CoP SAP 6.4

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6.4 Prediction of Post-Challenge Viral Load with Single Virus-Specific Antibody

The first step is to predict a post-challenge viral load (chosen from Section 3.3) using a virus-specific antibody (from Section 3.2). Different models are used depending on whether the post-challenge viral load is binary or numeric.

6.4.1 Numeric Viral Load

For numeric viral load, several models will be fit using the log of the response value. Let y_{jk} and x_{jk} be the outcome (e.g., log of the viral load) and the virus-specific antibody, respectively, for the k^{th} animal in the j^{th} arm. Let μ_{jk} be the mean response associated with y_{jk}. For this model, the vaccine arm is not modeled, so that two animals from different vaccine arms with the same value of virus-specific antibody will have the same predicted response. Several different models will be fit to the data, and best model will be selected by repeated cross validation with 500 replicates, where a certain proportion of the animals (e.g., 10%) are randomly left out of the model building and those left-out animals will be used to compare the fits of different models by adjusted R-squared. The animals selected for the test set will be stratified by challenge day; 1-2 animals will be selected per challenge day with the added constraint that both animals selected from a given day will not both be placebo.

The simplest model tried will be the linear model: $\mu_{jk} = \beta_0 + \beta_1 x_{jk}$. Another model is an exponential model (see e.g., McMahan, et al, 2020, Fig. 2). A third set of models are segmented regression models, with 2 breakpoints, using the segmented R package (Muggeo, 2020). A fourth set of models are fit with natural cubic splines with 5 degrees of freedom, using the default knots in the ns function in the spline R package. Finally, a four parameter logistic (4-PL) model may also be evaluated using the drm function in the drc R package (Ritz et al., 2015): $\mu_{jk} = B + ((A - B)/(1 + (x_{jk}/C)^D))$, where the 4-PL parameters are: A = lower asymptote, B = upper asymptote, C = midpoint, D = slope parameter. That model will be fit by least squares and the BFGS optimization method.

$f(x) = c + \frac{d-c}{1+\exp(b(\log(x)-\log(e)))}$

If the cross-validation produces a model with substantial non-monotonicity, we may remove that model type from consideration and repeat the CV without that model. This process may be repeated if necessary.

Once the model is selected by cross validation, the selected model will be fit to all of the data. If the selected model is not segmented regression, pointwise confidence intervals on the predicted values will be calculated using the parametric formula: $\hat{y}_{jk} \pm t_{\alpha/2,df} SE$, where $\hat{y}_{jk}$ = the estimated predicted value for the $k^t h$ animal in the $j^t h$ arm, SE = the standard error for the estimate of the predicted value, and $t_{\alpha/2,df}$ = critical value from the t distribution corresponding to $\alpha/2$ and n-p degrees of freedom (p includes the intercept, where applicable). This is analogous to the built-in predict functions in R. If the segmented regression model is selected by the cross-validation procedure, pointwise confidence intervals on the predicted values will be calculated by nonparametric bootstrap.

Table 6.4.1: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Numeric

Virus-Specific Antibody	Viral Load	Model Selected	Adjusted Rsq	Figure Number
log MN day challenge	AUC BAL N1	exp	0.522	6.4.2
log PsVNA ID80 day challenge	AUC Nasal Swab Subgenomic	lm	0.504	6.4.32
log PsVNA ID80 day challenge	AUC Nasal Swab N1	lm	0.500	6.4.24
log MN 2 weeks prior challenge	AUC Nasal Swab Subgenomic	lm	0.494	6.4.25
log MN 2 weeks prior challenge	AUC Nasal Swab N1	lm	0.474	6.4.17
log MSD ECL day challenge	AUC Nasal Swab N1	lm	0.472	6.4.20
log PsVNA ID80 2 weeks prior challenge	AUC Nasal Swab Subgenomic	lm	0.472	6.4.31
log MN day challenge	AUC Nasal Swab Subgenomic	lm	0.468	6.4.26
log PsVNA ID80 day challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.458	6.4.88
log MSD ECL 2 weeks prior challenge	AUC Nasal Swab N1	lm	0.456	6.4.19
log MSD ECL day challenge	AUC BAL N1	lm	0.448	6.4.4
log PsVNA ID80 2 weeks prior challenge	AUC Nasal Swab N1	lm	0.446	6.4.23
log PsVNA ID80 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.446	6.4.87
log MN day challenge	AUC Nasal Swab N1	lm	0.445	6.4.18
log PsVNA ID50 2 weeks prior challenge	AUC Nasal Swab Subgenomic	lm	0.443	6.4.29
log MSD ECL day challenge	AUC Nasal Swab Subgenomic	lm	0.441	6.4.28
log PsVNA ID50 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.440	6.4.85
log PsVNA ID80 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	lm	0.439	6.4.95

Table 6.4.1: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Numeric *(continued)*

Virus-Specific Antibody	Viral Load	Model Selected	Adjusted Rsq	Figure Number
log MN 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	lm	0.438	6.4.89
log MSD ECL 2 weeks prior challenge	AUC Nasal Swab Subgenomic	lm	0.434	6.4.27
log PsVNA ID80 day challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	lm	0.434	6.4.96
log MN 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.431	6.4.81
log MN day challenge	AUC BAL Subgenomic	exp	0.426	6.4.10
log PsVNA ID50 day challenge	AUC Nasal Swab N1	lm	0.424	6.4.22
log PsVNA ID50 2 weeks prior challenge	AUC Nasal Swab N1	lm	0.423	6.4.21
log PsVNA ID50 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	lm	0.423	6.4.93
log MSD ECL 2 weeks prior challenge	AUC BAL N1	lm	0.407	6.4.3
log PsVNA ID50 day challenge	AUC Nasal Swab Subgenomic	lm	0.404	6.4.30
log MSD ECL day challenge	AUC BAL Subgenomic	lm	0.392	6.4.12
log MN 2 weeks prior challenge	AUC BAL N1	exp	0.389	6.4.1
log PsVNA ID50 day challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.385	6.4.86
log MSD ECL 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.381	6.4.83
log PsVNA ID50 day challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	exp	0.367	6.4.94
log MN day challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.366	6.4.82

Table 6.4.1: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Numeric *(continued)*

Virus-Specific Antibody	Viral Load	Model Selected	Adjusted Rsq	Figure Number
log MN day challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	lm	0.365	6.4.90
log PsVNA ID80 day challenge	AUC BAL N1	exp	0.363	6.4.8
log MSD ECL 2 weeks prior challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	lm	0.360	6.4.91
log MSD ECL day challenge	AUC OP Swab N1	lm	0.357	6.4.36
log PsVNA ID80 day challenge	AUC OP Swab N1	lm	0.355	6.4.40
log MSD ECL 2 weeks prior challenge	AUC OP Swab N1	lm	0.343	6.4.35
log MSD ECL day challenge	log VL Day2 PostChallenge NasalSwab N1	lm	0.343	6.4.84
log MSD ECL 2 weeks prior challenge	AUC BAL Subgenomic	lm	0.341	6.4.11
log PsVNA ID80 2 weeks prior challenge	AUC BAL N1	lm	0.335	6.4.7
log MN day challenge	log VL Day2 PostChallenge BAL N1	lm	0.334	6.4.50
log MN day challenge	AUC OP Swab N1	lm	0.330	6.4.34
log MSD ECL day challenge	log VL Day2 PostChallenge NasalSwab Subgenomic	lm	0.330	6.4.92
log PsVNA ID80 2 weeks prior challenge	AUC OP Swab N1	lm	0.326	6.4.39
log MN 2 weeks prior challenge	AUC OP Swab N1	lm	0.324	6.4.33
log MN day challenge	log VL Day2 PostChallenge BAL Subgenomic	lm	0.322	6.4.58
log PsVNA ID50 2 weeks prior challenge	AUC OP Swab N1	lm	0.316	6.4.37

Table 6.4.1: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Numeric *(continued)*

Virus-Specific Antibody	Viral Load	Model Selected	Adjusted Rsq	Figure Number
log MN 2 weeks prior challenge	AUC BAL Subgenomic	exp	0.310	6.4.9
log PsVNA ID50 2 weeks prior challenge	AUC BAL N1	lm	0.303	6.4.5
log PsVNA ID50 day challenge	AUC BAL N1	exp	0.284	6.4.6
log PsVNA ID80 2 weeks prior challenge	log VL Day2 PostChallenge BAL Subgenomic	lm	0.262	6.4.63
log PsVNA ID80 day challenge	AUC BAL Subgenomic	exp	0.261	6.4.16
log PsVNA ID80 day challenge	log VL Day2 PostChallenge BAL N1	lm	0.260	6.4.56
log PsVNA ID80 day challenge	log VL Day2 PostChallenge BAL Subgenomic	exp	0.260	6.4.64
log PsVNA ID50 2 weeks prior challenge	log VL Day2 PostChallenge BAL N1	lm	0.259	6.4.53
log MSD ECL day challenge	log VL Day2 PostChallenge BAL Subgenomic	lm	0.259	6.4.60
log PsVNA ID50 2 weeks prior challenge	log VL Day2 PostChallenge BAL Subgenomic	lm	0.259	6.4.61
log MN 2 weeks prior challenge	log VL Day2 PostChallenge BAL Subgenomic	lm	0.257	6.4.57
log PsVNA ID80 2 weeks prior challenge	log VL Day2 PostChallenge BAL N1	lm	0.253	6.4.55
log PsVNA ID50 day challenge	AUC OP Swab N1	lm	0.249	6.4.38
log PsVNA ID80 2 weeks prior challenge	AUC BAL Subgenomic	exp	0.247	6.4.15
log MSD ECL day challenge	AUC OP Swab Subgenomic	lm	0.247	6.4.44
log MSD ECL day challenge	log VL Day2 PostChallenge BAL N1	lm	0.244	6.4.52
log MN 2 weeks prior challenge	log VL Day2 PostChallenge BAL N1	lm	0.241	6.4.49

Table 6.4.1: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Numeric *(continued)*

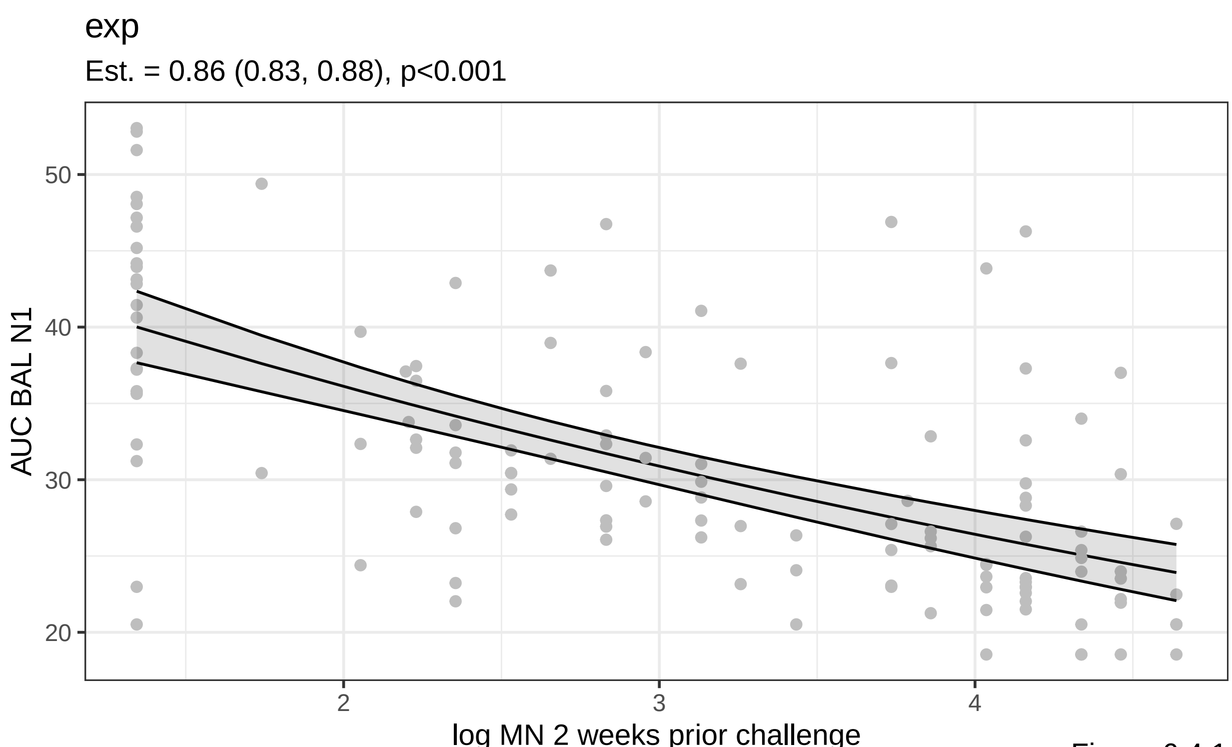
Virus-Specific Antibody	Viral Load	Model Selected	Adjusted Rsq	Figure Number
log MSD ECL 2 weeks prior challenge	log VL Day2 PostChallenge BAL Subgenomic	lm	0.237	6.4.59
log PsVNA ID80 day challenge	AUC OP Swab Subgenomic	lm	0.235	6.4.48
log MSD ECL 2 weeks prior challenge	AUC OP Swab Subgenomic	lm	0.231	6.4.43
log MN 2 weeks prior challenge	AUC OP Swab Subgenomic	lm	0.230	6.4.41
log MSD ECL 2 weeks prior challenge	log VL Day2 PostChallenge BAL N1	lm	0.228	6.4.51
log PsVNA ID80 2 weeks prior challenge	AUC OP Swab Subgenomic	lm	0.226	6.4.47
log PsVNA ID50 2 weeks prior challenge	AUC OP Swab Subgenomic	lm	0.222	6.4.45
log MN day challenge	AUC OP Swab Subgenomic	lm	0.211	6.4.42
log PsVNA ID50 day challenge	log VL Day2 PostChallenge BAL Subgenomic	exp	0.208	6.4.62
log PsVNA ID50 2 weeks prior challenge	AUC BAL Subgenomic	exp	0.205	6.4.13
log PsVNA ID50 day challenge	log VL Day2 PostChallenge BAL N1	exp	0.199	6.4.54
log PsVNA ID80 day challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.196	6.4.80
log PsVNA ID80 2 weeks prior challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.194	6.4.79
log MN 2 weeks prior challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.186	6.4.73
log PsVNA ID50 2 weeks prior challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.182	6.4.77

Table 6.4.1: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Numeric *(continued)*

Virus-Specific Antibody	Viral Load	Model Selected	Adjusted Rsq	Figure Number
log PsVNA ID50 day challenge	AUC BAL Subgenomic	exp	0.180	6.4.14
log PsVNA ID50 day challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.167	6.4.78
log PsVNA ID80 day challenge	log VL Day2 PostChallenge OPswab N1	lm	0.158	6.4.72
log MN 2 weeks prior challenge	log VL Day2 PostChallenge OPswab N1	lm	0.157	6.4.65
log PsVNA ID80 2 weeks prior challenge	log VL Day2 PostChallenge OPswab N1	lm	0.155	6.4.71
log PsVNA ID50 2 weeks prior challenge	log VL Day2 PostChallenge OPswab N1	lm	0.143	6.4.69
log PsVNA ID50 day challenge	AUC OP Swab Subgenomic	lm	0.138	6.4.46
log MSD ECL 2 weeks prior challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.129	6.4.75
log MSD ECL day challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.128	6.4.76
log PsVNA ID50 day challenge	log VL Day2 PostChallenge OPswab N1	lm	0.124	6.4.70
log MN day challenge	log VL Day2 PostChallenge OPswab Subgenomic	lm	0.120	6.4.74
log MSD ECL day challenge	log VL Day2 PostChallenge OPswab N1	lm	0.112	6.4.68
log MSD ECL 2 weeks prior challenge	log VL Day2 PostChallenge OPswab N1	lm	0.110	6.4.67
log MN day challenge	log VL Day2 PostChallenge OPswab N1	lm	0.101	6.4.66

There are 82 pairs of virus-specific antibodies/viral loads (out of 96 total pairs) where the best model fit is linear; 14 where the best model fit is exponential; 0 where the best model fit is segmented linear (with 2 breakpoints); 0 where the best model fit is natural cubic splines with 5 degrees of freedom; and 0 where the best model fit is 4-parameter logistic.

Predicted Values



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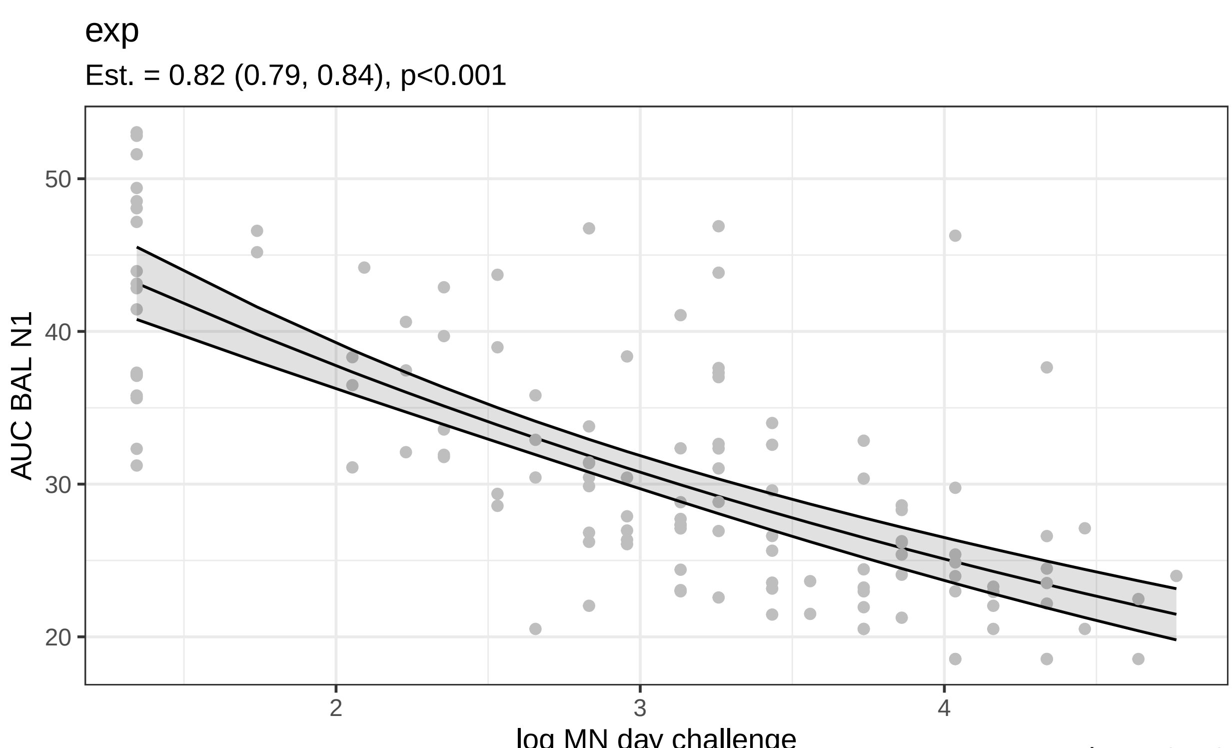

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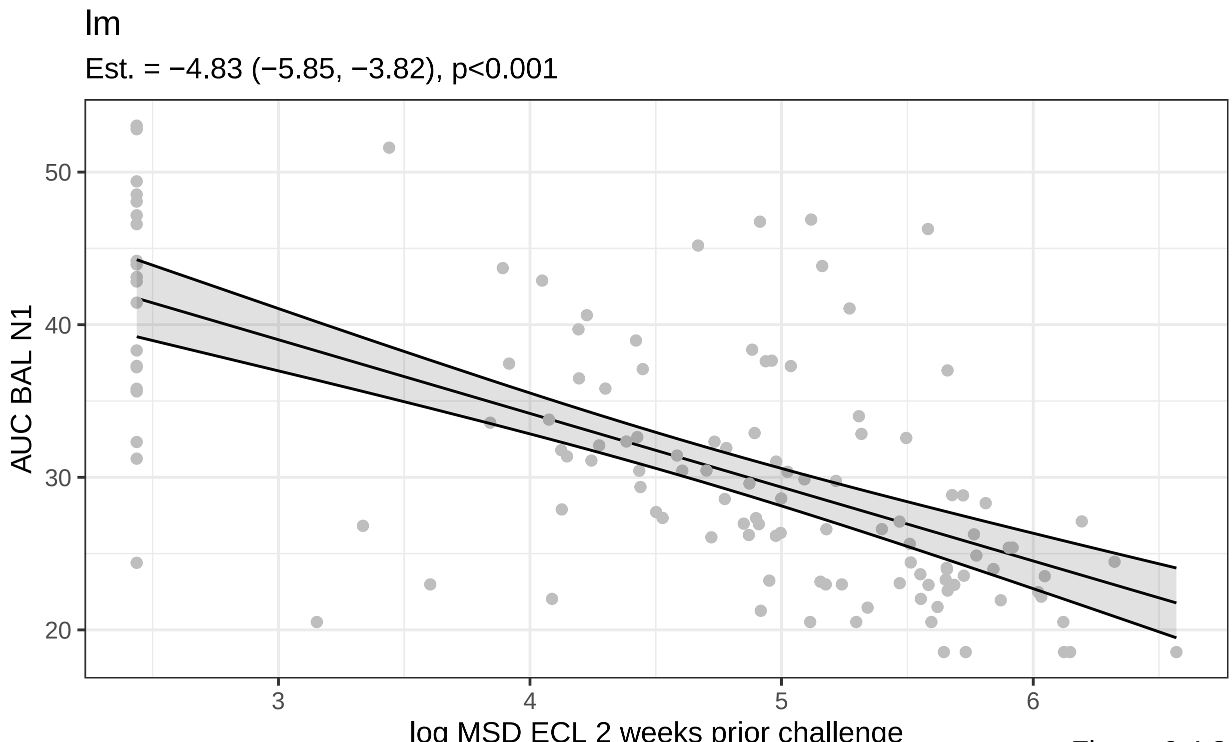

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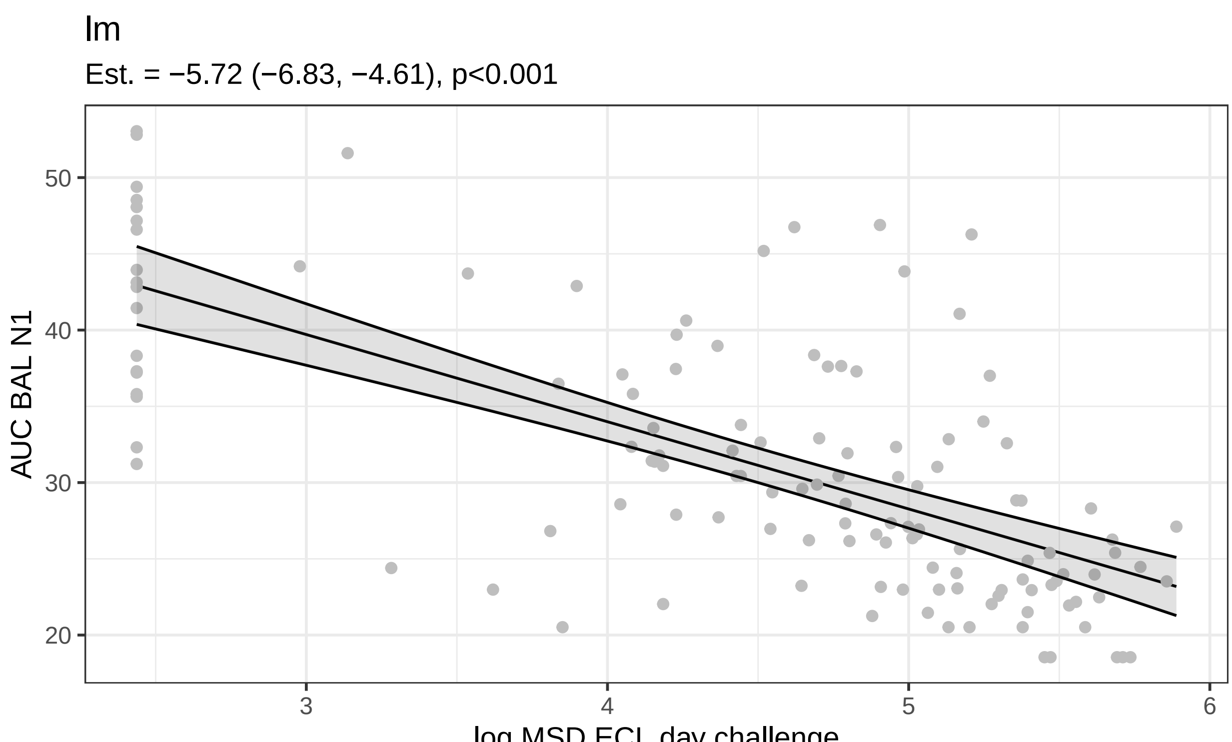

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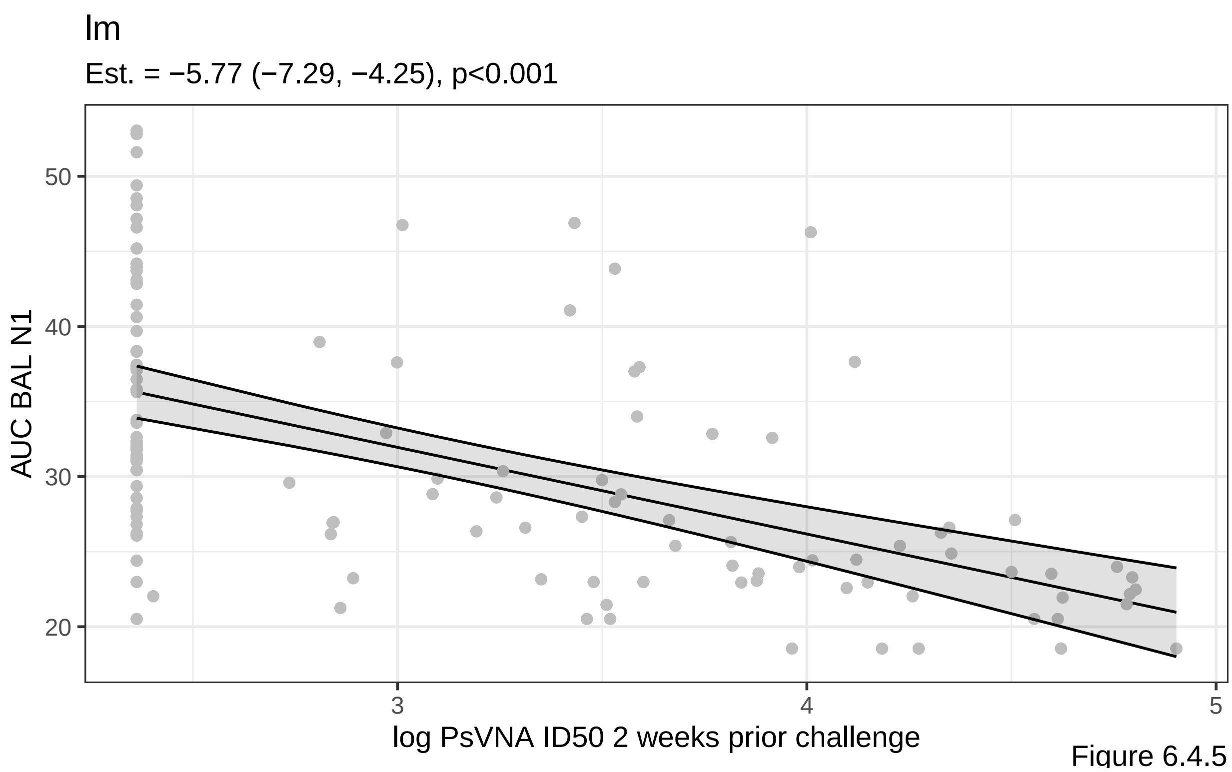

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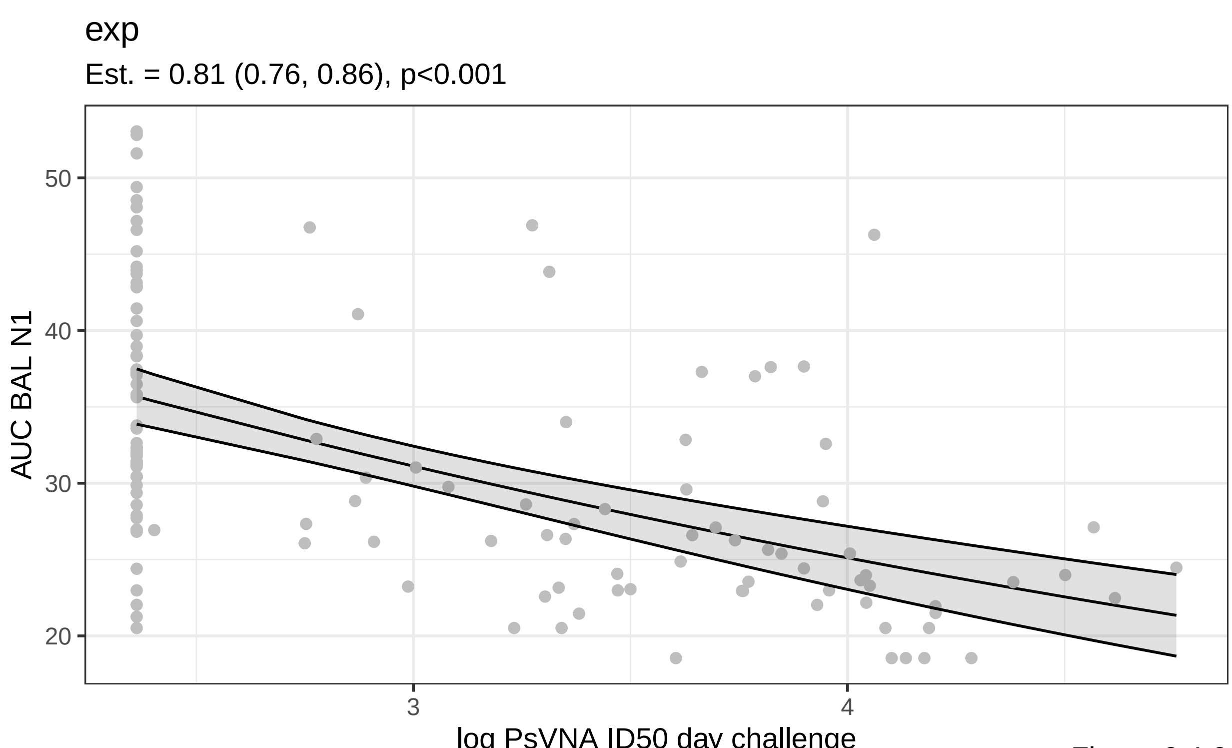


Figure 6.4.6

lm

Est. = −5.08 (−6.33, −3.84), p<0.001

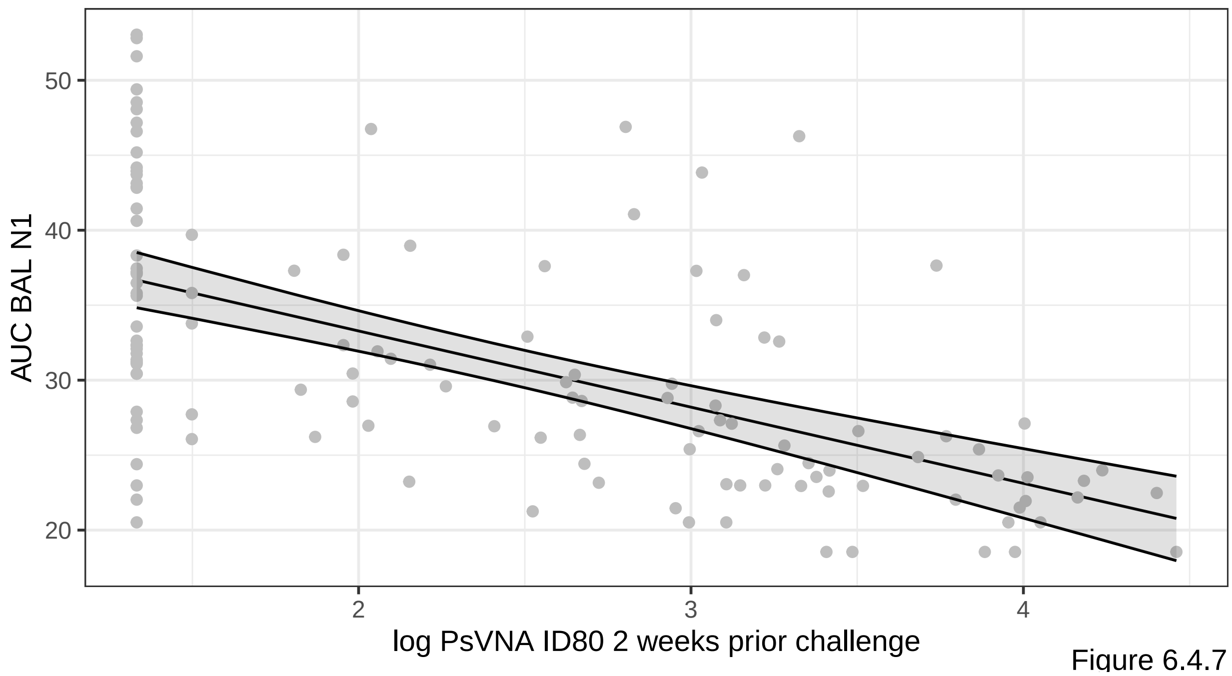
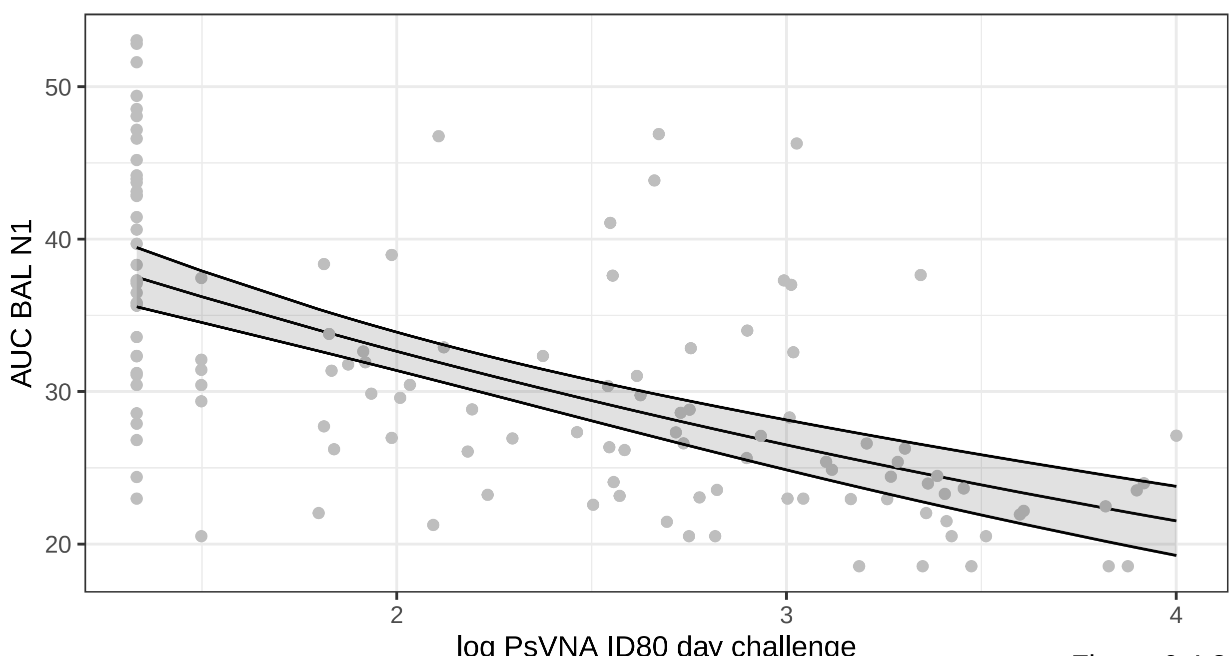


Figure 6.4.7

exp

Est. = 0.81 (0.77, 0.85), p<0.001



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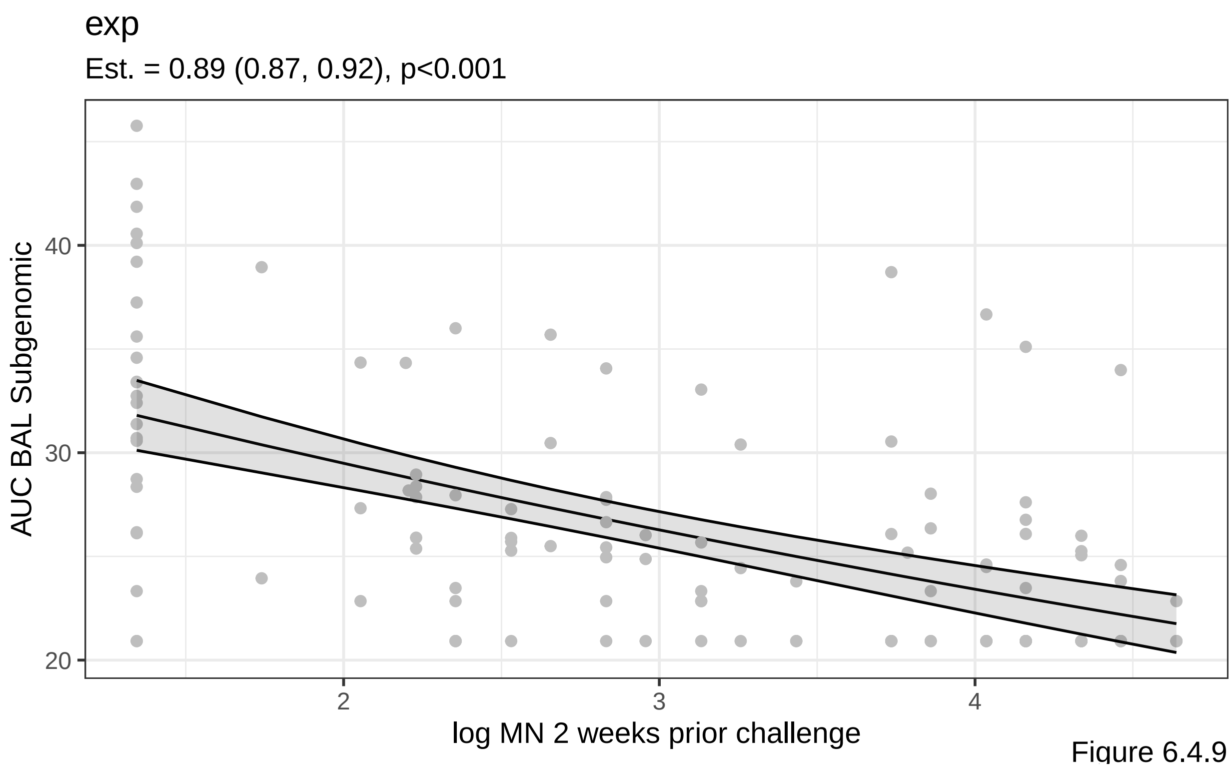

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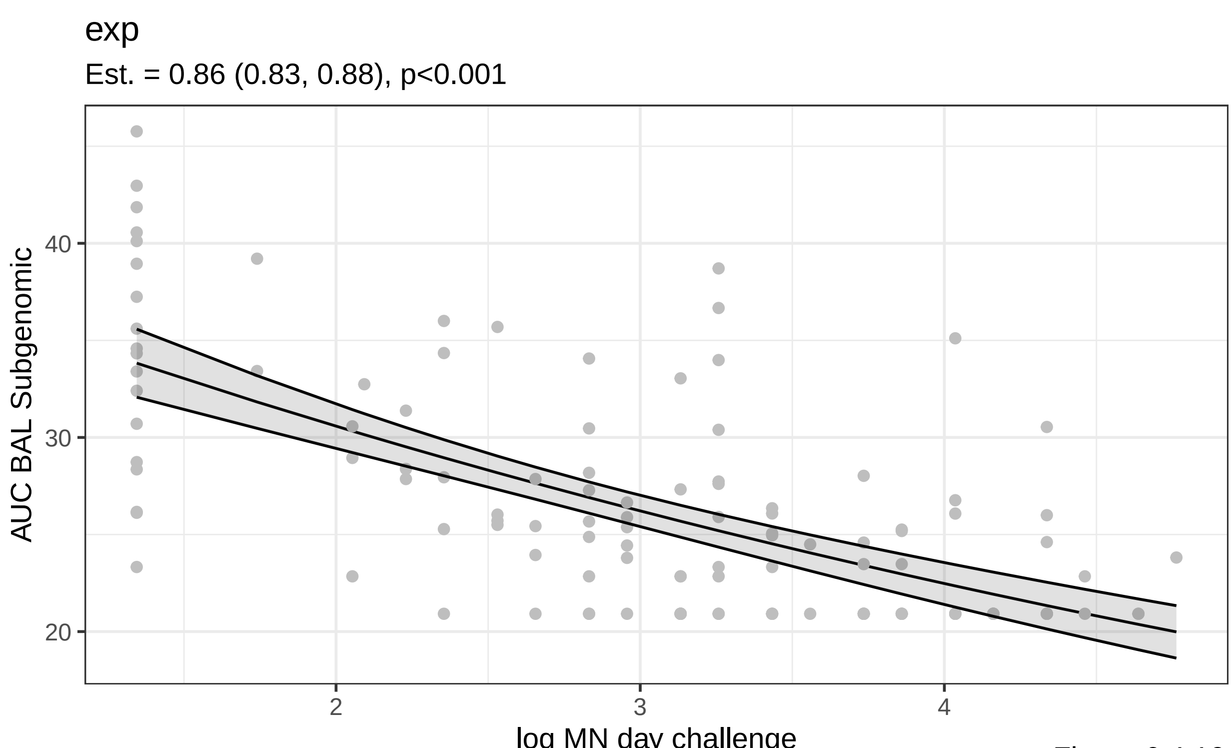


