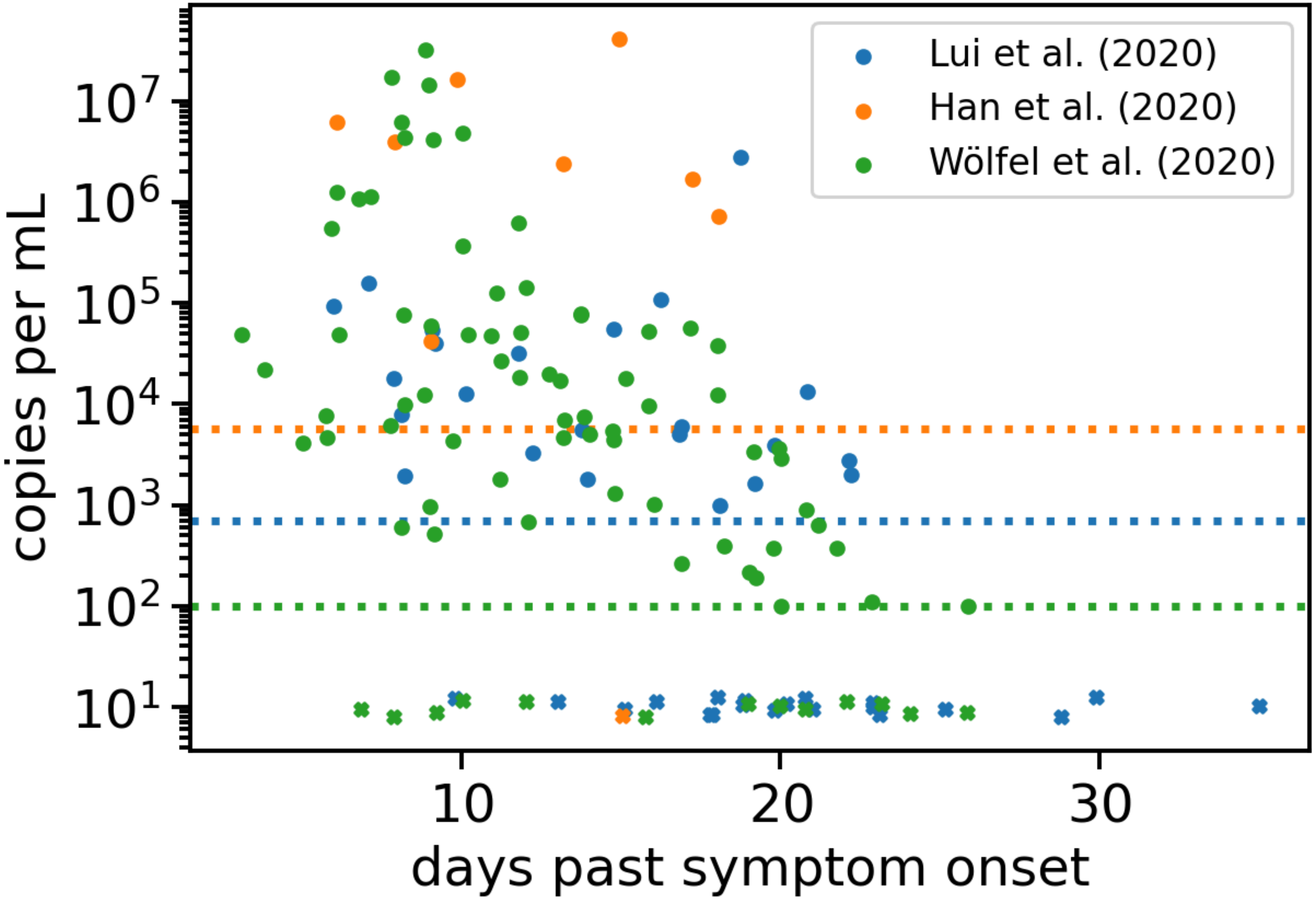
FECAL SHEDDING MODELS FOR SARS-COV-2 RNA

