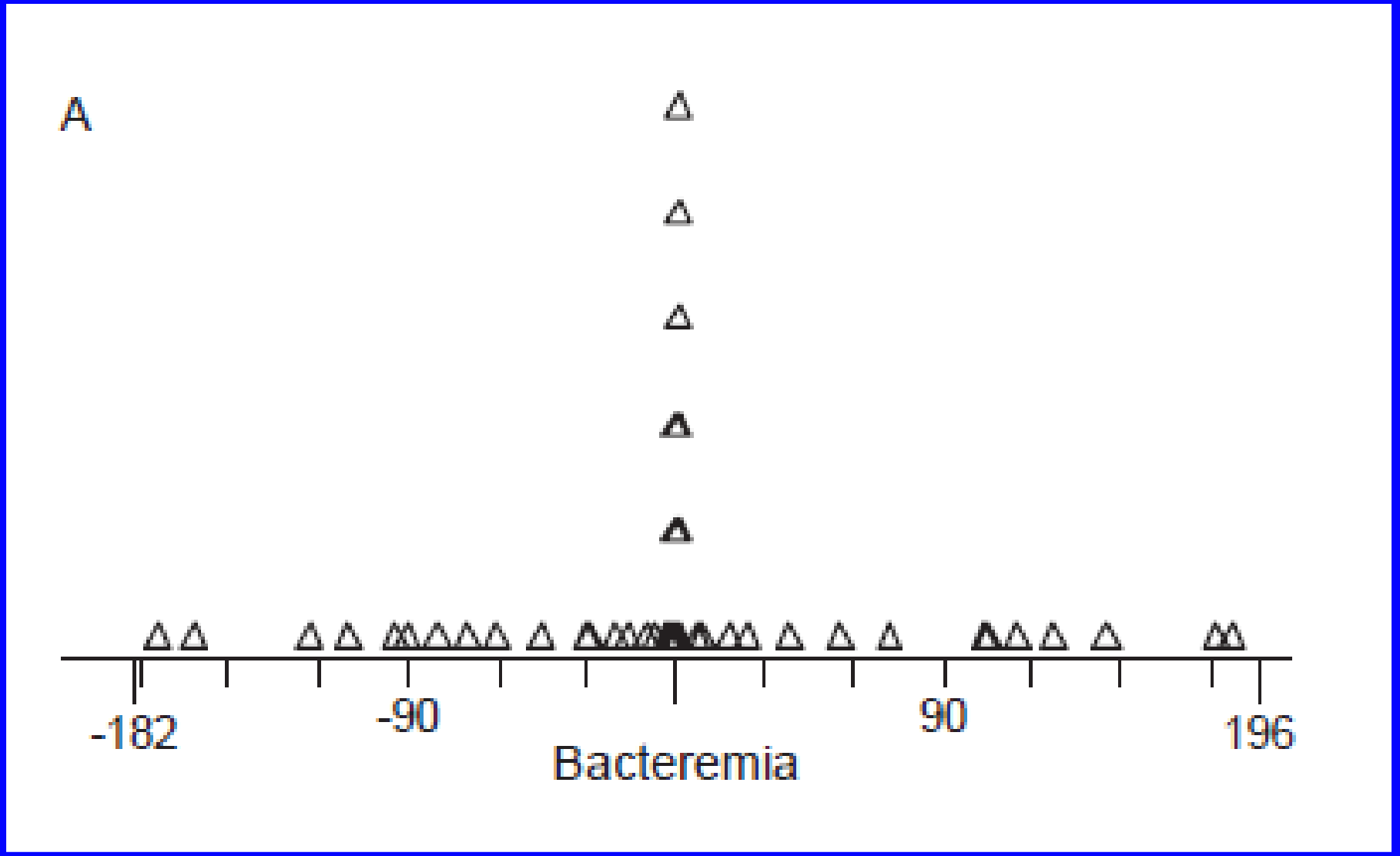
Mechanism for MI: acute inflammation in lungs releases cytokines. Activate inflammatory cells in atherosclerotic plaques → rupture, occlusion of vessel and myocardial infarction Corrales-Medina, Musher et al Lancet Infect Dis 10:83-92, 2010

Alternate mechanism: ↑cytokines persist for >30 days. Increase cardiac dysfunction at mitochondrial level with prolonged risk for heart failure

Other infections, not just pneumonia. *Staphylococcus aureus* bacteremia: Records of 588 patients with *Staph. aureus* bacteremia studied for ½ yr before and ½ yr after (called "self-controlled case series analysis") . 42 had an MI during observation period; 11 of the 42 clustered around the time of bacteremia