Figure 6.4.10

lm

Est. = −3.05 (−3.79, −2.32), p<0.001

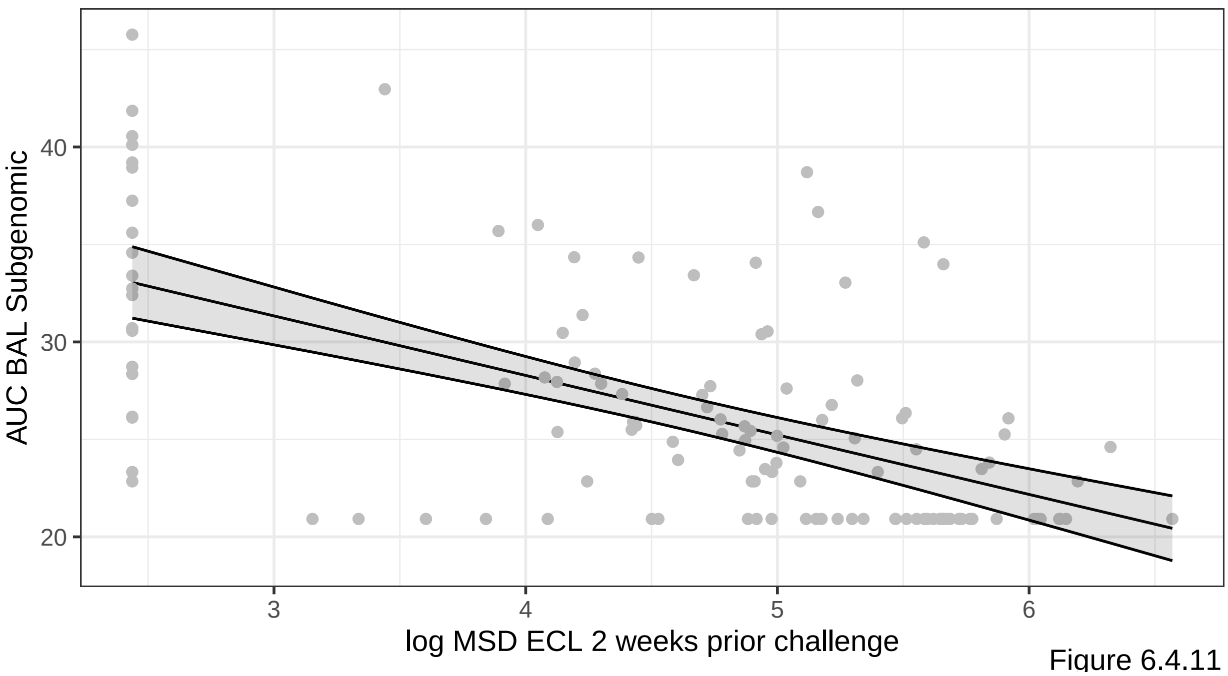
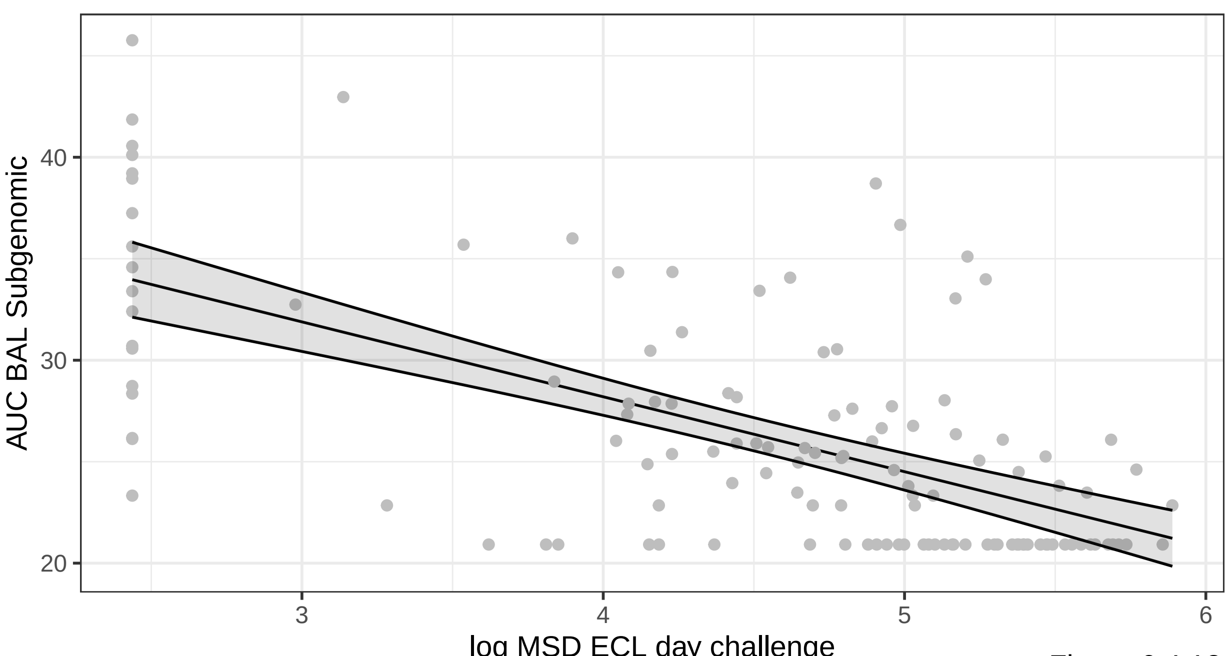


Figure 6.4.11

lm

Est. = −3.69 (−4.49, −2.89), p<0.001



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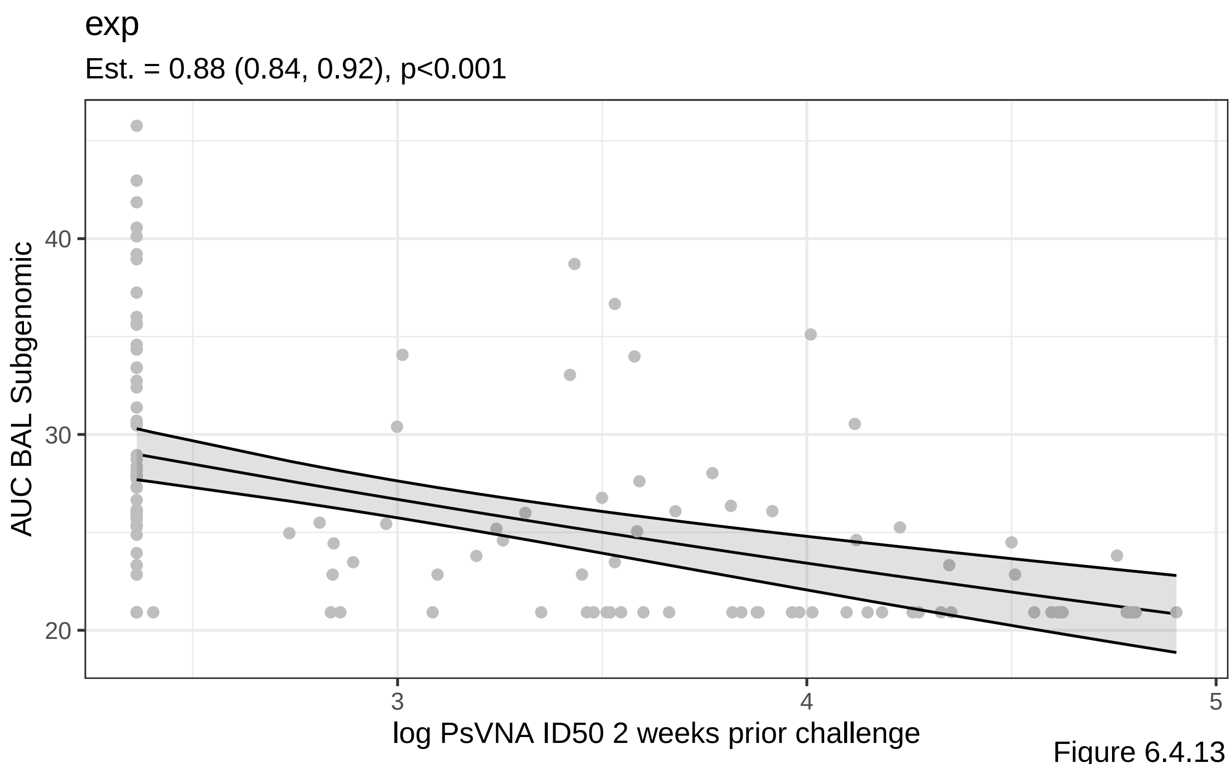

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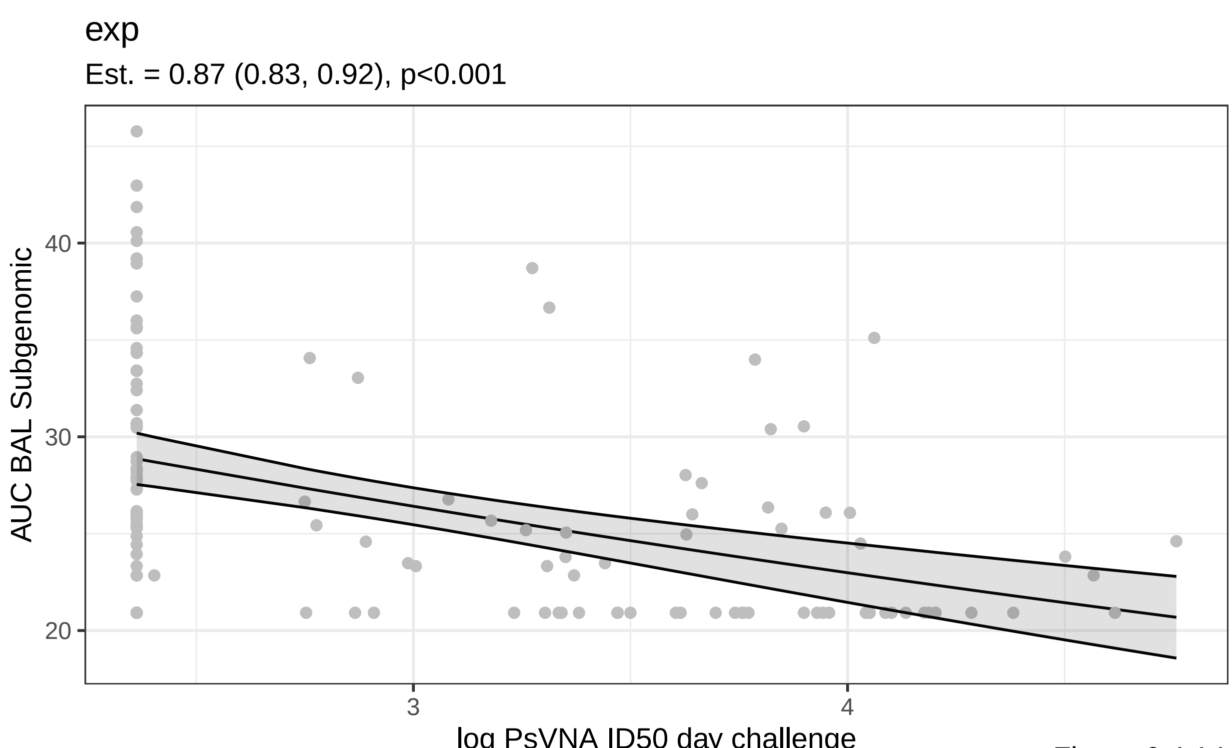

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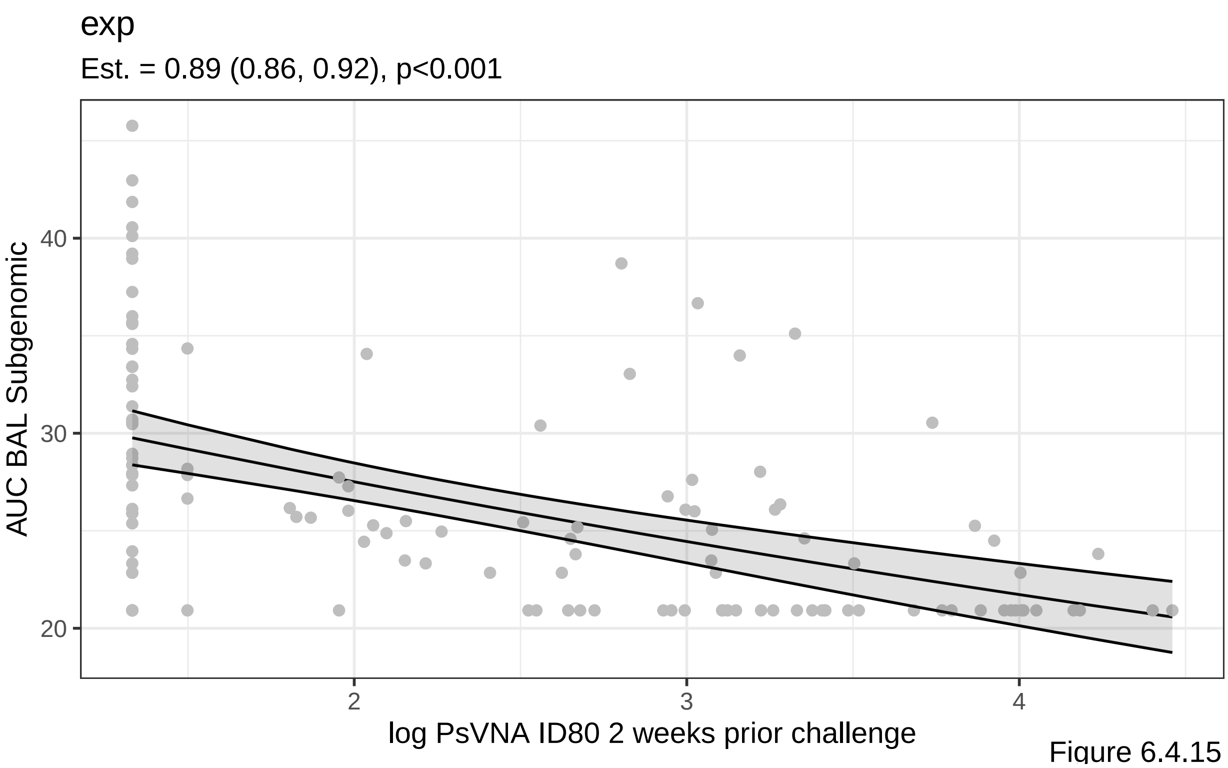

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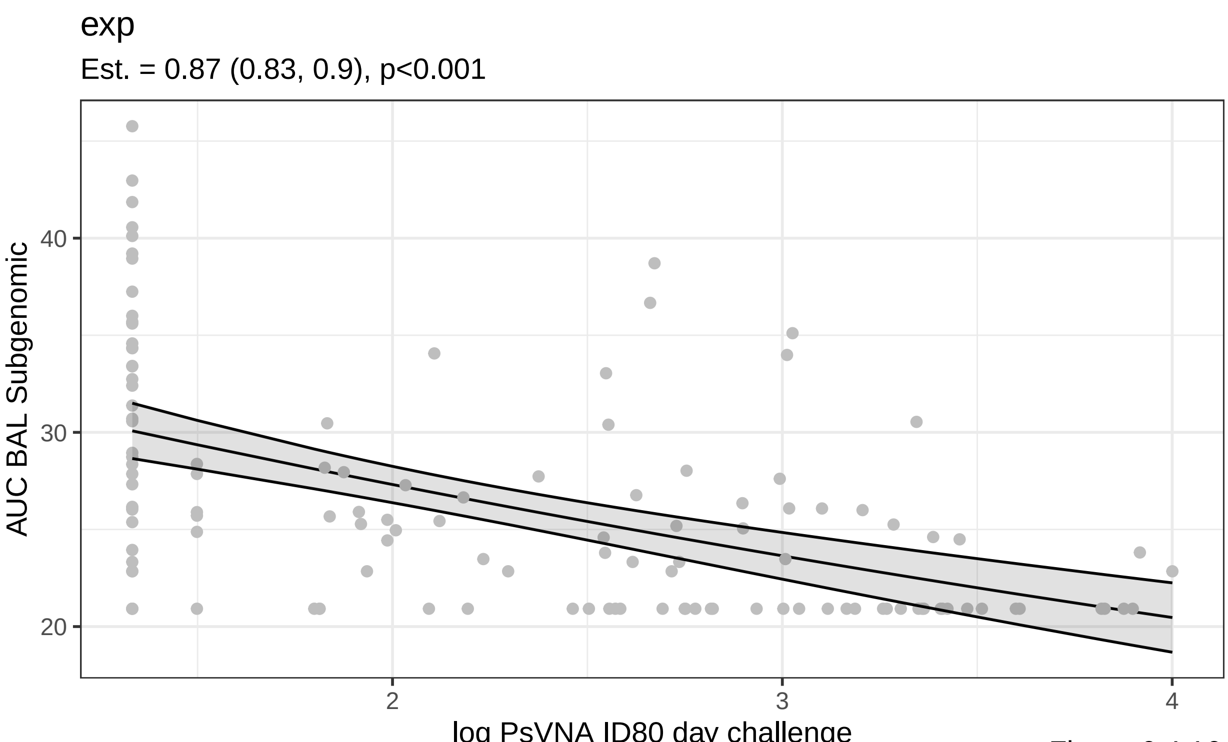

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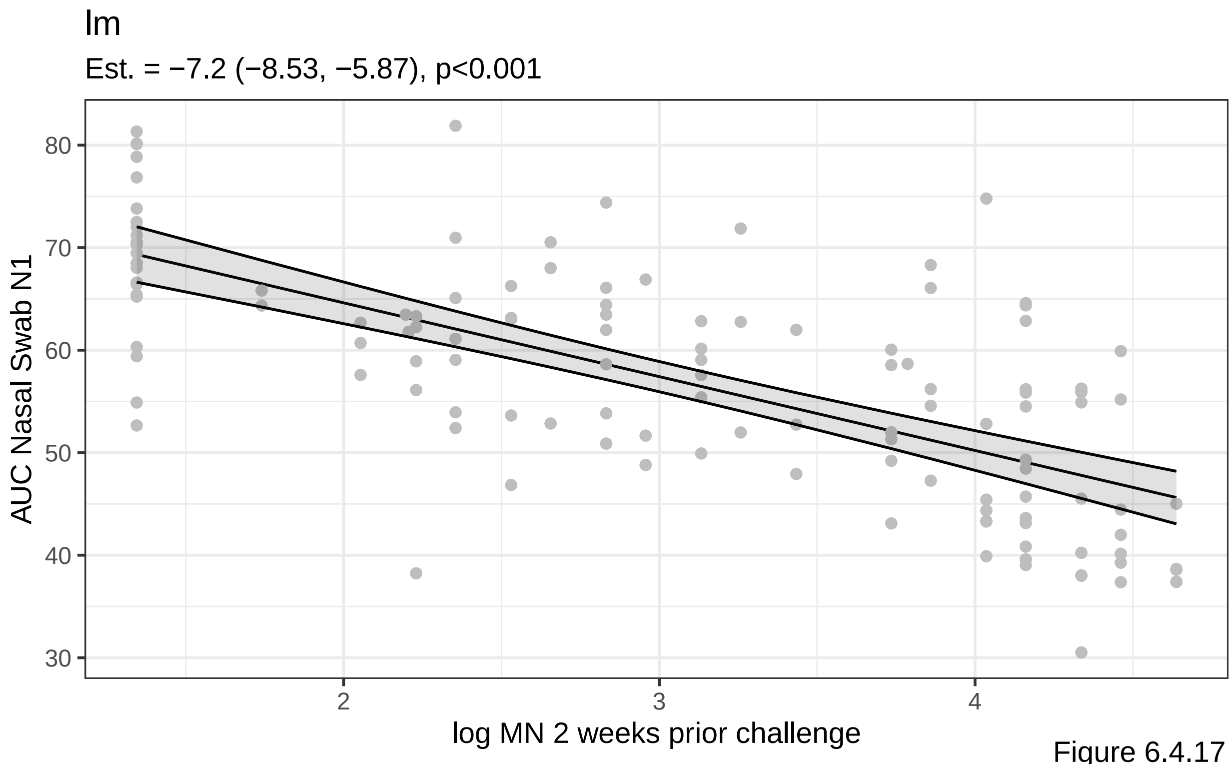

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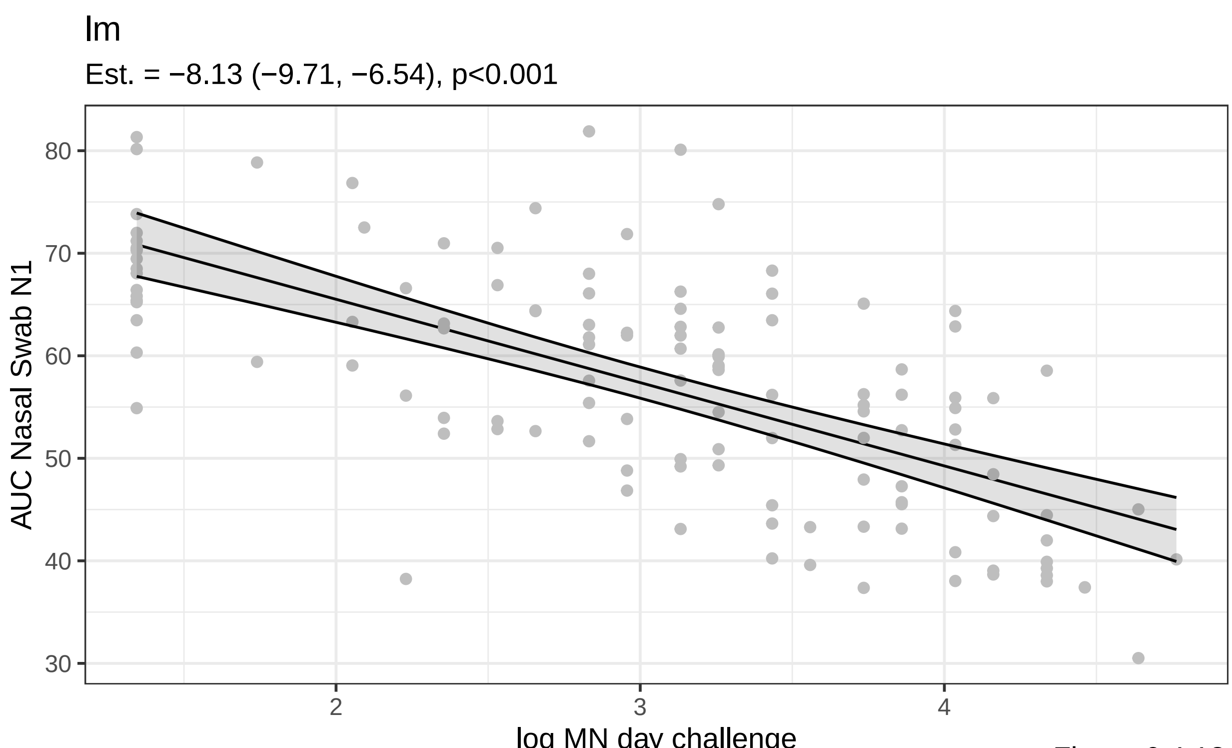

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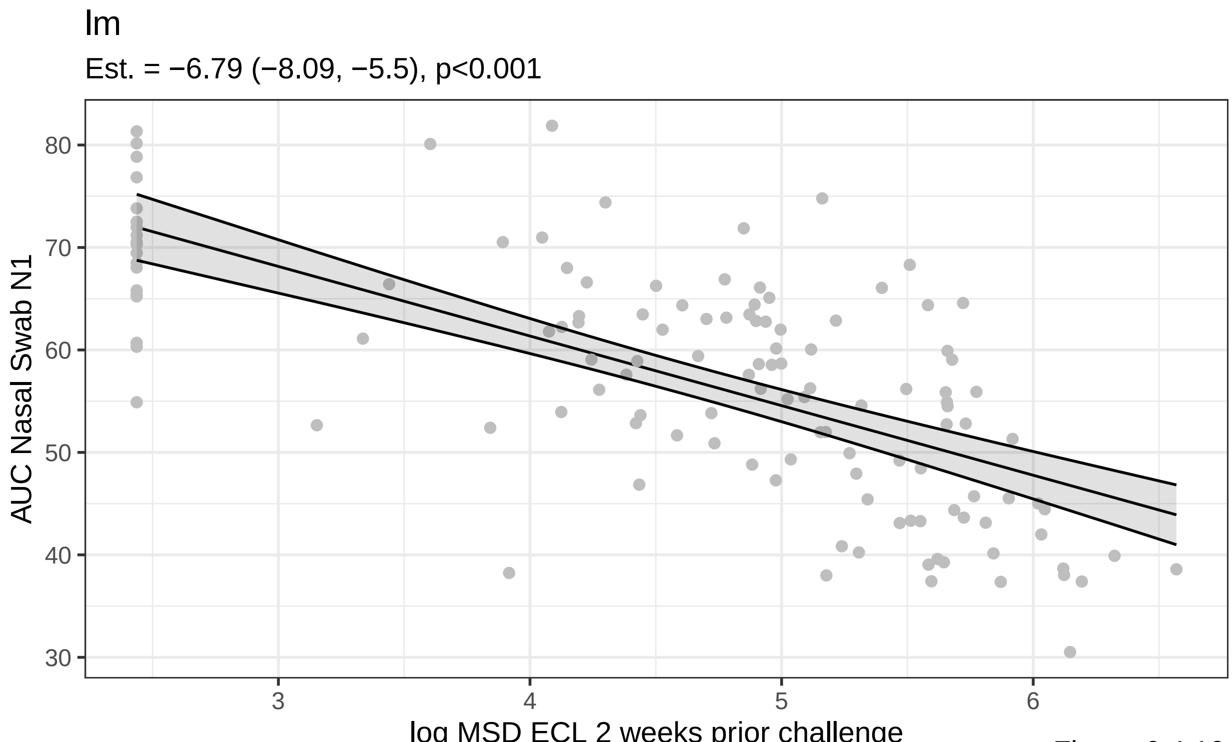

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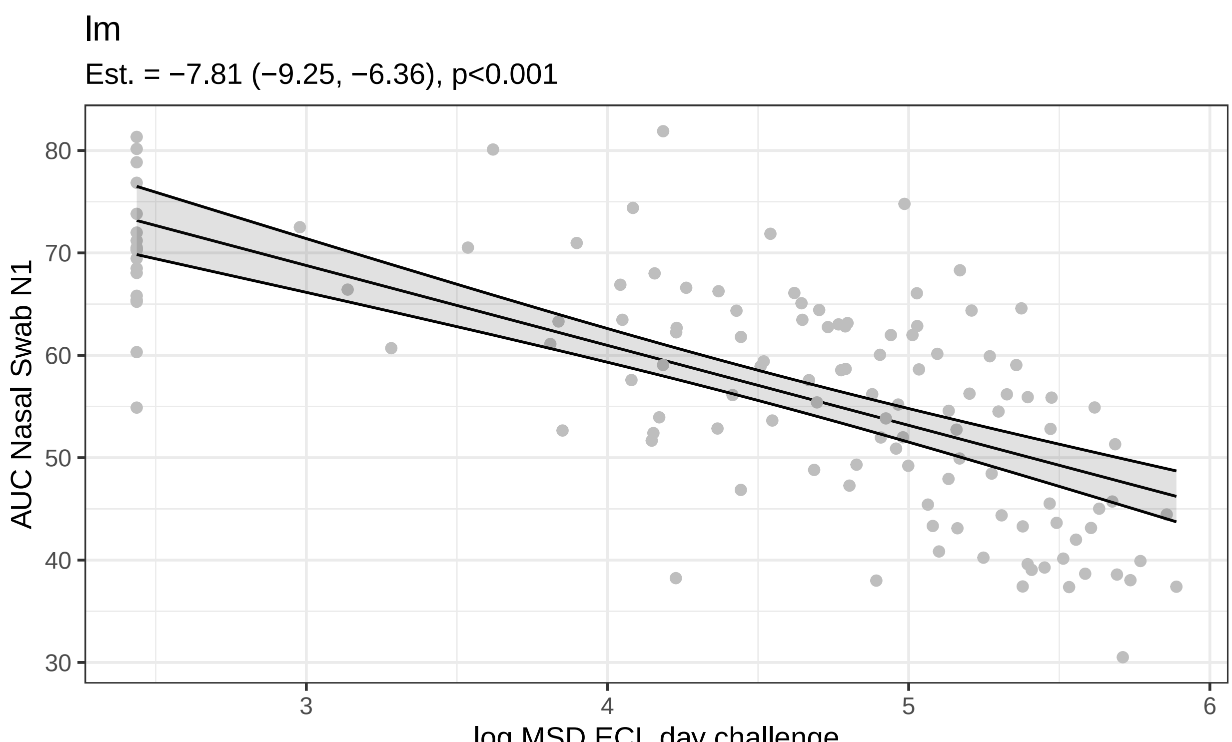

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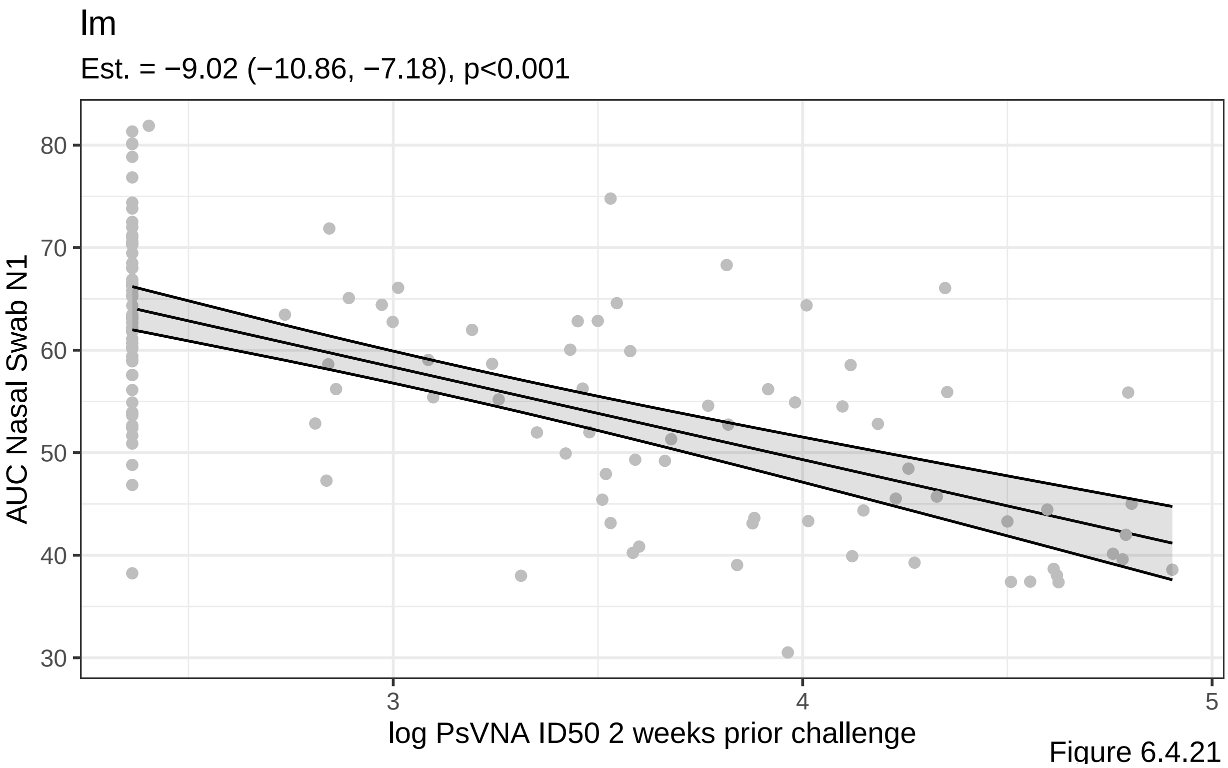

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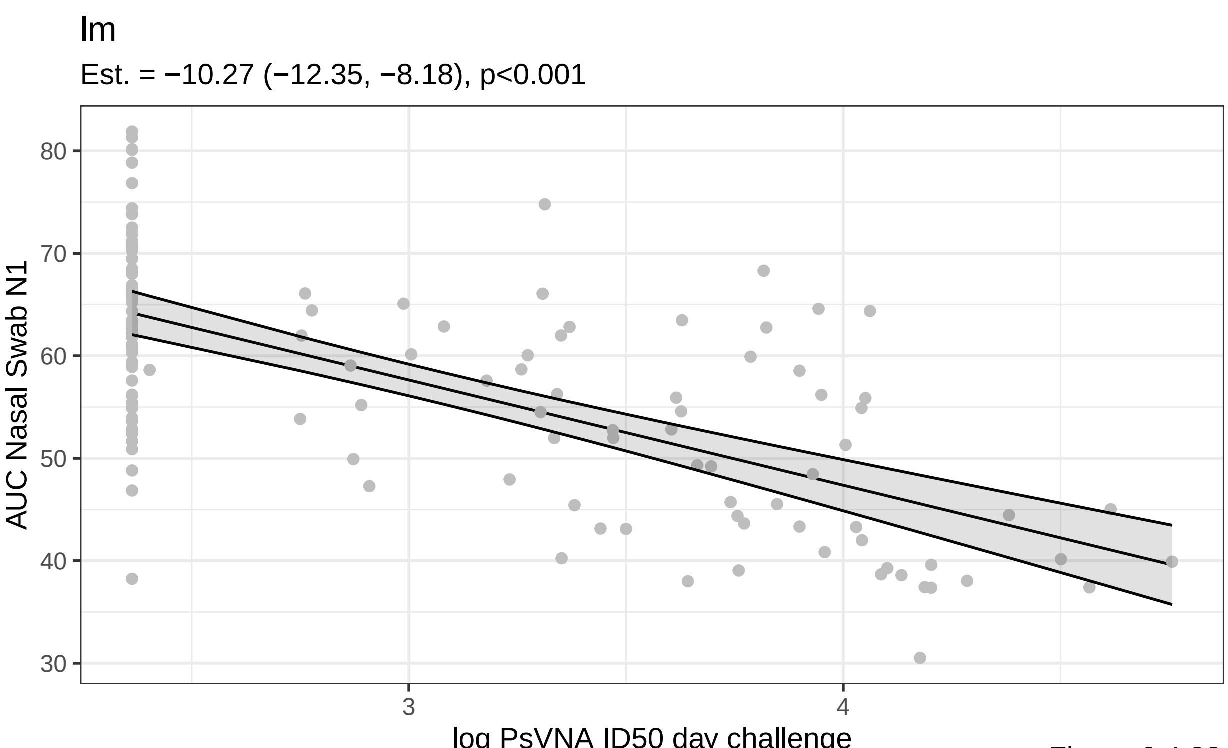

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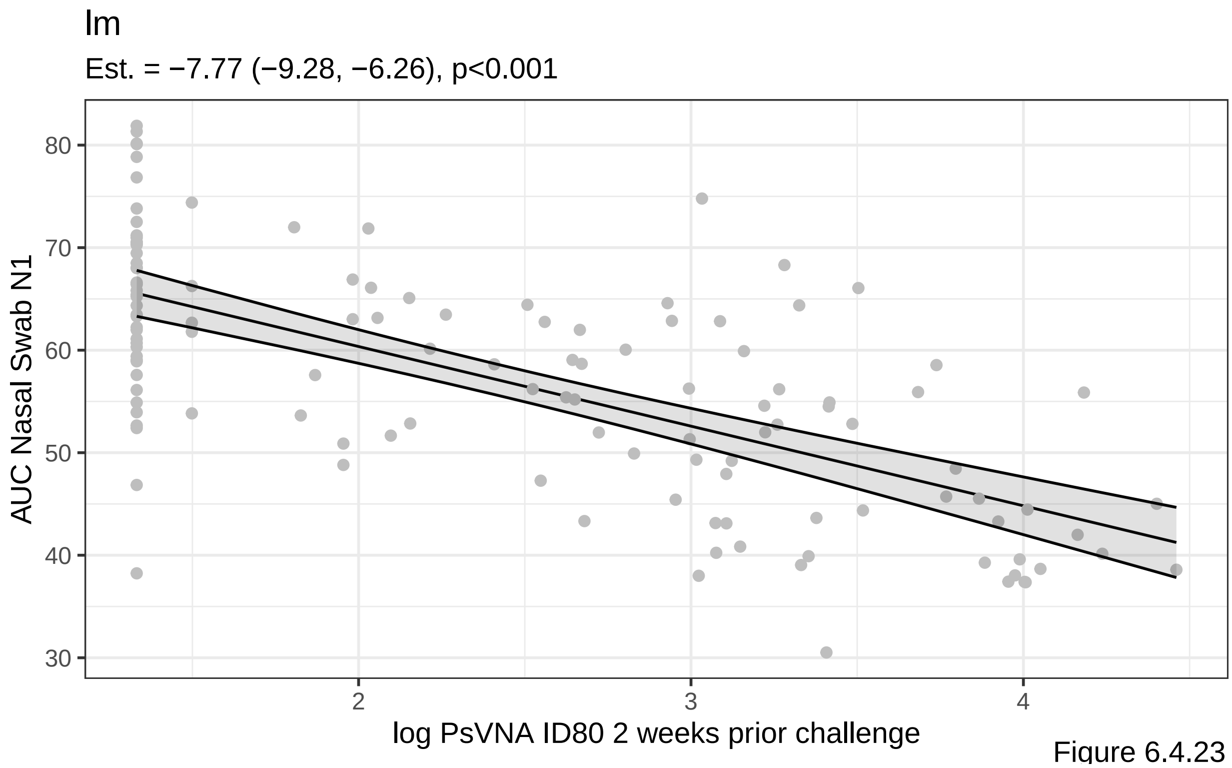

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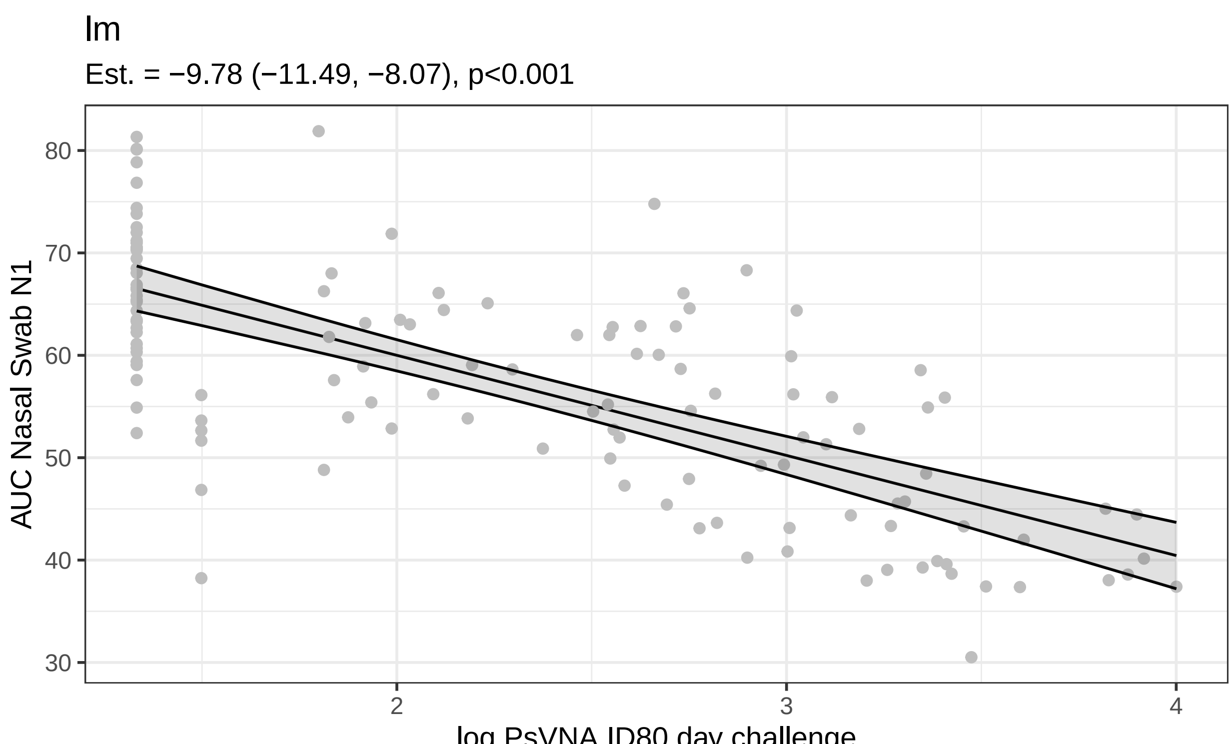

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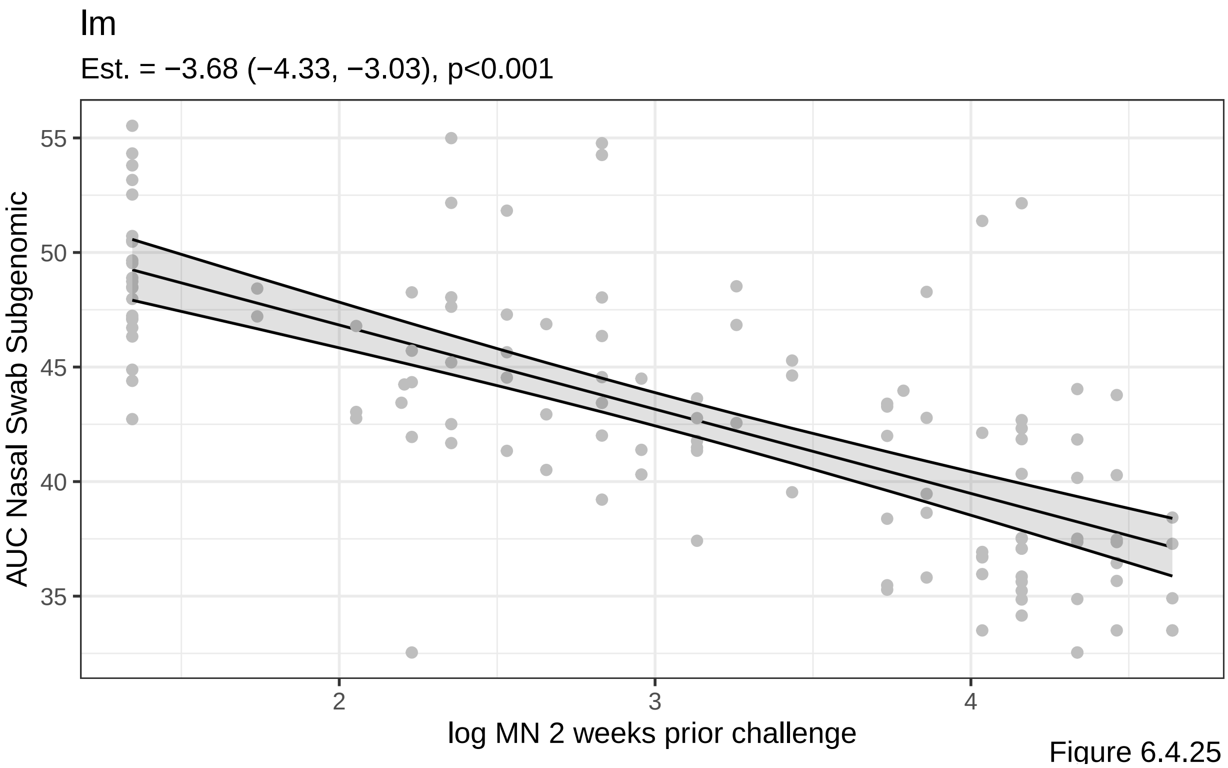