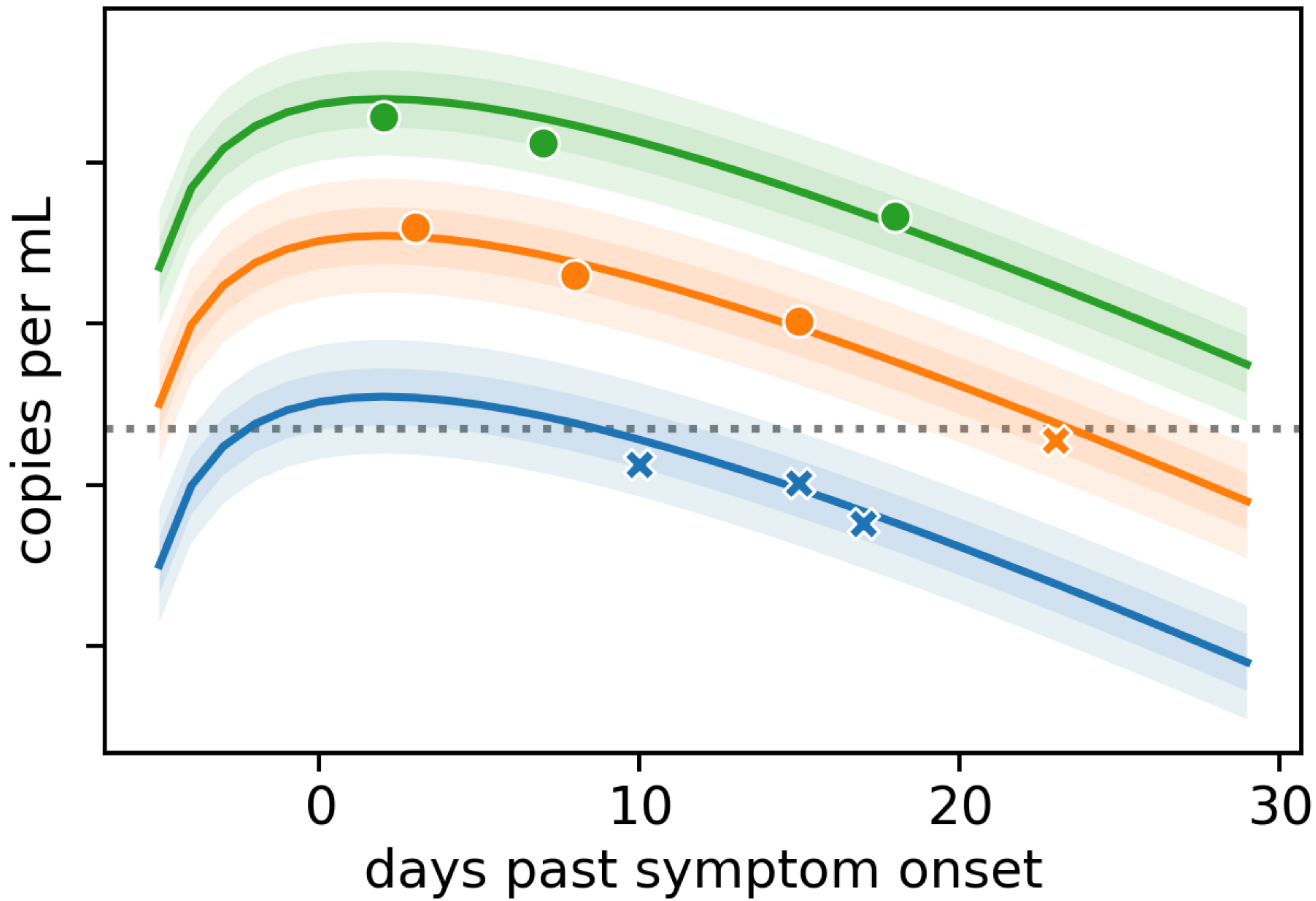
Till Hoffmann

Harvard T.H. Chan School of Public Health

QUESTIONS

- Does everyone shed SARS-CoV-2 RNA?
- How many gene copies do people shed?
- How is viral RNA shed over time?


copies per mL
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10
20
30
days past symptom onset
● Lui et al. (2020)
● Han et al. (2020)
● Wölfel et al. (2020)


copies per mL
0
10
20
30
days past symptom onset

SHEDDING MODEL

$$\mu_i \mid M, S, Q \sim \text{GeneralizedGamma}\left(M, S, Q\right)$$

SHEDDING MODEL

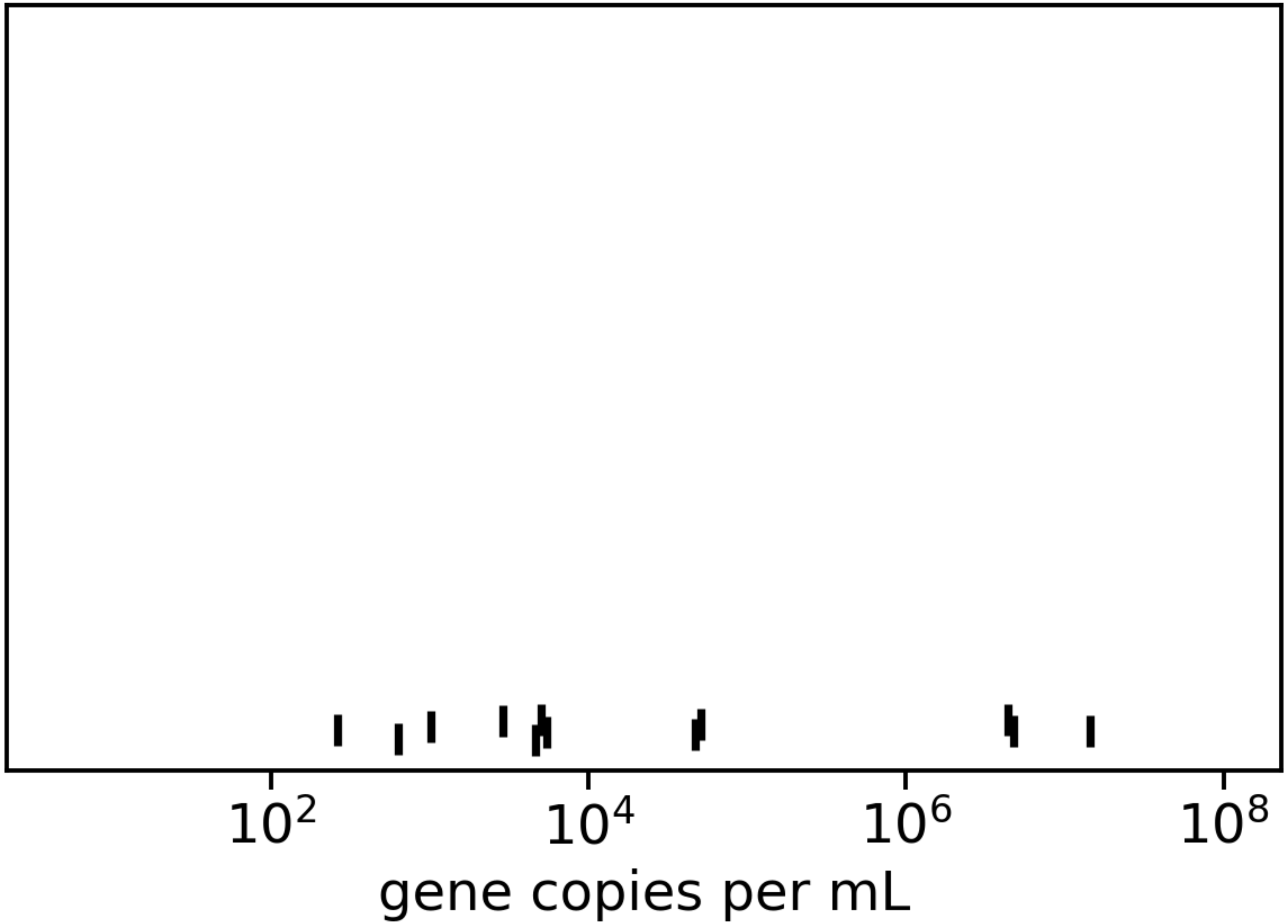
$$\mu_i \mid M, S, Q \sim \text{GeneralizedGamma}\left(M, S, Q\right)$$

