PCR TEST SENSITIVITY VS. TIME

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BACKGROUND: From peak sensitivity at Covid symptom onset, polymerase chain-reaction (PCR) test sensitivity declines over time.

Sensitivity is probability of positive test given a patient has Covid.

GOAL: Develop a Bayesian model to estimate sensitivity vs. time.

FINDINGS:

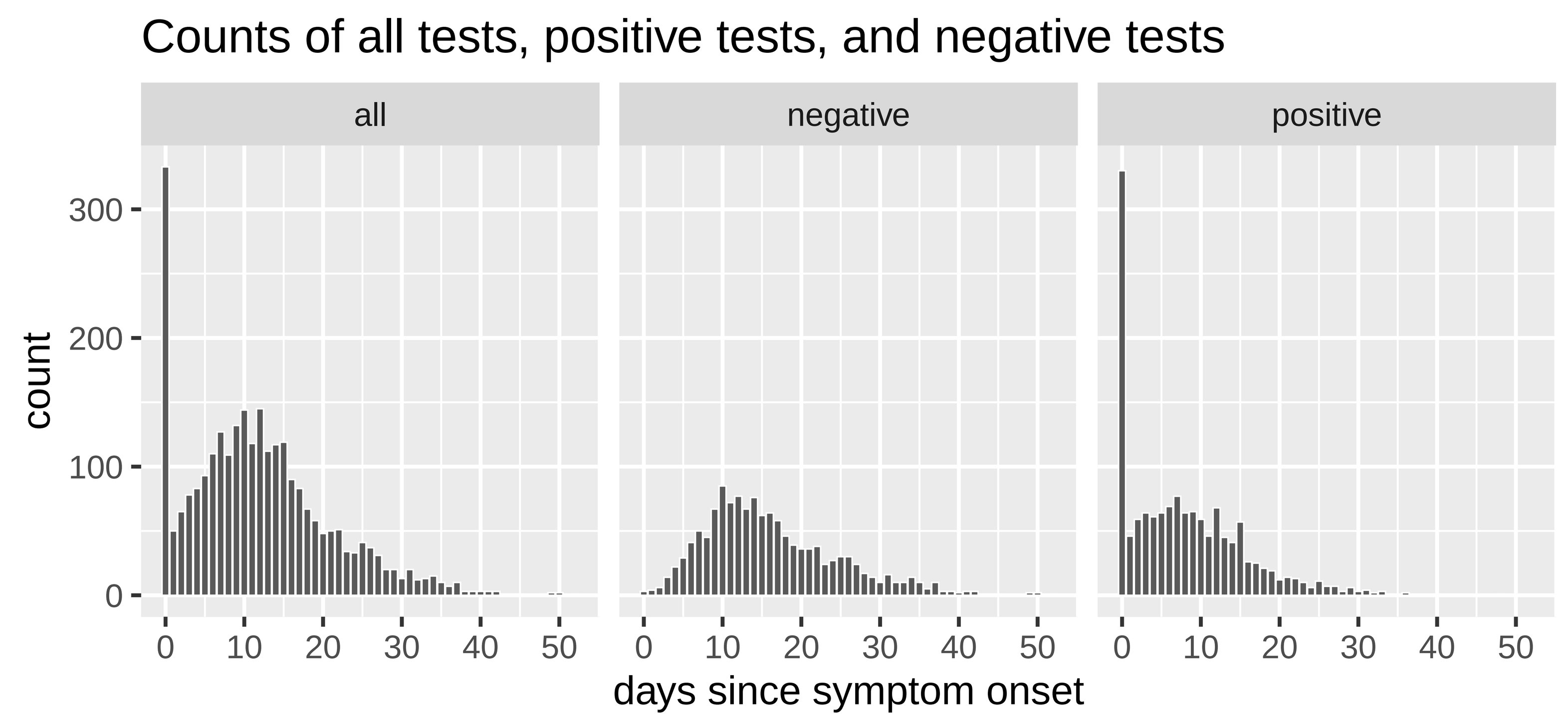
- **Mixed population:** The fits suggest patients had mixture of short and long Covid.fit
- **Pharmacokinetics:** Log regression is solution to one-compartment clearance model, with mixture for two populations.

APPLICATIONS:

- **Estimating prevalence** from tests,
- **Estimating viral load** over time, and
- **Calibrating test surveys** with time-to-hospitalization, time-to-death, and post-stratification.