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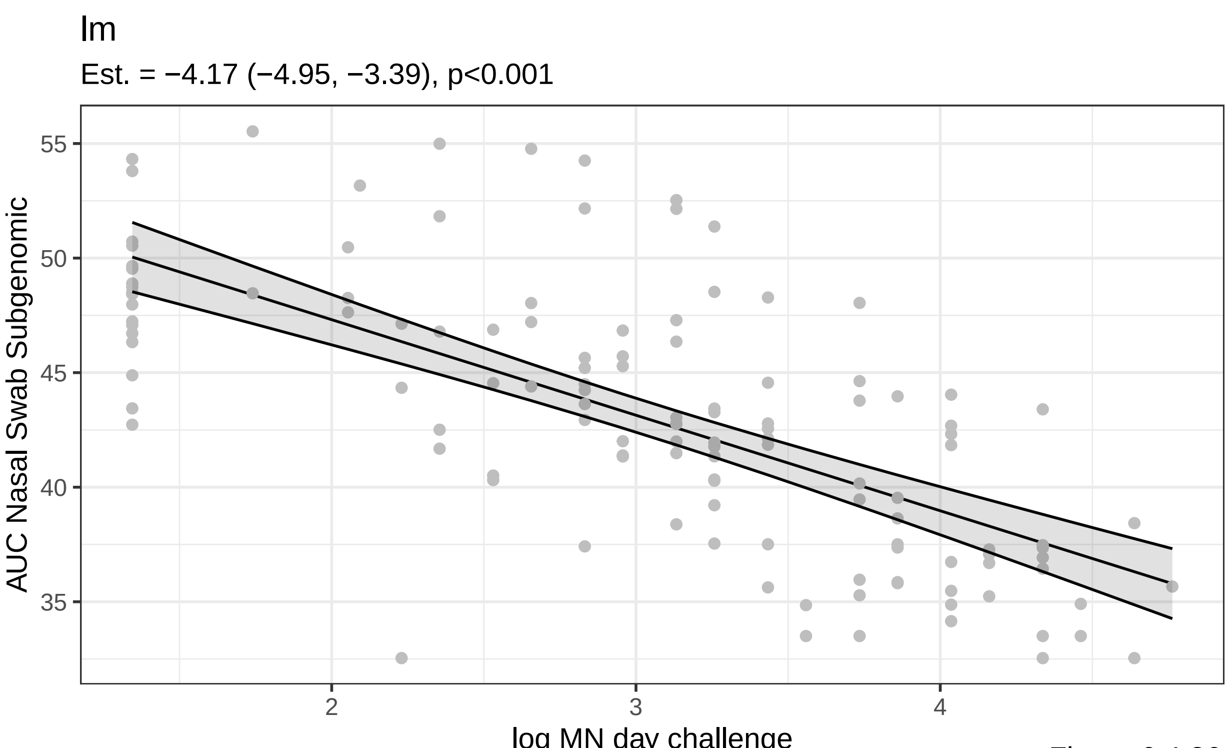
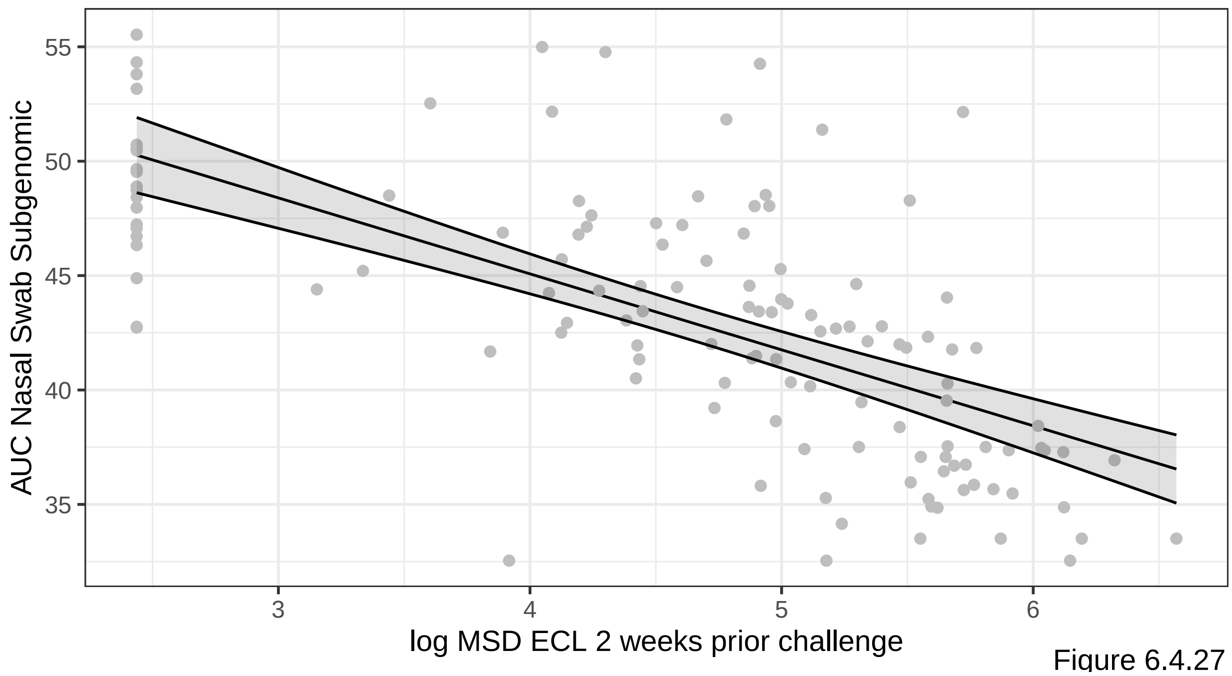


Figure 6.4.26

lm

Est. = −3.32 (−3.98, −2.66), p<0.001



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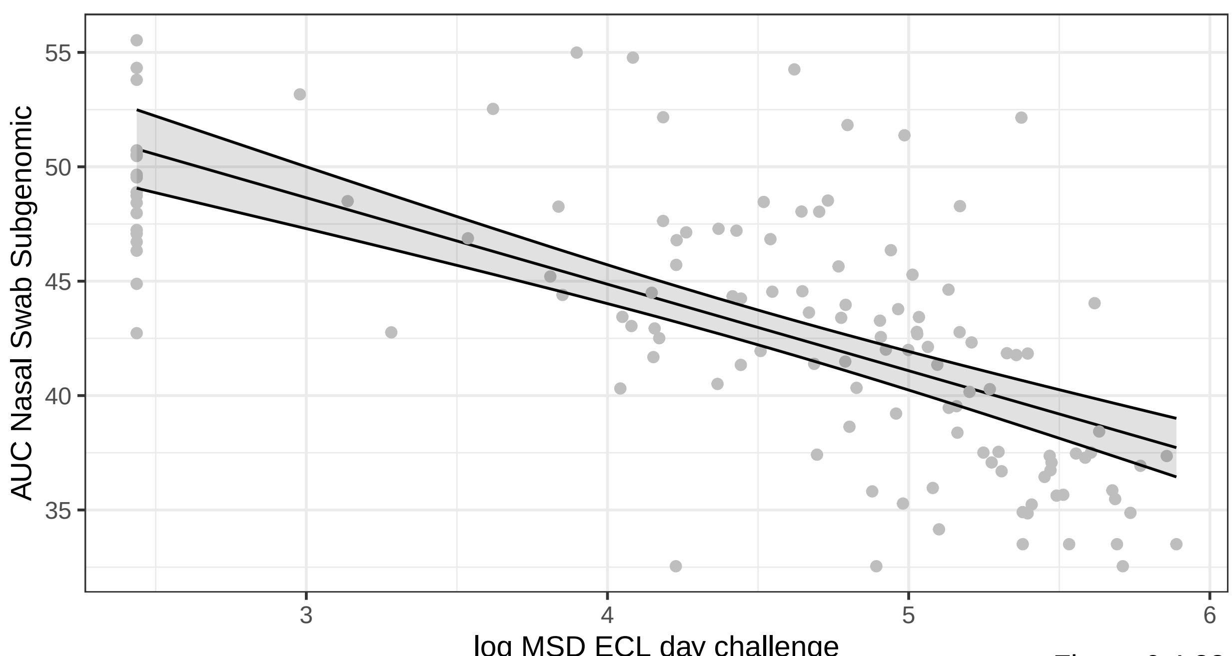
lm

Est. = −3.78 (−4.53, −3.04), p<0.001



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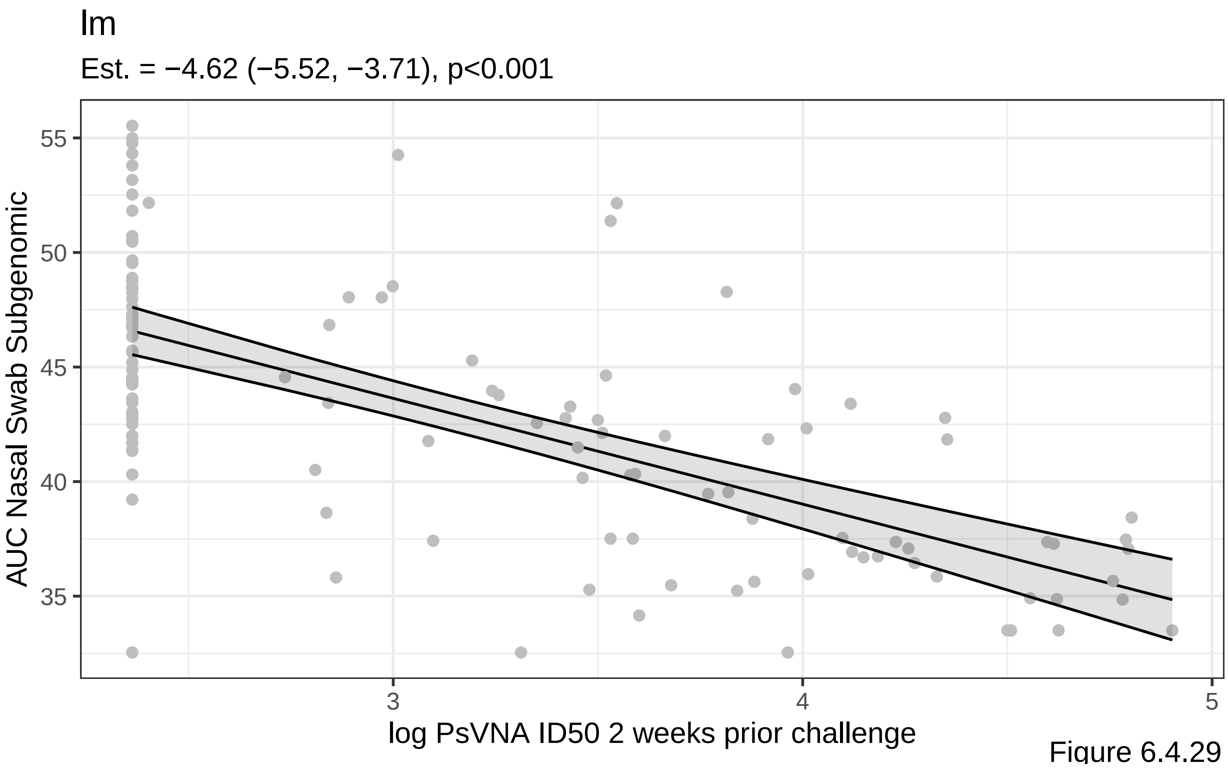

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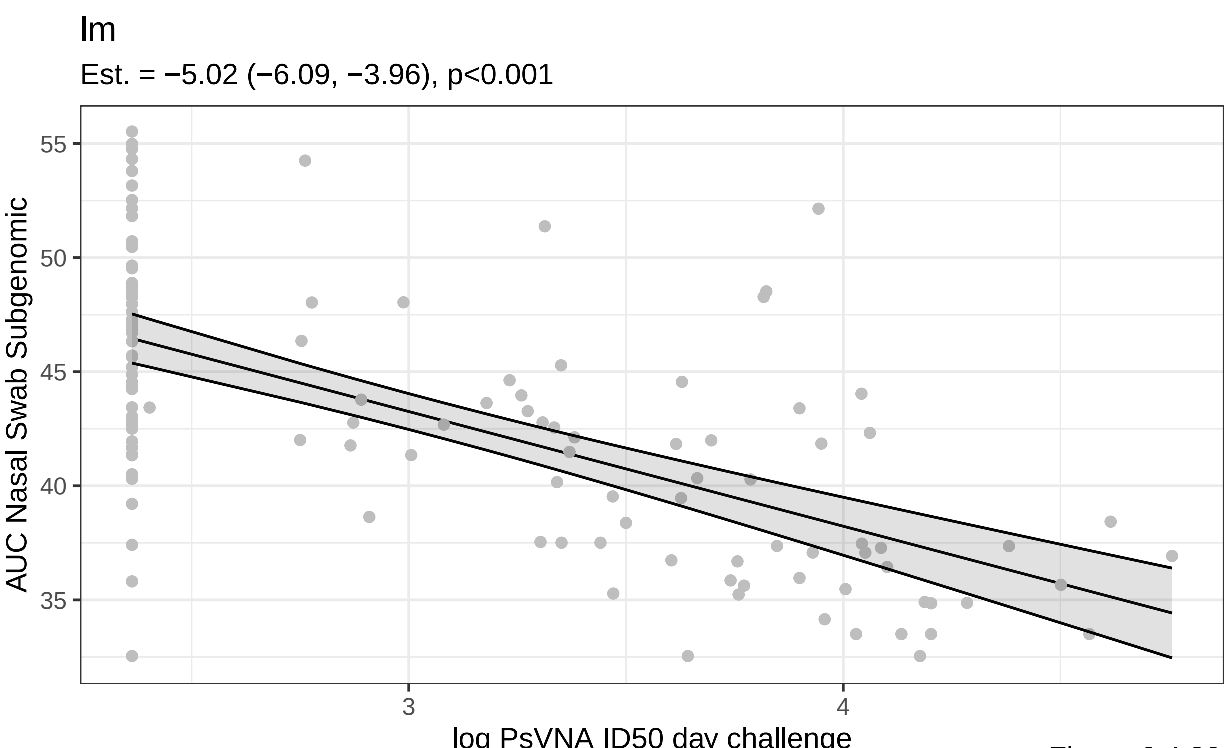

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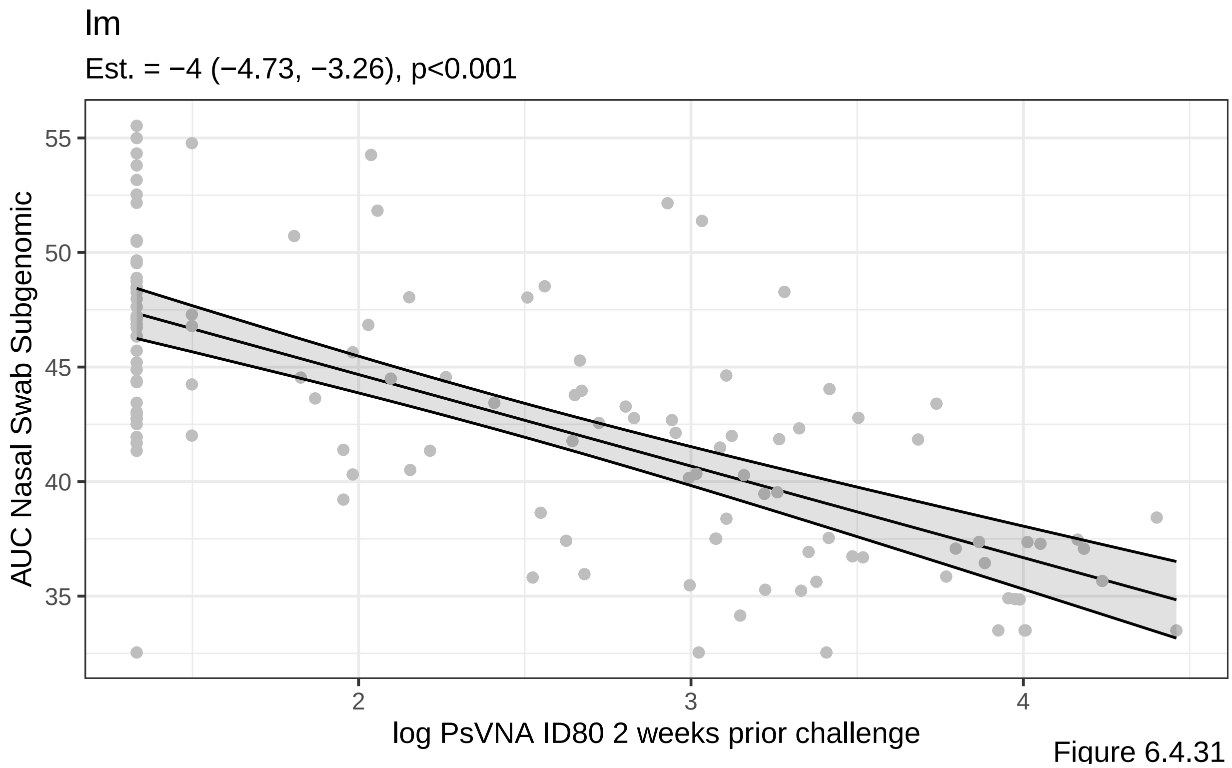

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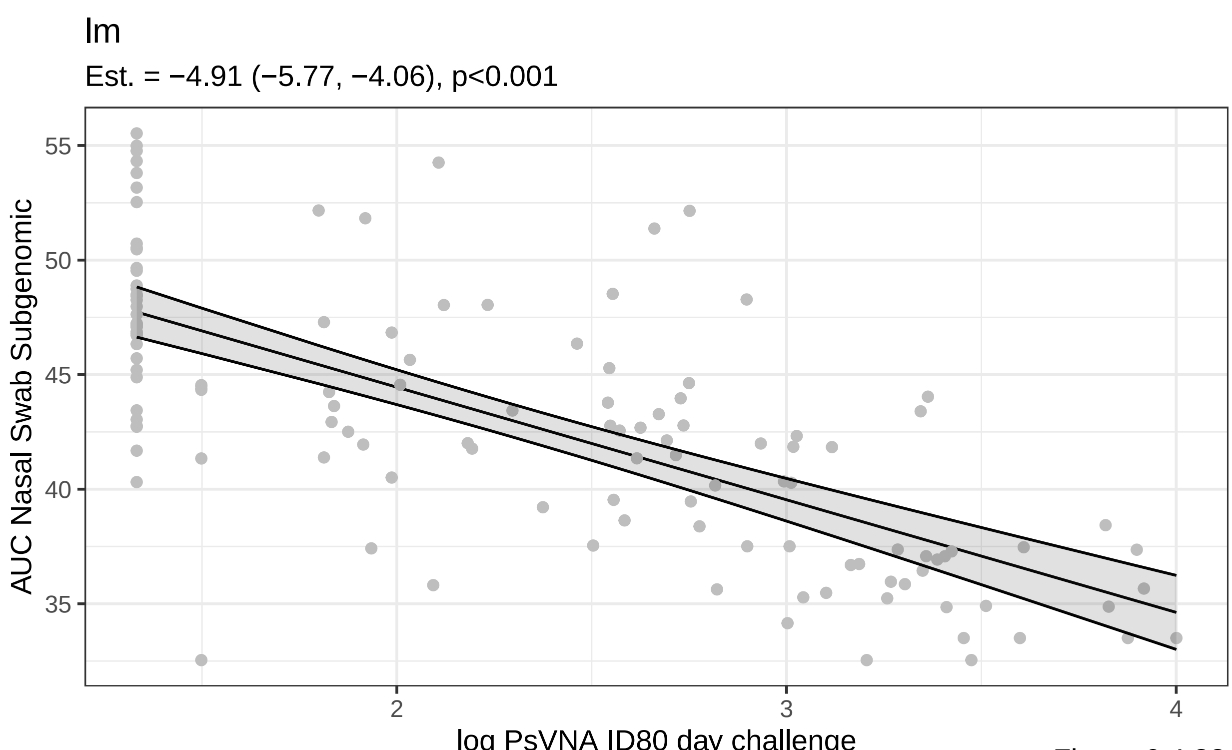