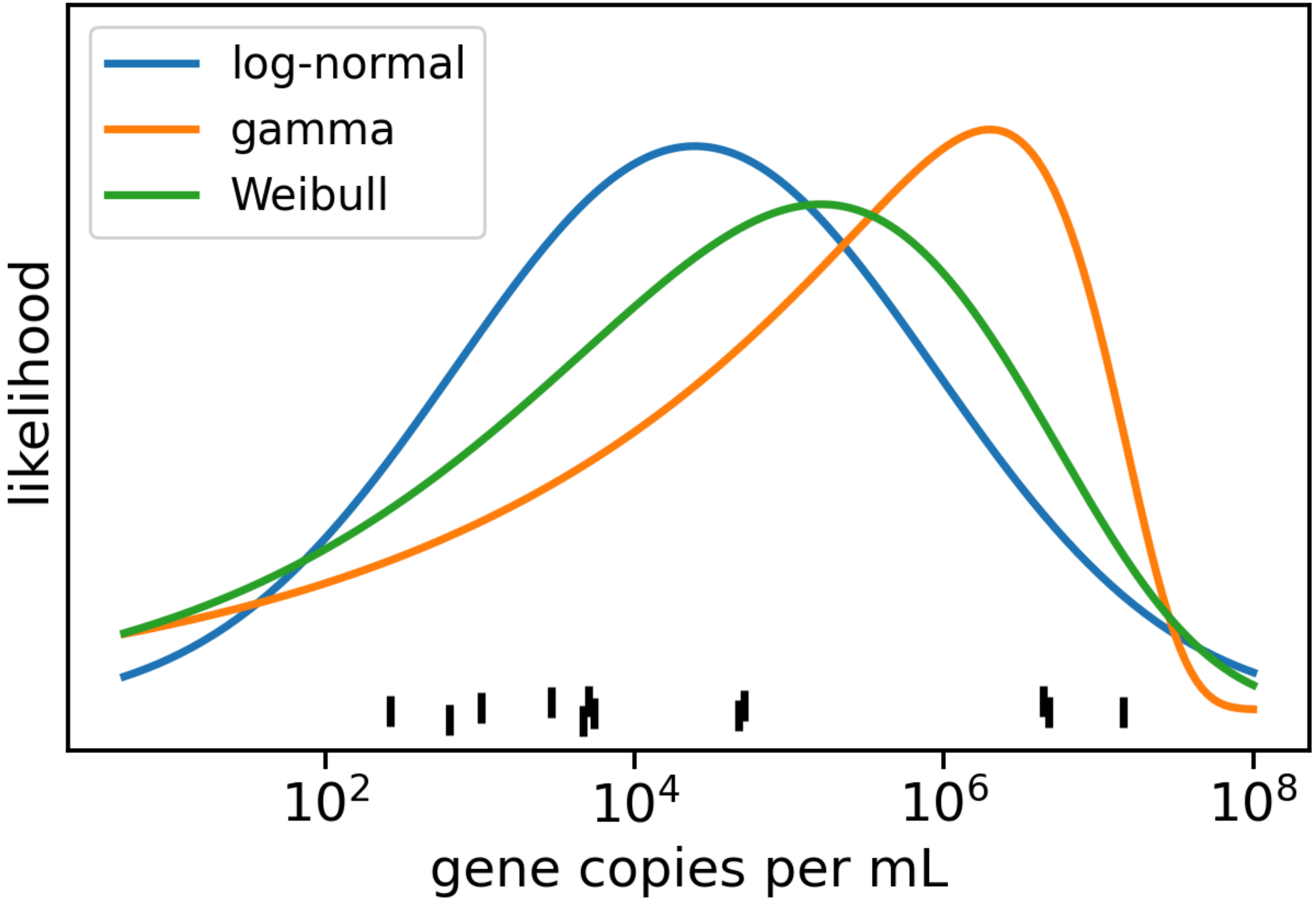
$$p\left(x_{ij} \mid \mu_i, \sigma, q\right) = \begin{cases} f\left(x_{ij} \mid \mu_i \times g\left(t_{ij}\right), \sigma, q\right) & \text{if } x_{ij} > \theta \\ & \end{cases}$$

