Motivational examples: diagnostic tests

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The obscure maths theorem that governs the reliability of Covid testing

There's been much debate about lateral flow tests – their accuracy depends on context and the theories of a 18th-century cleric

[Good, *J GEN INTERN MED* 2020]

Table 1 Estimates for Post-Test Probability of Acute COVID-19 Infection for Simulated Patient Scenarios

Clinical Scenarios	Pre-test probability (%)	PCR assay sensitivity (%)	Post-test probability of acute COVID-19 infection	
			Positive test (%)	Negative test (%)
Patient 1: high pre-test probability	70	70	100	41.2
		90	100	18.9
	90	70	100	73.0
		90	100	47.4
Patient 2: low pre-test probability	5	70	97.4	1.6
		90	97.9	0.5
	10	70	98.7	3.2
		90	99.0	1.1

Original Article

Bayesian analysis of tests with unknown specificity and sensitivity

Andrew Gelman, Bob Carpenter

First published: 13 August 2020 | https://doi.org/10.1111/rssc.12435 | Citations: 6

Motivational examples: clinical trial design

Design

CLINICAL TRIALS

Clinical Trials
1–10

DOI: 10.1177/1740774520943846
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SAGE

Anti-Thrombotic Therapy to Ameliorate Complications of COVID-19 (ATTACC): Study design and methodology for an international, adaptive Bayesian randomized controlled trial

Methods: An international, open-label, adaptive randomized controlled trial. Using a Bayesian framework, the trial will declare results as soon as pre-specified posterior probabilities for superiority, futility, or harm are reached. The trial uses response-adaptive randomization to maximize the probability that patients will receive the more beneficial treatment approach, as treatment effect information accumulates within the trial. By leveraging a common data safety monitoring

[Houston *et al.*, *Clinical Trials*, 17(5):491-500, 2020]

Motivational examples: study/trial analyses

The NEW ENGLAND JOURNAL of MEDICINE
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Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19

The REMAP-CAP Investigators*

lumab group, and 0 (interquartile range, –1 to 15) in the control group. The median adjusted cumulative odds ratios were 1.64 (95% credible interval, 1.25 to 2.14) for tocilizumab and 1.76 (95% credible interval, 1.17 to 2.91) for sarilumab as compared with control, yielding posterior probabilities of superiority to control of more than 99.9% and of 99.5%, respectively. An analysis of 90-day survival showed improved survival in the pooled interleukin-6 receptor antagonist groups, yielding a hazard ratio for the comparison with the control group of 1.61 (95% credible interval, 1.25 to 2.08) and a posterior probability of superiority of more than 99.9%. All secondary analyses supported efficacy of these interleukin-6 receptor antagonists.

ORIGINAL

Dexamethasone 12 mg versus 6 mg for patients with COVID-19 and severe hypoxaemia: a pre-planned, secondary Bayesian analysis of the COVID STEROID 2 trial

Abstract

Purpose: We compared dexamethasone 12 versus 6 mg daily for up to 10 days in patients with coronavirus disease 2019 (COVID-19) and severe hypoxaemia in the international, randomised, blinded COVID STEROID 2 trial. In the primary, conventional analyses, the predefined statistical significance thresholds were not reached. We conducted a pre-planned Bayesian analysis to facilitate probabilistic interpretation.

Methods: We analysed outcome data within 90 days in the intention-to-treat population (data available in 967 to 982 patients) using Bayesian models with various sensitivity analyses. Results are presented as median posterior probabilities with 95% credible intervals (CrIs) and probabilities of different effect sizes with 12 mg dexamethasone.

Results: The adjusted mean difference on days alive without life support at day 28 (primary outcome) was 1.3 days (95% CrI −0.3 to 2.9; 94.2% probability of benefit). Adjusted relative risks and probabilities of benefit on serious adverse reactions was 0.85 (0.63 to 1.16; 84.1%) and on mortality 0.87 (0.73 to 1.03; 94.8%) at day 28 and 0.88 (0.75 to 1.02; 95.1%) at day 90. Probabilities of benefit on days alive without life support and days alive out of hospital at day 90 were 85 and 95.7%, respectively. Results were largely consistent across sensitivity analyses, with relatively low probabilities of clinically important harm with 12 mg on all outcomes in all analyses.

The NEW ENGLAND JOURNAL of MEDICINE
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Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

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Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
	(N=18,198)		(N=18,325)			
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
	(N=19,965)		(N=20,172)			
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

* The total population without baseline infection was 36,523; total population including those with and those without prior evidence of infection was 40,137.
† The surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
‡ The credible interval for vaccine efficacy was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.
§ Posterior probability was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.