# Comment

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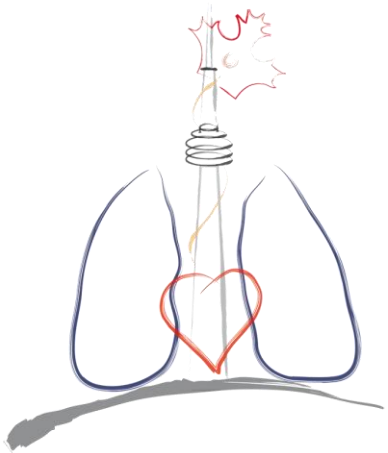
Sunnybrook
HEALTH SCIENCES CENTRE
when it matters MOST



UNIVERSITY OF TORONTO
Interdepartmental Division of Critical Care Medicine

# Disclosures

- I am not a statistician
- I can’t explain Bayesian statistics in 5 minutes

# My 3 Steps to Recovery from Frequentist Addiction©

1. Take a deep breath and relax, it's ok
2. Forget everything you never really new about frequentist statistics
3. Remember the bedside


KEEP
CALM
YOU ARE ALREADY
A
BAYESIAN

# 1. Take a deep breath and relax, it's ok

## EXPERIMENTAL DESIGN FOR DRUG DEVELOPMENT: A BAYESIAN APPROACH

Journal of Biopharmaceutical Statistics, 1(1), 81–101 (1991)

*Donald A. Berry*

## Guidance for Industry and FDA Staff

## Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials

Document issued on: February 5, 2010

The draft of this document was issued on 5/23/2006

# 1. Take a deep breath and relax, it's ok

## Why Are Clinicians Not Embracing the Results from Pivotal Clinical Trials in Severe Sepsis? A Bayesian Analysis

2008

Andre C. Kalil[1]*, Junfeng Sun[2]

PLoS ONE 3(5): e2291

| CLINICAL TRIALS (Favorable Evidence) | Early Goal-Directed Therapy | Activated Protein C | Activated Protein C (APACHE II >25) | Low-Dose Steroids (Non-Responders) | Low-Tidal Volume | Intensive Insulin Therapy (>5 days in ICU) |
|---|---|---|---|---|---|---|
| **Published P values** (Frequentist) | 0.009 | 0.005 | 0.0002 | 0.02 | 0.007 | 0.005 |
| **Sample Size of Unfavorable Evidence** (Bayesian Priors) | CURRENT PROBABILITY OF NEW TREATMENT BEING NO BETTER THAN CONTROL | | | | | |
| **ENTHUSIASTIC** (Sample Size = 1) | 0.01 | 0.009 | 0.0003 | 0.03 | 0.009 | 0.003 |
| **MILD SKEPTIC** (Sample Size = 200) | 0.05 | 0.02 | 0.002 | 0.10 | 0.02 | 0.02 |
| **MILD-MODERATE SKEPTIC** (Sample Size = 500) | 0.14 | 0.03 | 0.007 | 0.21 | 0.05 | 0.05 |
| **MODERATE SKEPTIC** (Sample Size = 1000) | 0.25 | 0.05 | 0.03 | 0.33 | 0.10 | 0.12 |
| **SEVERE SKEPTIC** (Sample Size = 2000) | 0.41 | 0.12 | 0.09 | 0.47 | 0.21 | 0.23 |