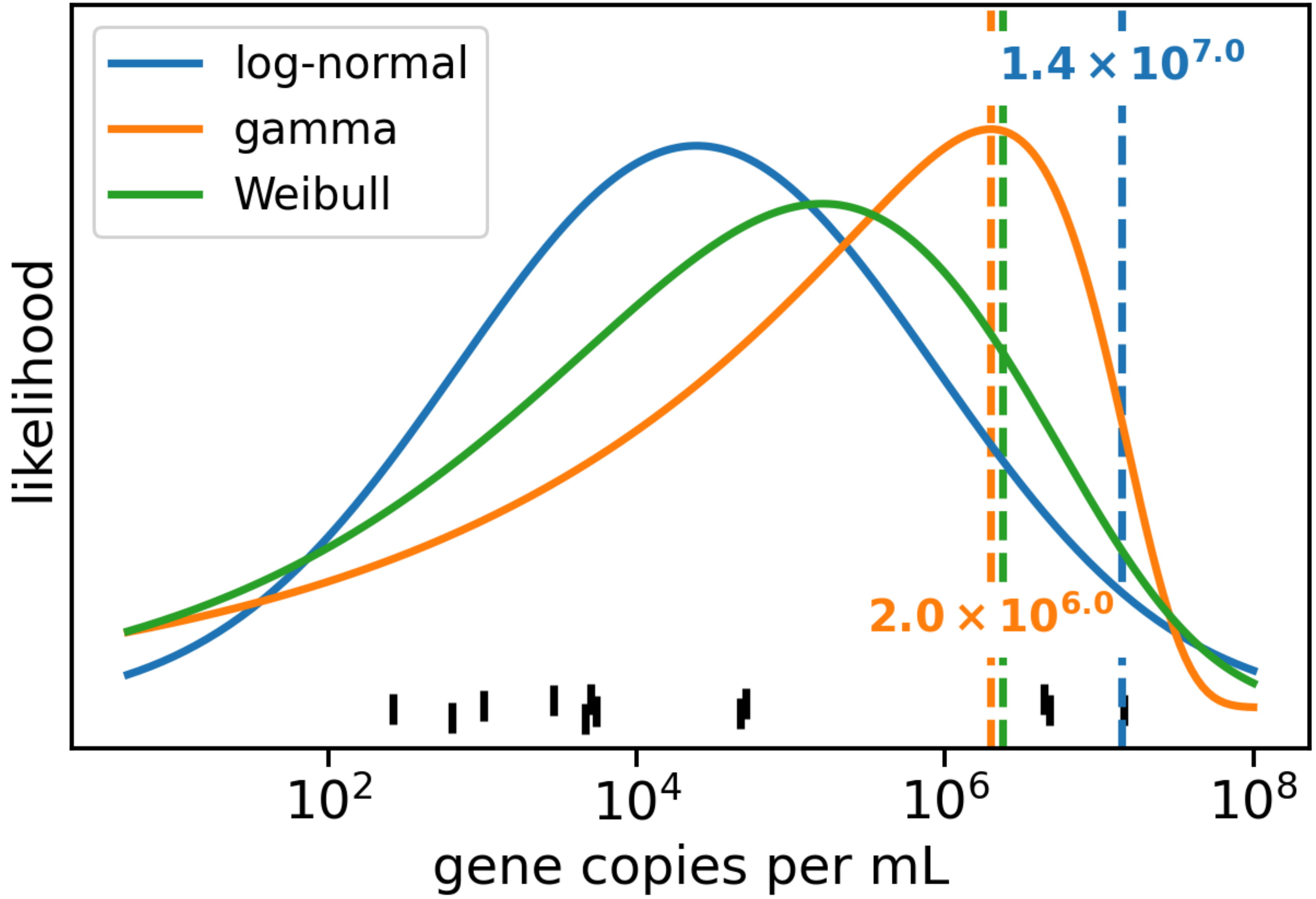
SHEDDING MODEL

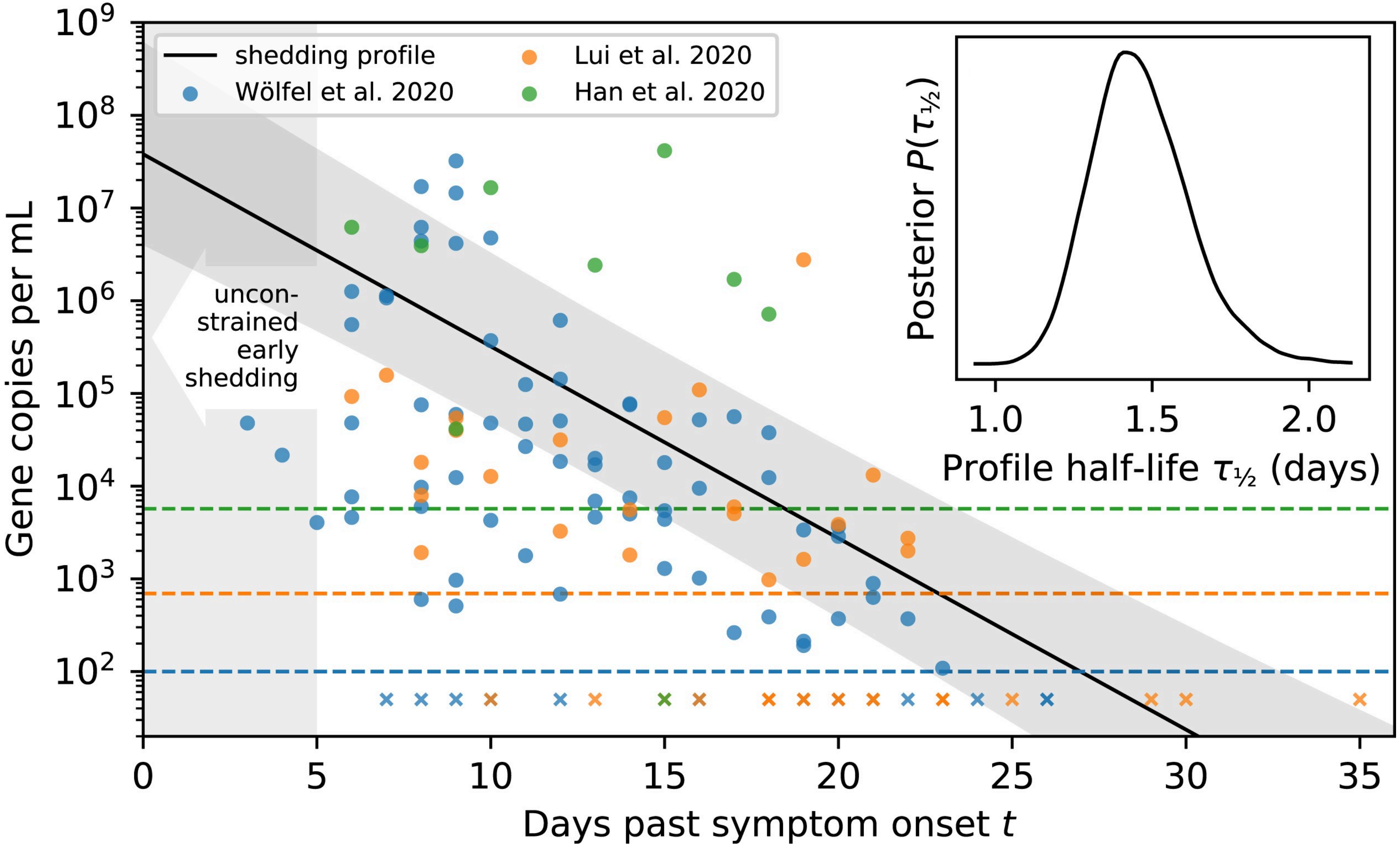
$$\mu_i \mid M, S, Q \sim \text{GeneralizedGamma}\left(M, S, Q\right)$$