Figure 6.4.32

lm

Est. = −4.15 (−5.19, −3.11), p<0.001

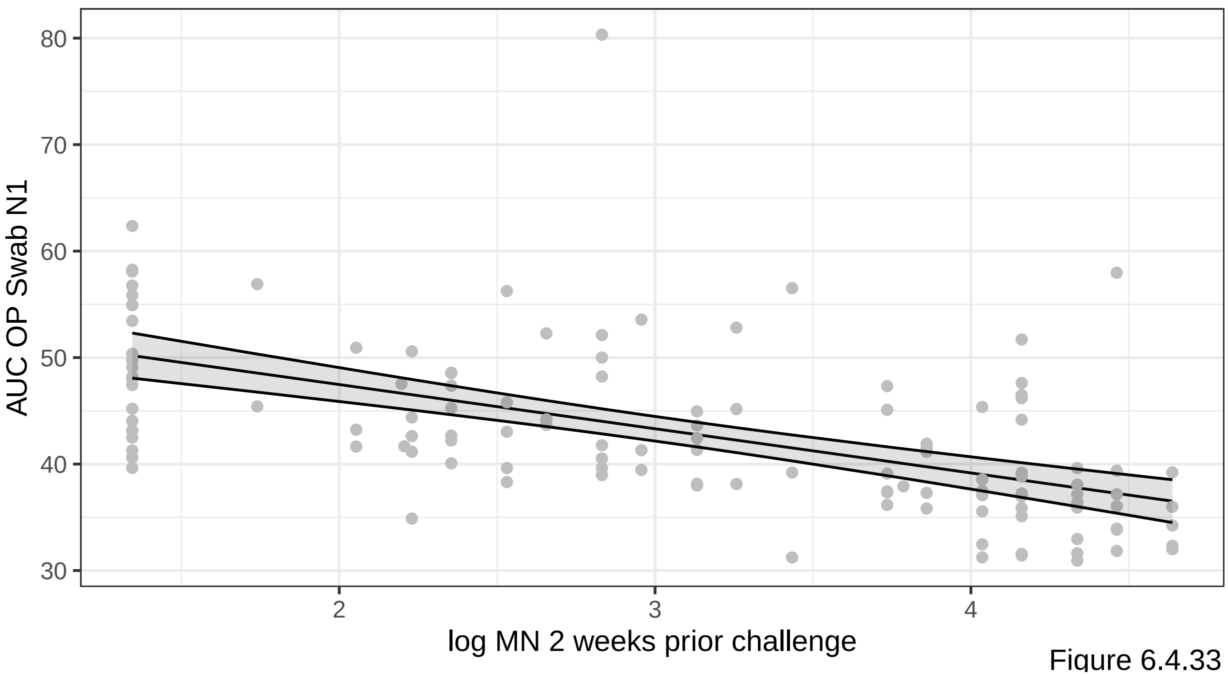


Figure 6.4.33

lm

Est. = −4.87 (−6.07, −3.66), p<0.001

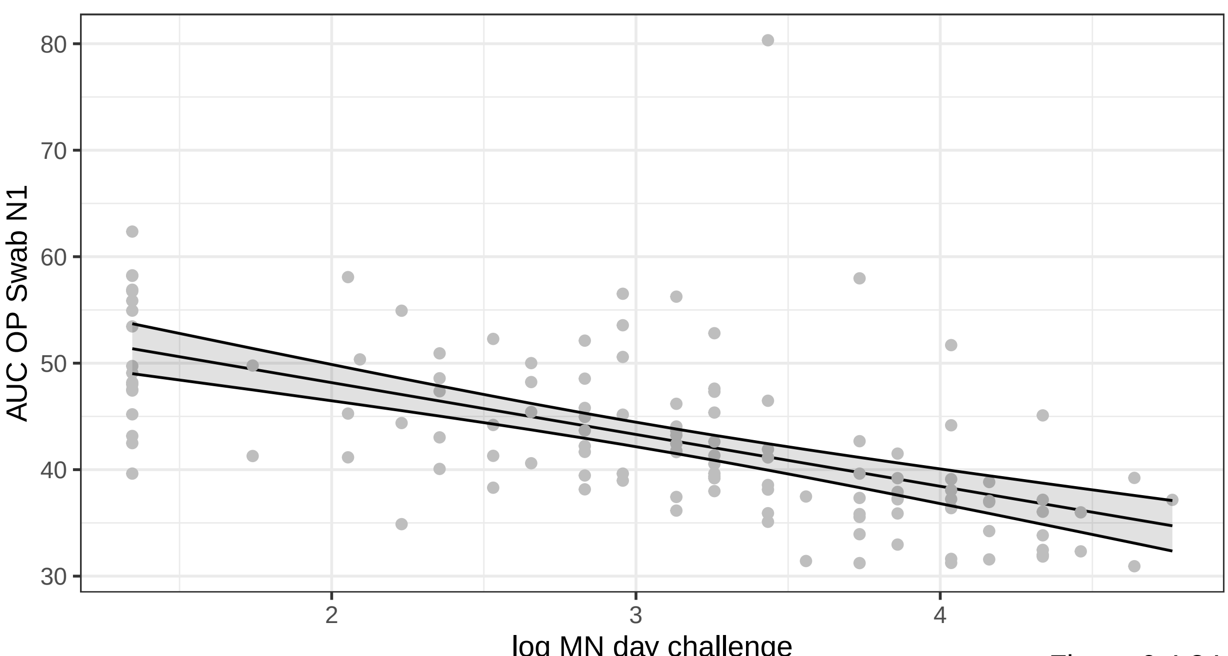


Figure 6.4.34

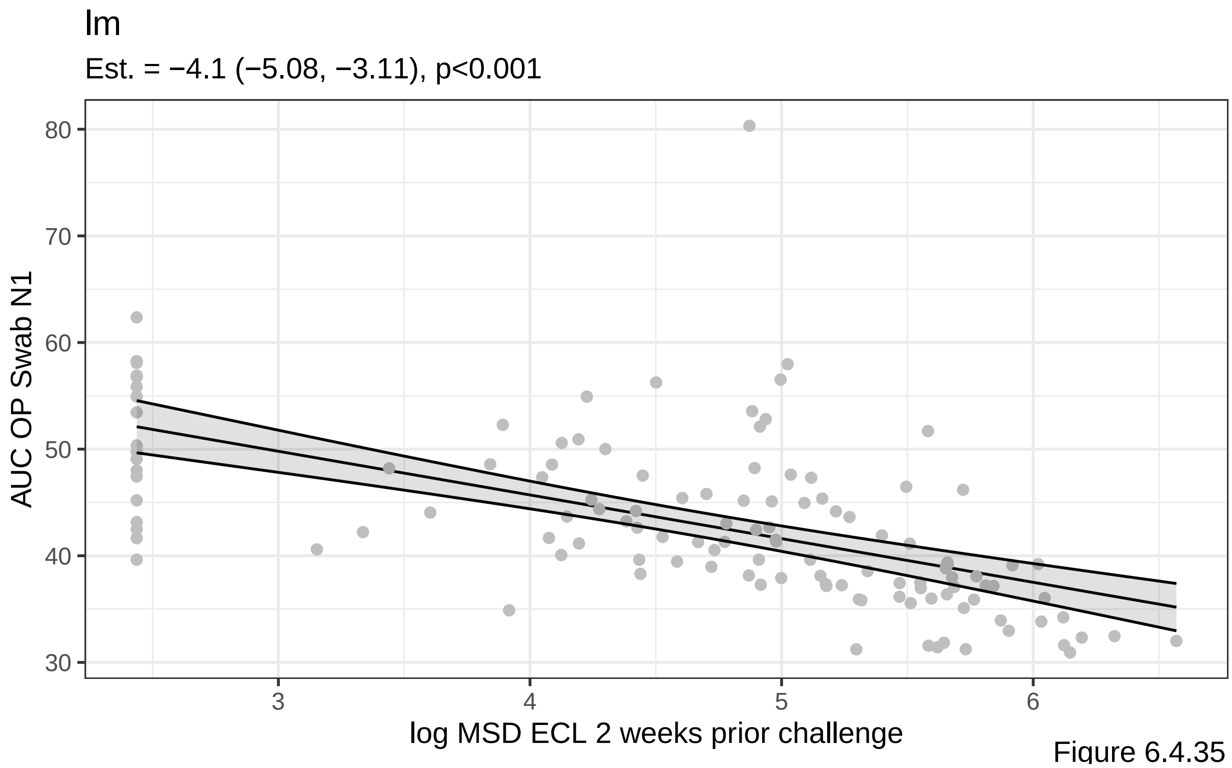


Figure 6.4.35

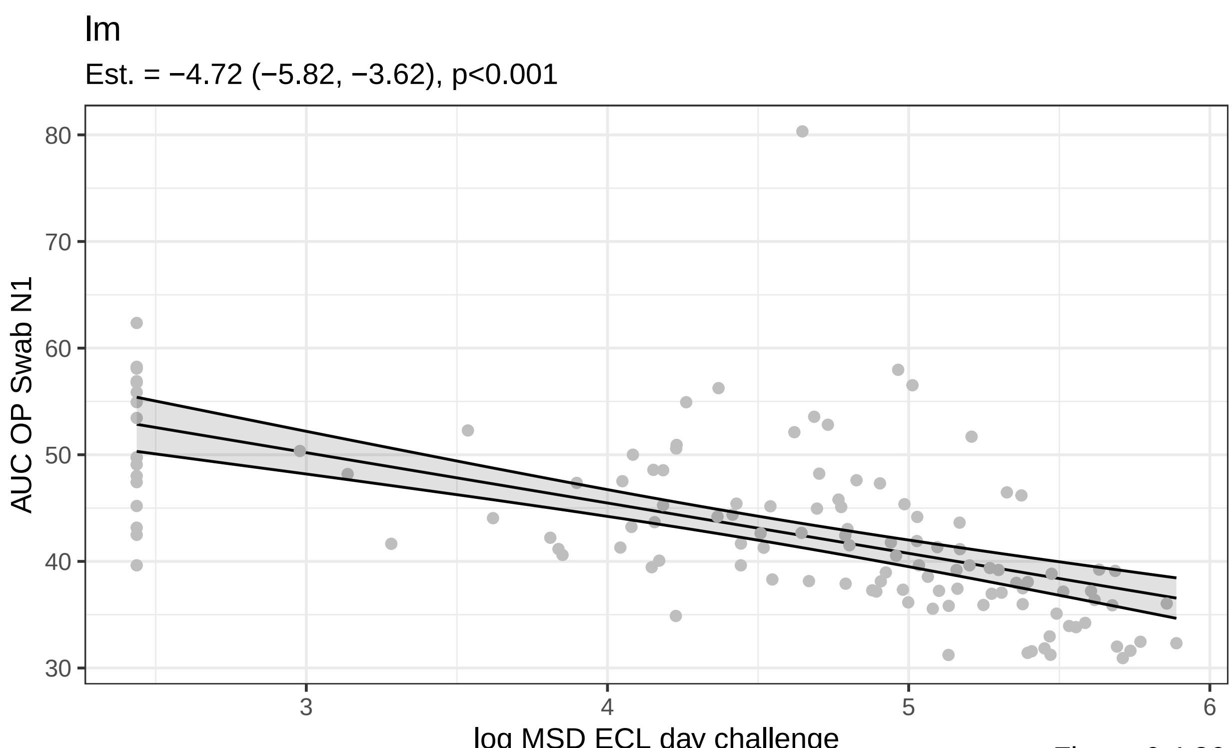


Figure 6.4.36

lm

Est. = −5.43 (−6.81, −4.04), p<0.001

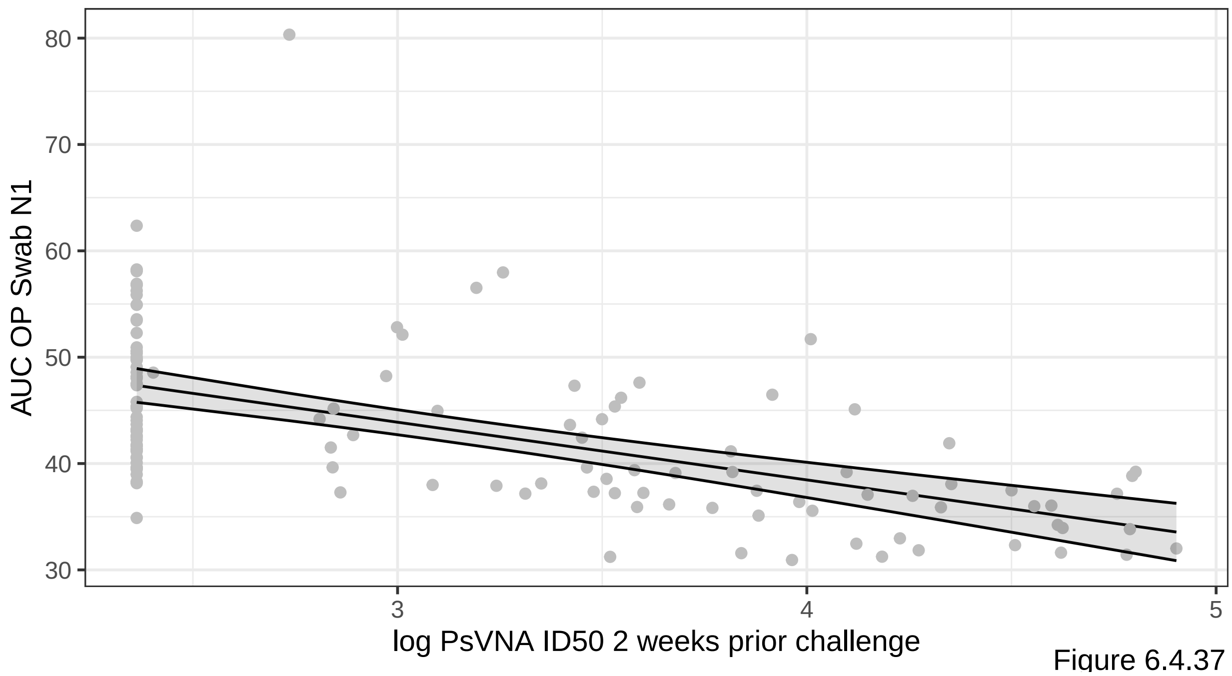


Figure 6.4.37

lm

Est. = −5.52 (−7.16, −3.87), p<0.001

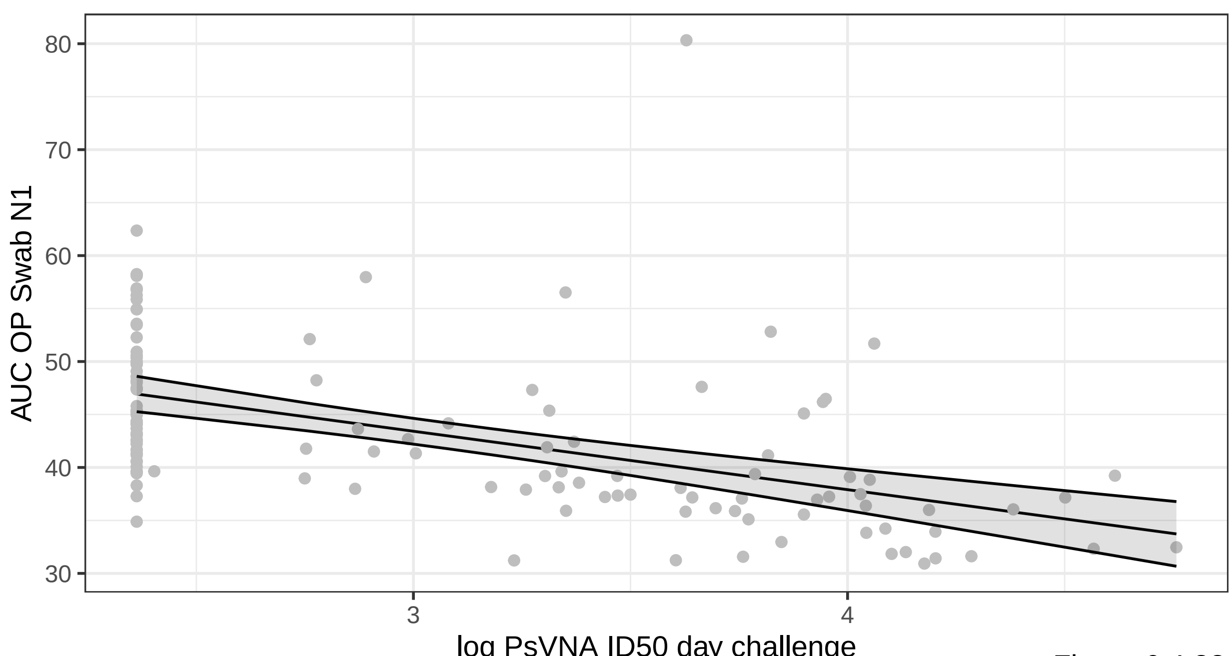


Figure 6.4.38

lm

Est. = −4.62 (−5.77, −3.46), p<0.001

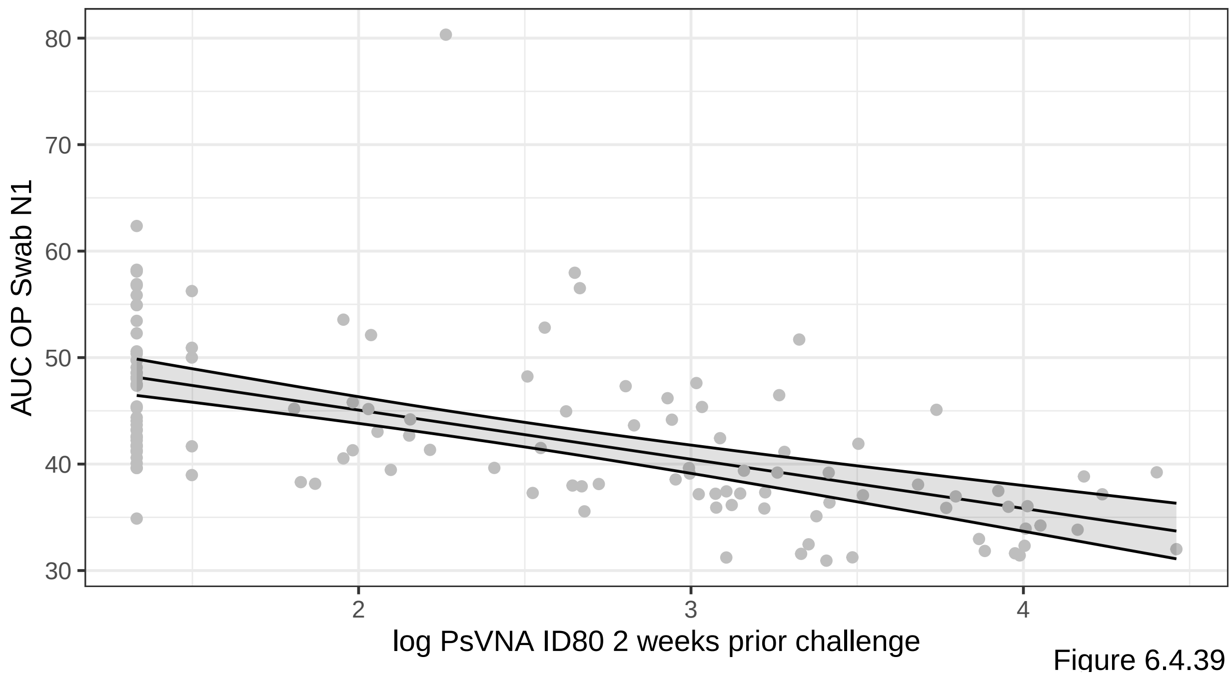


Figure 6.4.39

lm

Est. = −5.73 (−7.08, −4.39), p<0.001

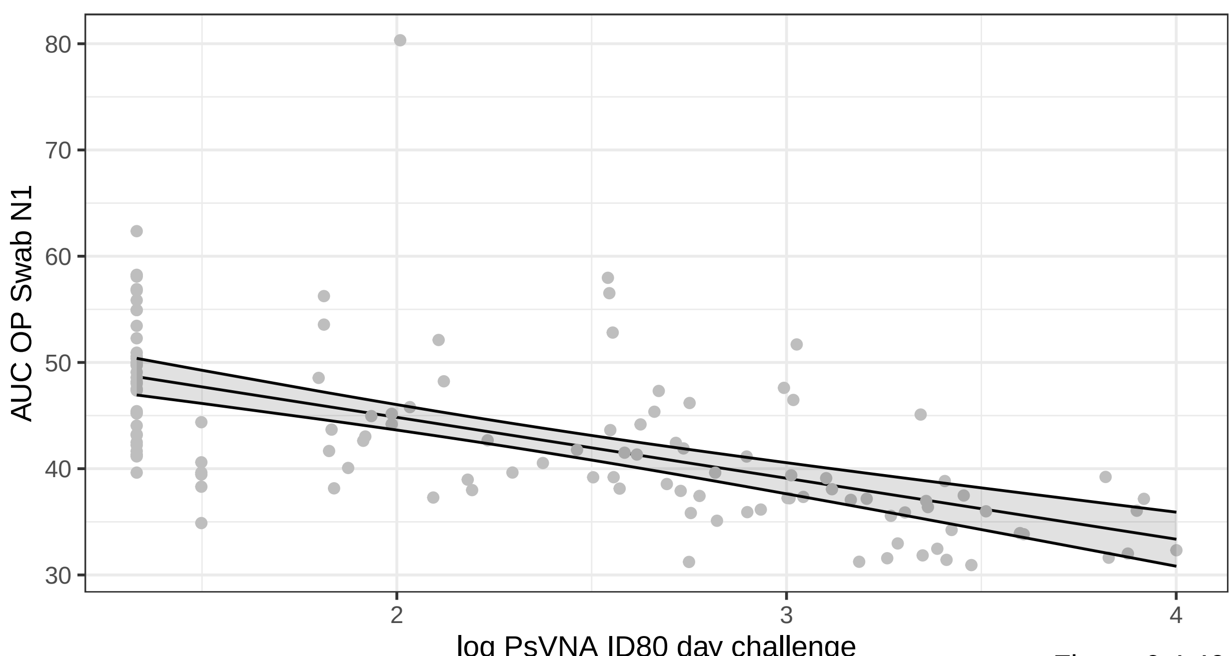


Figure 6.4.40

lm

Est. = −2.08 (−2.73, −1.43), p<0.001

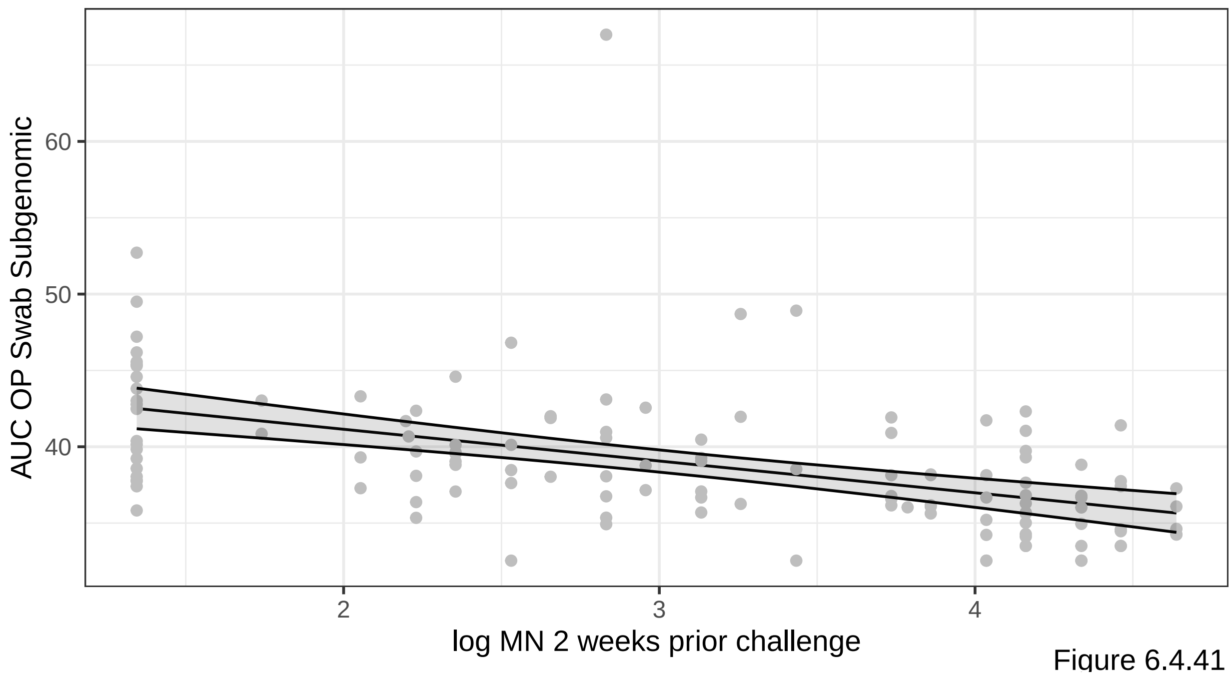


Figure 6.4.41

lm

Est. = −2.32 (−3.09, −1.55), p<0.001

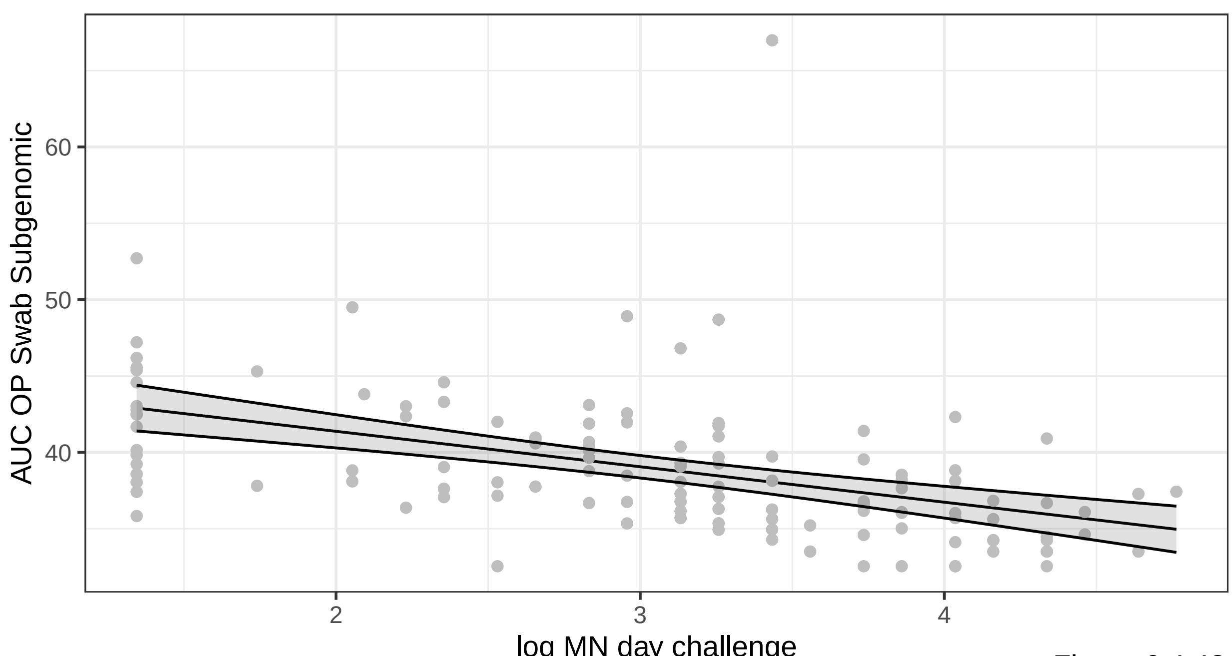


Figure 6.4.42

lm

Est. = −2 (−2.63, −1.37), p<0.001

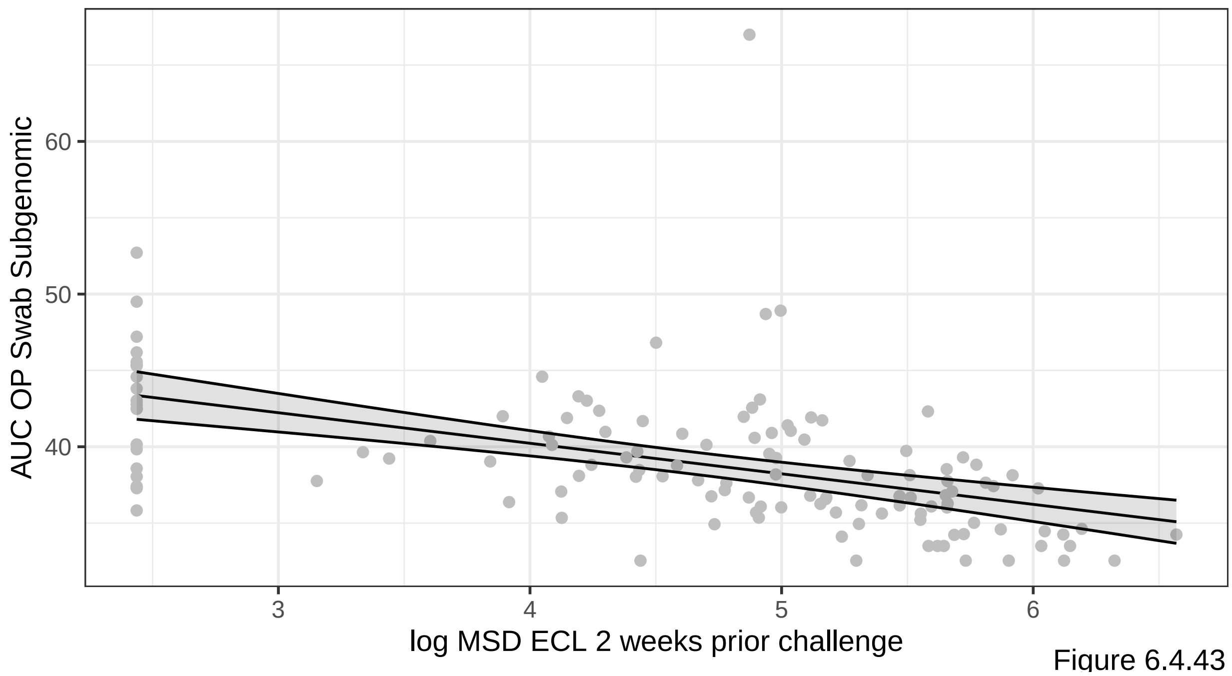


Figure 6.4.43

lm

Est. = −2.33 (−3.04, −1.63), p<0.001

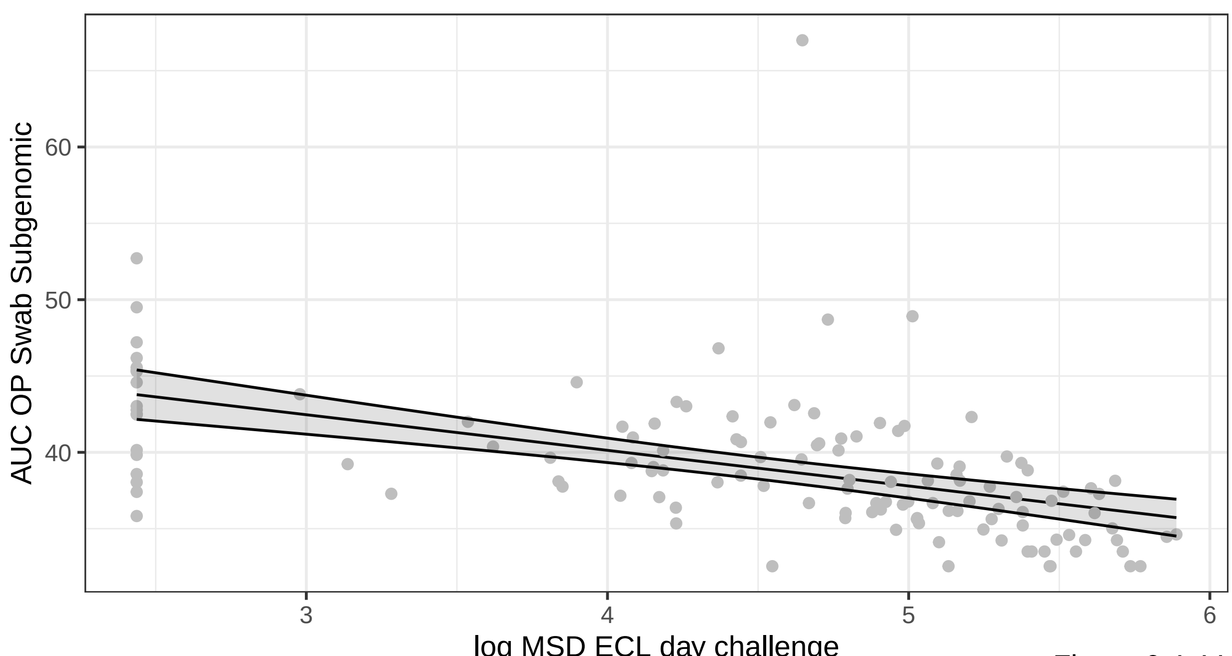


Figure 6.4.44

lm

Est. = −2.71 (−3.58, −1.84), p<0.001

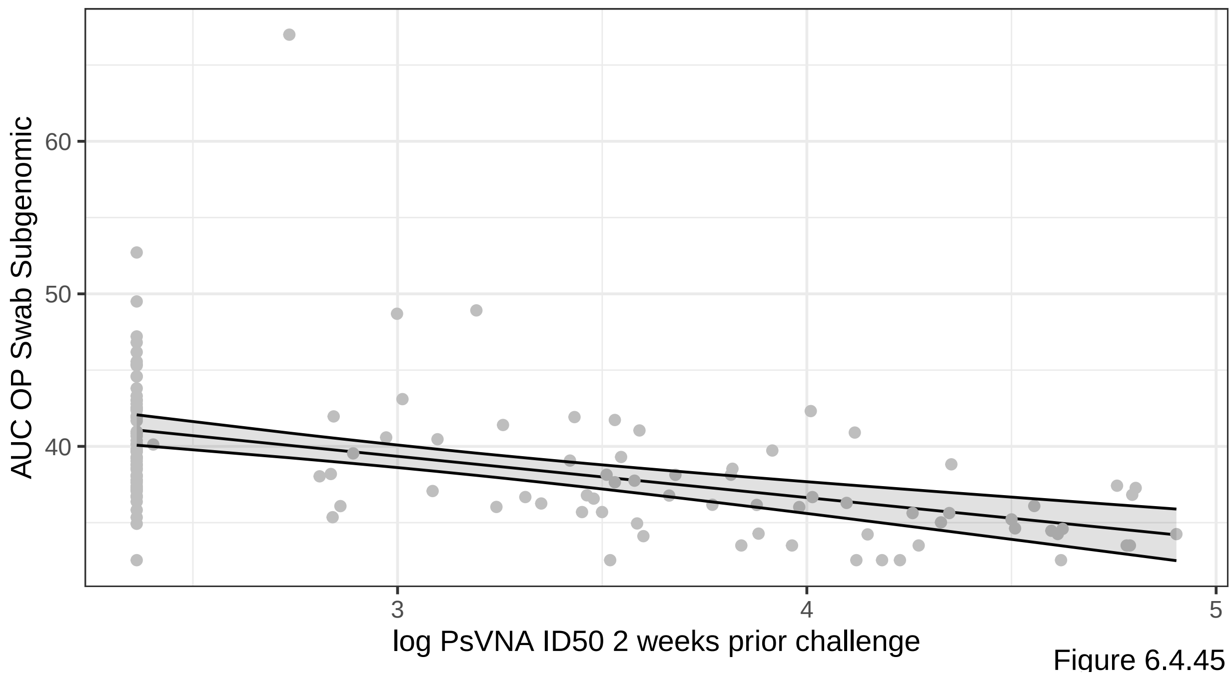


Figure 6.4.45

lm

Est. = −2.48 (−3.52, −1.43), p<0.001

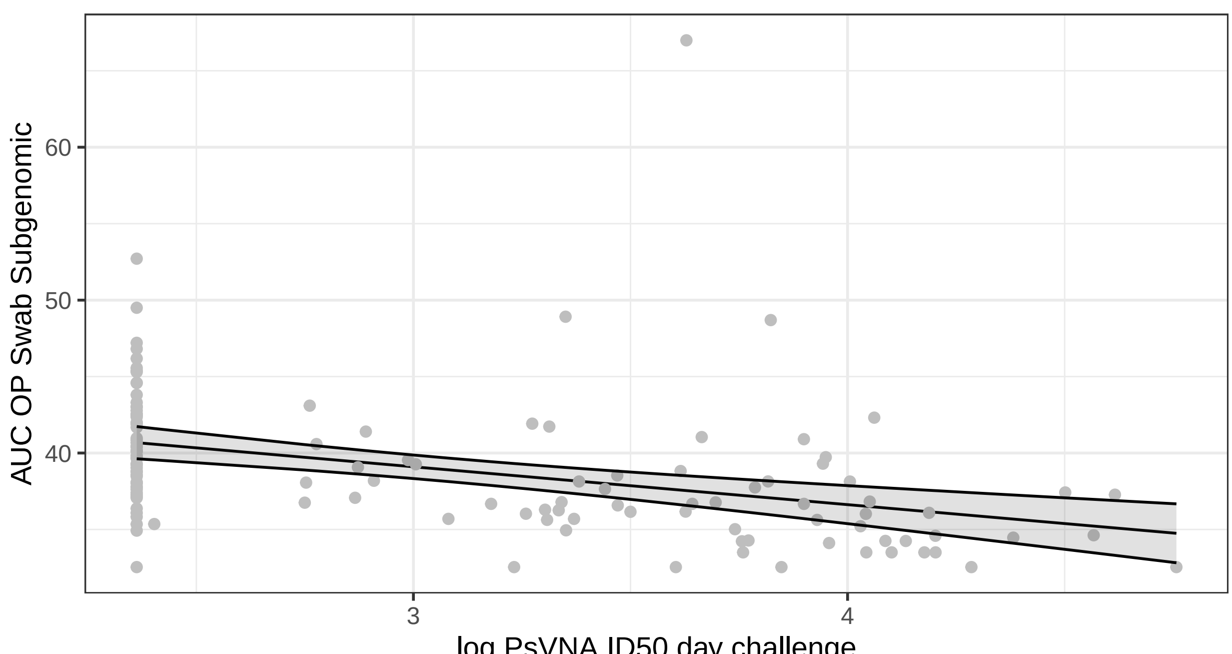


Figure 6.4.46

lm

Est. = −2.29 (−3.02, −1.56), p<0.001

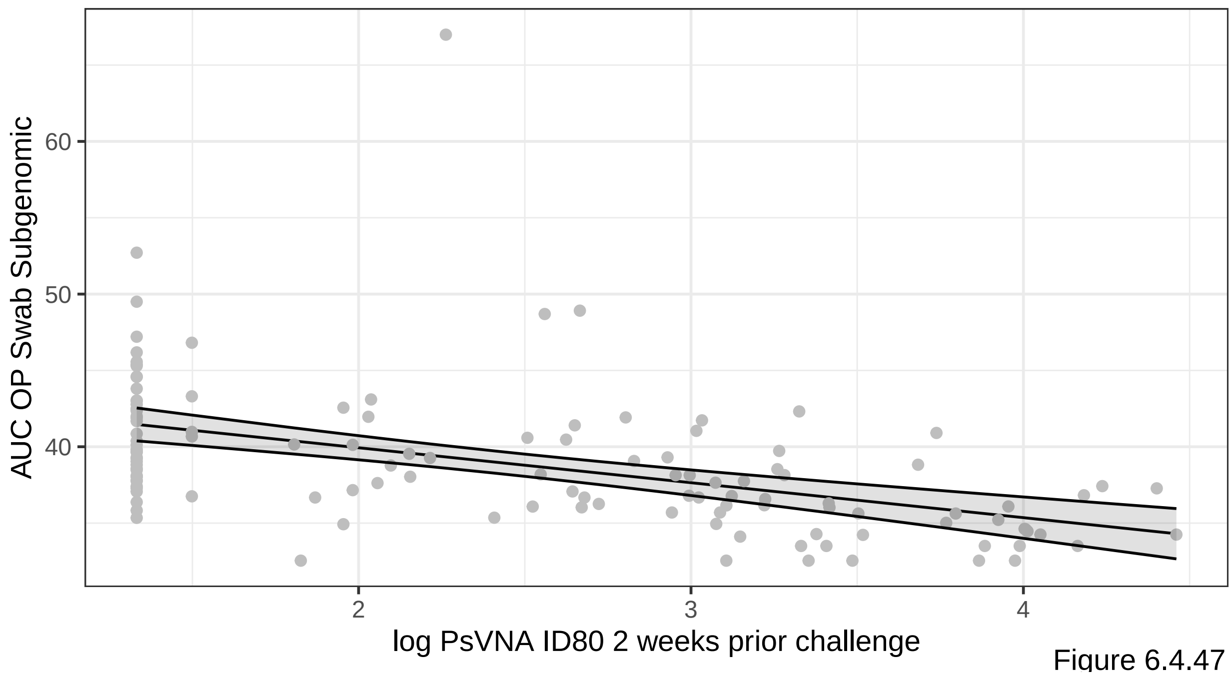


Figure 6.4.47

lm

Est. = −2.78 (−3.64, −1.91), p<0.001

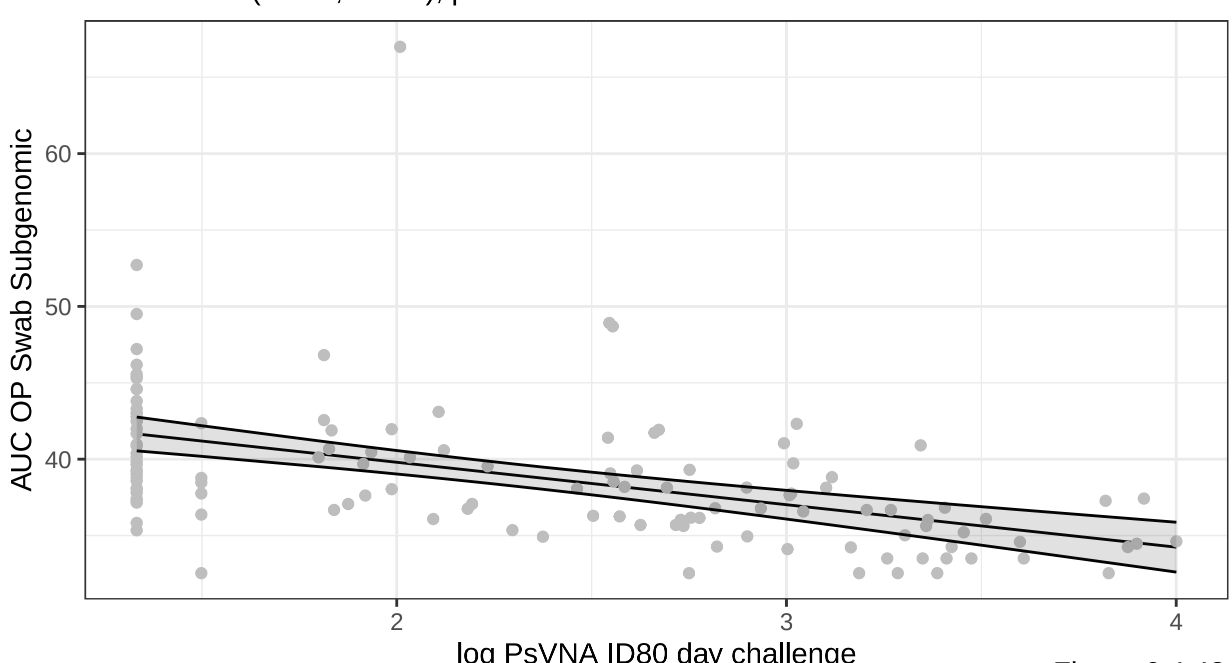


Figure 6.4.48

lm

Est. = −0.66 (−0.86, −0.45), p<0.001

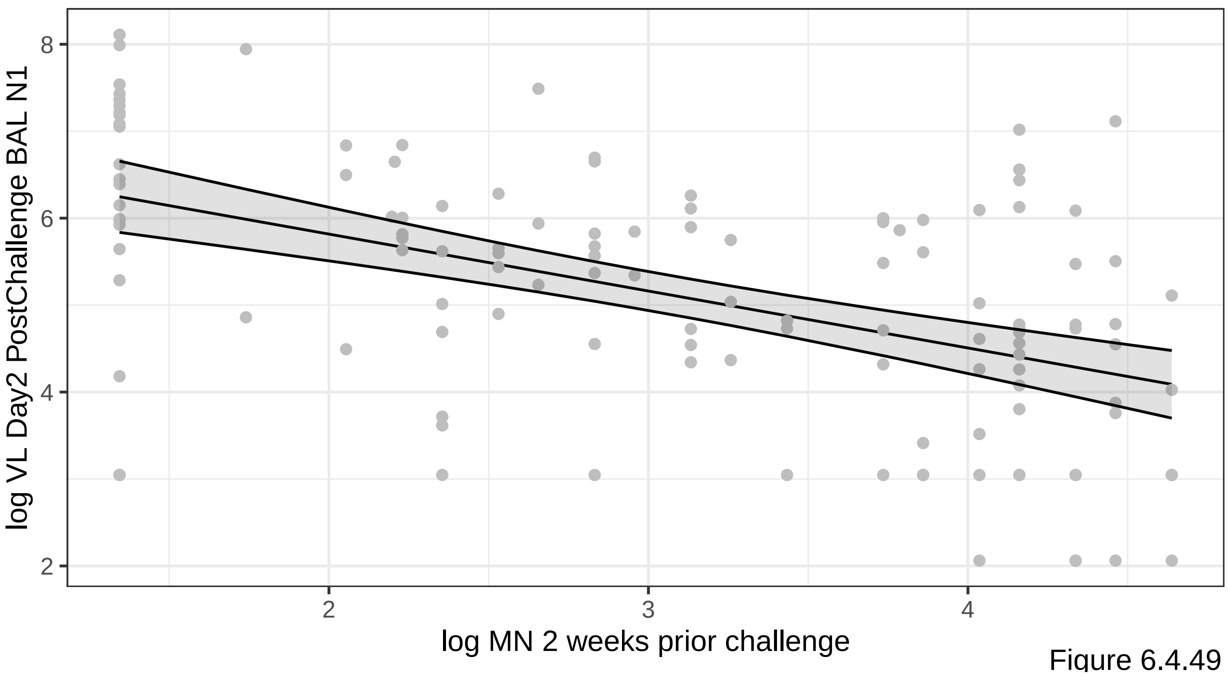


Figure 6.4.49

lm

Est. = −0.89 (−1.11, −0.67), p<0.001

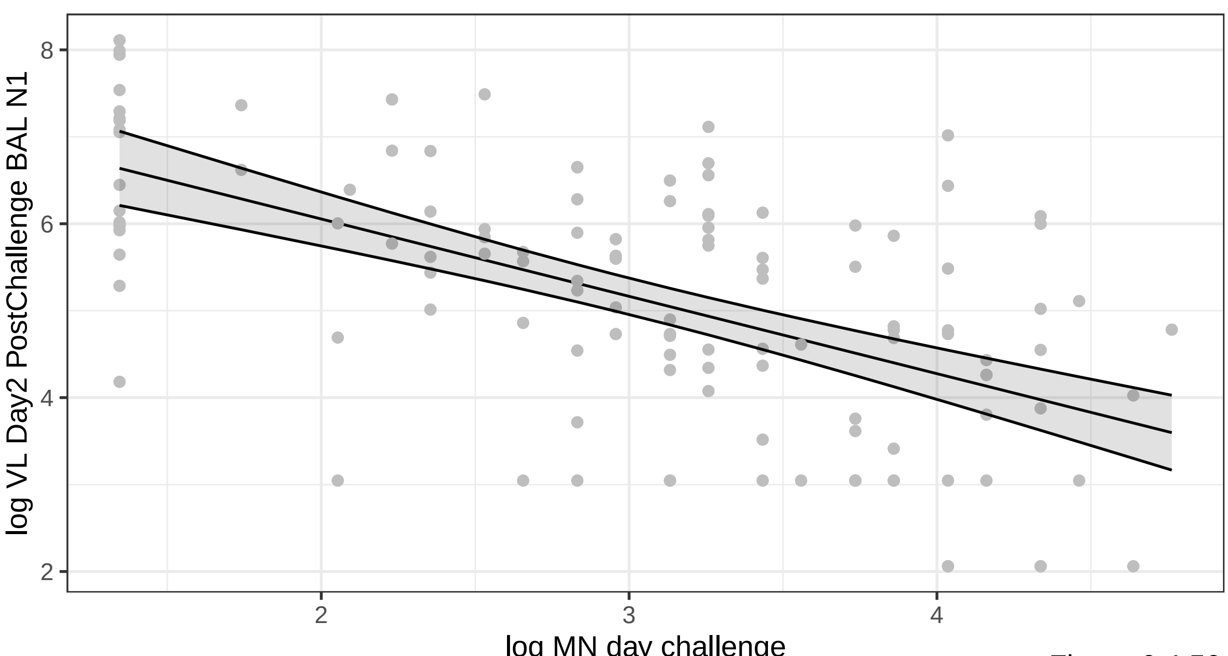


Figure 6.4.50

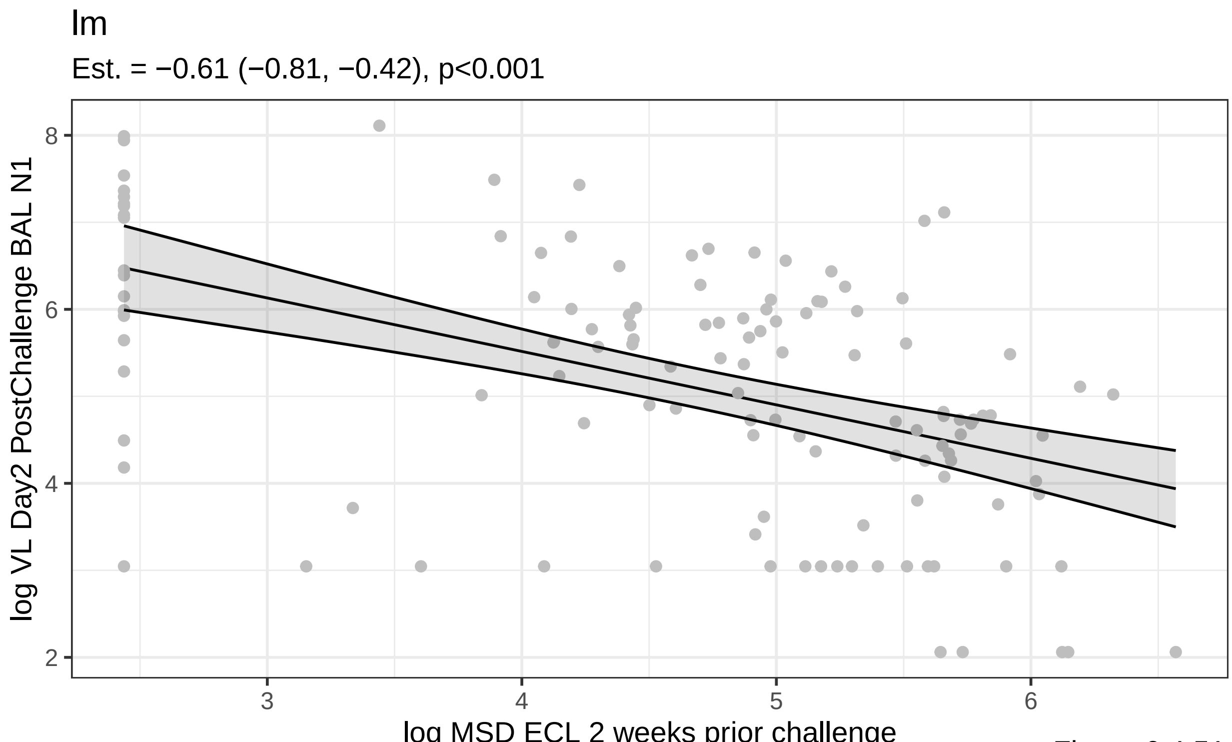


Figure 6.4.51

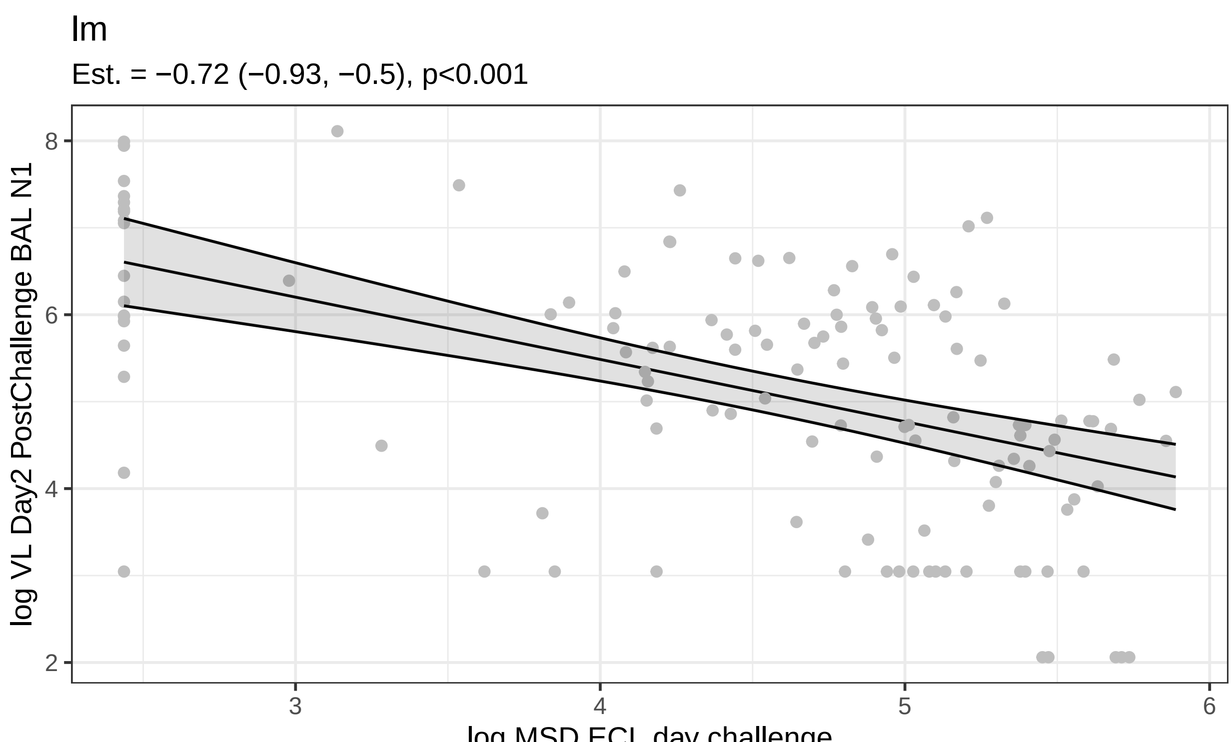


Figure 6.4.52

lm

Est. = −0.9 (−1.16, −0.64), p<0.001

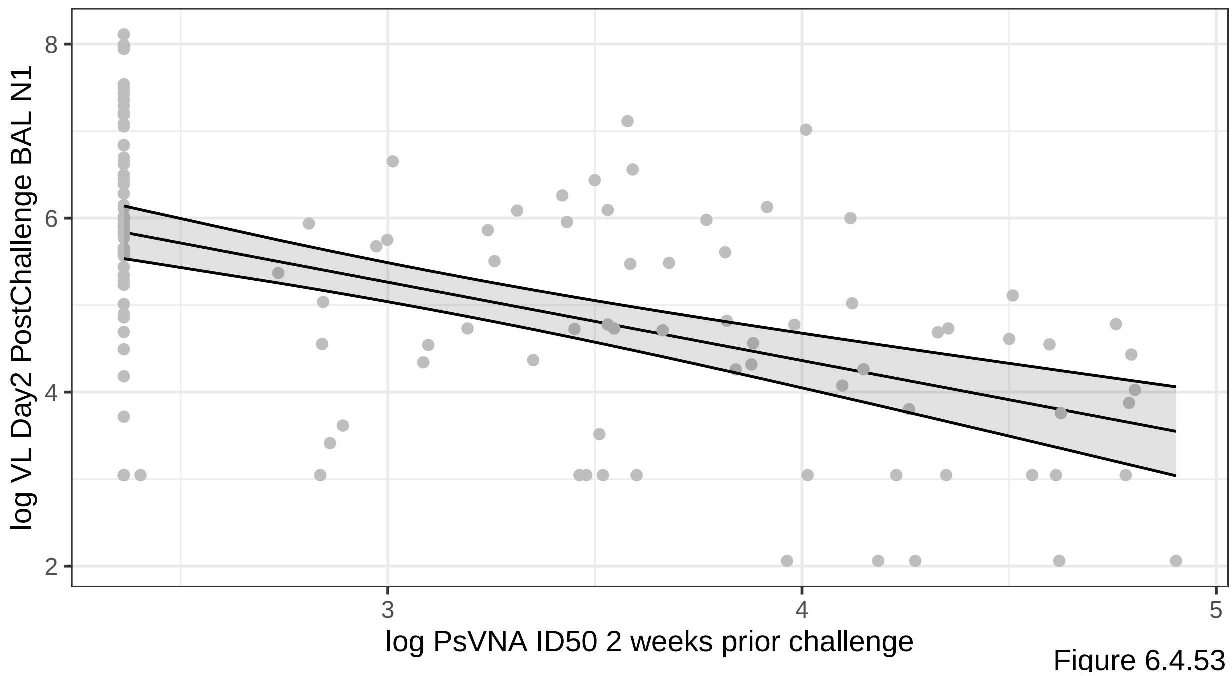


Figure 6.4.53

exp

Est. = 0.83 (0.78, 0.89), p<0.001

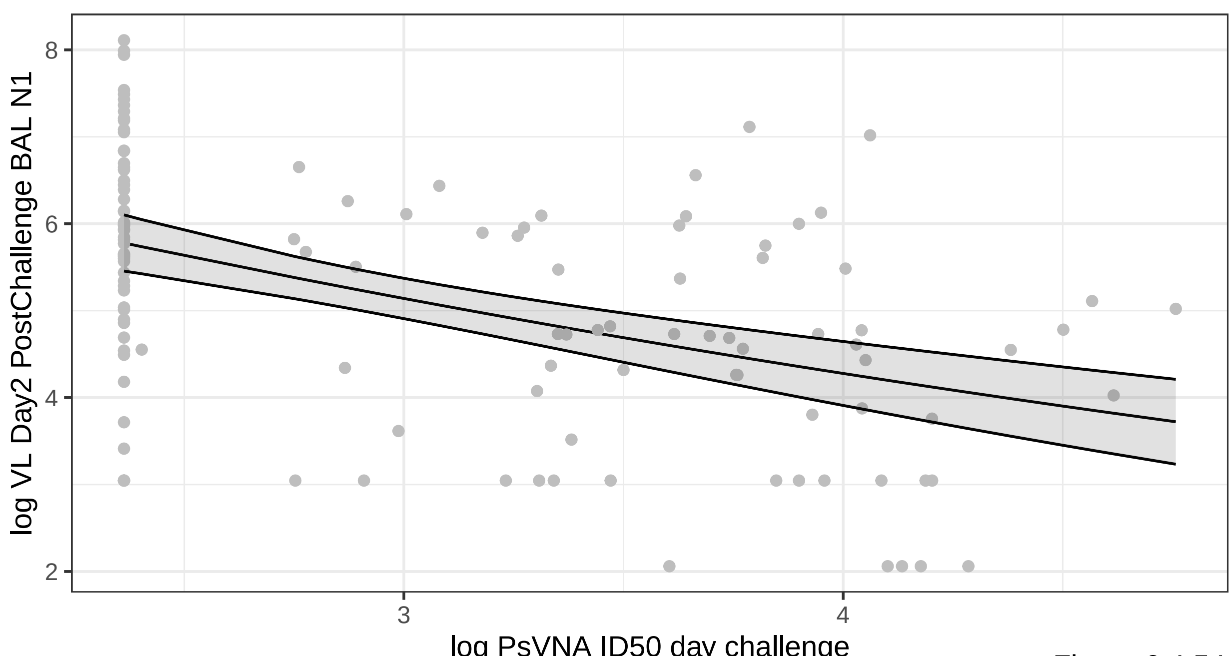


Figure 6.4.54

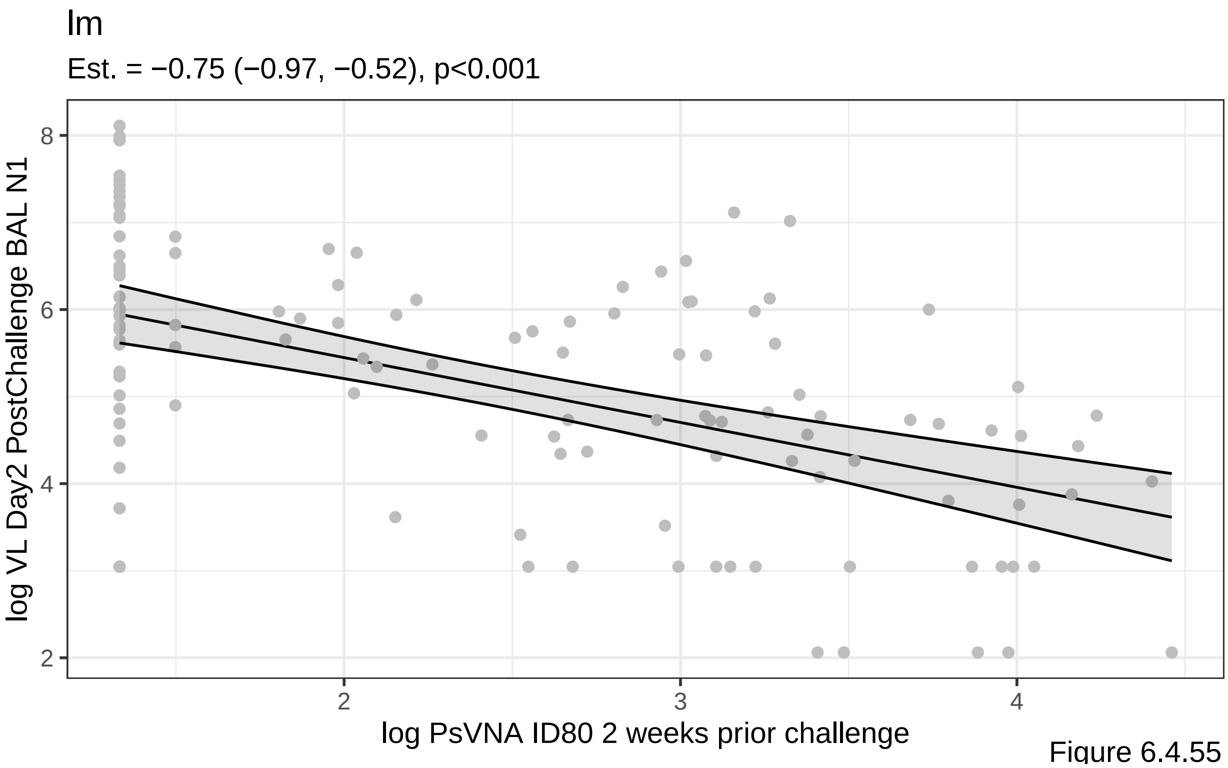


Figure 6.4.55

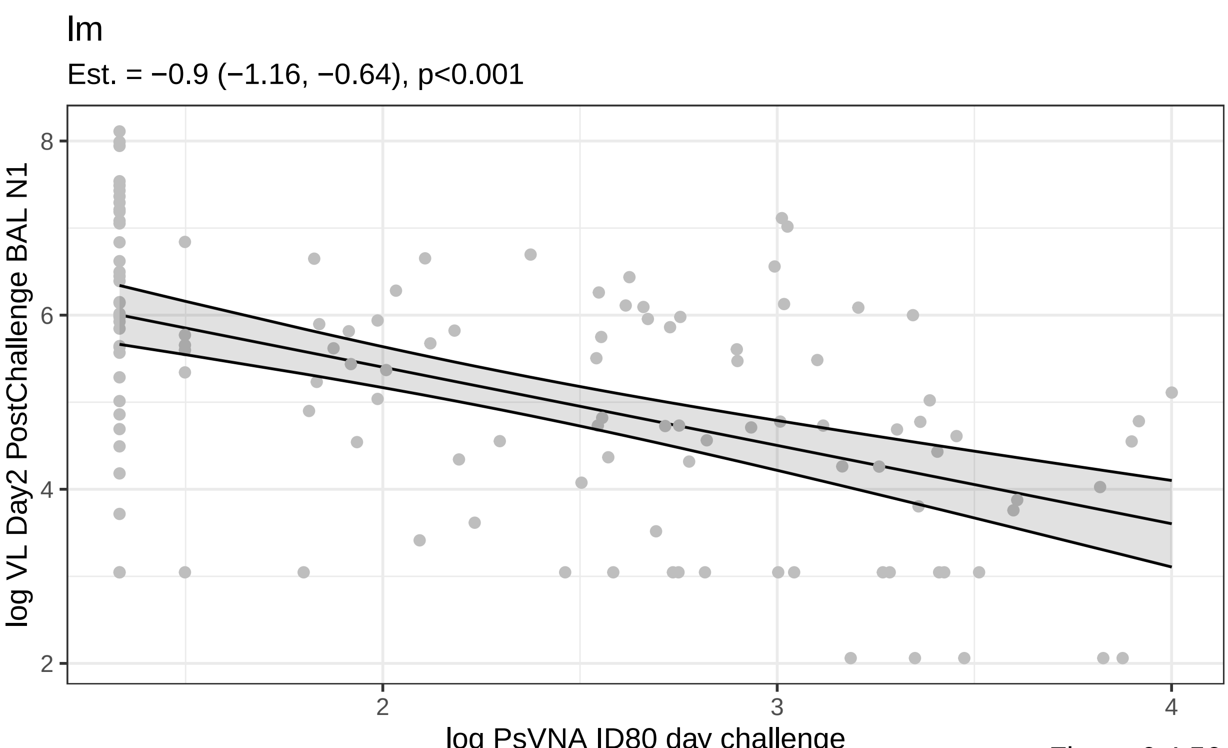


Figure 6.4.56

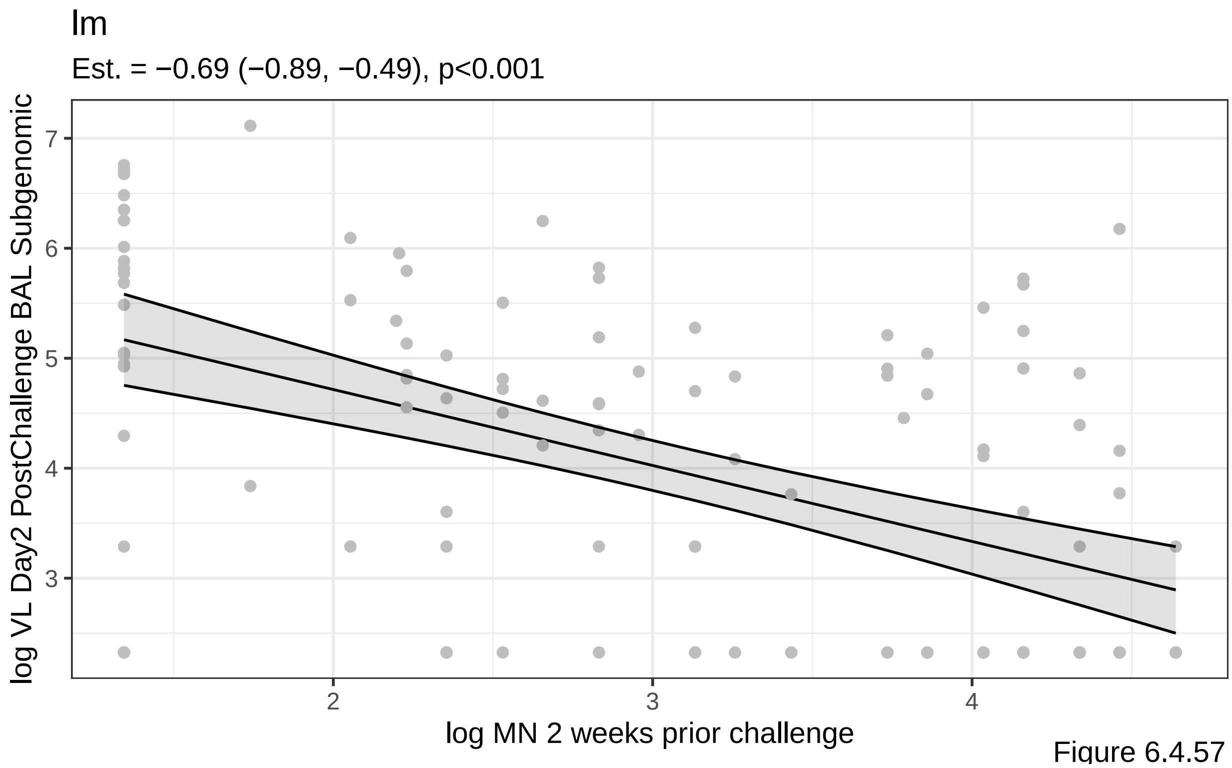


Figure 6.4.57

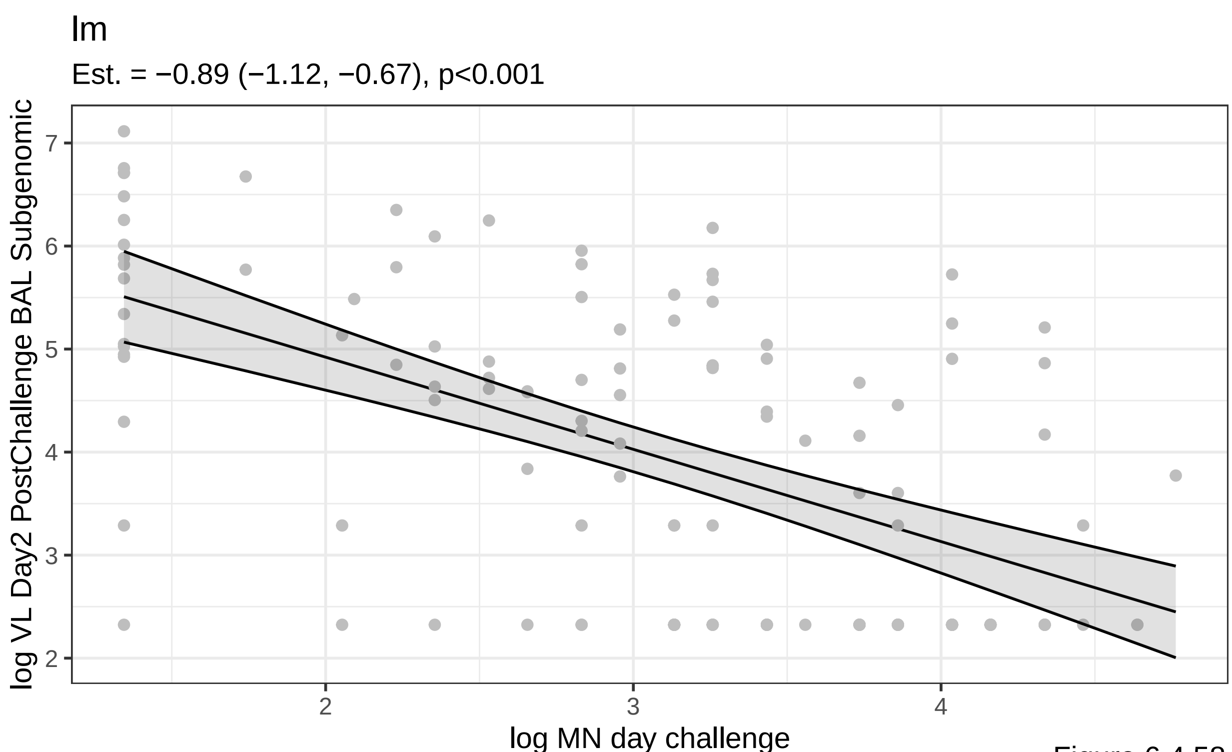


Figure 6.4.58

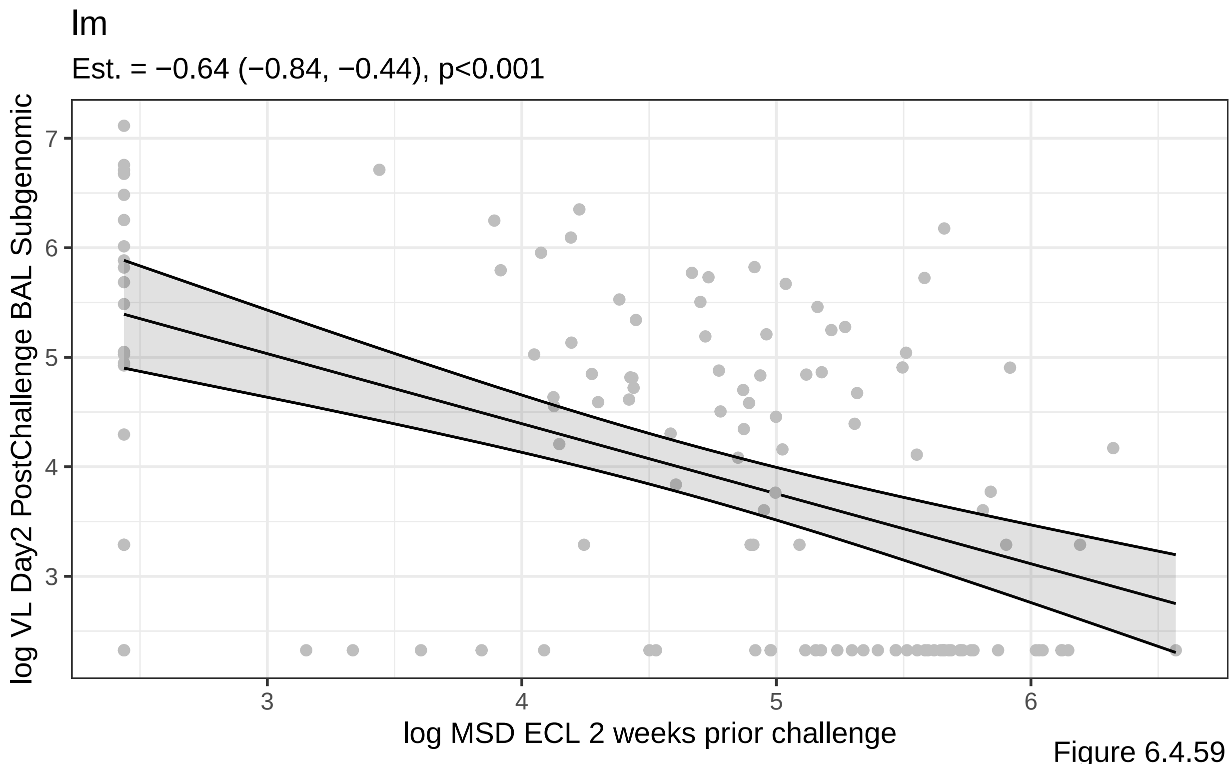


Figure 6.4.59

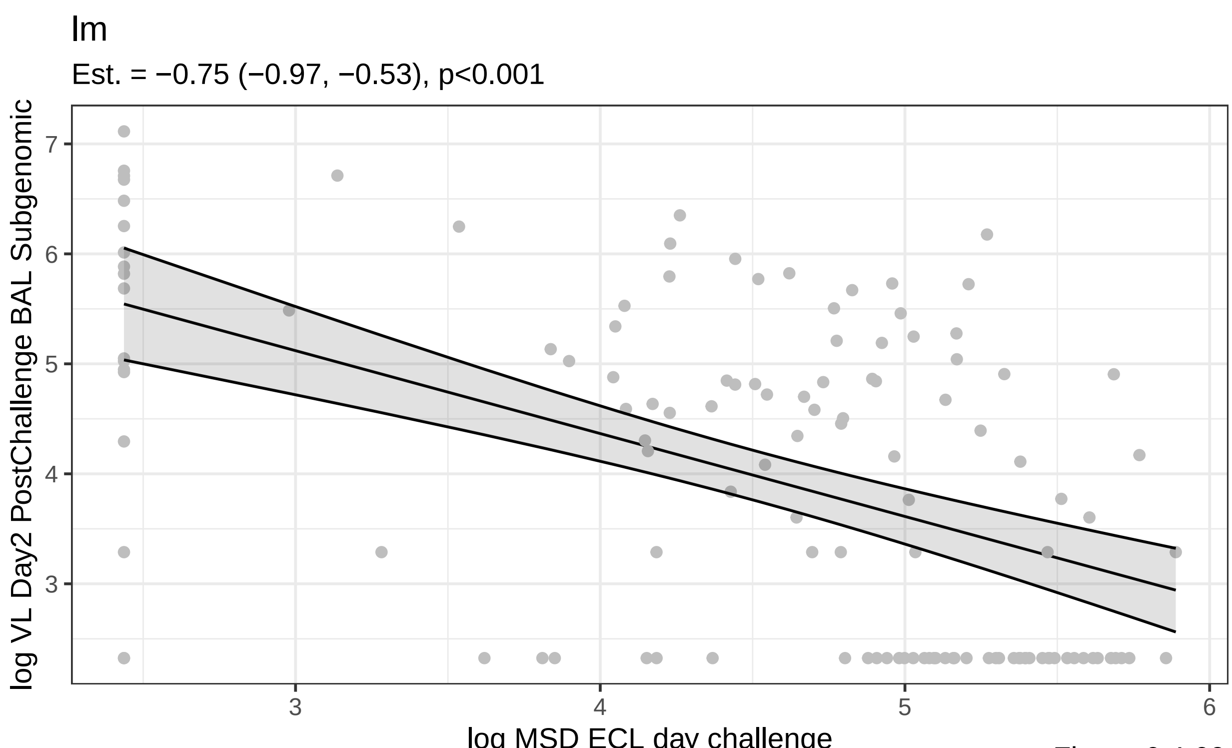


Figure 6.4.60

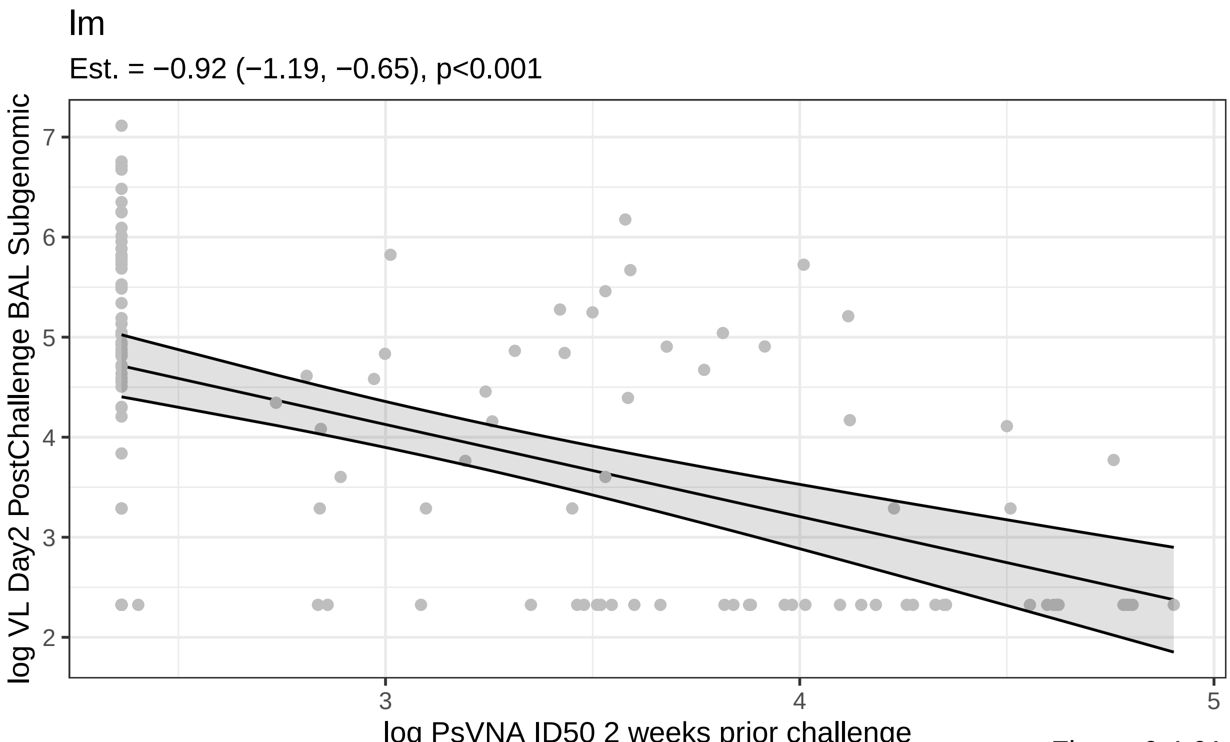


Figure 6.4.61

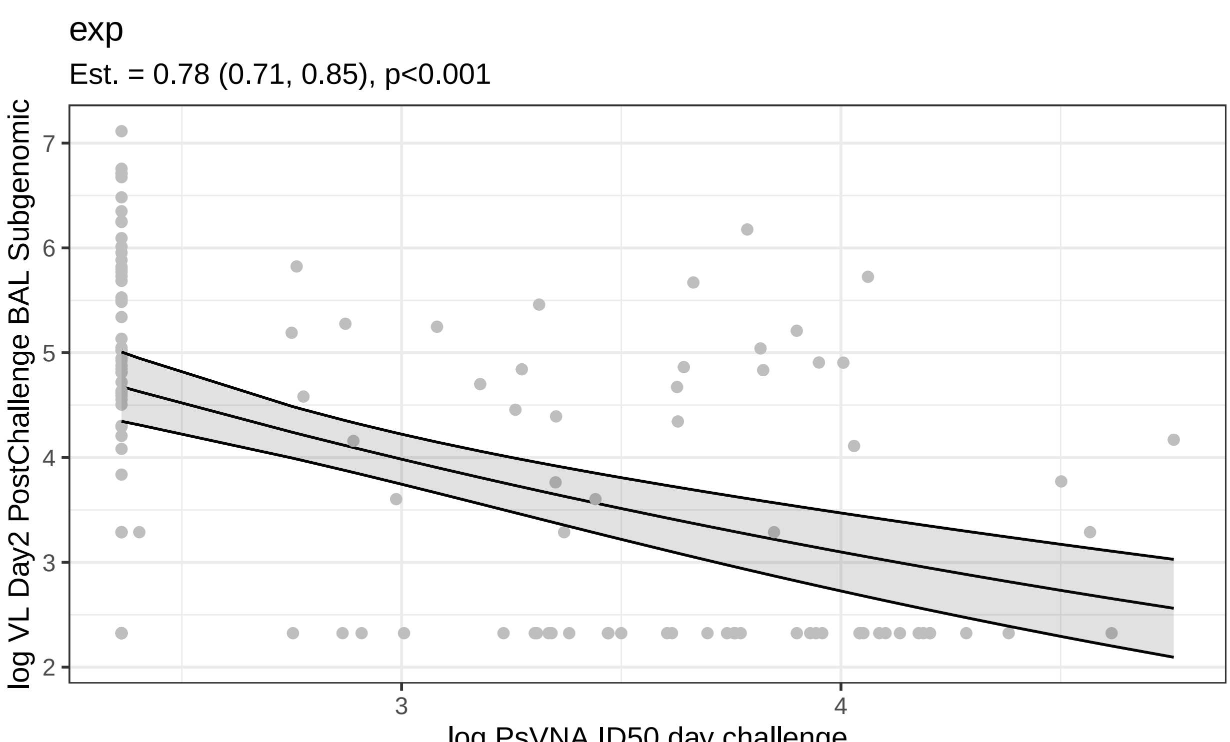


Figure 6.4.62

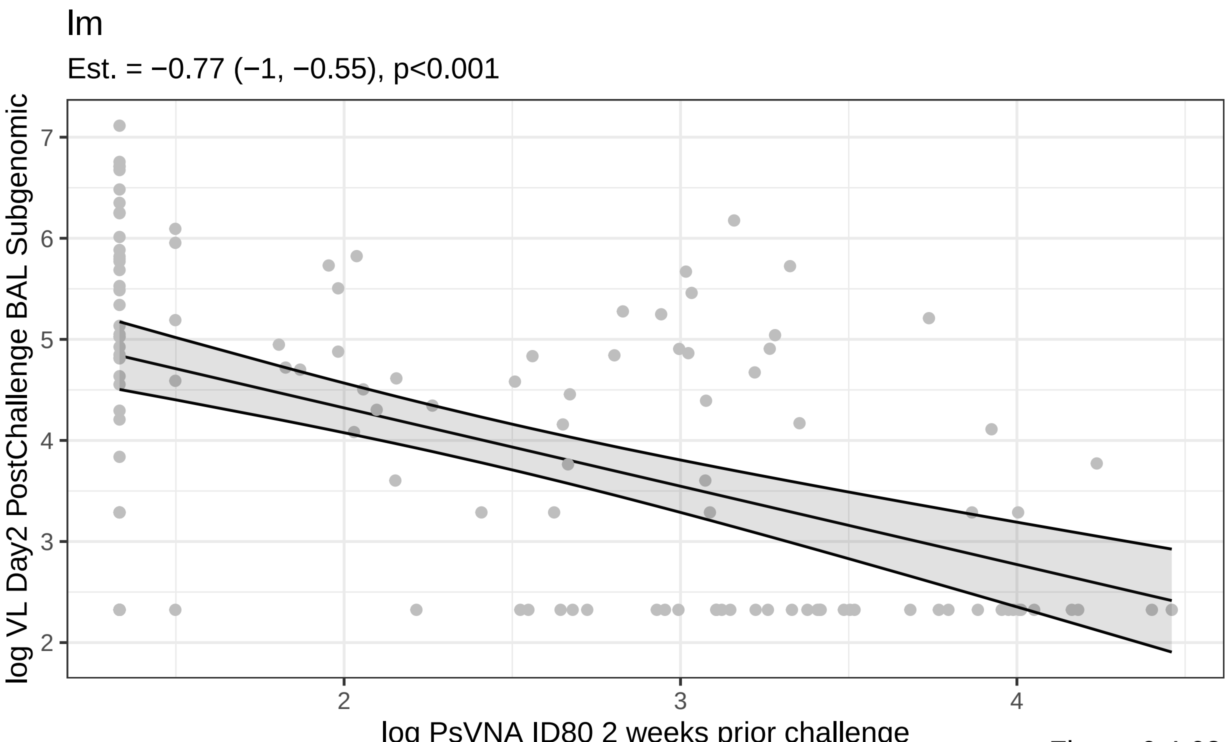


Figure 6.4.63

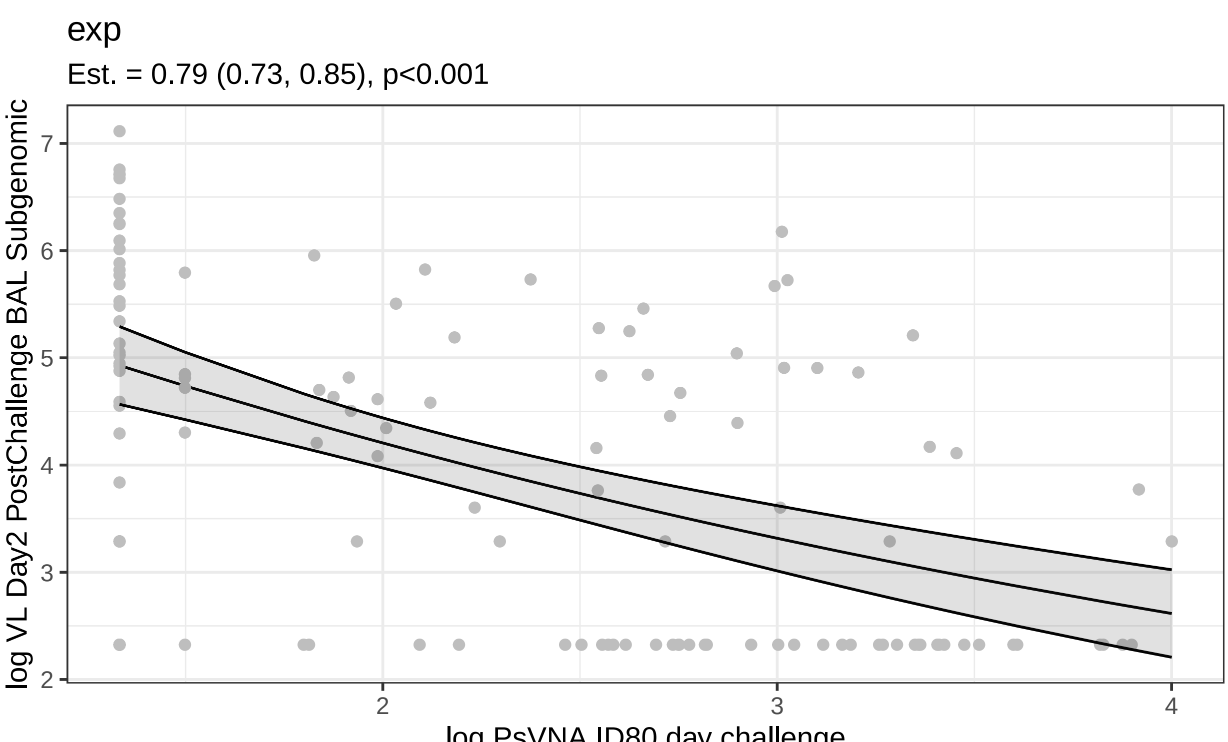


Figure 6.4.64

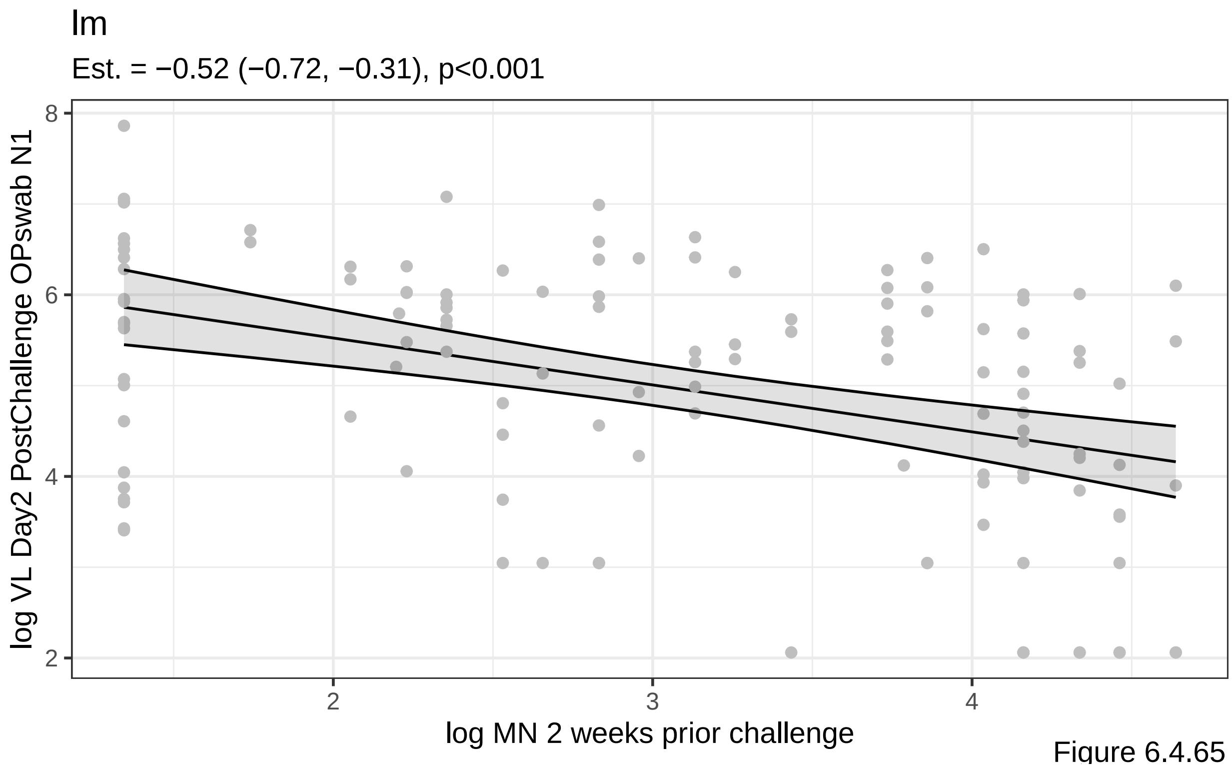


Figure 6.4.65

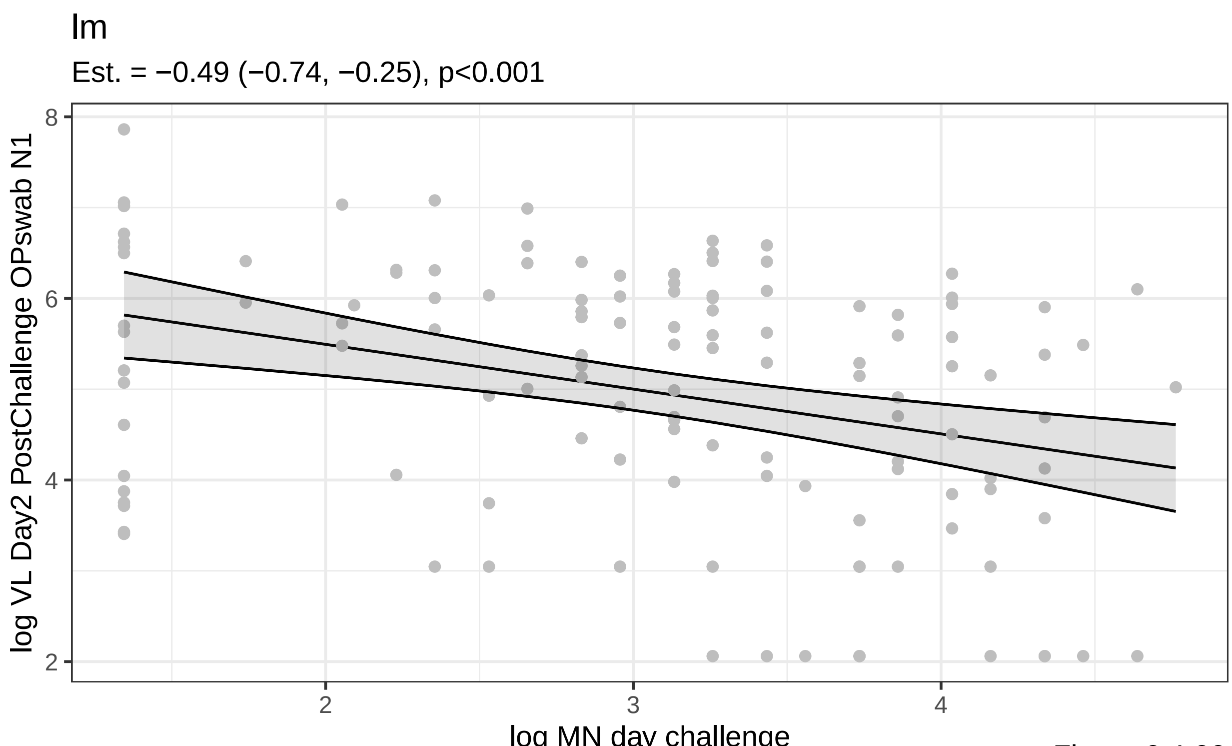


Figure 6.4.66

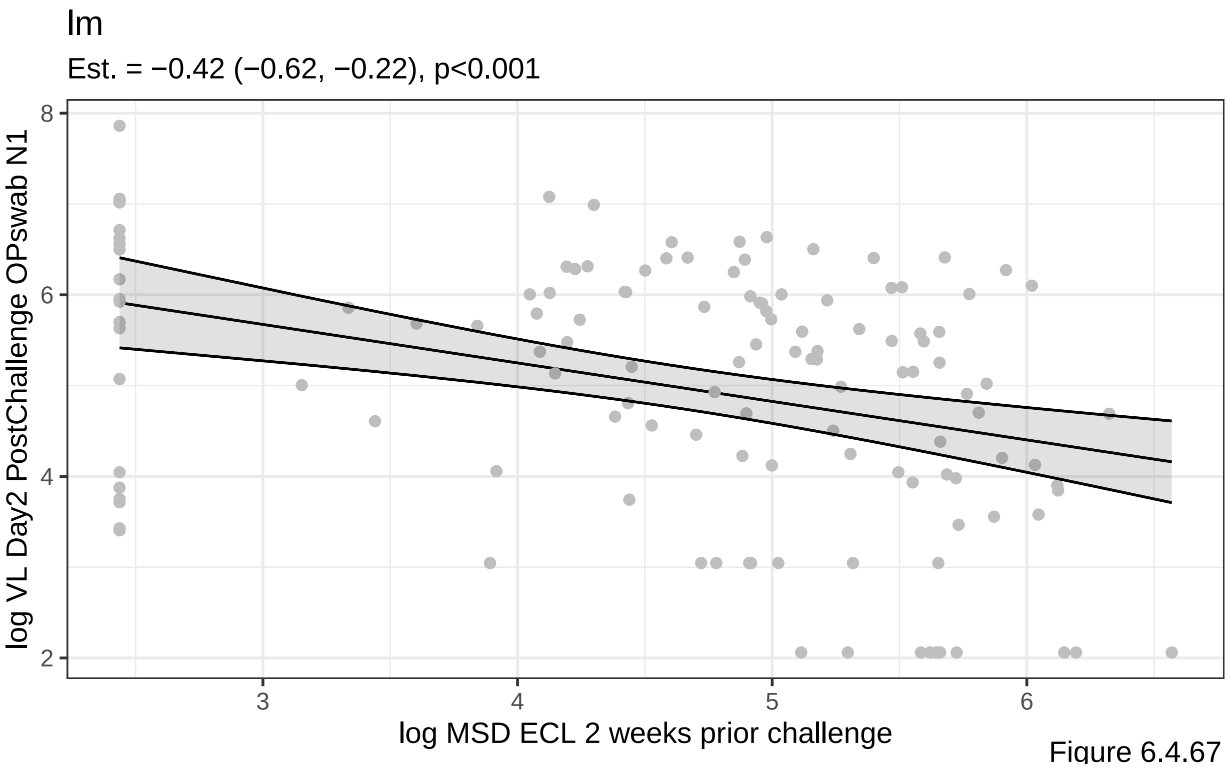


Figure 6.4.67

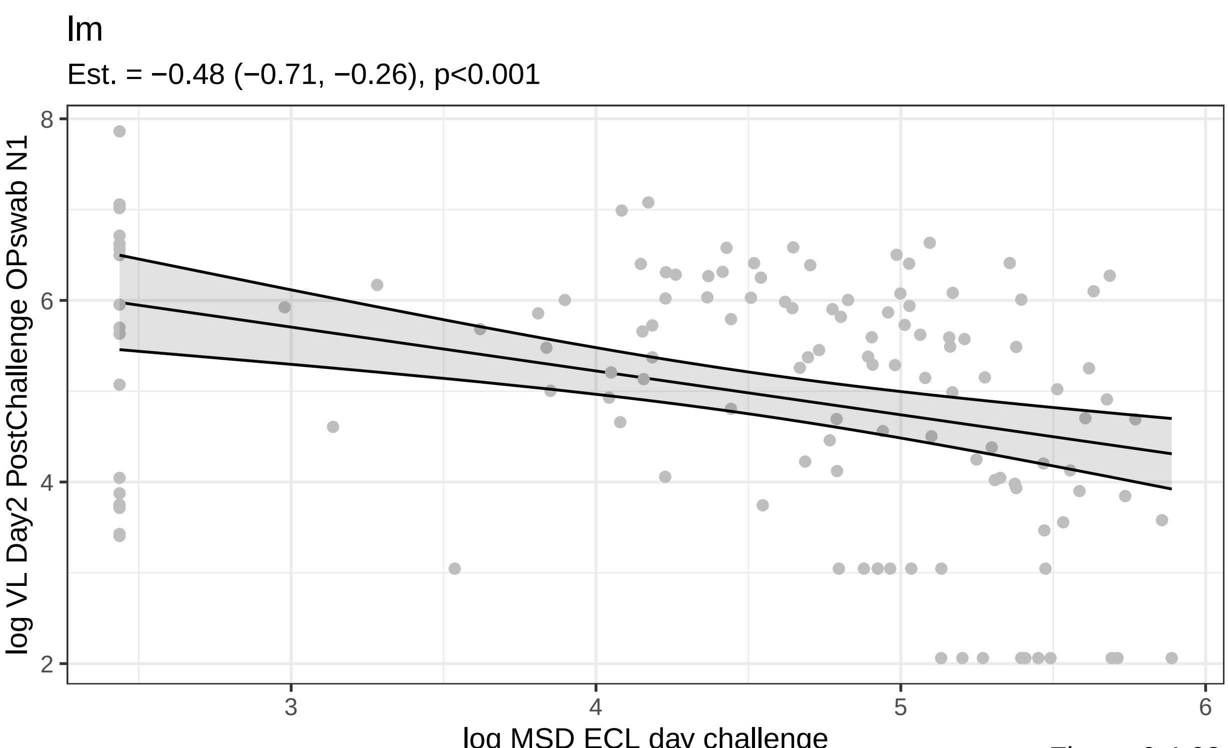


Figure 6.4.68