# 1. Take a deep breath and relax, it's ok

## Extracorporeal membrane oxygenation (ECMO) reconsidered

— 2010 —

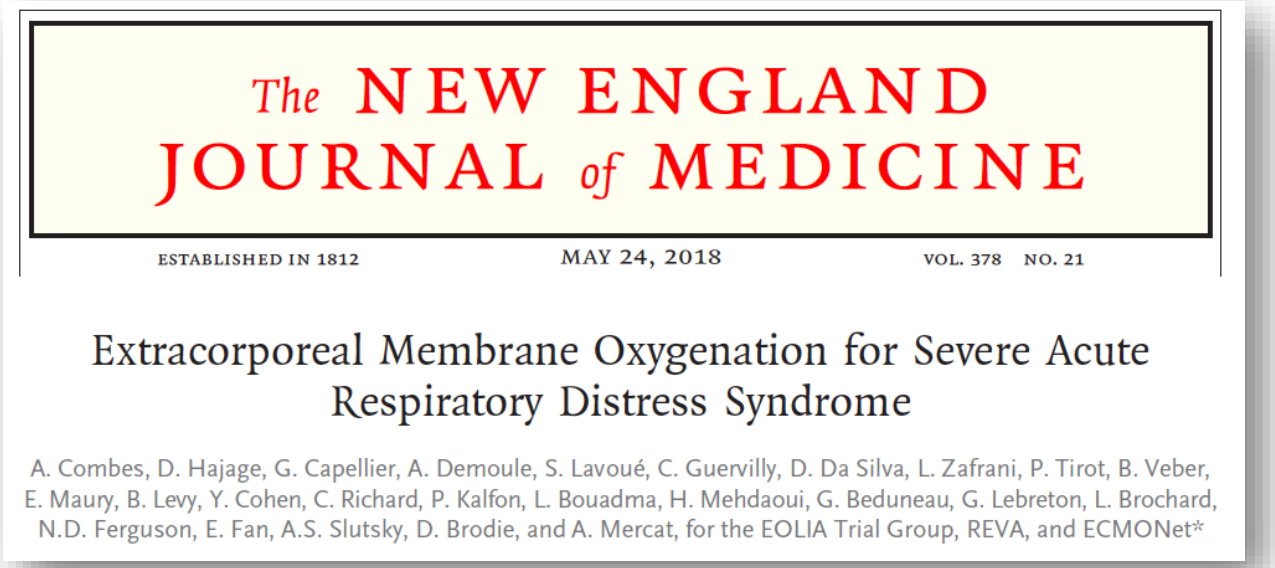
John L Moran, Richard P Chalwin and Petra L Graham

**ABSTRACT**

The role of extracorporeal membrane oxygenation (ECMO) in the treatment of the acute respiratory distress syndrome (ARDS) is controversial, notwithstanding the recent publication of the results of the CESAR (Conventional Ventilation or ECMO for Severe Adult Respiratory Failure) trial. Using Bayesian meta-analytic methods from three randomised controlled trials (RCTs) of ECMO in ARDS, we estimate the mortality odds ratio to be 0.78 (95% credible interval, 0.25–3.04), $P(OR > 1) = 30\%$. Thus, a null effect of ECMO is not excluded and there appears only weak evidence of efficacy. We survey particular problems

Crit Care Resusc 2010; 12: 131–135

# 2. Forget everything you never really new abut statistics



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 24, 2018 VOL. 378 NO. 21

Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome

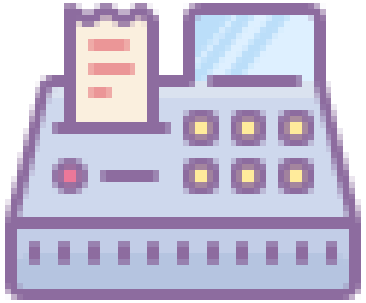
A. Combes, D. Hajage, G. Capellier, A. Demoule, S. Lavoué, C. Guervilly, D. Da Silva, L. Zafrani, P. Tirot, B. Veber, E. Maury, B. Levy, Y. Cohen, C. Richard, P. Kalfon, L. Bouadma, H. Mehdaoui, G. Beduneau, G. Lebreton, L. Brochard, N.D. Ferguson, E. Fan, A.S. Slutsky, D. Brodie, and A. Mercat, for the EOLIA Trial Group, REVA, and ECMONet*

| End Point | ECMO Group (N=124) | Control Group (N=125) | Relative Risk or Difference (95% CI)† | P Value |
|---|---|---|---|---|
| Primary end point: mortality at 60 days — no. (%) | 44 (35) | 57 (46) | 0.76 (0.55 to 1.04) | 0.09 |

- What is the probability ECMO reduces mortality?
- What is the probability that the EOLIA results are from chance?
- What is the probability that the ECMO-effect is between .55 and 1.04?