$$p\left(x_{ij} \mid \mu_i, \sigma, q\right) = \begin{cases} f\left(x_{ij} \mid \mu_i \times g\left(t_{ij}\right), \sigma, q\right) & \text{if } x_{ij} > \theta \\ F\left(\theta \mid \mu_i \times g\left(t_{ij}\right), \sigma, q\right) & \text{otherwise} \end{cases}$$

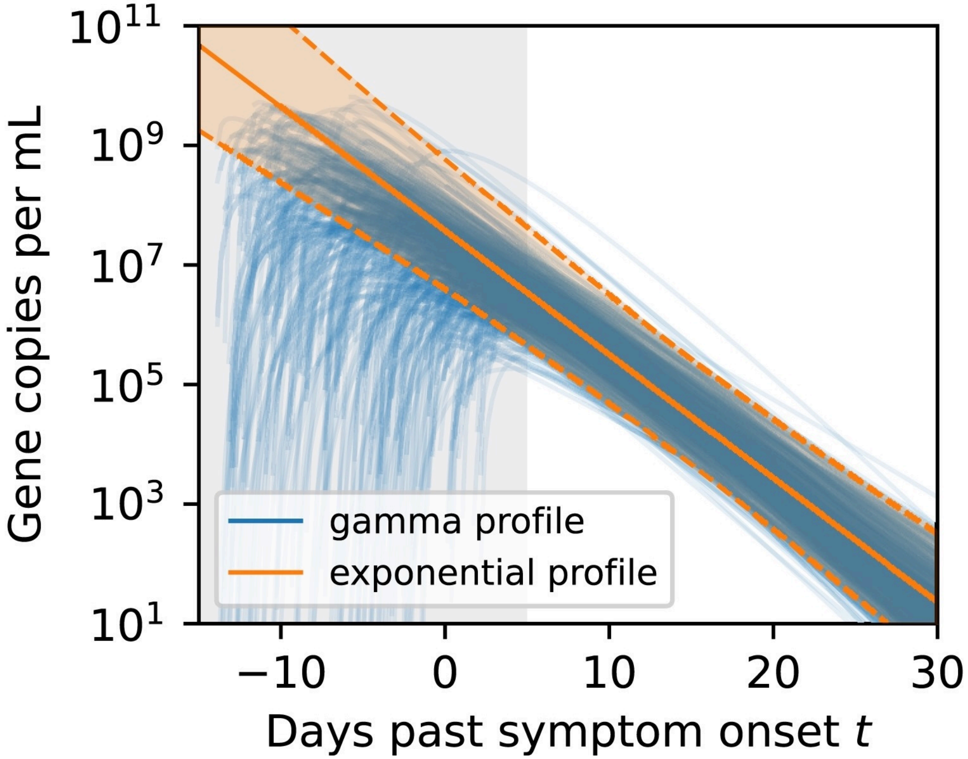

10^2
10^4
10^6
10^8
gene copies per mL

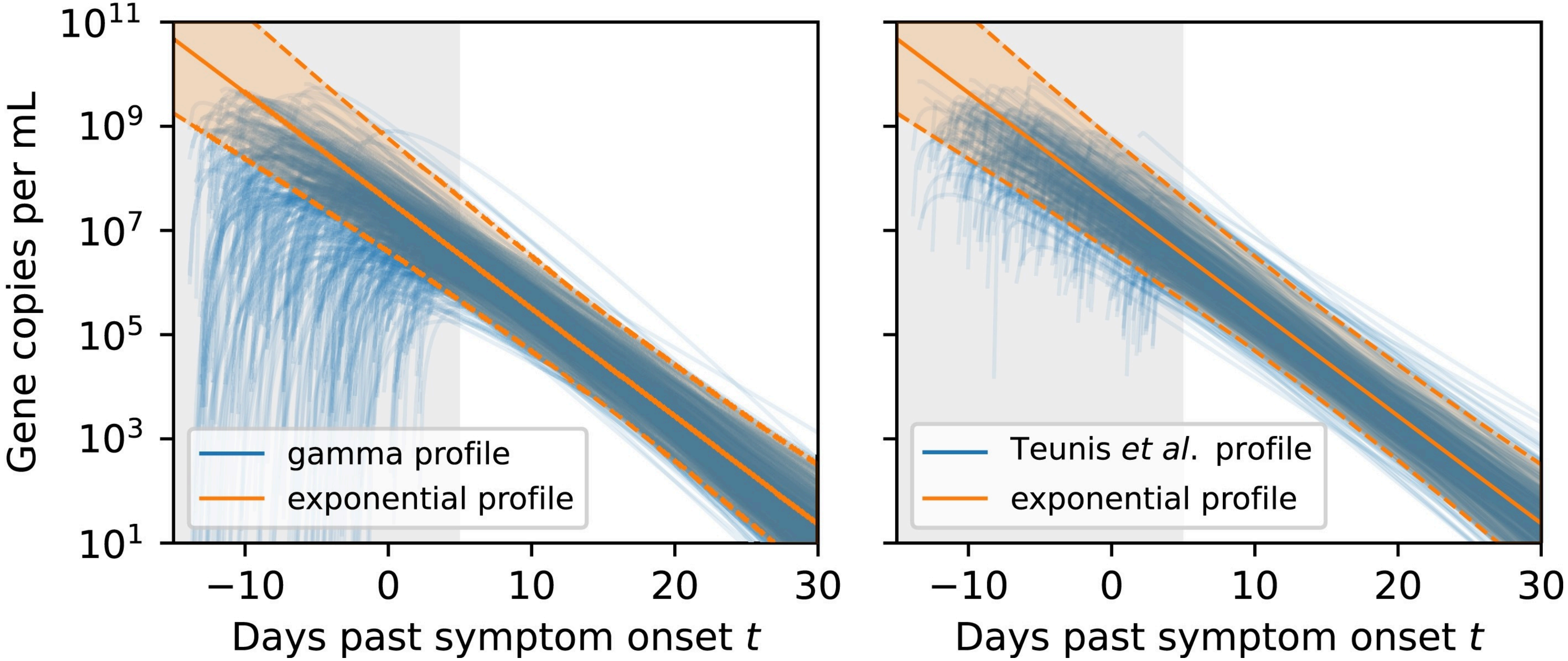

log-normal
gamma
Weibull
likelihood
10^2
10^4
10^6
10^8
gene copies per mL


log-normal
gamma
Weibull
$1.4 \times 10^{7.0}$
$2.0 \times 10^{6.0}$
likelihood
10^2
10^4
10^6
10^8
gene copies per mL



shedding profile
Wölfel et al. 2020
Lui et al. 2020
Han et al. 2020
Gene copies per mL
10^9
10^8
10^7
10^6
10^5
10^4
10^3
10^2
uncon-strained early shedding
Days past symptom onset t
0
5
10
15
20
25
30
35
Posterior $P(\tau_{1/2})$
1.0
1.5
2.0