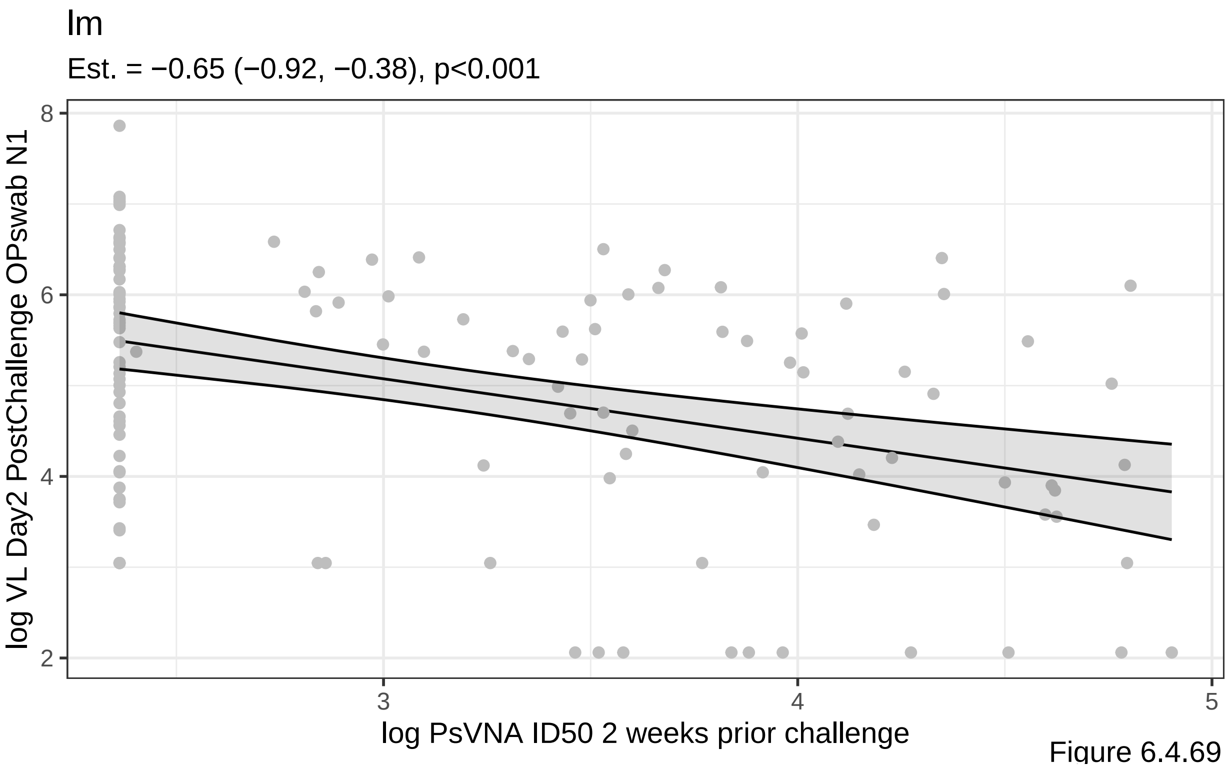


Figure 6.4.69

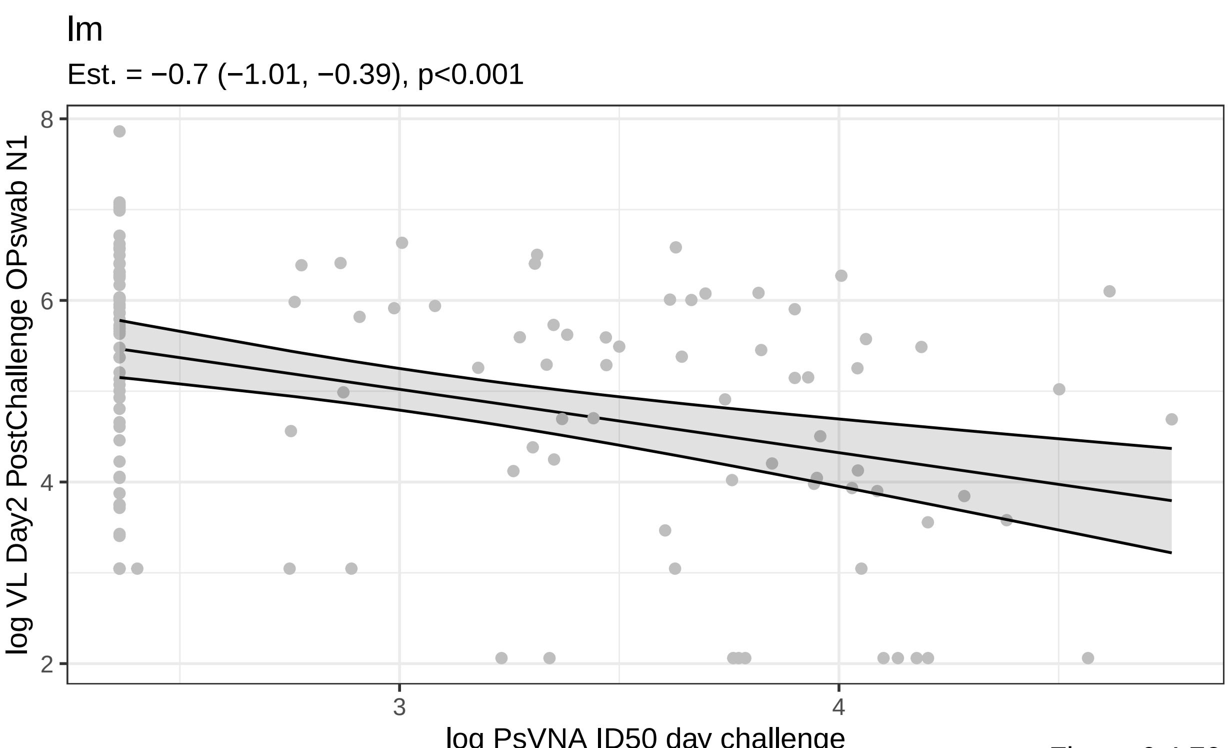


Figure 6.4.70

lm

Est. = −0.57 (−0.79, −0.34), p<0.001

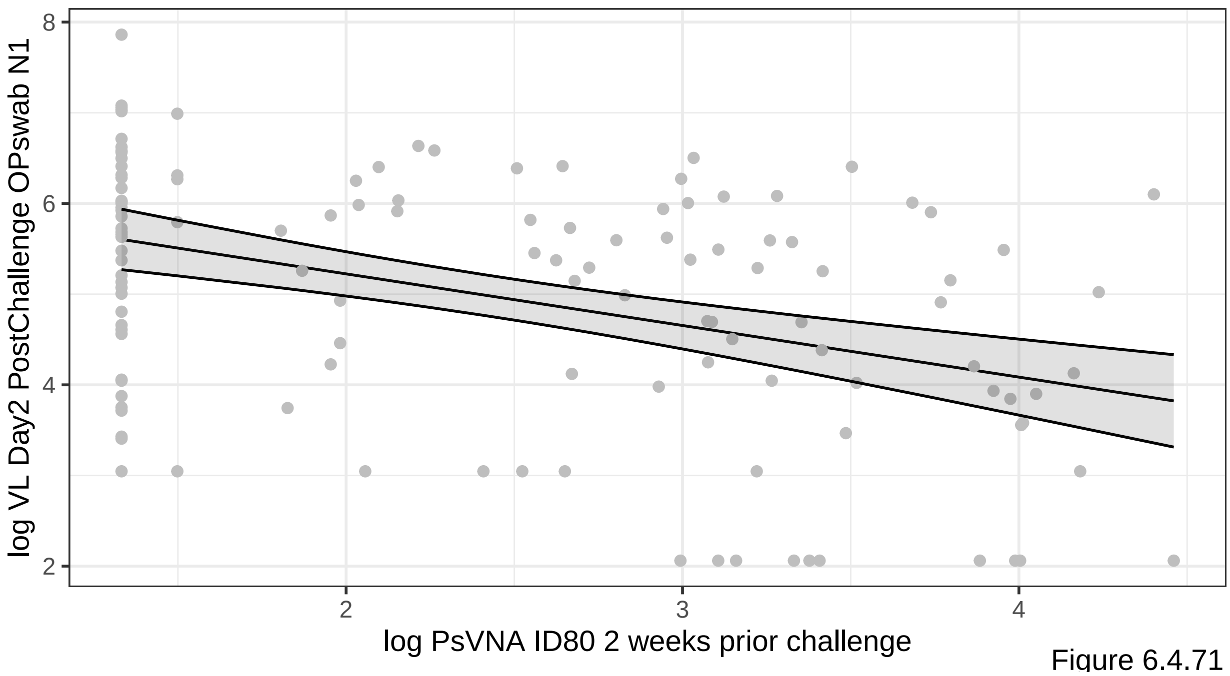


Figure 6.4.71

lm

Est. = −0.69 (−0.95, −0.42), p<0.001

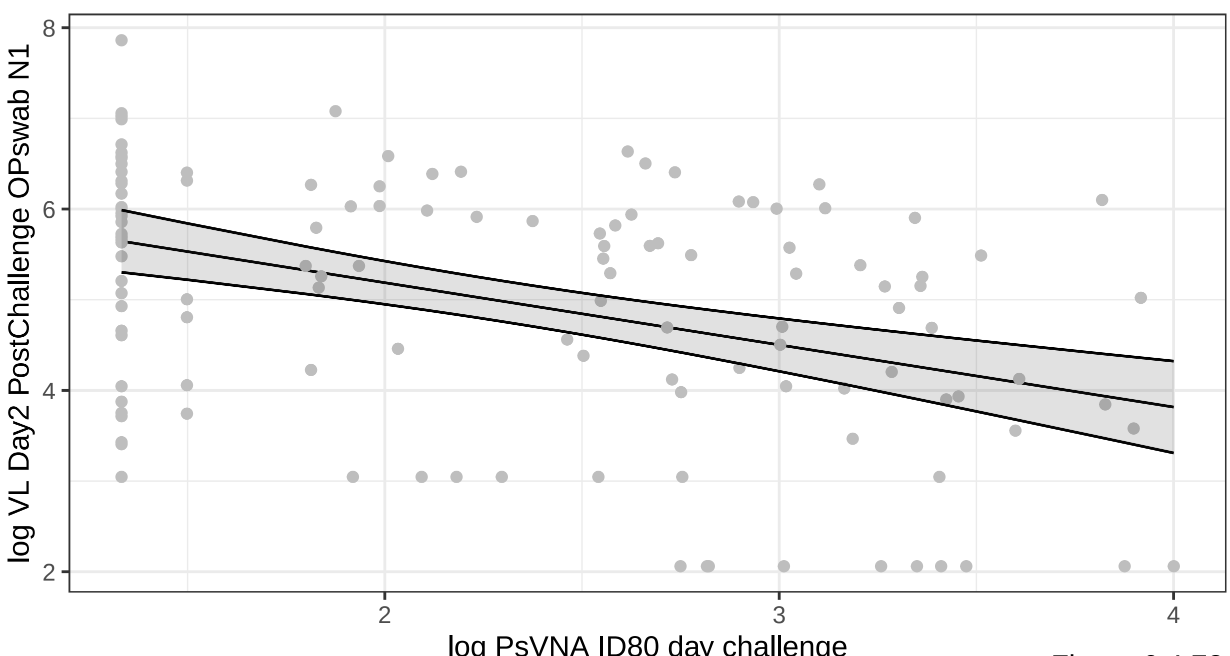


Figure 6.4.72

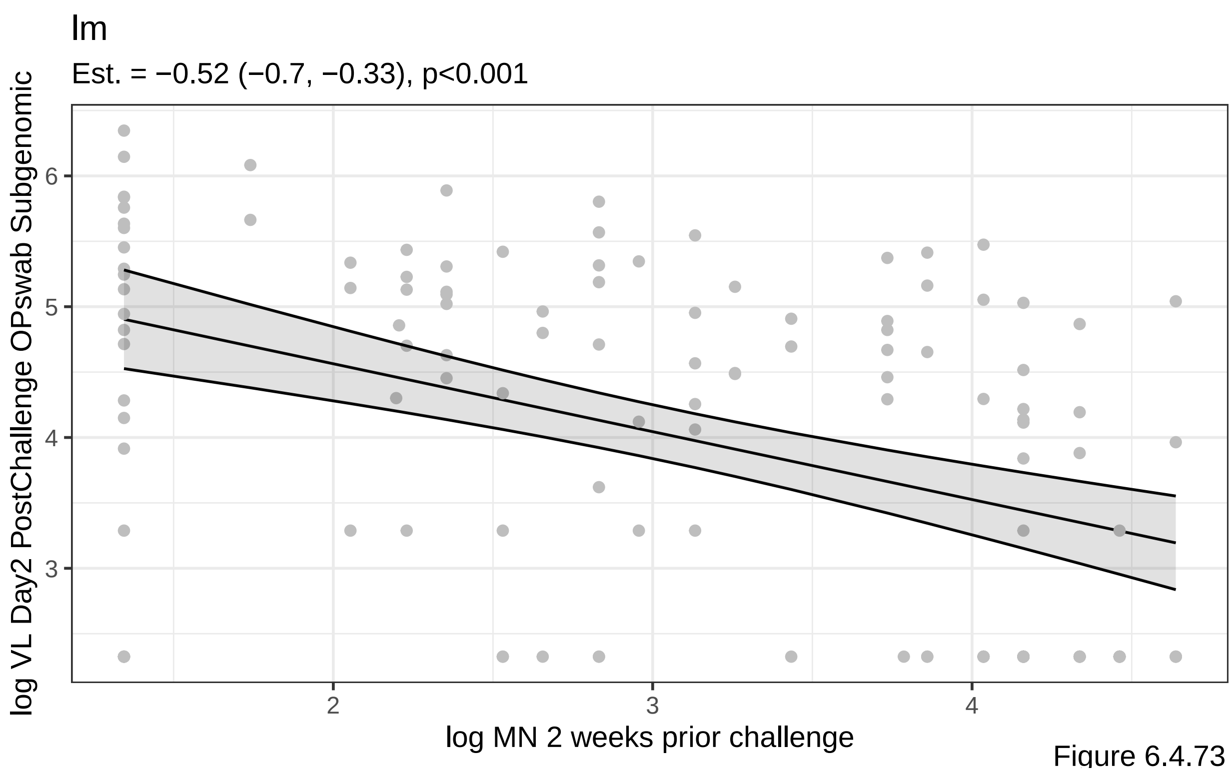


Figure 6.4.73

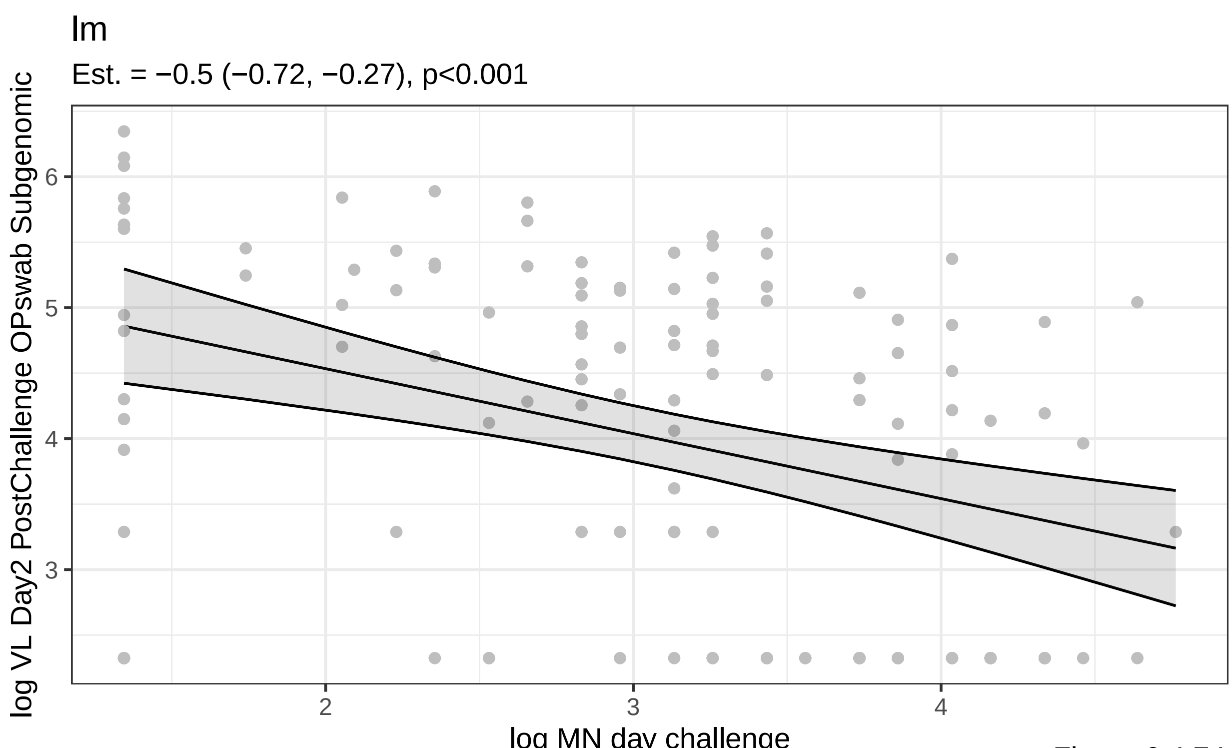


Figure 6.4.74

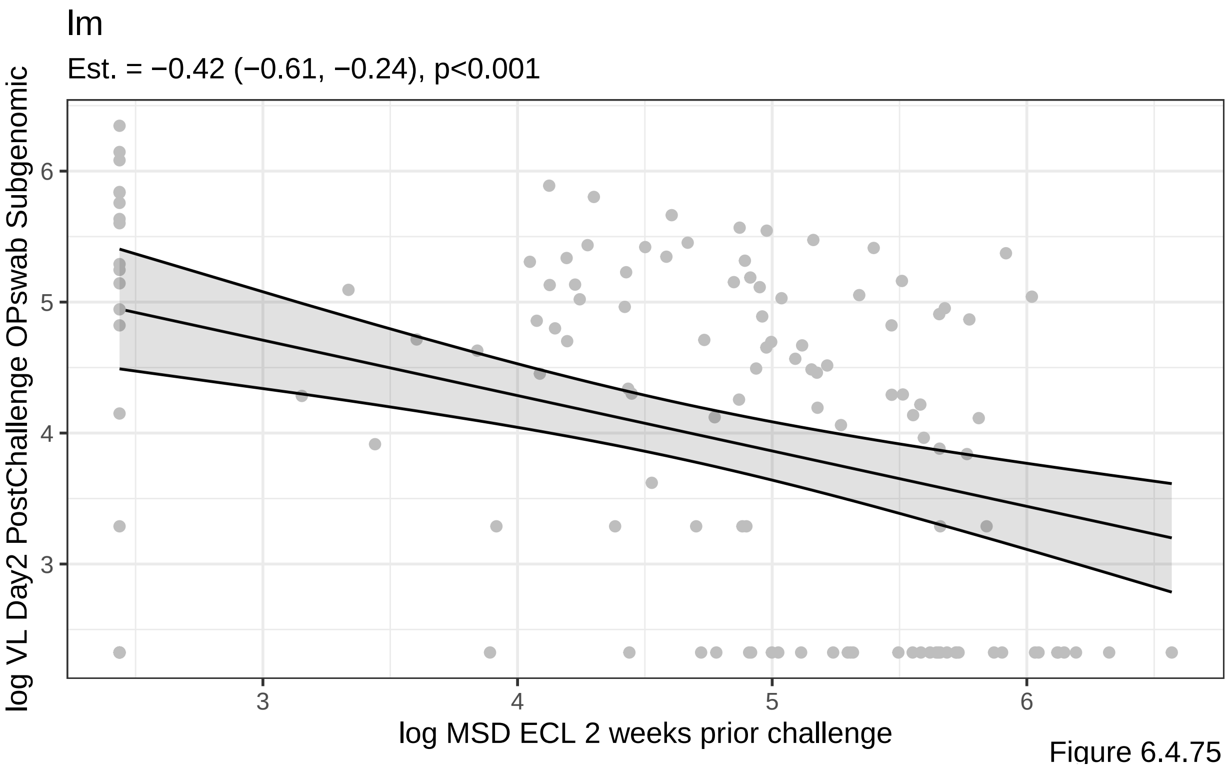


Figure 6.4.75

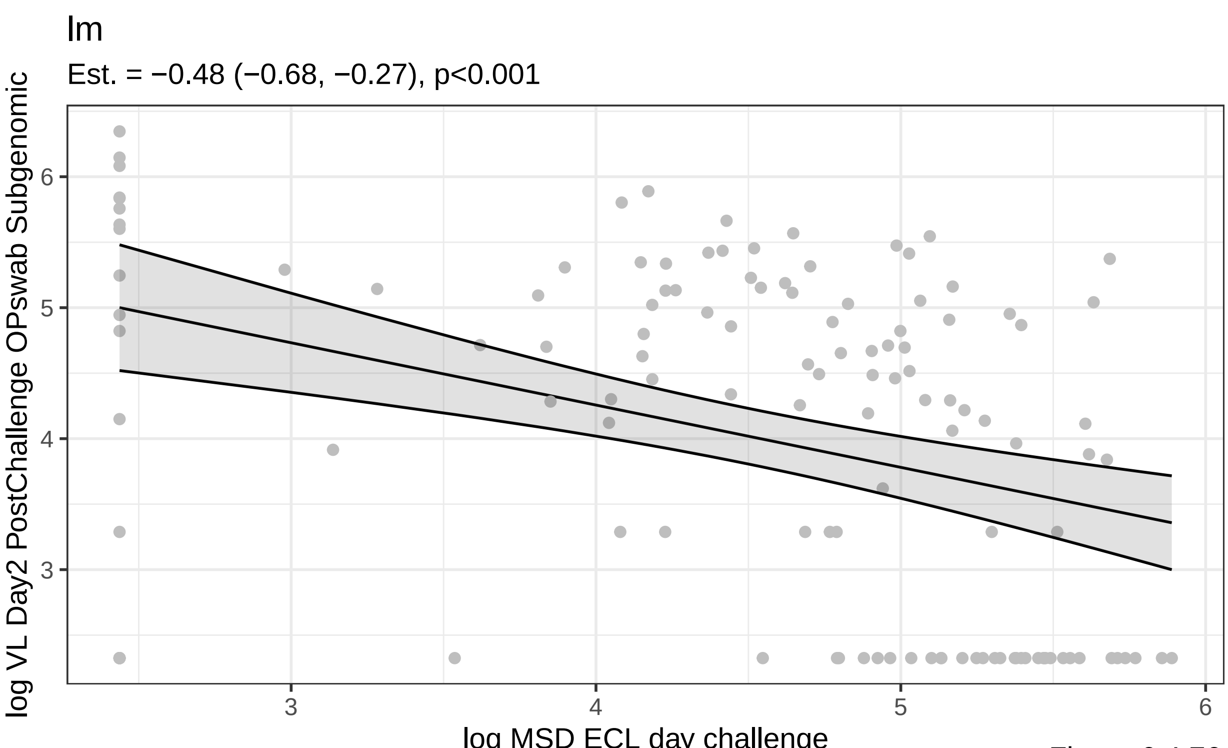


Figure 6.4.76

lm

Est. = −0.68 (−0.93, −0.44), p<0.001

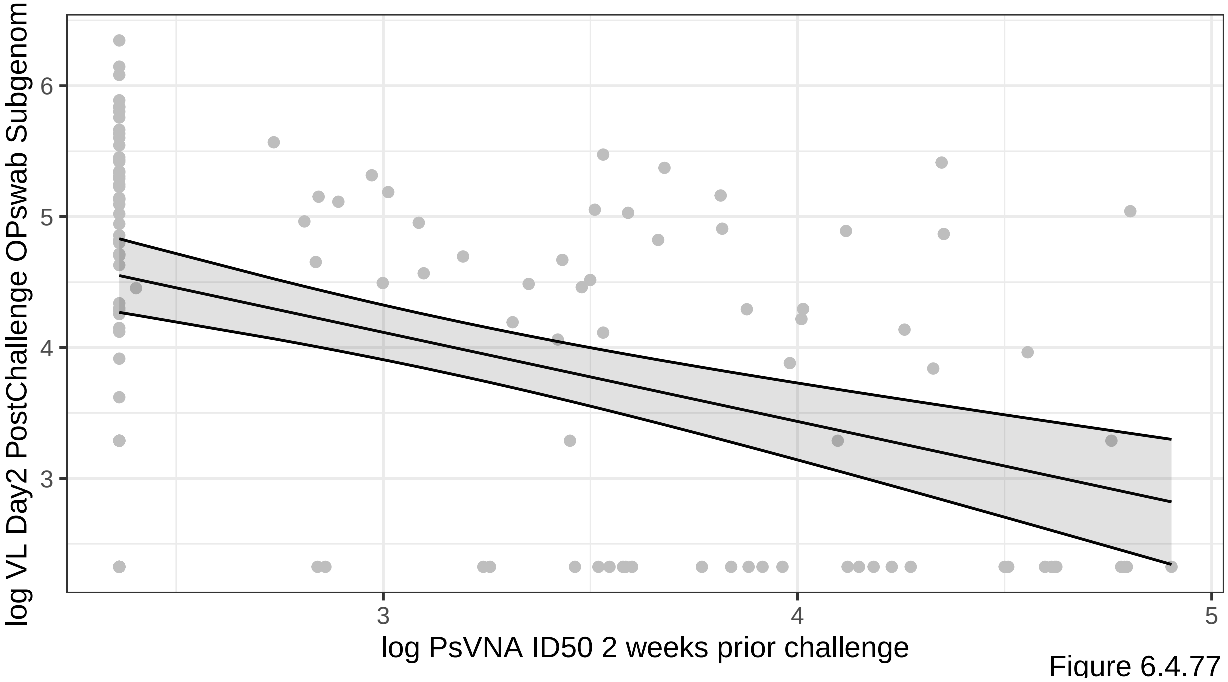


Figure 6.4.77

lm

Est. = −0.74 (−1.03, −0.46), p<0.001

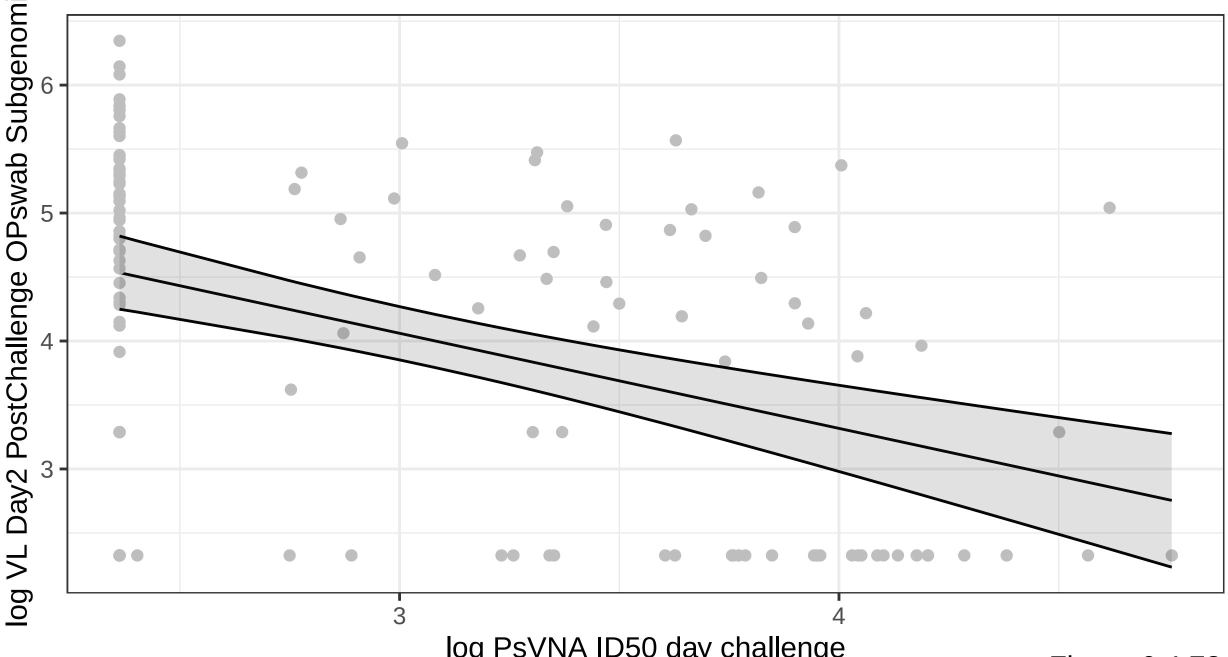


Figure 6.4.78

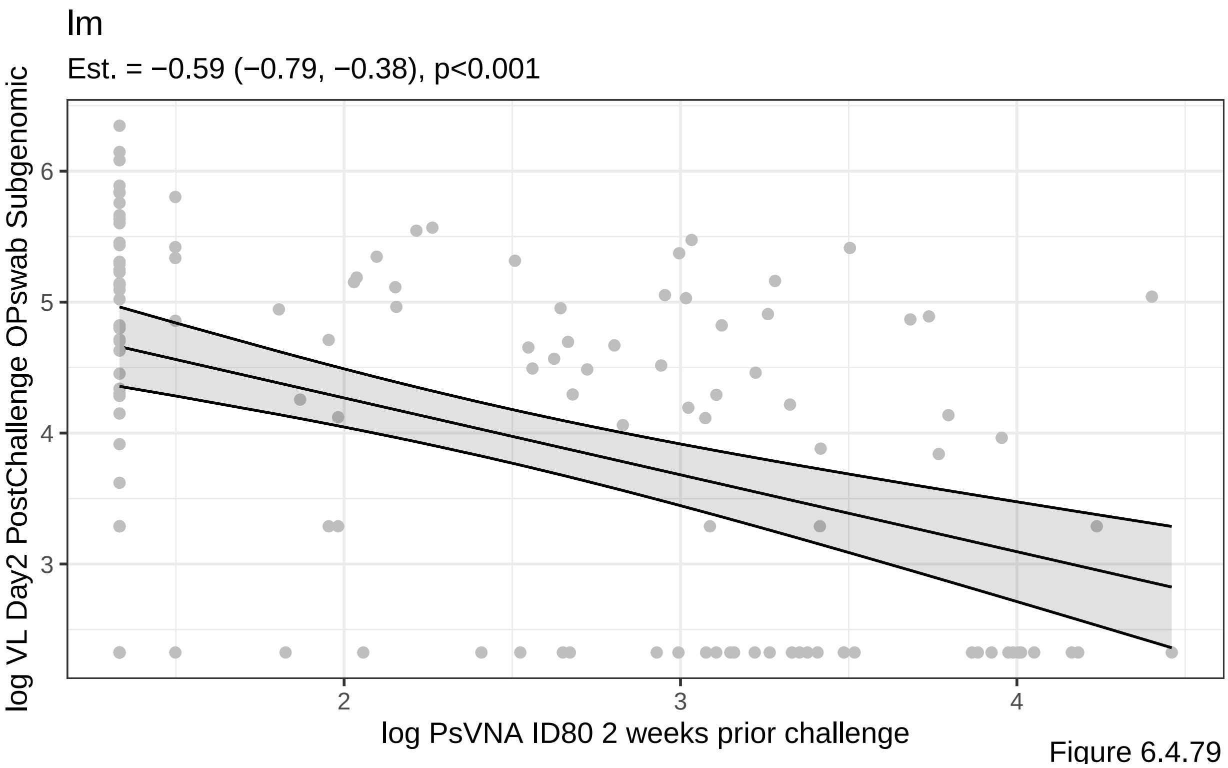


Figure 6.4.79

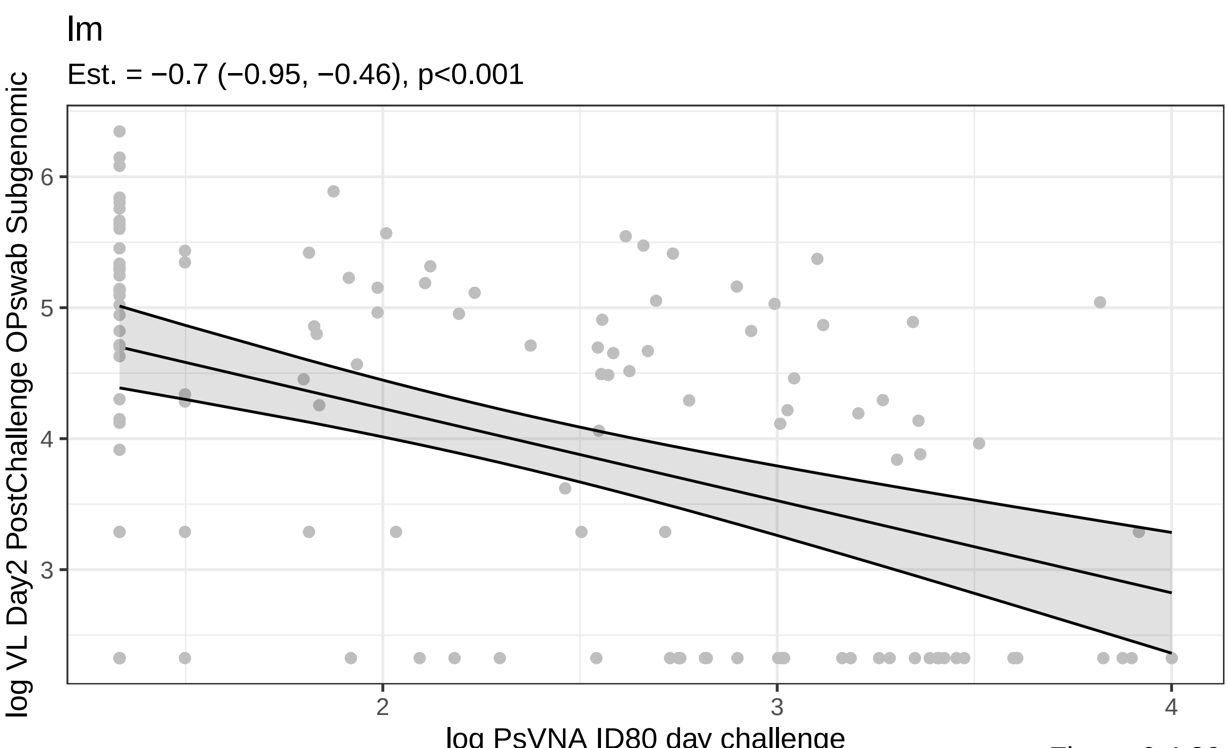


Figure 6.4.80

lm

Est. = −0.78 (−0.94, −0.63), p<0.001

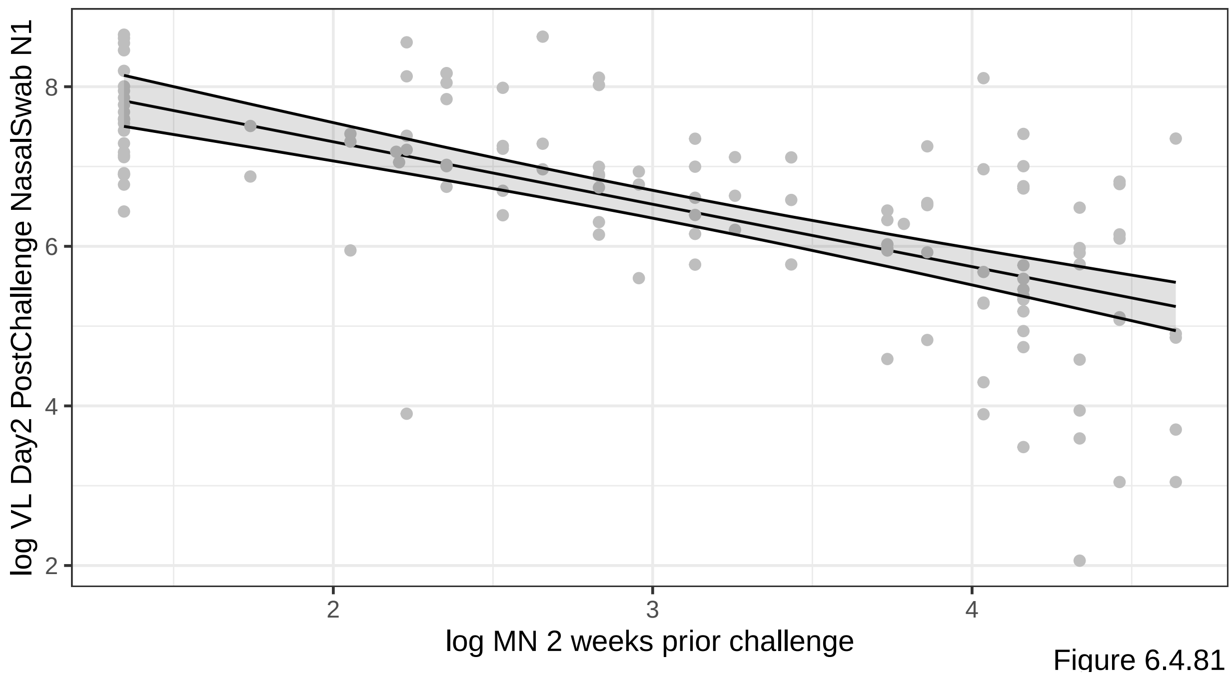


Figure 6.4.81

lm

Est. = −0.84 (−1.03, −0.65), p<0.001

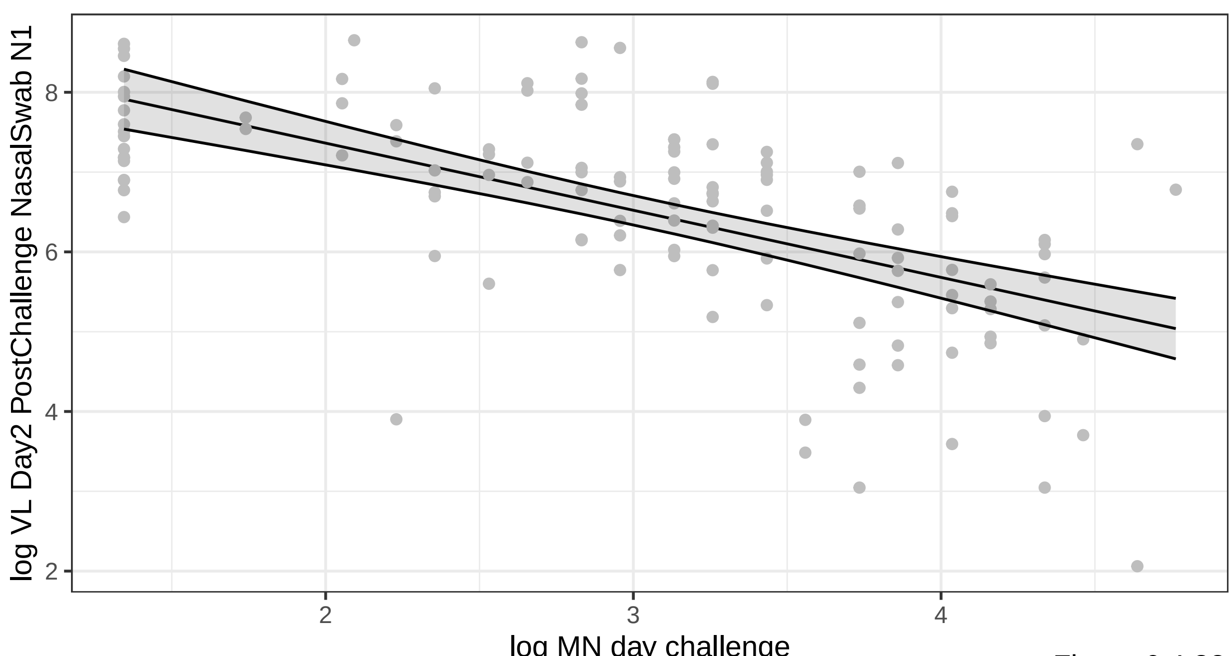


Figure 6.4.82

lm

Est. = −0.71 (−0.87, −0.55), p<0.001

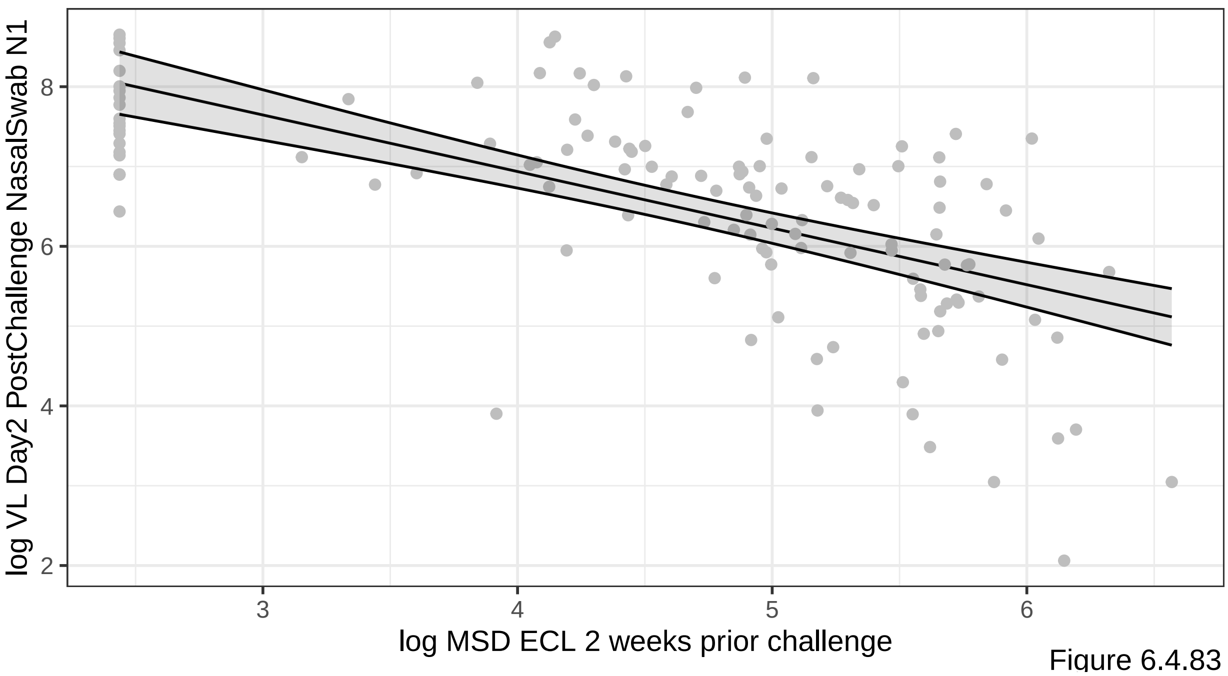


Figure 6.4.83

lm

Est. = −0.76 (−0.95, −0.58), p<0.001

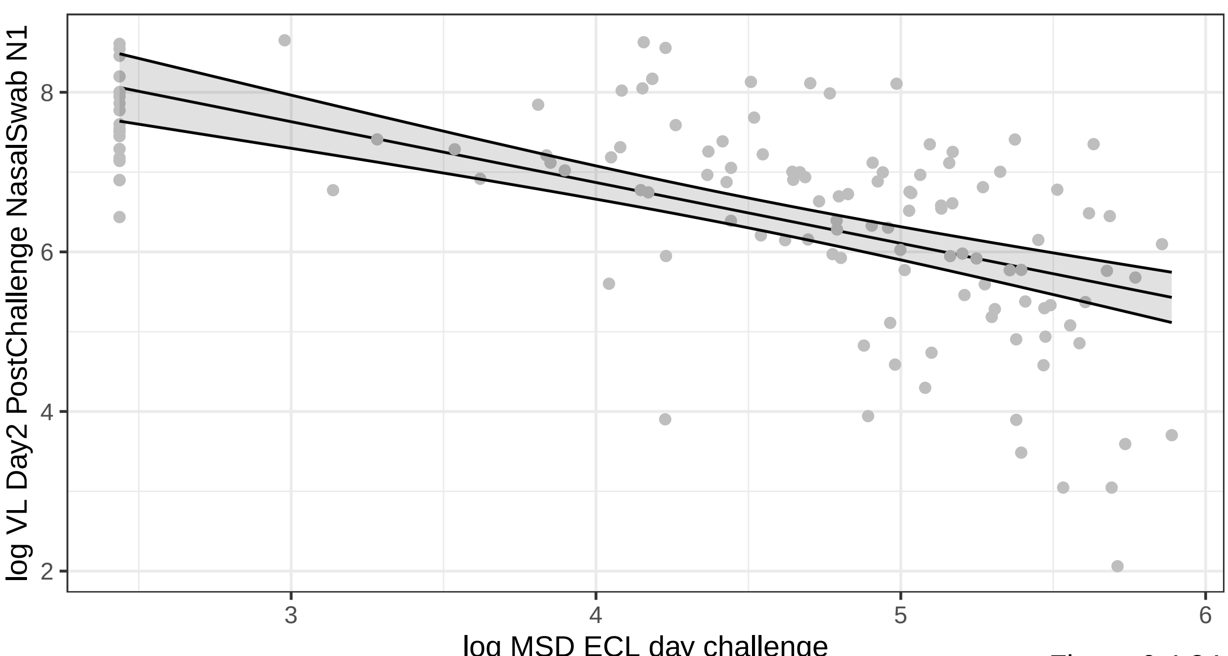


Figure 6.4.84

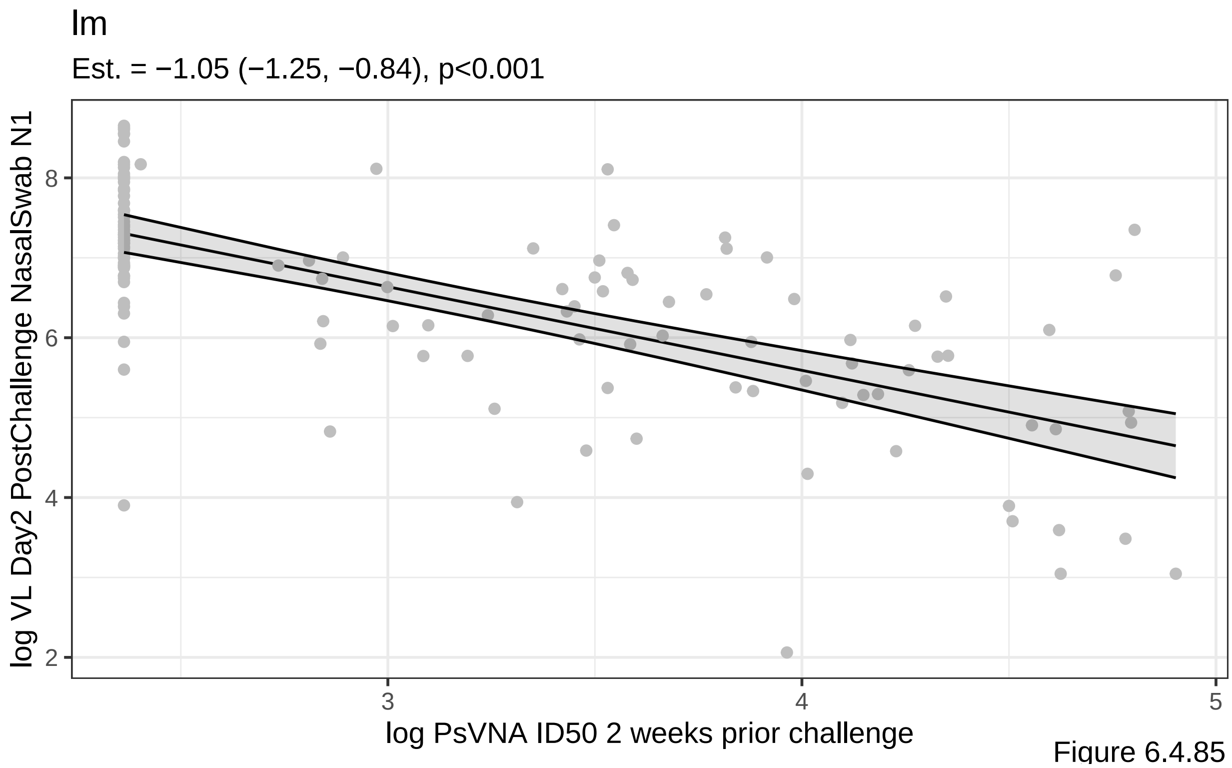


Figure 6.4.85

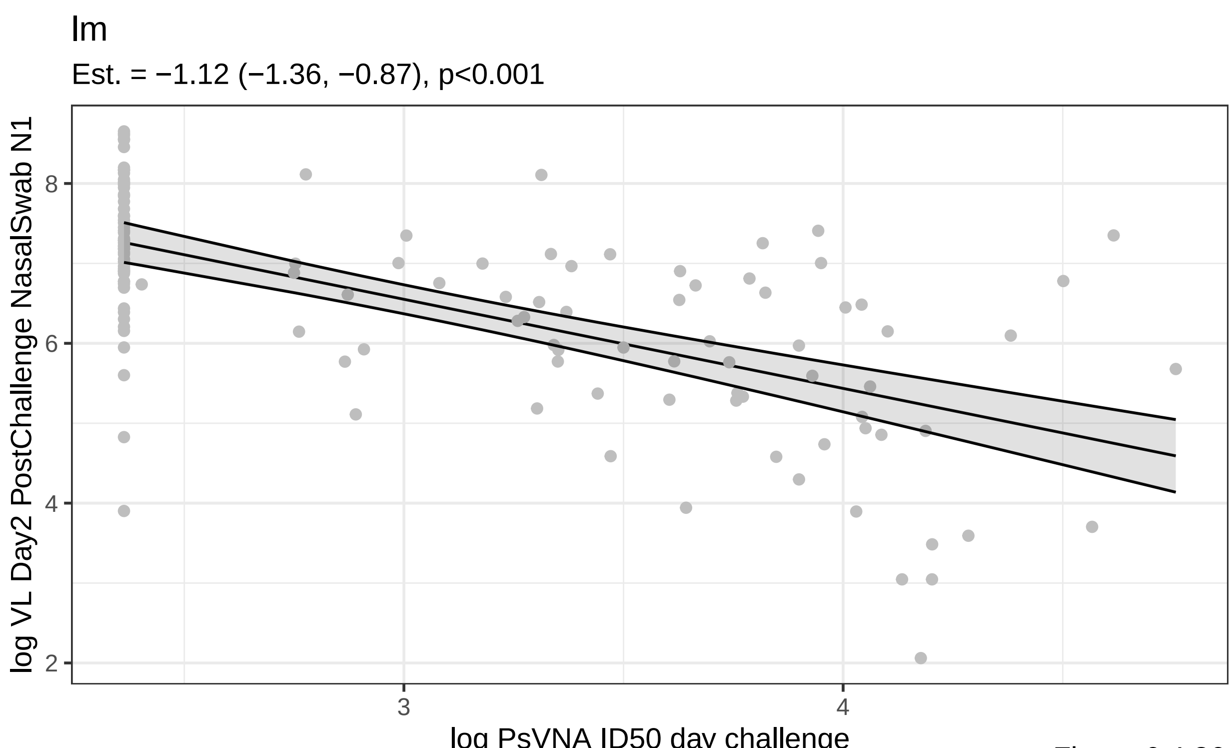


Figure 6.4.86

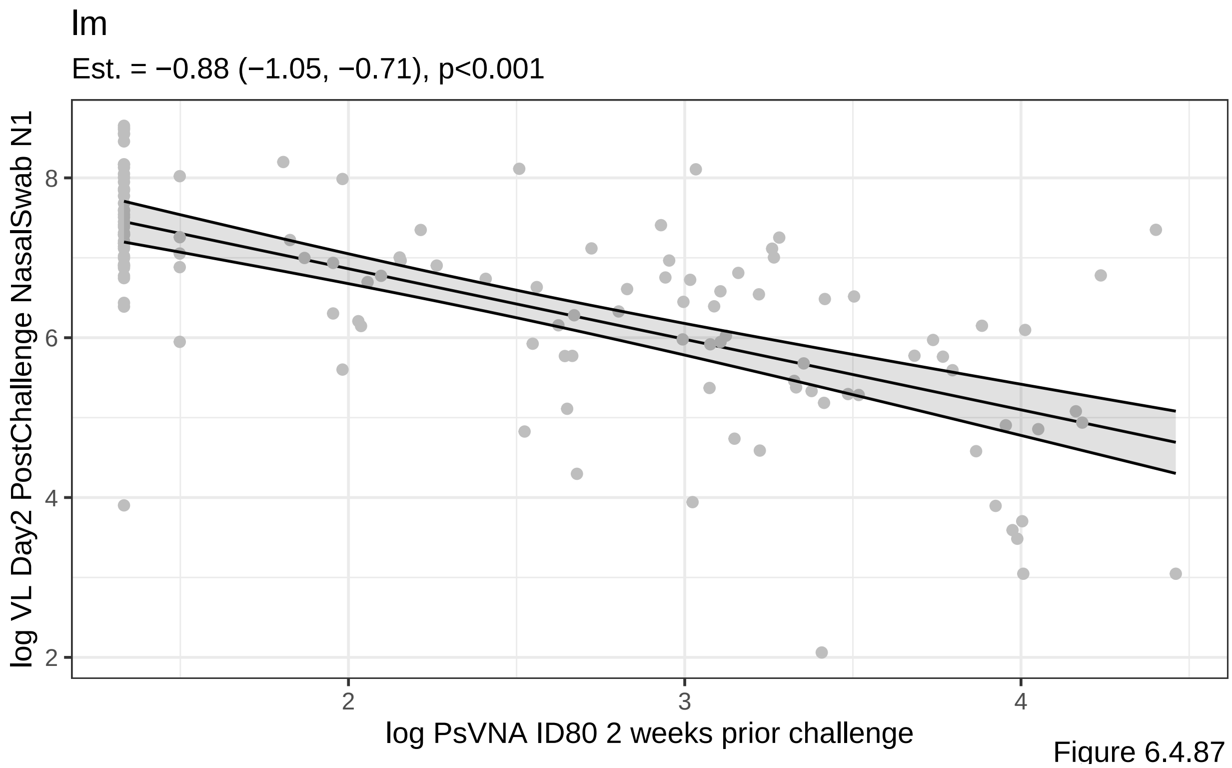


Figure 6.4.87

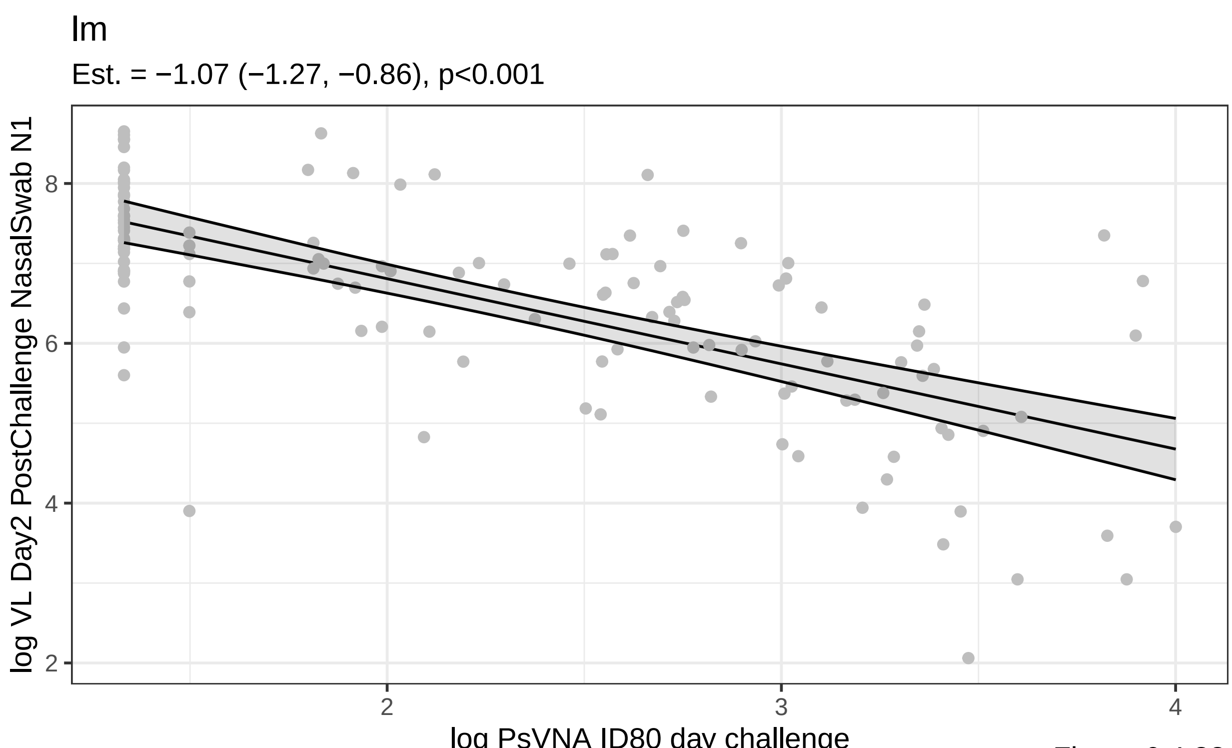


Figure 6.4.88

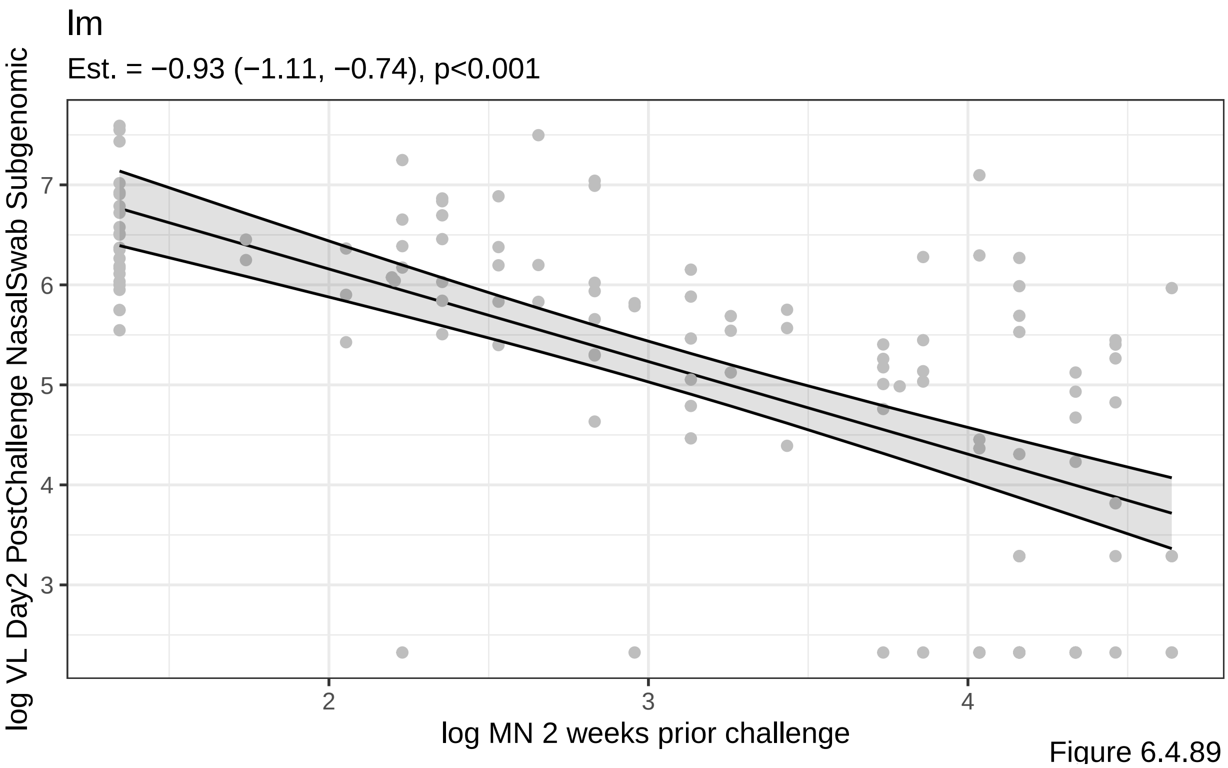
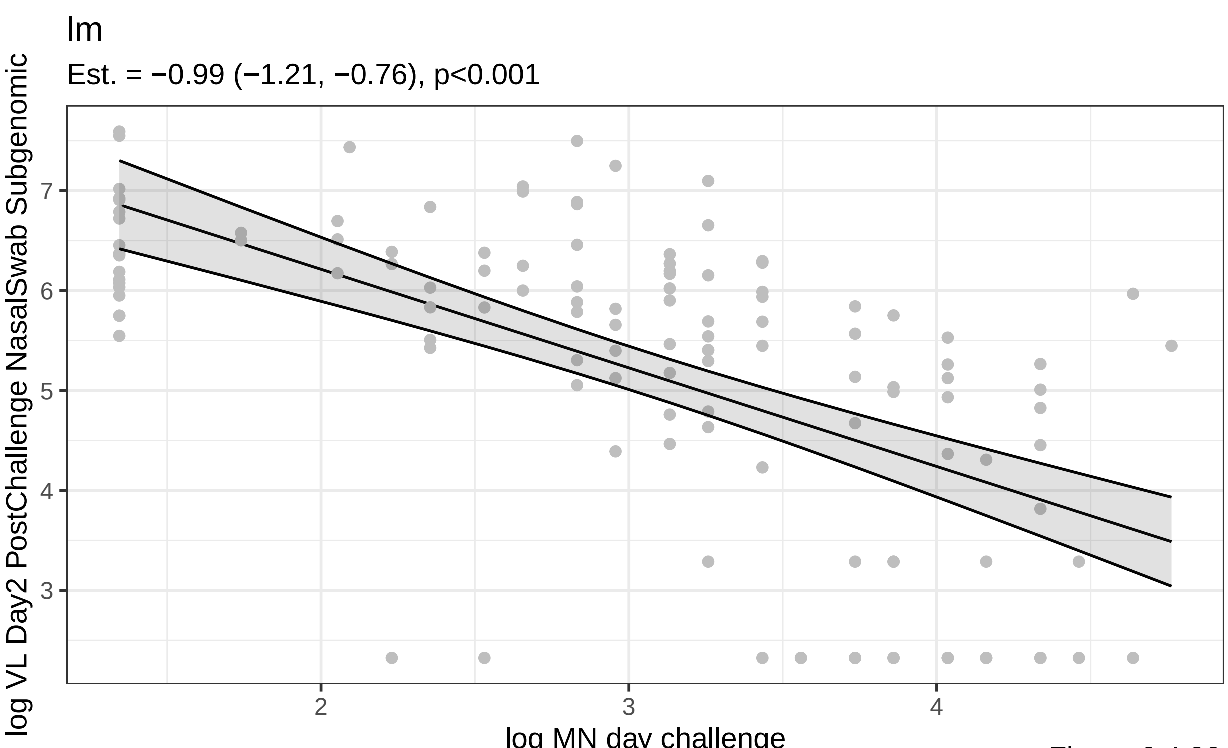


Figure 6.4.89



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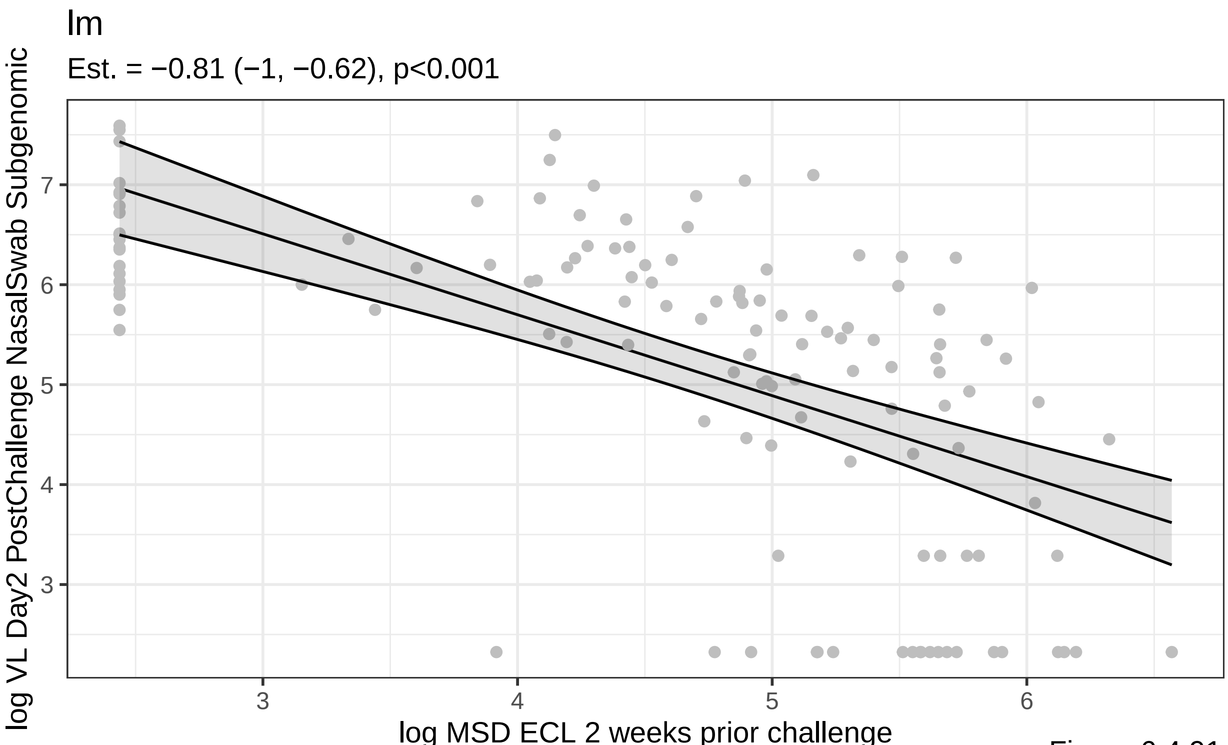


Figure 6.4.91

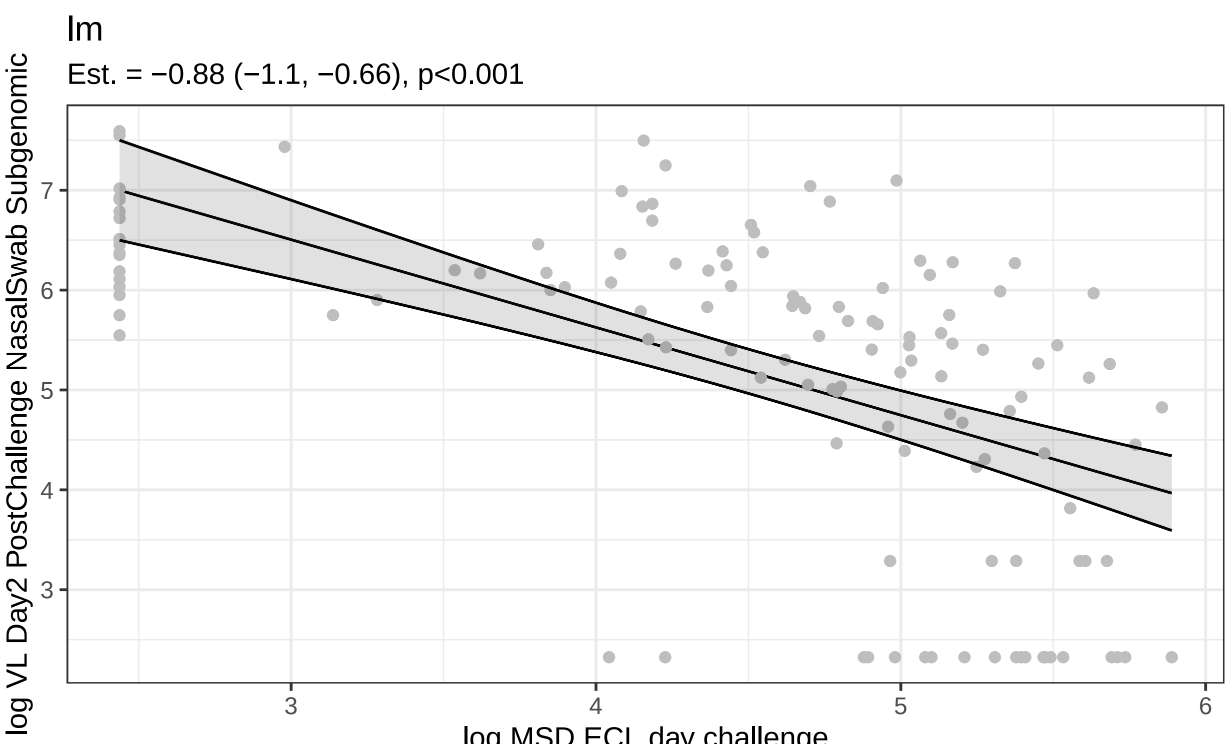


Figure 6.4.92

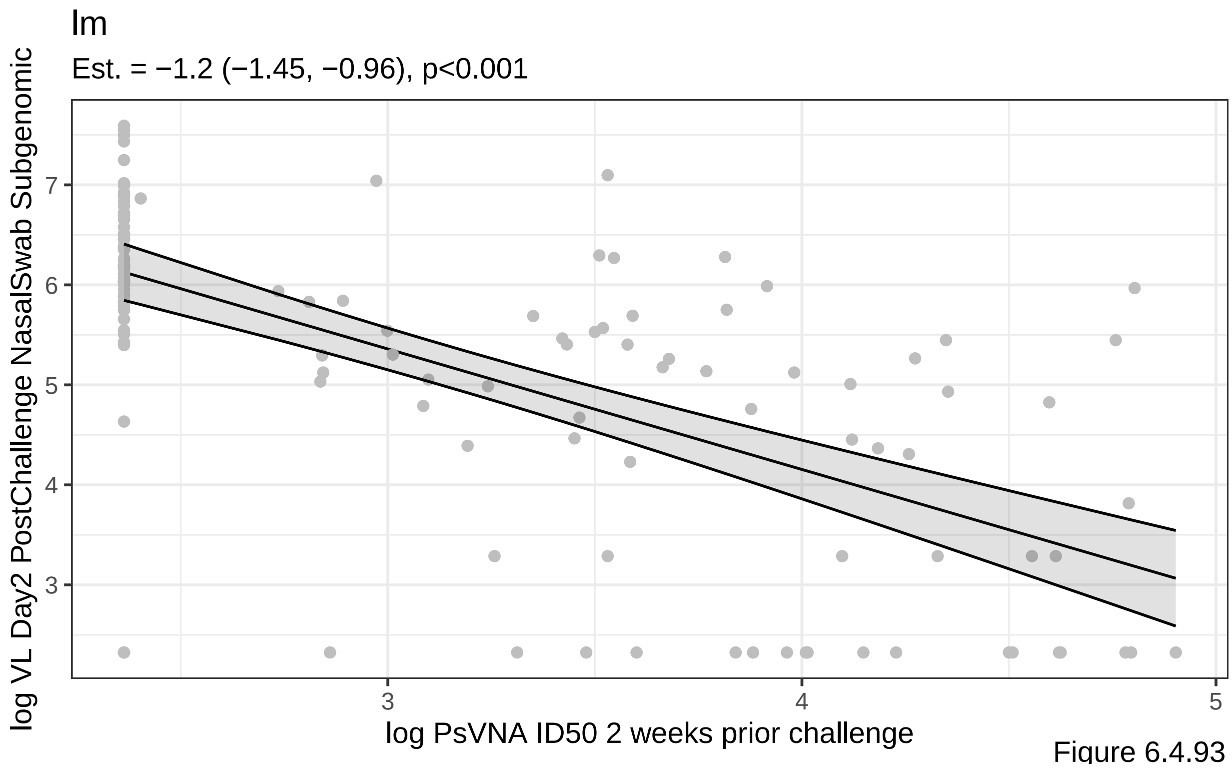


Figure 6.4.93

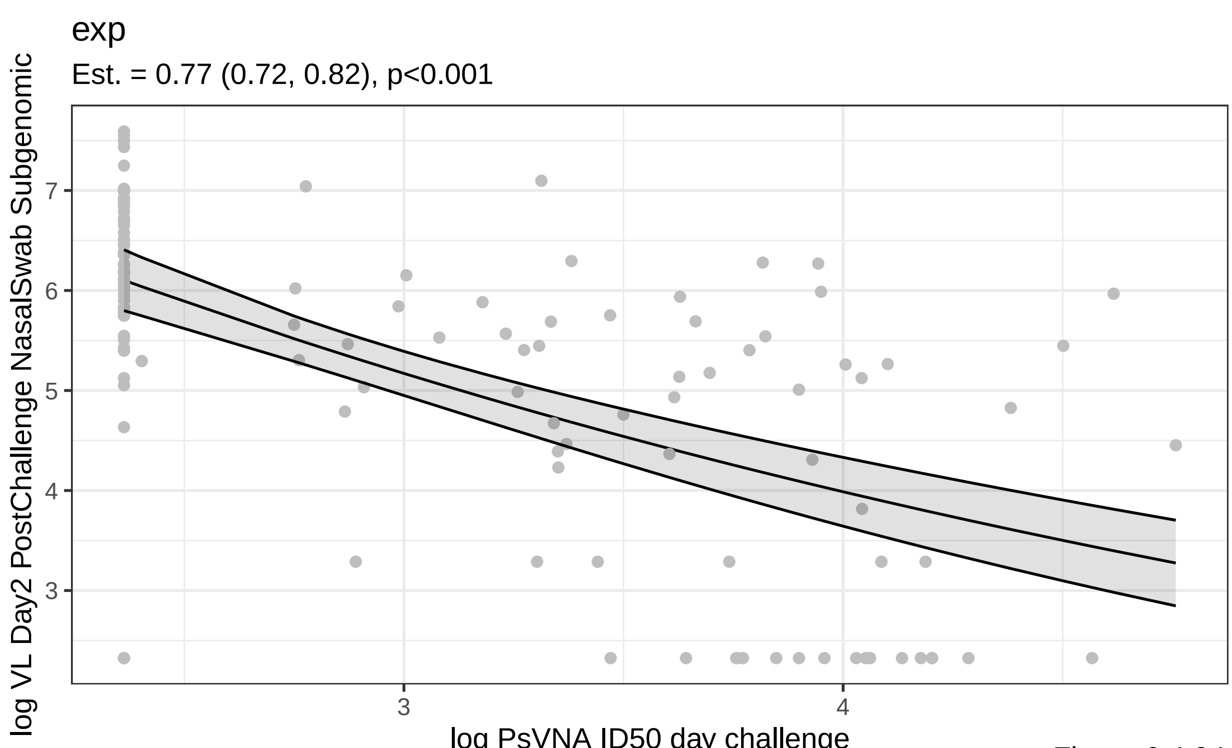


Figure 6.4.94

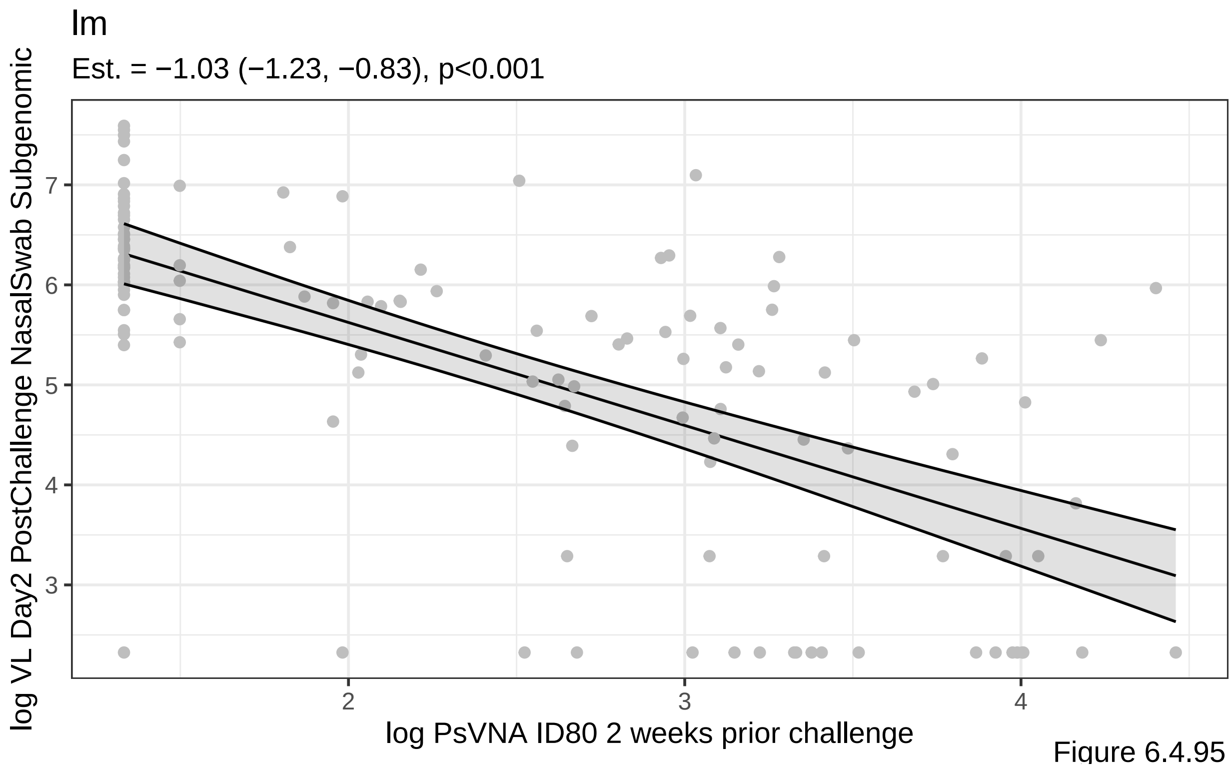


Figure 6.4.95

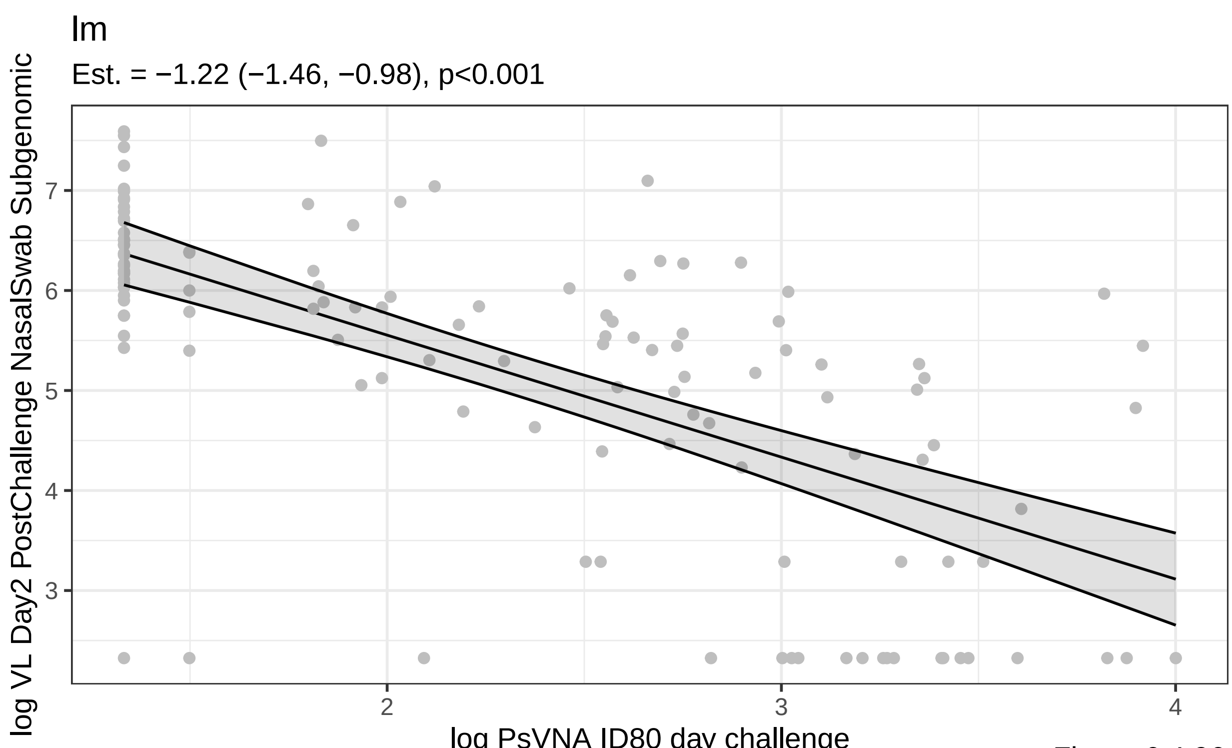


Figure 6.4.96

6.4.2 Binary Viral Load

For binary viral load, a logistic model is fit with an intercept and one main effect for virus-specific antibody. The notation is the same as in Section 6.4.1, except now y_{jk} represents a binary response. As in the previous section, several models will be tried and the best one selected by cross-validation. Instead of comparing the models using adjusted R-squared, we use the binary analog, the adjusted coefficient of discrimination (Tjur, 2009, Fay et al., 2012). The models tried are the following: the logistic model:

$log_e\{\mu_{jk}/(1-\mu_{jk})\} = \beta_0 + \beta_1 x_{jk}$

Analogously to Section 6.4.1, the linear predictor portion of the model may be modeled in different ways: it could be fit as a segmented line with 2 breakpoints, or fit with natural cubic splines with 5 degrees of freedom. As in section 6.4.1, the best model by cross-validation will be fit to all of the data (enforcing monotonicity if needed), with confidence intervals on the prediction calculated using the parametric formula as above or nonparametric bootstrap (for segmented regression).