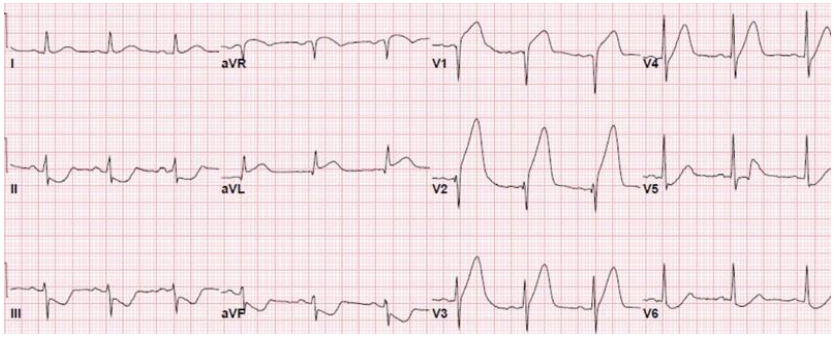
# 3. Remember the bedside

TnT 35 ng/L, Sensitivity 95%, Specificity 80%

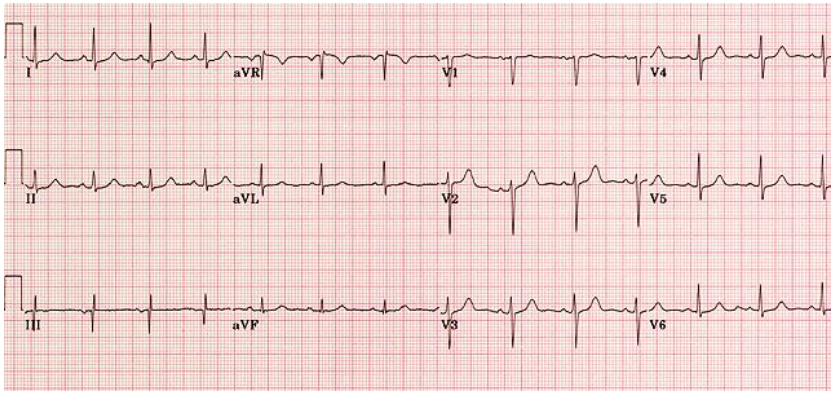


## What is the probability the patient is having an MI?

57 yo man typical chest pain

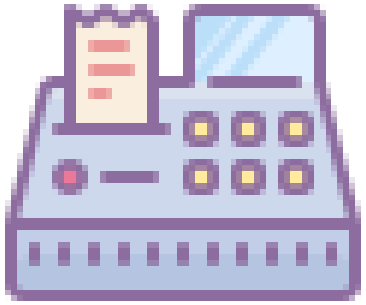



39 yo woman atypical chest pain

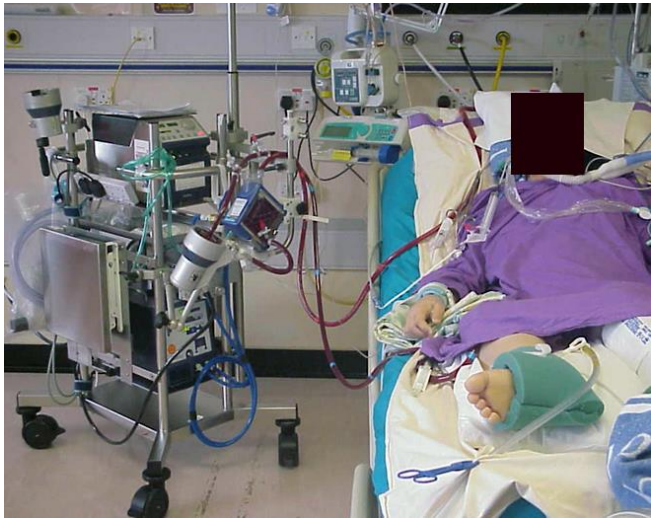


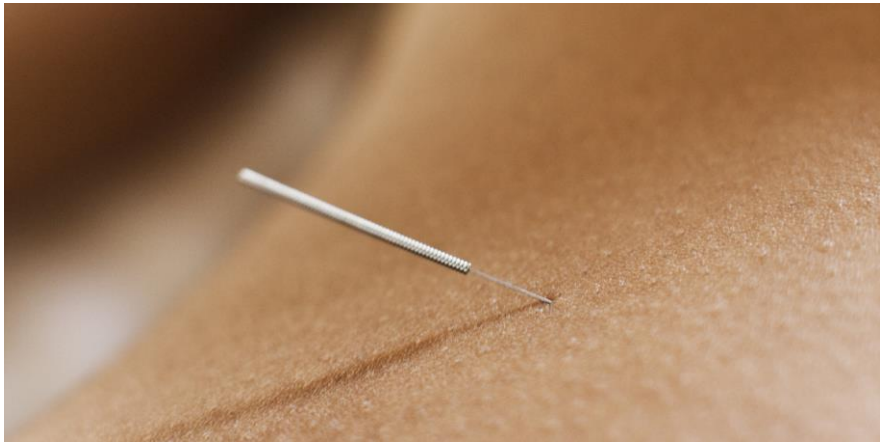
# 3. Remember the bedside
# A new treatment for severe ARDS

RR 0.76, P=0.03, 95% CI (0.55 – 0.73)



What is the probability the treatment reduces mortality?





# Are All Significant *P* Values Created Equal?

## The Analogy Between Diagnostic Tests and Clinical Research

Warren S. Browner, MD, MPH, Thomas B. Newman, MD, MPH

(*JAMA* 1987;257:2459-2463)

- Post test probability ≈ Pre test probability x Sens/1-Spec
- P (MI | + troponin) ≈ P(MI) x Sens/1-Spec
- P (ECMO | EOLIA) ≈ P(ECMO) x f (CI, P value)

We need post test probabilities to make decisions

frequentist statistics only provide

*"Sensitivity" and "Specificity"*