Profile half-life $\tau_{1/2}$ (days)


Gene copies per mL
10^{11}
10^{9}
10^{7}
10^{5}
10^{3}
10^{1}
−10
0
10
20
30
Days past symptom onset t
gamma profile
exponential profile


Gene copies per mL
10^{11}
10^{9}
10^{7}
10^{5}
10^{3}
10^{1}
−10
0
10
20
30
Days past symptom onset t
gamma profile
exponential profile
Teunis *et al*. profile
exponential profile

SUB-POPULATION MODEL

For patients with all-negative samples,

$$p\left(x_{i\bullet} \mid \mu_i, \sigma, q, \rho\right) = (1-\rho) + \rho \prod_{j=1}^{m_i} F\left(\theta \mid \mu_i \times g\left(t_{ij}\right), \sigma, q\right).$$

CONCLUSIONS

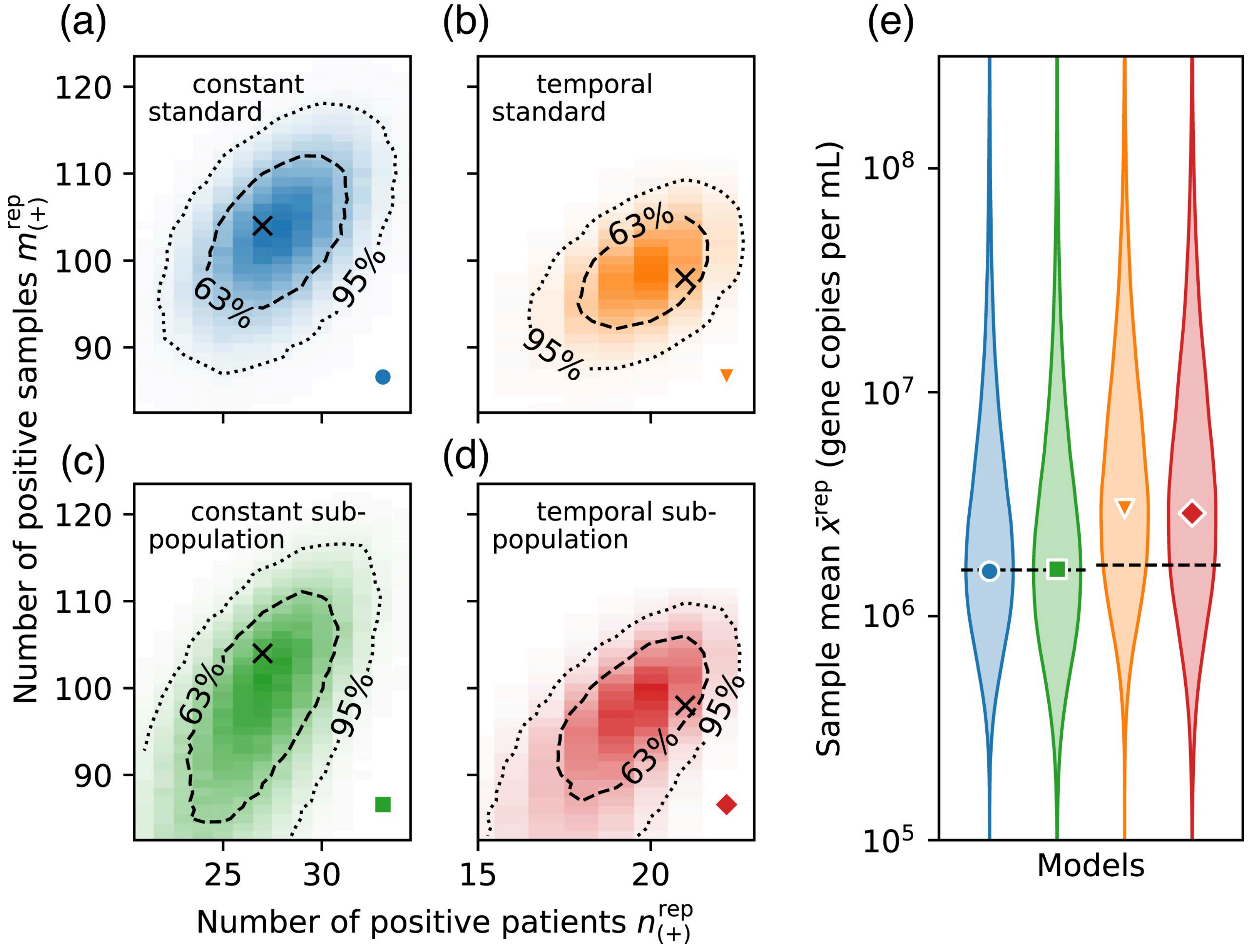
- Modeling essential to constrain viral RNA shedding.
- Early shedding can reconcile clinical and wastewater-based data.
- Data are consistent with everyone shedding, but to different degrees.