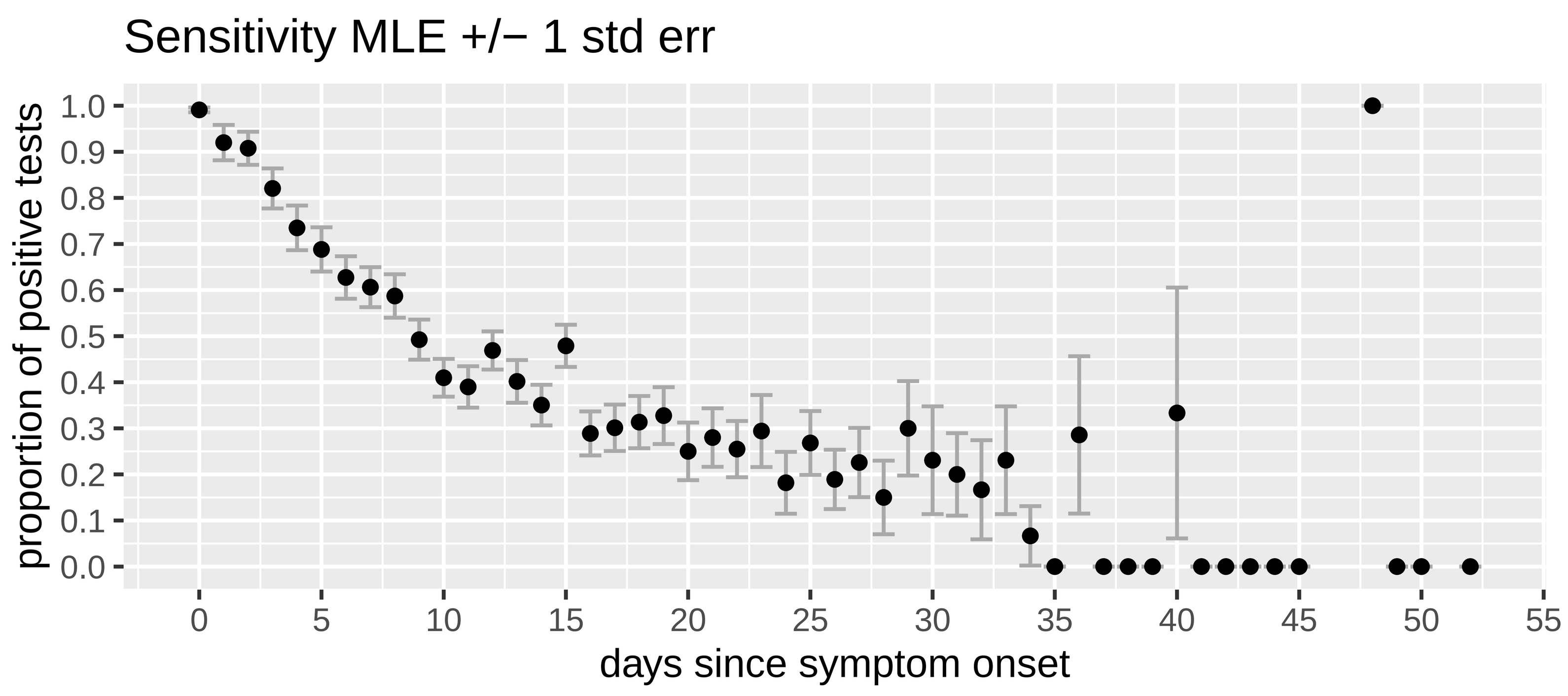
1. Data

The data was collected from all patients admitted to one UK hospital with Covid in mid-2020.



Sue Mallet et al. (2020) "At what times during infection is SARS-CoV-2 detectable and no longer detectable using RT-PCR-based tests?" *BMC Medicine*

2. Unconstrained MLE with standard errors



3. Bayesian models

Hetero (logit): $y_n \sim \mathrm{bernoulli}(\mathrm{logit}^{-1}(\theta_{t_n}));\quad \theta_t \sim \mathrm{normal}(0,3);\quad \theta_{t+1} < \theta_t$

Hetero (log): $y_n \sim \mathrm{bernoulli}(\exp(\theta_{t_n}));\quad \theta_t \sim \mathrm{normal}(0,3);\quad \theta_{t+1} < \theta_t < 0$

RW(1) (logit): $y_n \sim \mathrm{bernoulli}(\mathrm{logit}^{-1}(\theta_{t_n}));\quad \theta_{t+1} \sim \mathrm{normal}(\theta_t, \sigma);\quad \sigma \sim \mathrm{normal}(0,1);$
$\theta_{t+1} < \theta_t;\quad \sigma > 0$

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$\theta_{t+1} < \theta_t < 0;\quad \sigma > 0$

RW(2) (logit): $y_n \sim \mathrm{bernoulli}(\mathrm{logit}^{-1}(\theta_{t_n}));\quad \theta_{t+2} \sim \mathrm{normal}(\theta_{t-1} + (\theta_{t-1} - \theta_{t-2}), \sigma);$
$\sigma \sim \mathrm{normal}(0,0.5);\quad \theta_{t+1} < \theta_t;\quad \sigma > 0$

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Regression (logit): $y_n \sim \mathrm{bernoulli}(\mathrm{logit}^{-1}(\alpha + \beta \cdot t_n));\quad \alpha, \beta \sim \mathrm{normal}(0,0.5);\quad \beta < 0$