Table 6.4.2: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Binary

Virus-Specific Antibody	Binary Viral Load	Model Selected	Adjusted CoD	Figure Number
log MSD ECL 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab N1	ns5	1.000	6.4.131
log MSD ECL day challenge	bin VL Day2 PostChallenge NasalSwab N1	ns5	1.000	6.4.132
log PsVNA ID50 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab N1	ns5	1.000	6.4.133
log PsVNA ID50 day challenge	bin VL Day2 PostChallenge NasalSwab N1	ns5	1.000	6.4.134
log PsVNA ID80 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab N1	ns5	1.000	6.4.135
log PsVNA ID80 day challenge	bin VL Day2 PostChallenge NasalSwab N1	ns5	1.000	6.4.136
log MN day challenge	bin VL Day2 PostChallenge NasalSwab N1	ns5	0.475	6.4.130
log MSD ECL 2 weeks prior challenge	bin VL Day2 PostChallenge BAL Subgenomic	ns5	0.280	6.4.107
log MSD ECL 2 weeks prior challenge	bin VL Day2 PostChallenge BAL N1	log	0.259	6.4.99
log MSD ECL day challenge	bin VL Day2 PostChallenge BAL Subgenomic	ns5	0.250	6.4.108
log PsVNA ID50 2 weeks prior challenge	bin VL Day2 PostChallenge BAL Subgenomic	log	0.223	6.4.109

Table 6.4.2: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Binary *(continued)*

Virus-Specific Antibody	Binary Viral Load	Model Selected	Adjusted CoD	Figure Number
log PsVNA ID80 day challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	ns5	0.223	6.4.144
log PsVNA ID50 day challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	ns5	0.216	6.4.142
log MSD ECL day challenge	bin VL Day2 PostChallenge OPswab Subgenomic	ns5	0.215	6.4.124
log MN day challenge	bin VL Day2 PostChallenge BAL Subgenomic	log	0.209	6.4.106
log PsVNA ID80 2 weeks prior challenge	bin VL Day2 PostChallenge BAL Subgenomic	log	0.203	6.4.111
log MN 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab Subgenomic	ns5	0.203	6.4.121
log PsVNA ID80 day challenge	bin VL Day2 PostChallenge BAL Subgenomic	log	0.199	6.4.112
log MSD ECL 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab Subgenomic	seg	0.194	6.4.123
log MN day challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	ns5	0.188	6.4.138
log MN 2 weeks prior challenge	bin VL Day2 PostChallenge BAL Subgenomic	log	0.179	6.4.105
log PsVNA ID80 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	log	0.174	6.4.143
log PsVNA ID50 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	log	0.173	6.4.141

Table 6.4.2: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Binary *(continued)*

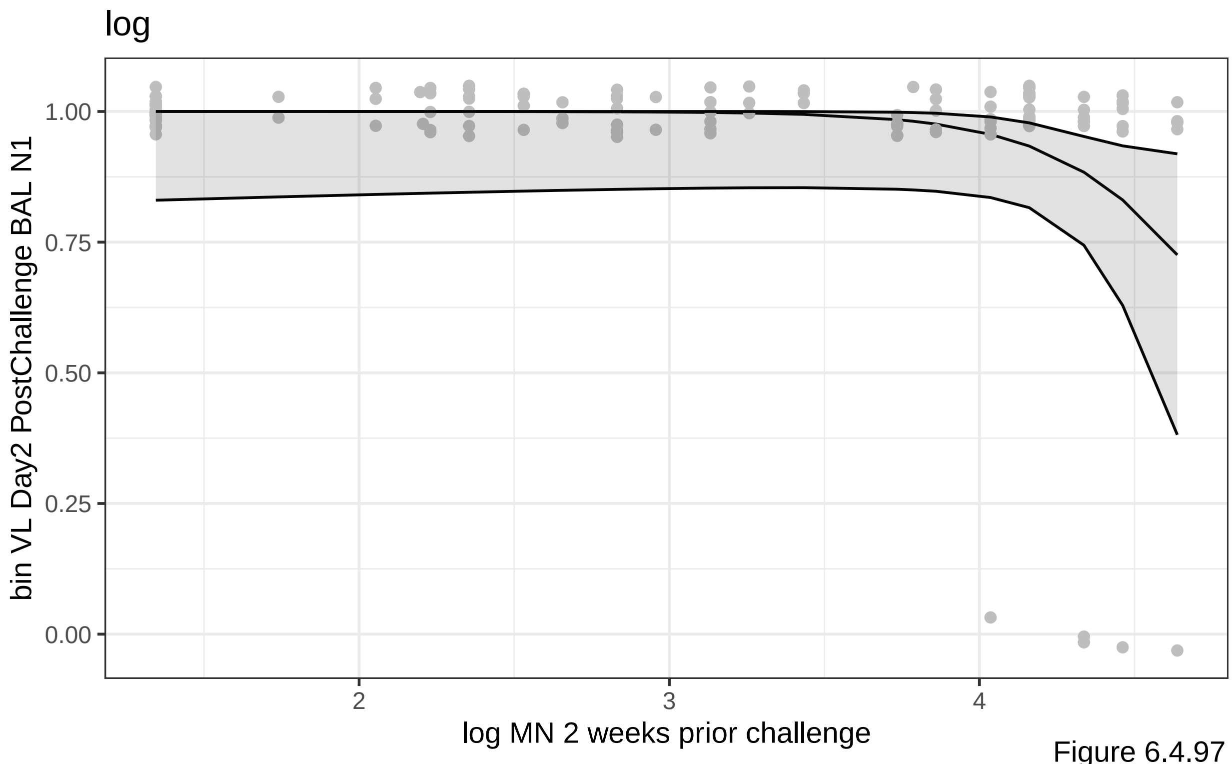
Virus-Specific Antibody	Binary Viral Load	Model Selected	Adjusted CoD	Figure Number
log MN 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	log	0.168	6.4.137