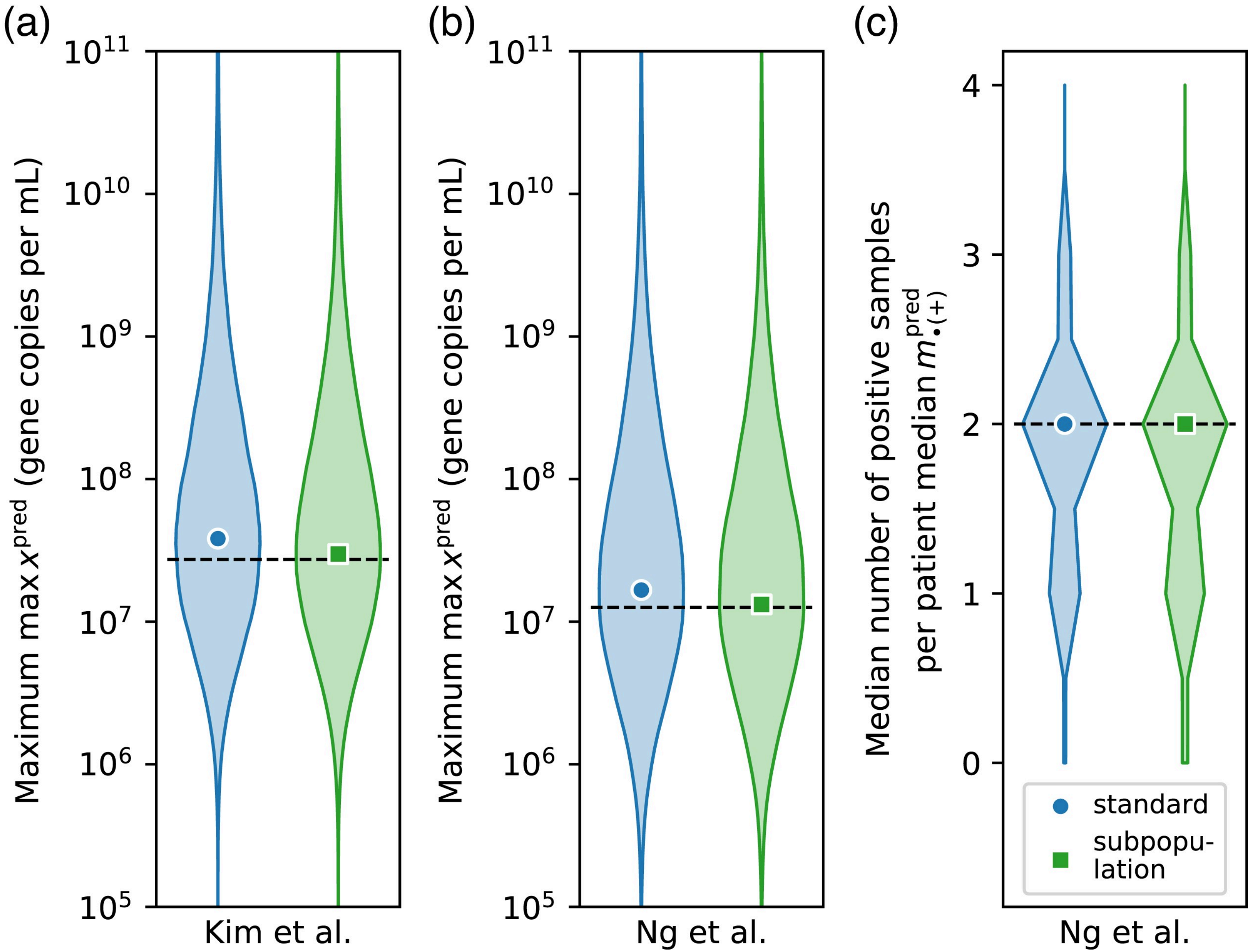
WHAT’S NEXT?