Corrales-Medina, Bozkurt, Musher et al Scand J Infect Dis 41:511-4, 2009

Self-controlled case series analysis, *Staph aureus* bacteremia and myocardial infarction



Summary of timing of MI in 588 patients with *S. aureus* bacteremia

In older male patients, often with significant cardiovascular risk, *S. aureus* bacteremia associated with a **7.9 fold ↑ risk of acute MI within 14 days around the diagnosis of the infection**

In the 48 h around the diagnosis of bacteremia, **35.3 fold ↑ risk of acute MI**

Increased deaths have long been associated with influenza Langmuir Am J Epidemiol 1974

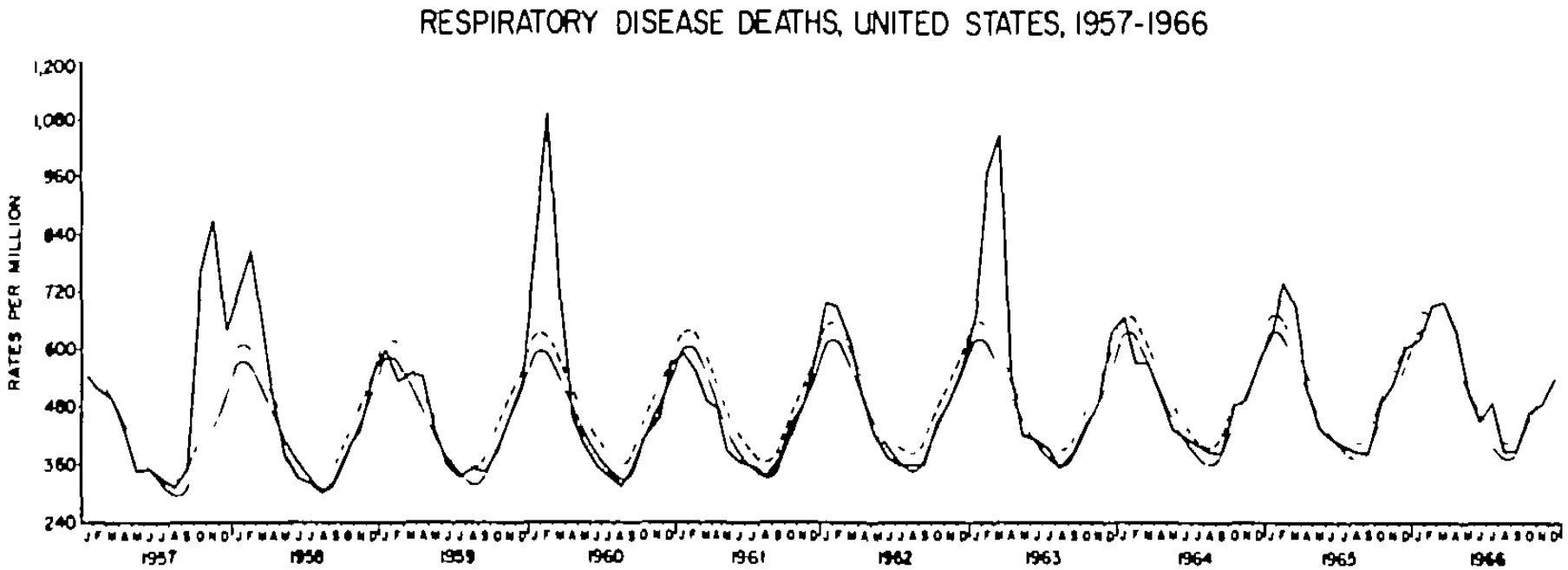
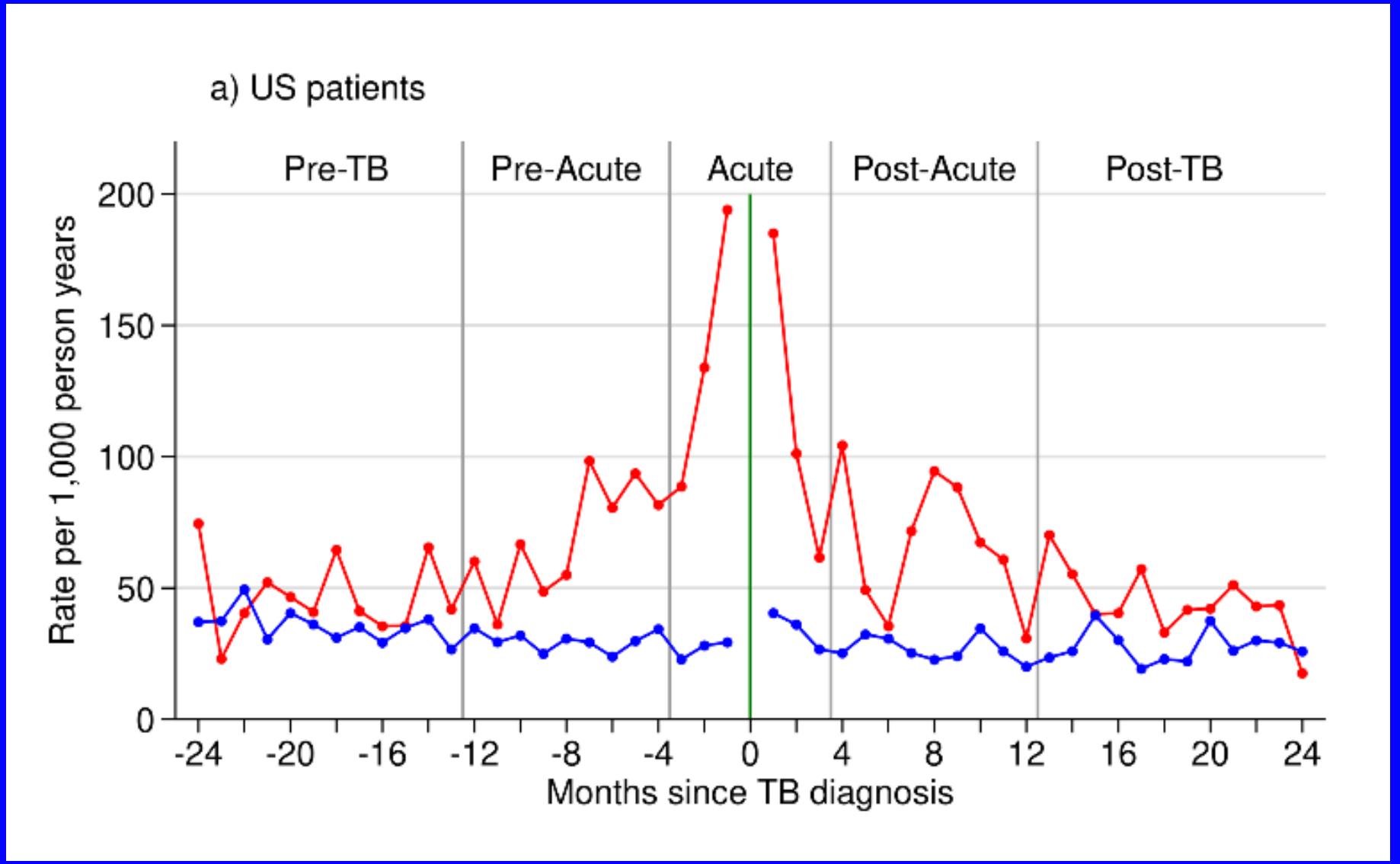