log PsVNA ID50 day challenge	bin VL Day2 PostChallenge BAL Subgenomic	log	0.164	6.4.110
log MN 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab N1	log	0.162	6.4.113
log MSD ECL 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	log	0.160	6.4.139
log MSD ECL day challenge	bin VL Day2 PostChallenge BAL N1	log	0.157	6.4.100
log MSD ECL 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab N1	log	0.153	6.4.115
log MSD ECL day challenge	bin VL Day2 PostChallenge OPswab N1	log	0.153	6.4.116
log PsVNA ID80 day challenge	bin VL Day2 PostChallenge BAL N1	log	0.152	6.4.104
log PsVNA ID80 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab Subgenomic	log	0.152	6.4.127
log PsVNA ID50 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab Subgenomic	log	0.149	6.4.125
log PsVNA ID80 day challenge	bin VL Day2 PostChallenge OPswab Subgenomic	log	0.149	6.4.128
log MN day challenge	bin VL Day2 PostChallenge OPswab Subgenomic	seg	0.143	6.4.122
log MN day challenge	bin VL Day2 PostChallenge BAL N1	log	0.141	6.4.98

Table 6.4.2: Model Selection Results Using Single Virus-Specific Antibody to Predict Post Challenge Viral Load - Binary *(continued)*

Virus-Specific Antibody	Binary Viral Load	Model Selected	Adjusted CoD	Figure Number
log PsVNA ID50 day challenge	bin VL Day2 PostChallenge OPswab Subgenomic	log	0.140	6.4.126
log MSD ECL day challenge	bin VL Day2 PostChallenge NasalSwab Subgenomic	log	0.134	6.4.140
log PsVNA ID80 day challenge	bin VL Day2 PostChallenge OPswab N1	log	0.131	6.4.120
log PsVNA ID80 2 weeks prior challenge	bin VL Day2 PostChallenge BAL N1	log	0.124	6.4.103
log PsVNA ID80 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab N1	log	0.116	6.4.119
log PsVNA ID50 2 weeks prior challenge	bin VL Day2 PostChallenge BAL N1	log	0.110	6.4.101
log PsVNA ID50 day challenge	bin VL Day2 PostChallenge OPswab N1	log	0.110	6.4.118
log MN day challenge	bin VL Day2 PostChallenge OPswab N1	log	0.104	6.4.114
log MN 2 weeks prior challenge	bin VL Day2 PostChallenge BAL N1	log	0.101	6.4.97
log PsVNA ID50 2 weeks prior challenge	bin VL Day2 PostChallenge OPswab N1	log	0.096	6.4.117
log PsVNA ID50 day challenge	bin VL Day2 PostChallenge BAL N1	log	0.074	6.4.102
log MN 2 weeks prior challenge	bin VL Day2 PostChallenge NasalSwab N1	log	0.007	6.4.129

There are 32 pairs of virus-specific antibodies/viral loads (out of 48 total pairs) where the best model fit is logistic; 2 where the best model fit is segmented (with 2 breakpoints); and 14 where the best model fit is natural cubic splines with 5 degrees of freedom.

Predicted Values



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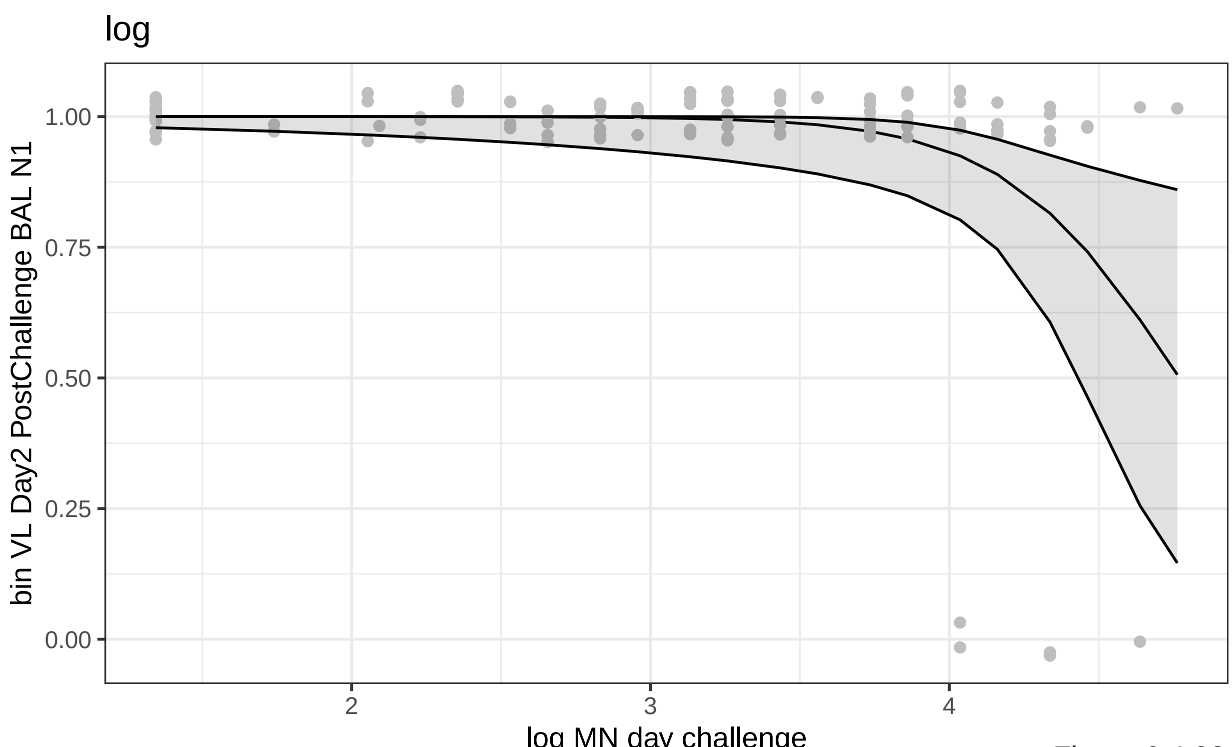

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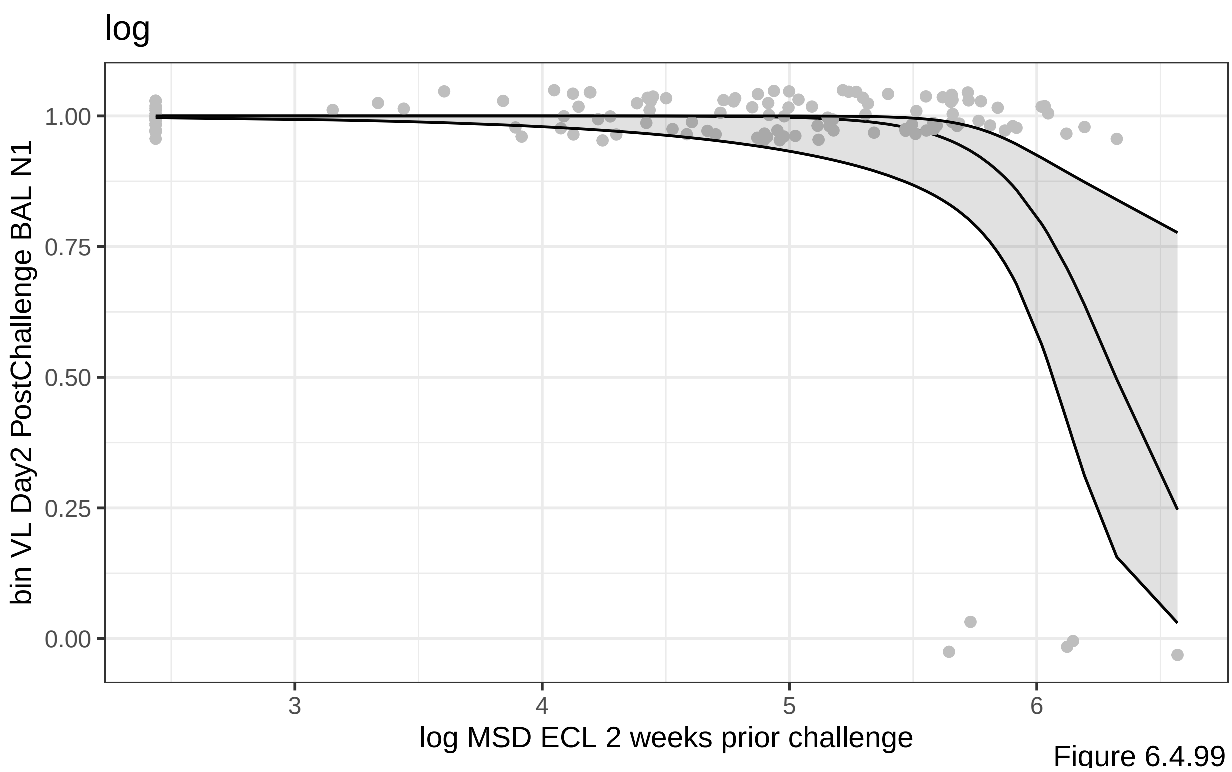

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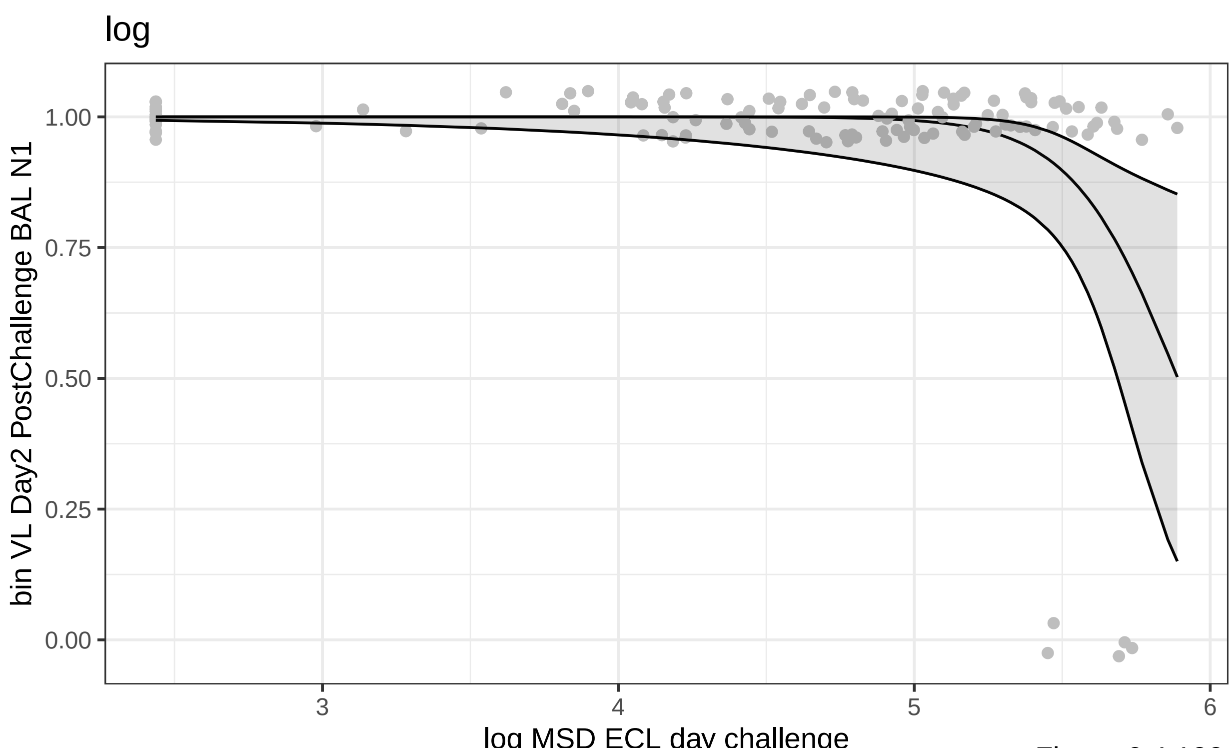