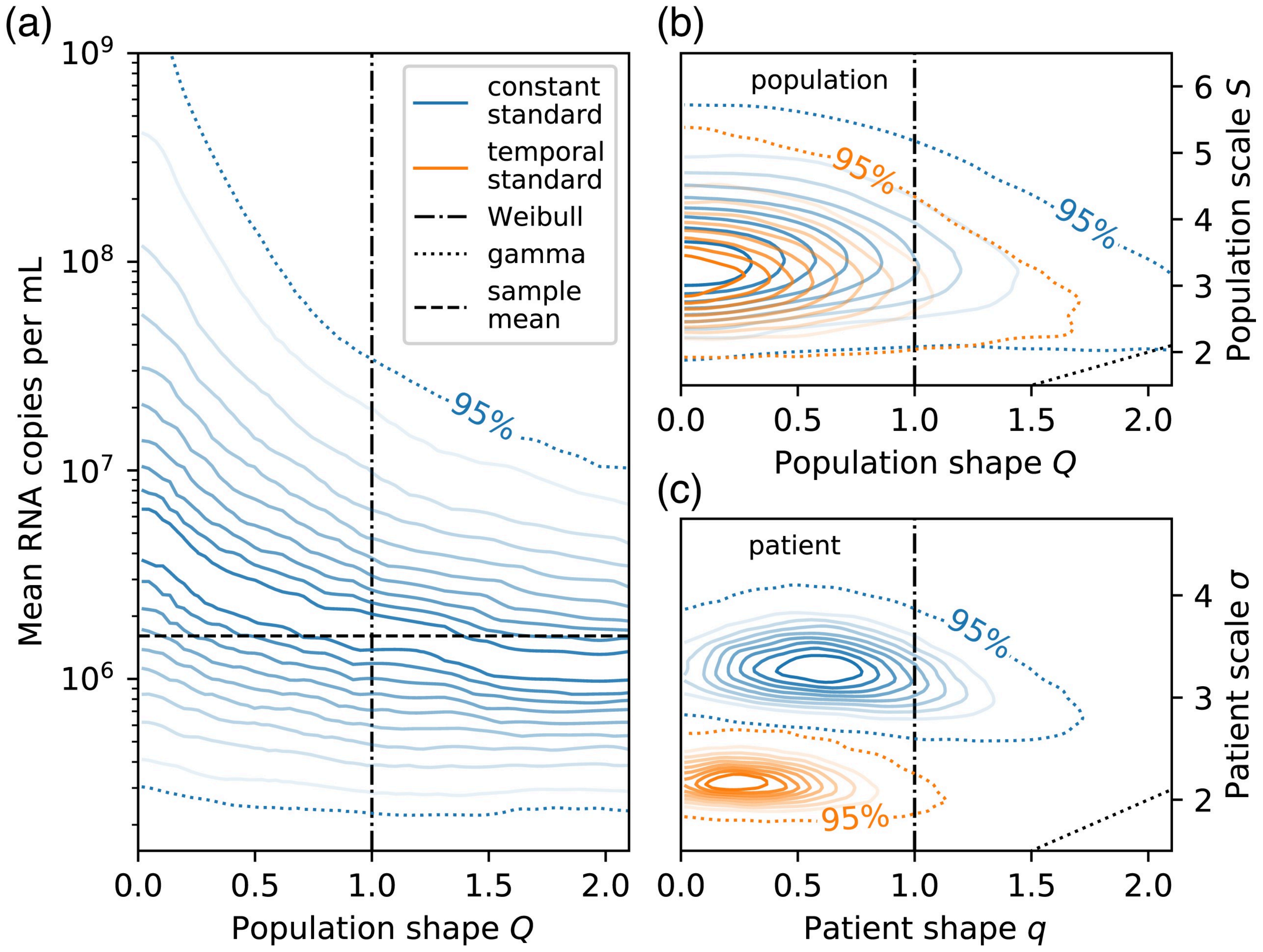
- Expand the Shedding Hub data.
- Non-parametric shedding profiles.
- Random effects for demographics, studies, gene targets, viral variants, ….

QUESTIONS

T Hoffmann and J Alsing (2023). “Faecal Shedding Models for SARS-CoV-2 RNA Among Hospitalised Patients and Implications for Wastewater-Based Epidemiology.” *Journal of the Royal Statistical Society C*, 330–345.


(a)
constant standard
(b)
temporal standard
(c)
constant sub-population
(d)
temporal sub-population
(e)
63%
95%
120
110
100
90
25
30
15
20
Number of positive samples $m_{(+)}^{\mathrm{rep}}$
Number of positive patients $n_{(+)}^{\mathrm{rep}}$
Sample mean $\bar{x}^{\mathrm{rep}}$ (gene copies per mL)
10^8
10^7
10^6
10^5
Models

(a)
(b)
(c)
Maximum max x^{pred} (gene copies per mL)
10^{11}
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
Kim et al.
Ng et al.
Median number of positive samples per patient median $m_{\bullet(+)}^{\mathrm{pred}}$
4
3
2
1
0
● standard
■ subpopulation
Ng et al.


(a)
10^9
10^8
10^7
10^6
Mean RNA copies per mL
95%
0.0
0.5
1.0
1.5
2.0
Population shape Q
constant standard
temporal standard
Weibull
gamma
sample mean
(b)
population
95%
95%
6
5
4
3
2
Population scale S
0.0
0.5
1.0
1.5
2.0
Population shape Q
(c)
patient
95%
95%
4
3
2
Patient scale σ
0.0
0.5
1.0
1.5
2.0
Patient shape q

SHEDDING PROFILES

- Exponential: $\exp\left(-\lambda\left(t-t_0\right)\right)$
- Gamma: $\left(t-t_0\right)^{a-1}\exp\left(-b\left(t-t_0\right)\right)$
- Teunis et al.: $\left[1-\exp\left(-a\left(t-t_0\right)\right)\right]\exp\left(-b\left(t-t_0\right)\right)$