# You need priors to use statistical information
# They will either be implicit or explicit

*Bayesian measures are subjective. Some people regard subjectivity as a liability. It may be. But all inferences are made by individuals and so they are necessarily subjective. An advantage of the Bayesian approach is that it makes subjectivity explicit.*

Donald A. Berry

# Steps 4-12

- OMG, this is amazing, why haven't we been doing this all along?
- Where do these priors come from?
- If Bayesian statistics tells us the probability the treatment works given priors and the evidence, what threshold should I use to change practice?  95% 51%
- Do Bayesian trials require fewer patients?
- What about multiple testing and stopping rules?
- Do Bayesian stats fix the crossover problem in Eolia?

**Special Communication**

# Are All Significant *P* Values Created Equal?

## The Analogy Between Diagnostic Tests and Clinical Research

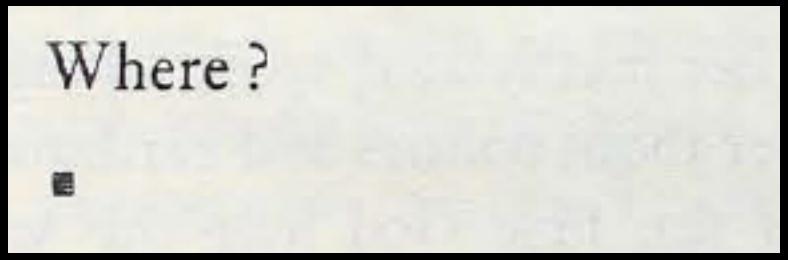
Warren S. Browner, MD, MPH, Thomas B. Newman, MD, MPH

JAMA 1987;257:2459-2463

# Toward Evidence-Based Medical Statistics. 1: The *P* Value Fallacy

Steven N. Goodman, MD, PhD

Ann Intern Med. 1999;130:995-1004

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