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Regress. mix (logit): $y_n \sim \mathrm{bernoulli}(\lambda \cdot \mathrm{logit}^{-1}(\alpha_1 + \beta_1 \cdot t_n) + (1-\lambda) \cdot \mathrm{logit}^{-1}(\alpha_2 + \beta_2 \cdot t_n)))$
$\lambda \sim \mathrm{beta}(2,2);\quad \alpha_k, \beta_k \sim \mathrm{normal}(0,1);\quad \beta_k < 0$

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$\lambda \sim \mathrm{beta}(2,2);\quad \alpha_k, \beta_k \sim \mathrm{normal}(0,1);\quad \alpha_k, \beta_k < 0.$

4. Model comparison regression fit

Approximate leave-one-out cross-validation estimates of expected log predictive density (ELPD) differences plus standard errors of differences. Estimated using Stan's `loo` package.

Model	Scale	ELPD (diff)	standard error (diff)
2nd-order random walk	log	0.0	0.0
Regression mixture	log	-0.4	1.5
1st-order random walk	log	-0.9	0.7
Regression	log	-2.8	2.7
Heterogeneous	log	-3.0	1.8
Heterogeneous	logit	-3.0	1.9
2nd-order random walk	logit	-6.7	3.7
1st-order random walk	logit	-8.4	3.8
Regression mixture	logit	-15.0	4.1
Regression	logit	-81.6	9.9

5. Log (mixture) regression coefficient estimates

Regression (log): $\widehat{\alpha} = -0.01;\quad \widehat{\beta} = -0.07$

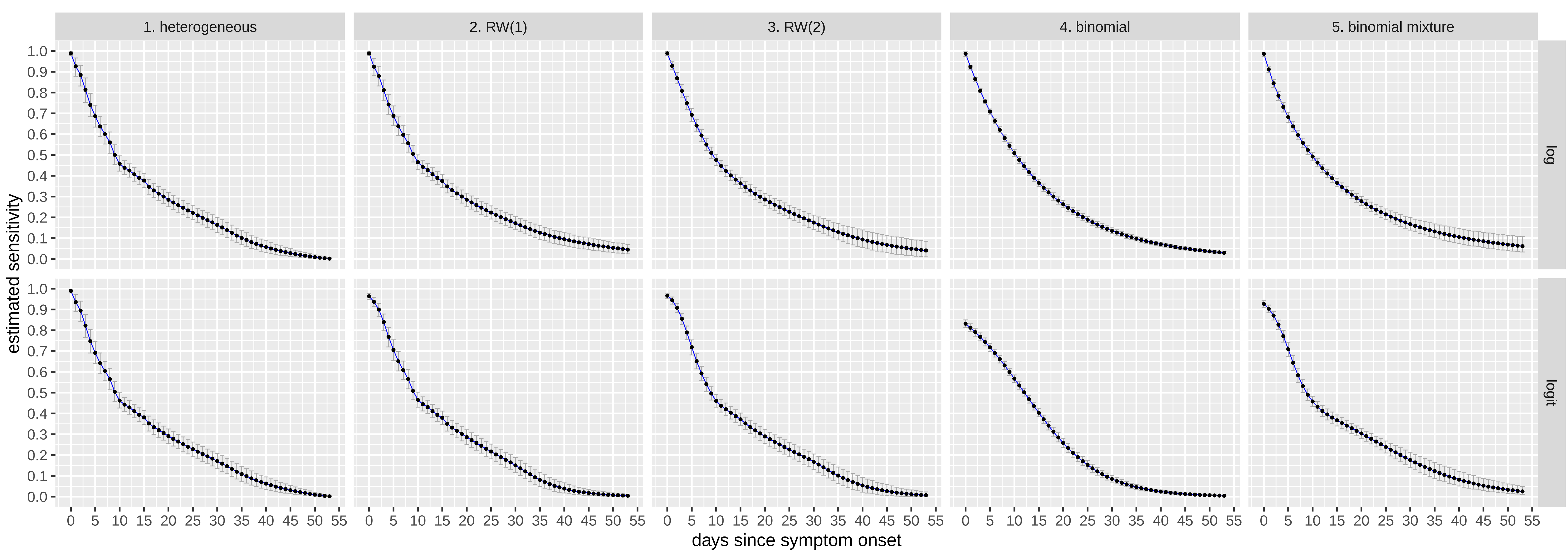
Regression (log mix): $\widehat{\alpha}_1 = -0.02;\ \widehat{\beta}_1 = -0.04;\quad \widehat{\alpha}_2 = -0.03;\ \widehat{\beta}_2 = -0.18;\quad \widehat{\lambda} = 0.6$

6. Reproducible GitHub repository

Stan

`https://github.com/bob-carpenter/pcr-sensitivity-vs-time`

7. Visual model comparison



International Society for Bayesian Analysis (ISBA), World Meeting, July 2024, Venice