FIG. 1. Thin line, expected; heavy line, observed; broken line, epidemic threshold.

St. Petersburg autopsy study documented MI with influenza outbreaks Madjid, Eur Heart J. 2007 **Influenza vaccine reduces risk of MI in subjects with CAD: 67% ↓ in vaccinated vs non-vax subjects.** Naghavi, Circulation 102:3039, 2000

Cardiac events and Dx of TB



Now let's turn to long-term effects of acute infection.

This is what interests your group.

Data less solid, and mechanism is what you are in process of elucidating

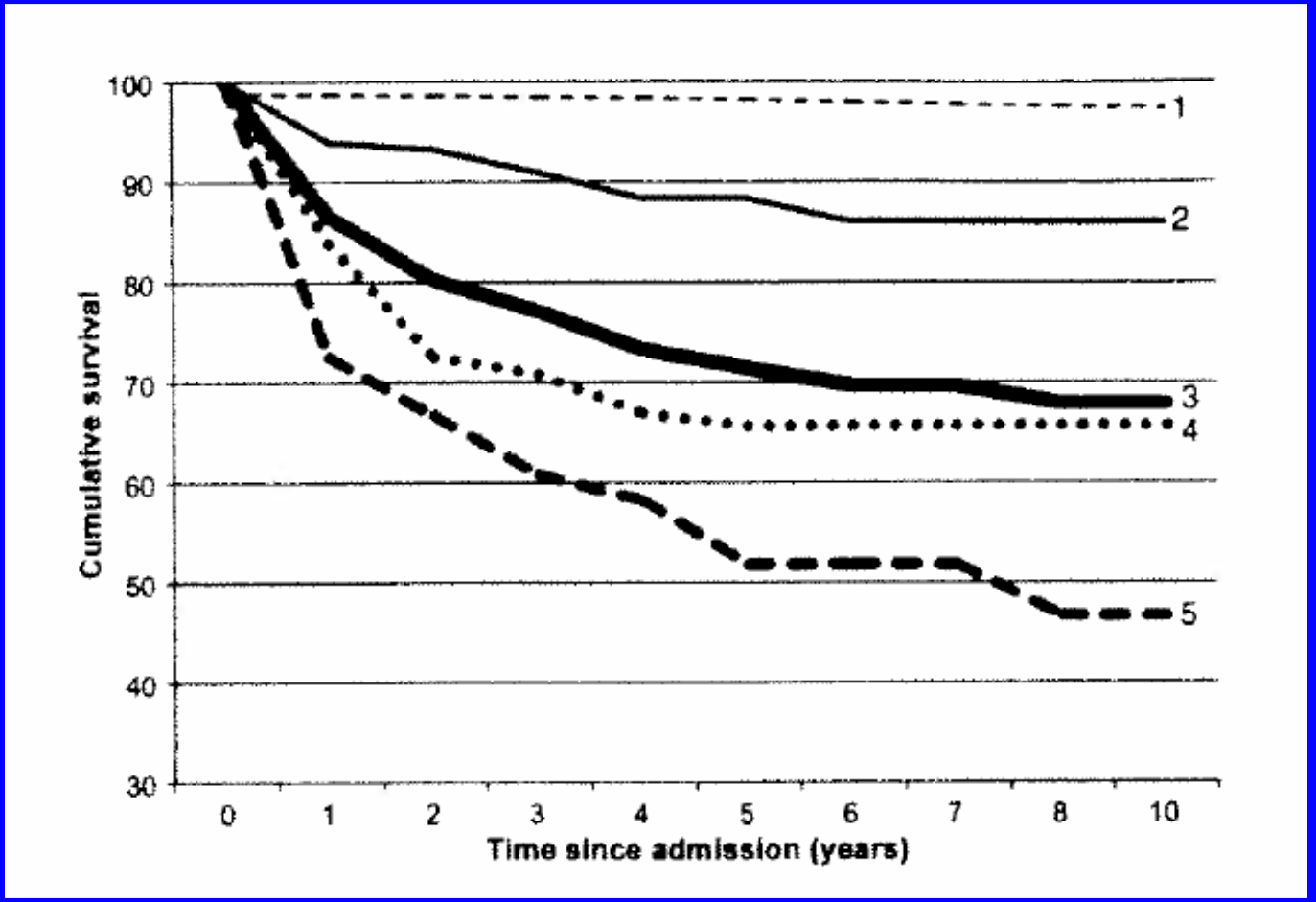
I always start with clinical observation; actually began with friends and family before patients.

Dwindling and deaths in the 1-2 years after seeming recovery from pneumonia.

Study of 10 year mortality after pneumococcal pneumonia shows a long-lasting increased mortality when compared to population at large

Survival (yrs) post pneumococcal pneumonia

Sandvall, Rueda, Musher Clin Infect Dis. 2013



1.Expected survival based on age of patients at Dx.

3. Cumulative survival all pneumonia patients

2, 4. 5. Increasing severity index scores at admission

Two other studies

Late mortality after sepsis. Prescott HC, et al. BMJ 2016;353:i2375. Propensity matched analysis. Compared mortality during 2 yrs after: (1) admission for sepsis; (2) admission for infection, not septic; (3) noninfectious inflammatory condition; (4) controls. In sepsis group, 42% mortality at 2 yr vs 21% in controls. Divergence continues

Glick et al Clin Infect Dis 2021 **One-Year Quality of Life Post–Pneumonia Diagnosis in Japanese Adults. "Substantial loss in quality of life in the year following a diagnosis of pneumonia"**

Review article Postinfectious Epigenetic Immune Modifications — A Double-Edged Sword

DiNardo, Netea, Musher, NEJMed 2021

Increased awareness of importance of sensitization of monocytes, natural killer cells, and dendritic cells.

This sensitization reflects long-lived epigenetic changes that profoundly enhance or suppress immune responses.

Immunologic stimuli — infections or immunizations — can have long-term consequences for the immune responsiveness of the host.

Conclusion

There us a striking incidence of acute cardiac events following acute infections

This mortality effect then persists for years

The increased risk of death is proportional to the severity of the infection

Different mechanisms for the short vs long term observations