obtain $\Omega = 3.3\%$, which is exactly the same as the result obtained by the simple mathematical calculation $4/121 \times 100$, and the mathematical model would become redundant. We would accept 3.3% as the proportion discordant, although the binomial 95% confidence interval is 1.3%–8.2%. Nonetheless, had the authors chosen to test >3 colonies per sample, they might have observed a larger number of discordant samples.

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References

Reply to Coen et al.

To the Editor—We provide additional information to address the concerns raised by Coen et al. [1] about our article [2]. Our enumerated answers to the questions concerning study methodology are followed by our response to the questions regarding the mathematical model.

1. We selected 3 colonies per sample as our initial sample number, to insure that the analysis would be technically manageable and would also provide sufficient data for generating a mathematical model to estimate the clonality of carriage. We agree that selecting additional colonies for analysis might have increased the number of discordant samples; however, the overall goal of the study was to demonstrate that discordant carriage occurs and that a mathematical model could be used to estimate the frequency of discordance for a population.

2. The one sample for which a denominator of 4 is listed (sample 1503) reflects the identification of an additional pulsed-field gel electrophoresis profile after the original 3 colonies were selected. This resulted in 4 strains being identified and processed, rather than the original 3.

3. We do not have sufficient data to address the question regarding the effect of antibiotics on cocolonization rates.

4. In terms of model development, we utilized data from a well-defined population to make the model more generalizable. As discussed in our article, only baseline samples from the methadone maintenance program cohort were included in the mathematical model. Samples 1117 and 1490 were not from baseline. The isolate (0785H) from the hospital population was part of a different population and was, therefore, also excluded from the model. Moreover, we clearly acknowledged the potential limitations in the generalizability of the model in the original article.

With regard to the mathematical model, Coen et al. make a number of assumptions that are not correct. We used the equation

$$P(SC) = P(SC|OC)(1 - \Omega) + P(SC|OD)(\Omega)$$

In this equation, $\Omega$ denotes the parameter used in our article—that is, $\Omega = P(OD)$. Since $P(SC|OC)$ must equal 1, the above equation reduces to

$$P(SC) = (1 - \Omega) + P(SC|OD)(\Omega)$$

It should be noted that the event “SC” stands for a sample that was originally discordant, meaning that the event is defined on the basis of the original sampling. When conducting second-stage sampling (or resampling) of already-observed events, the relevant probabilities may change. In our analysis, of the initial 4 discordant samples (on the basis of the original sample, these 4 samples must be truly discordant), 2 were concordant. This ratio (2/4) thus can be used to approximate the conditional probability, $P(SC|OC)$. Coen et al. incorrectly added 2 entirely different probabilities (on 2 entirely different events) together—that is, $(117/121 + 2/121)$, in which the first term $(117/121)$ is $P(SC)$ and the second term $(2/121)$ is a conditional probability of an event involving both original and second-stage sampling (i.e., resampling). This approach is invalid. The assumptions underlying our approach are valid, and we therefore believe that the model is correct as described.

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Reference

Clearance Duration as a Predictor of Sustained Viral Response in Patients with Chronic Hepatitis C Virus Genotype 1

To the Editor—We read with great interest the model described by Drusano and Preston [1] regarding the prediction of a sustained viral response (SVR) in patients infected with chronic hepatitis C virus (HCV) genotype 1 who were treated with