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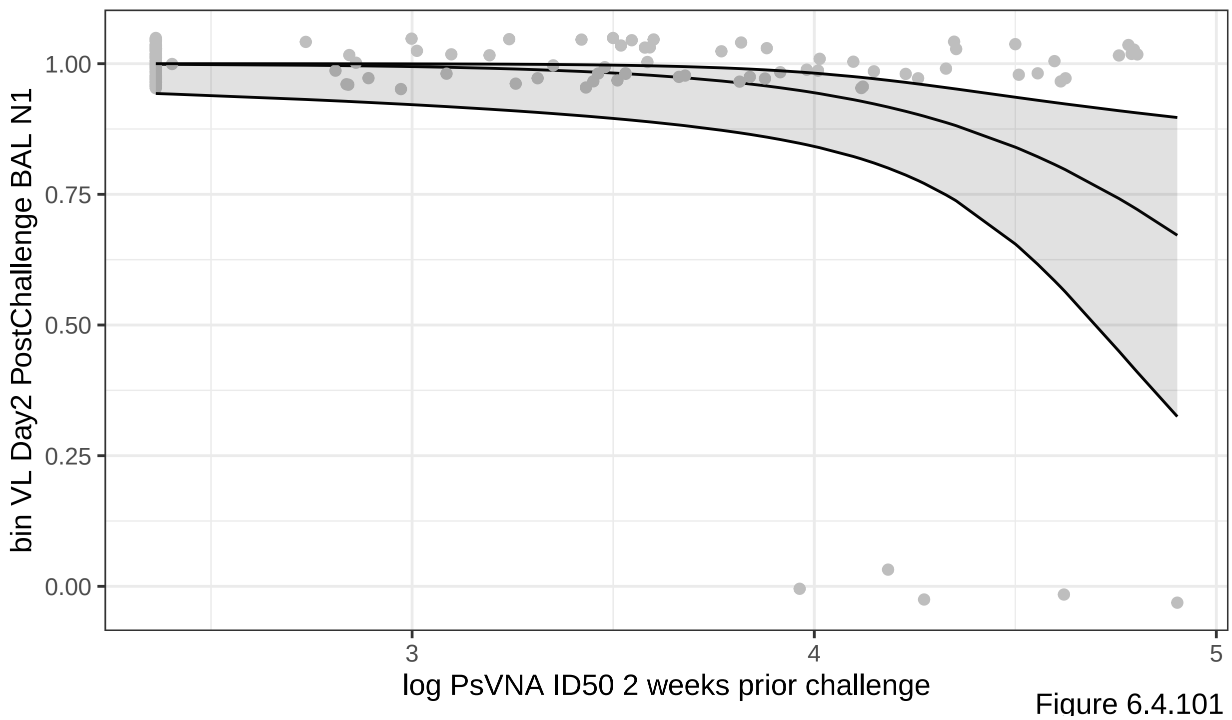

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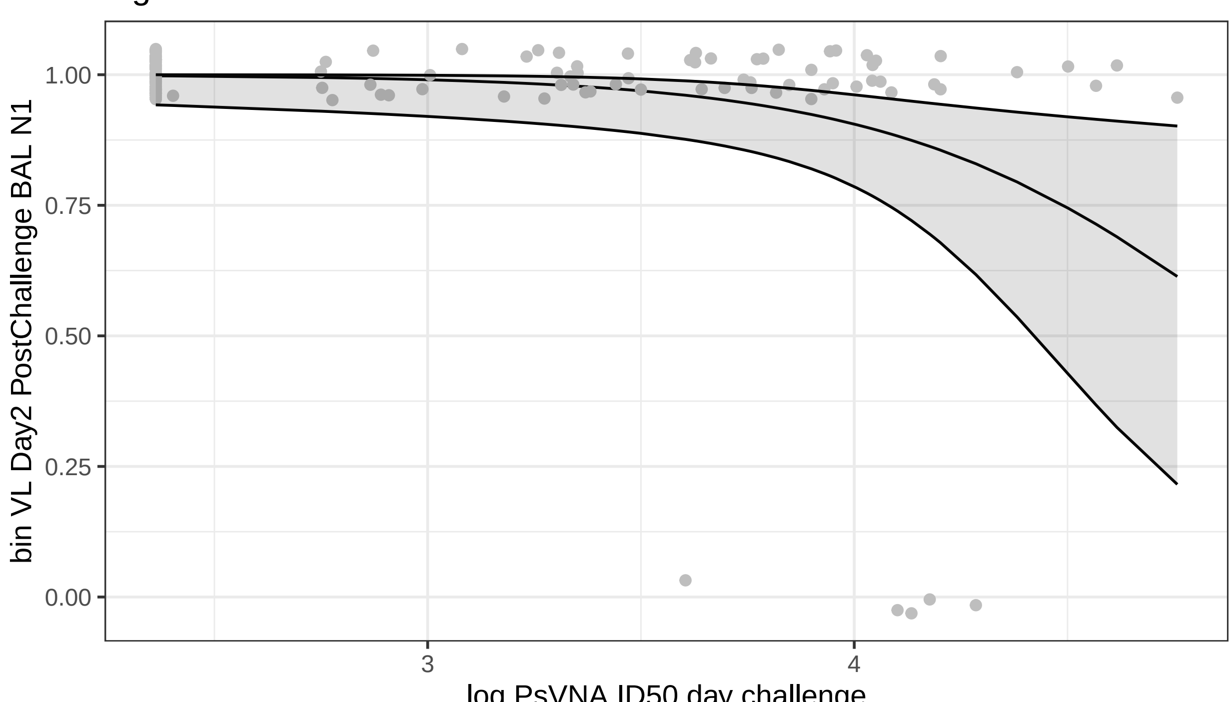

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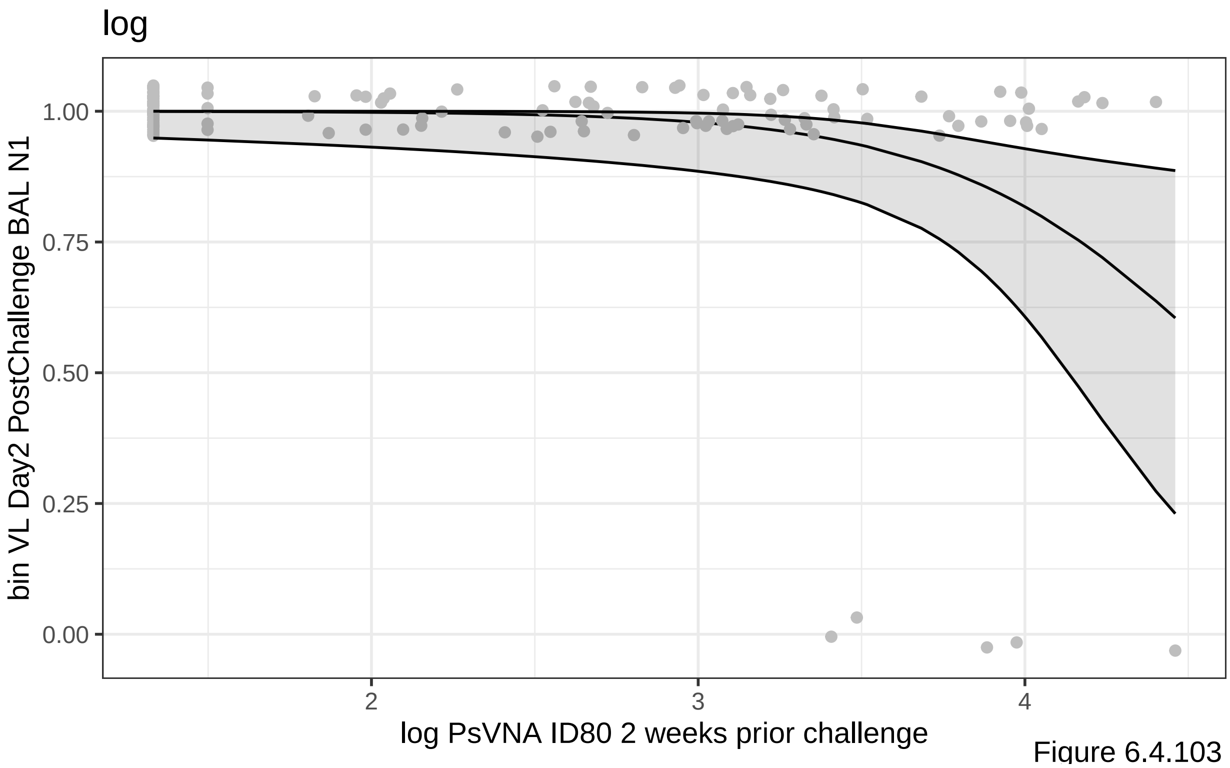

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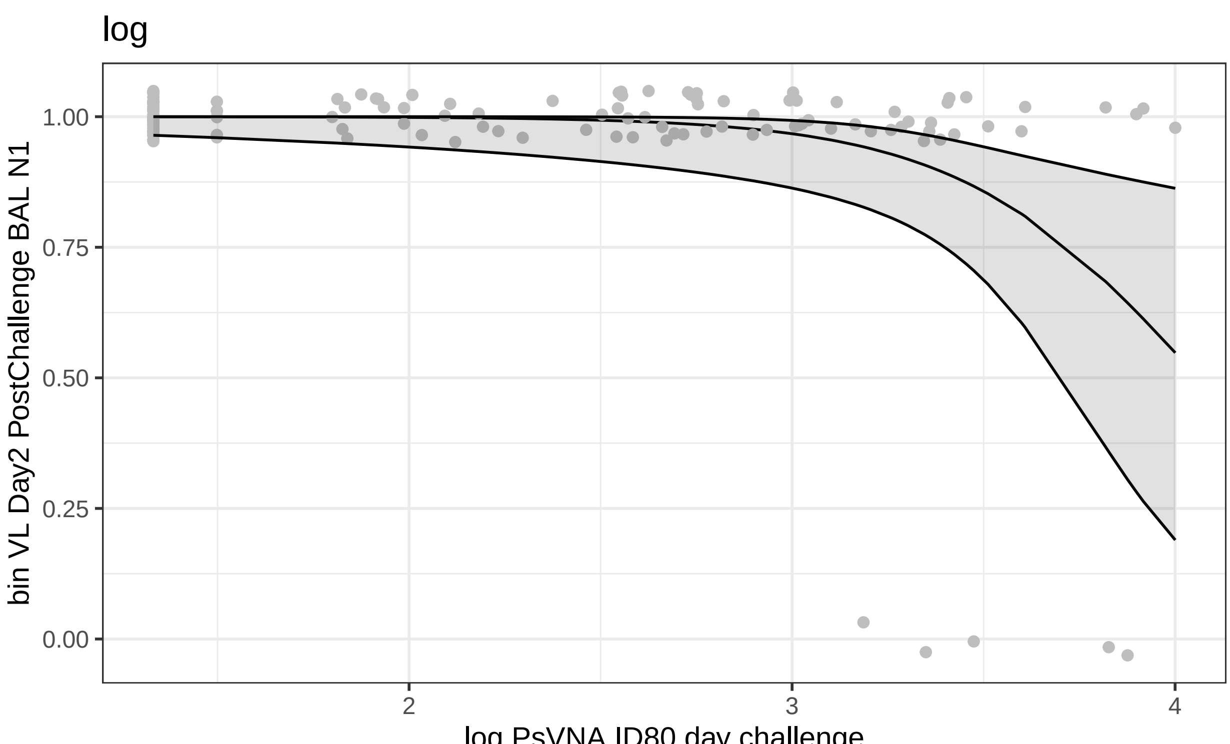

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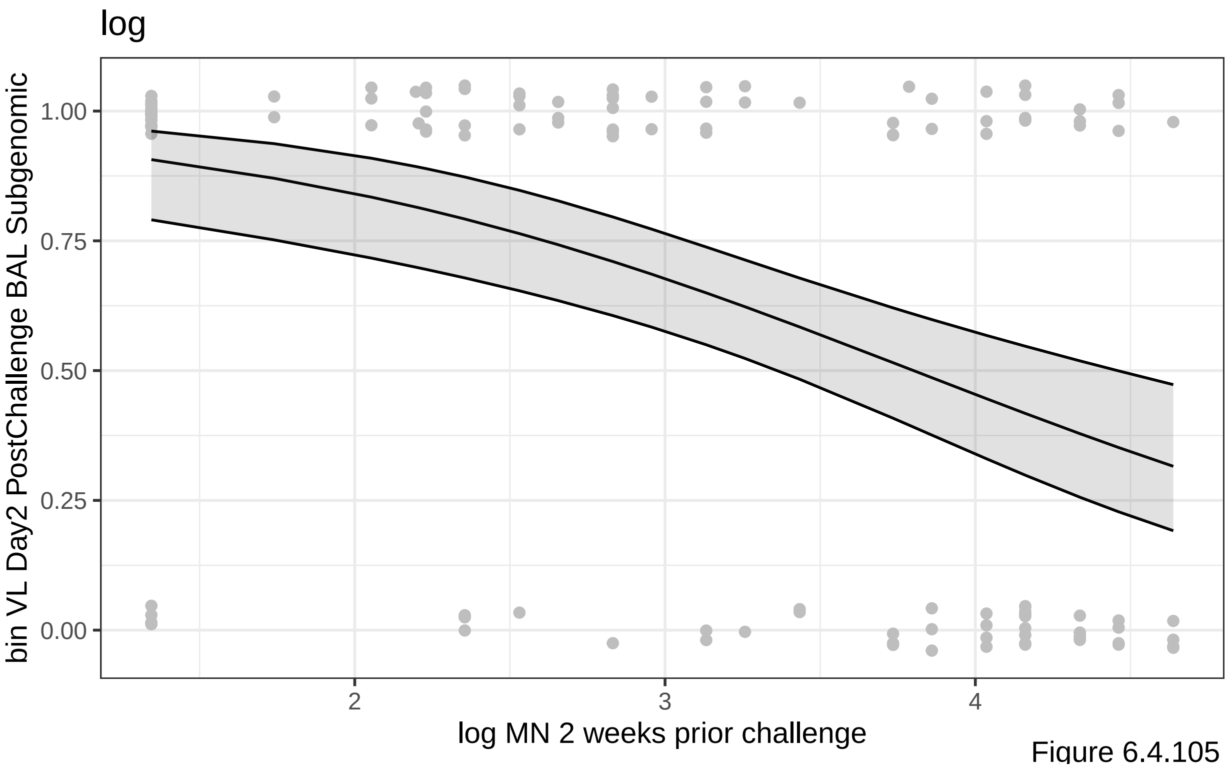

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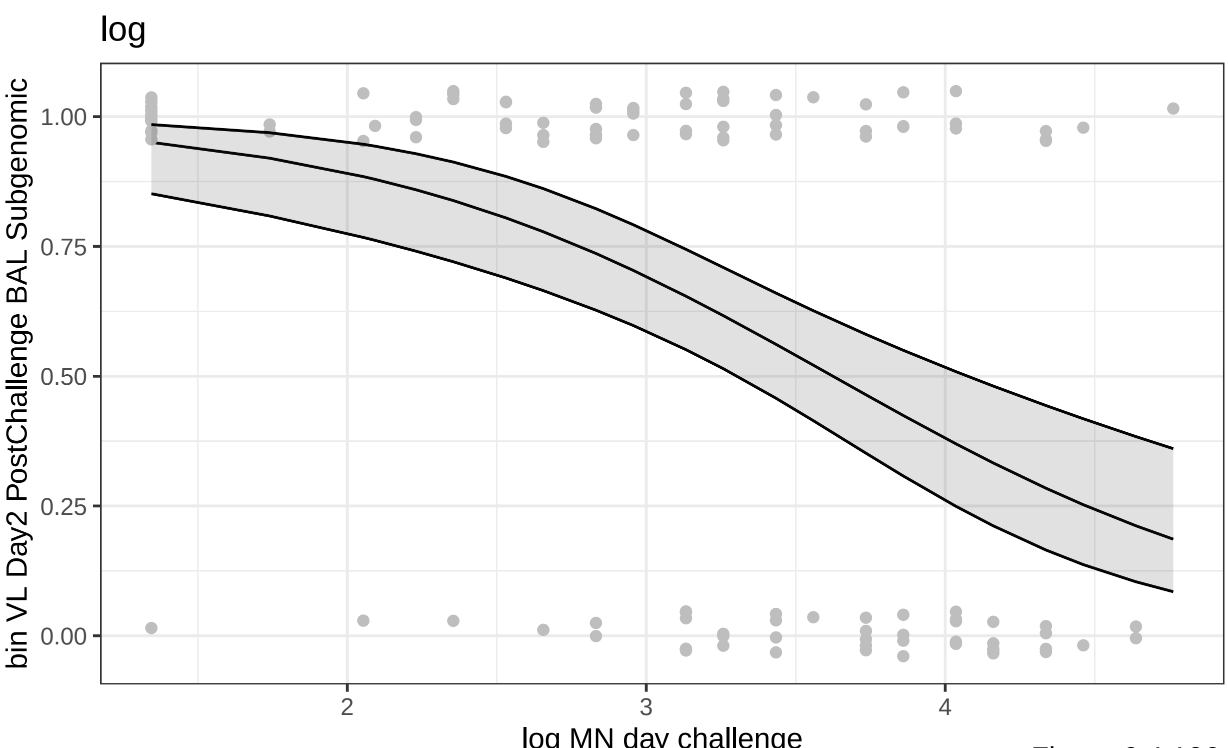

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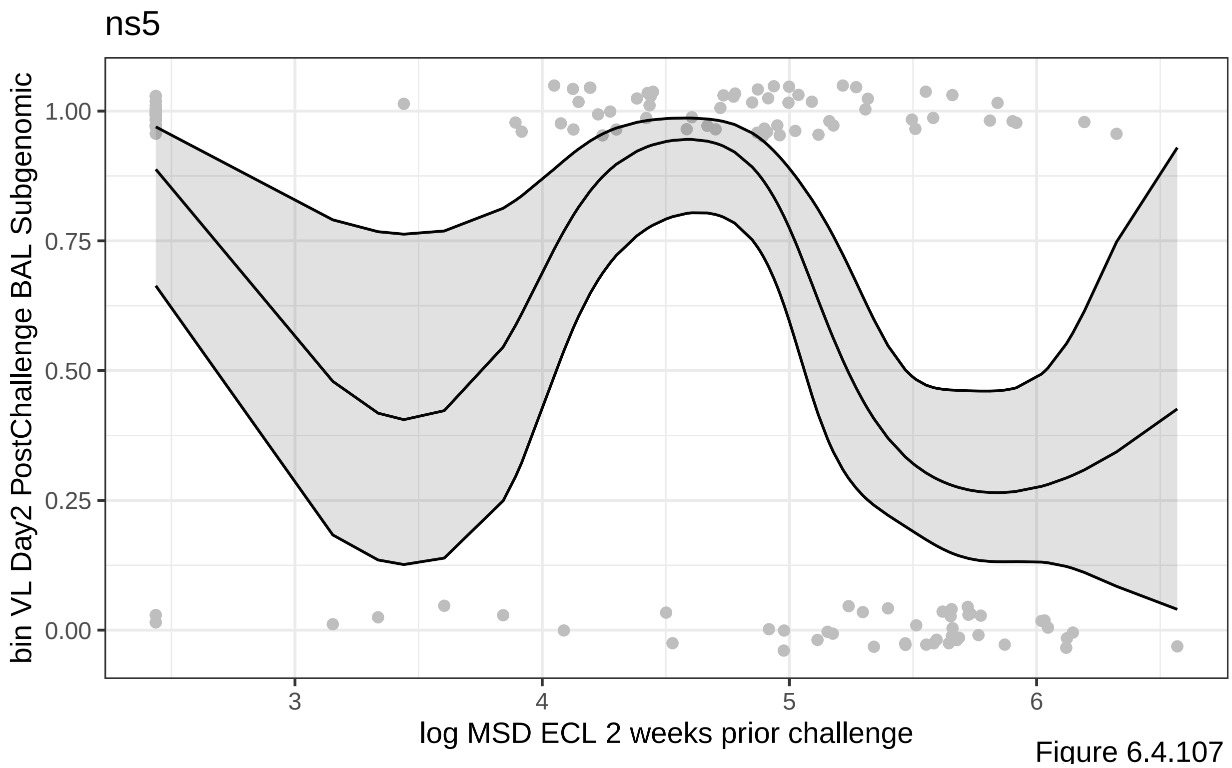

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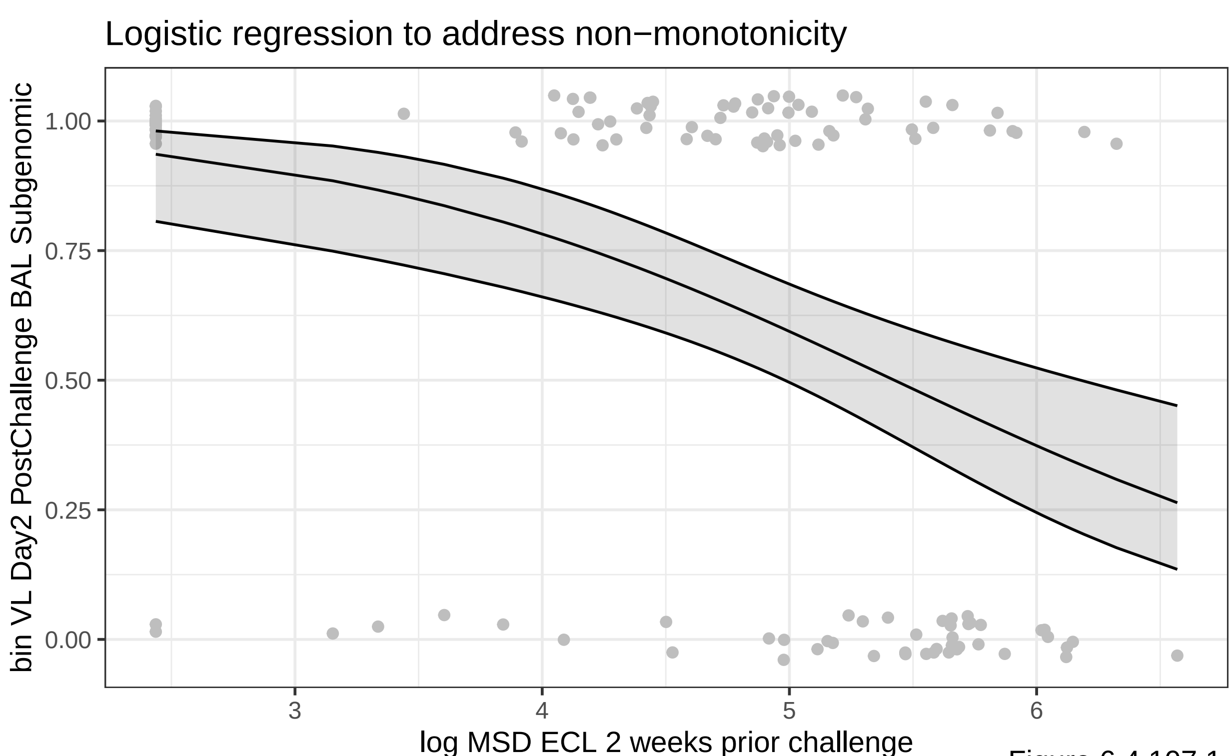

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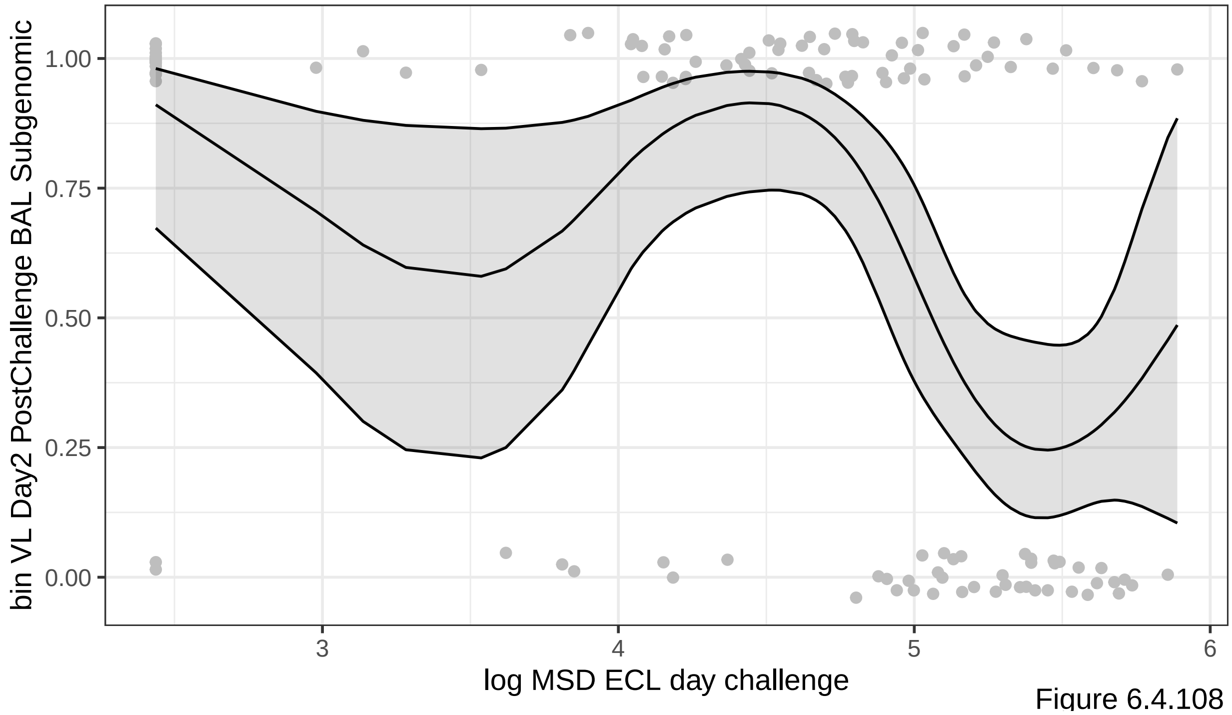
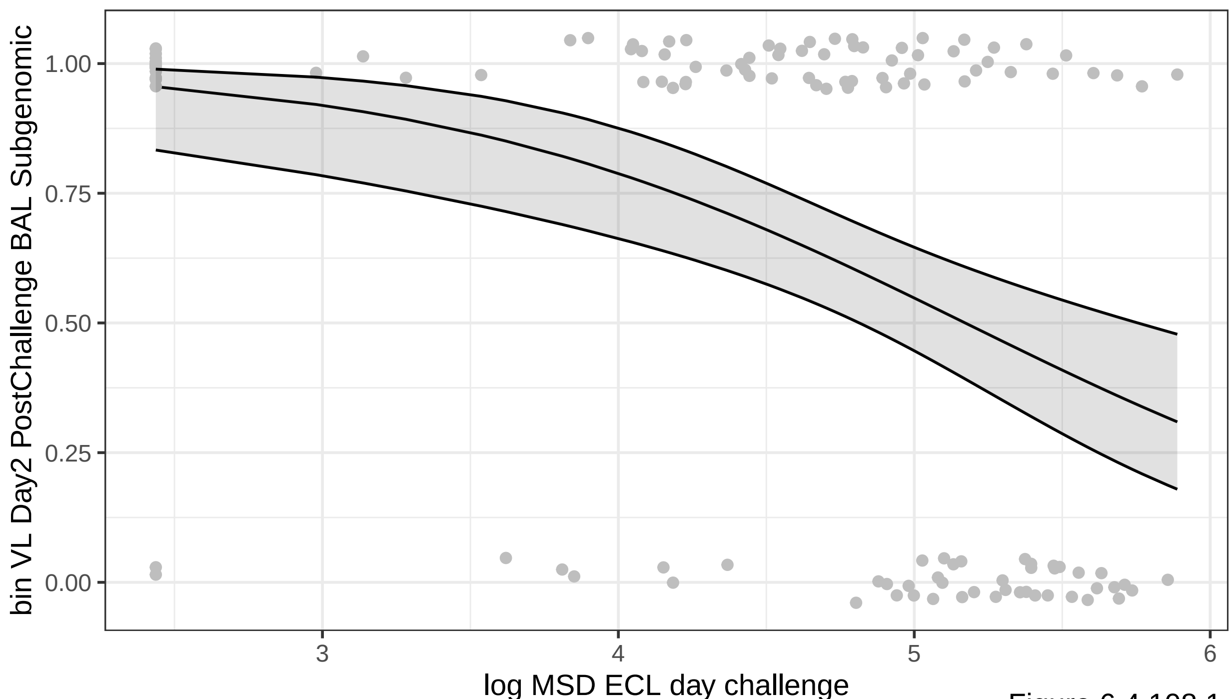


Figure 6.4.108

Logistic regression to address non−monotonicity



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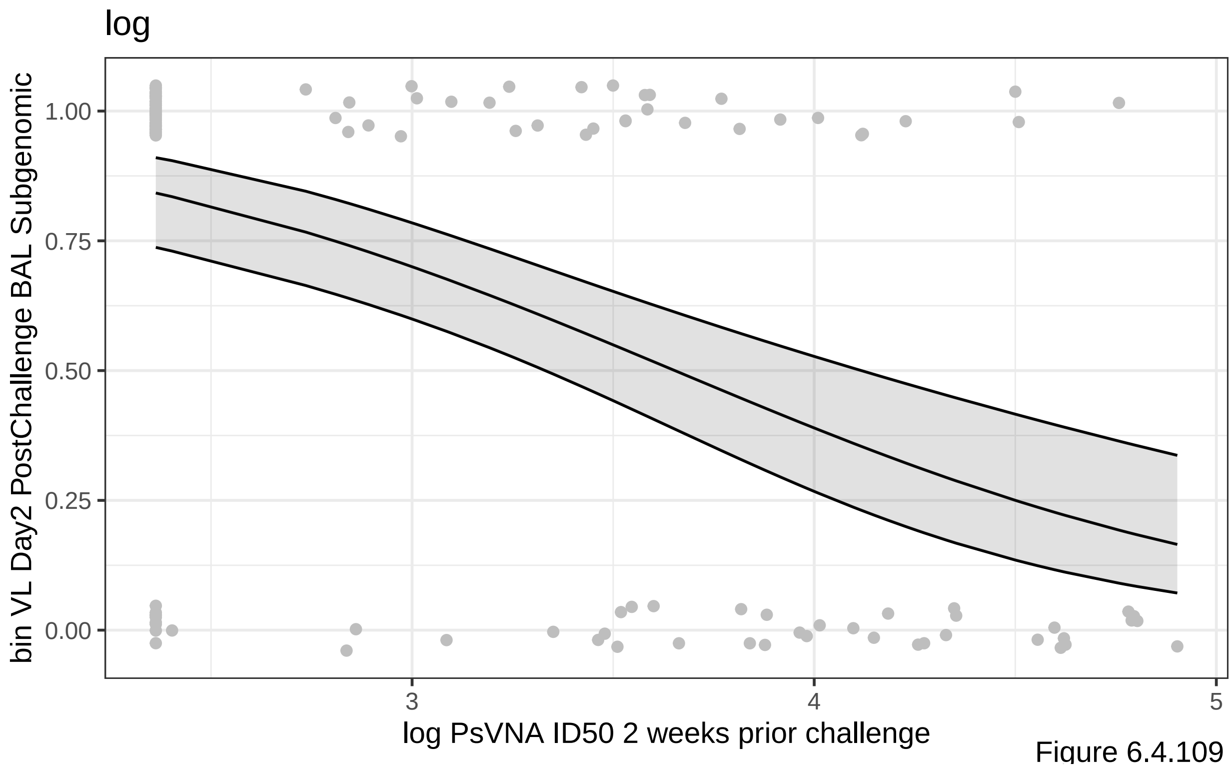

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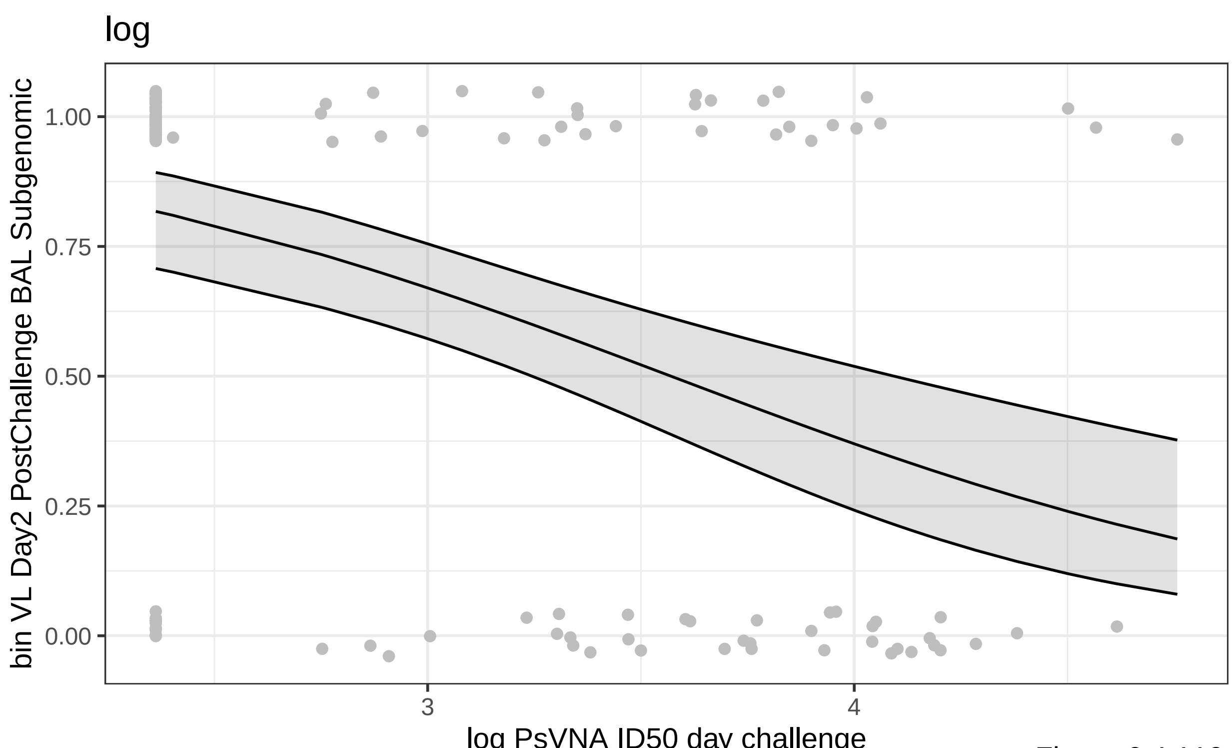

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log

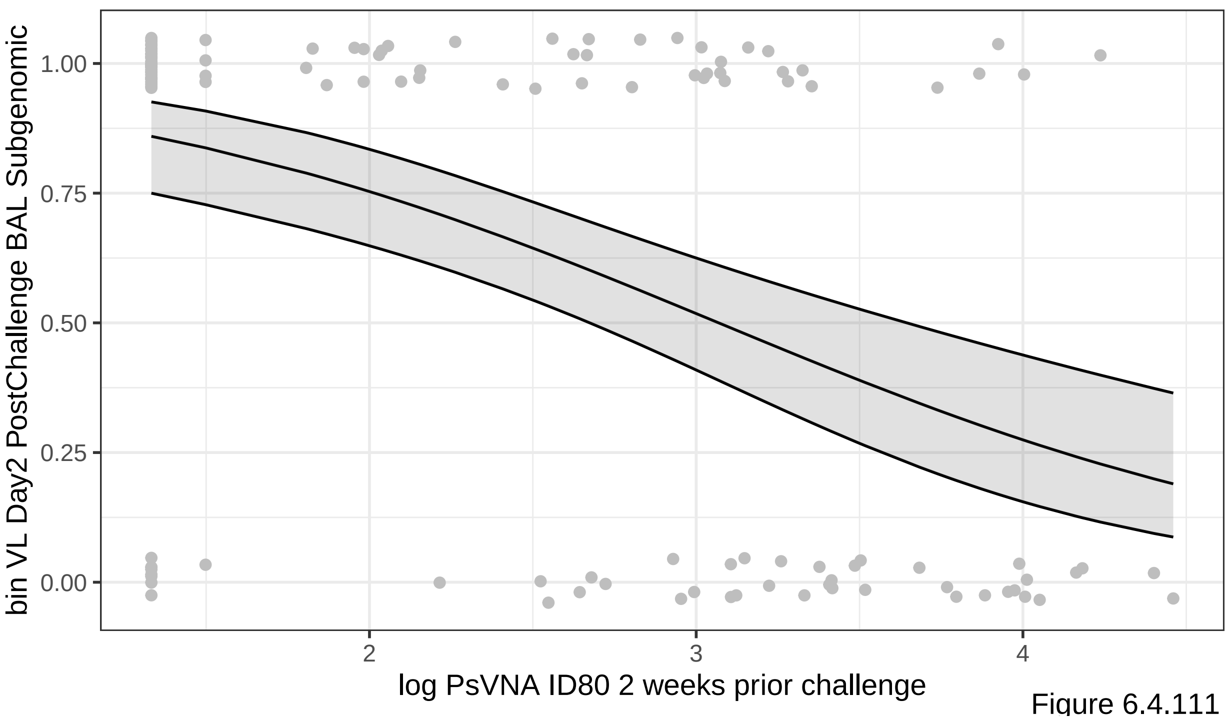

Figure 6.4.111

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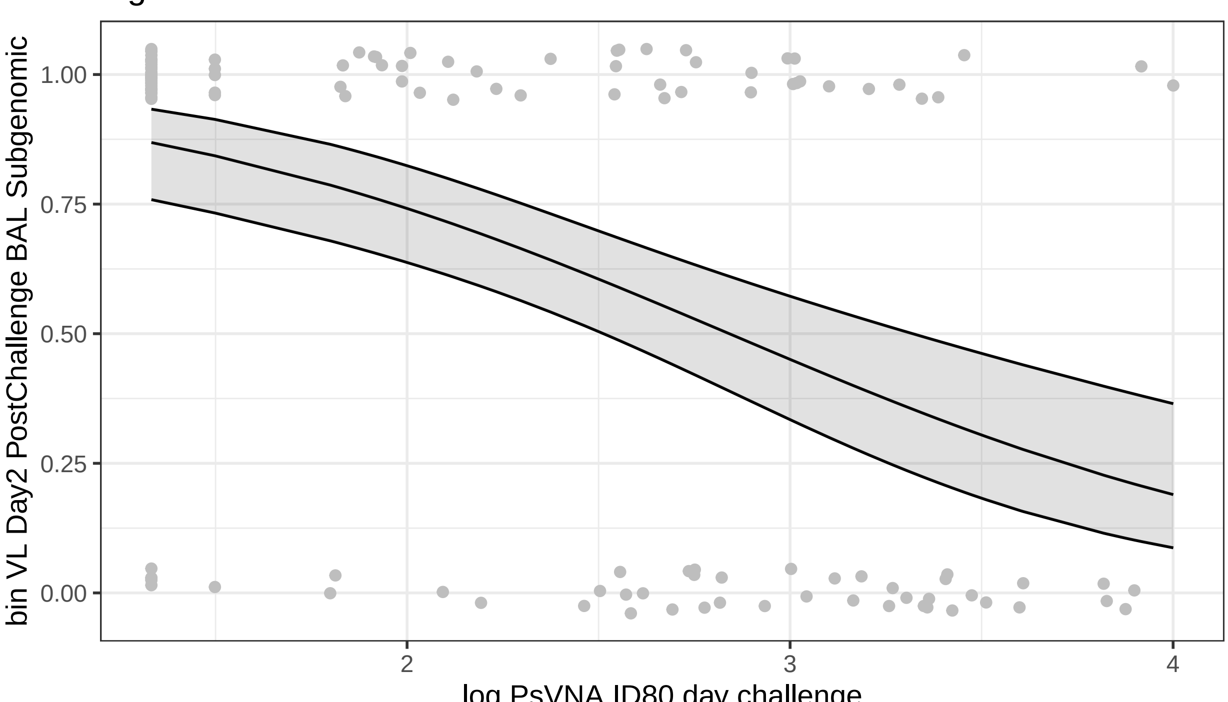

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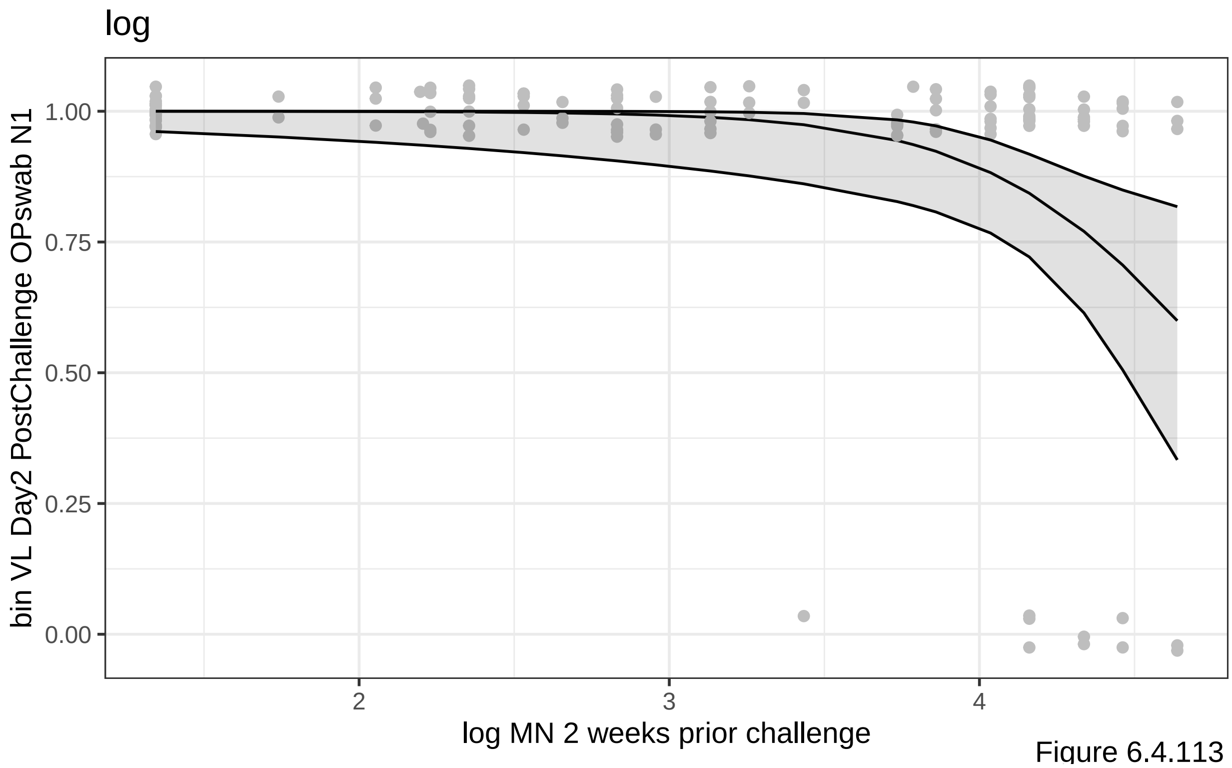

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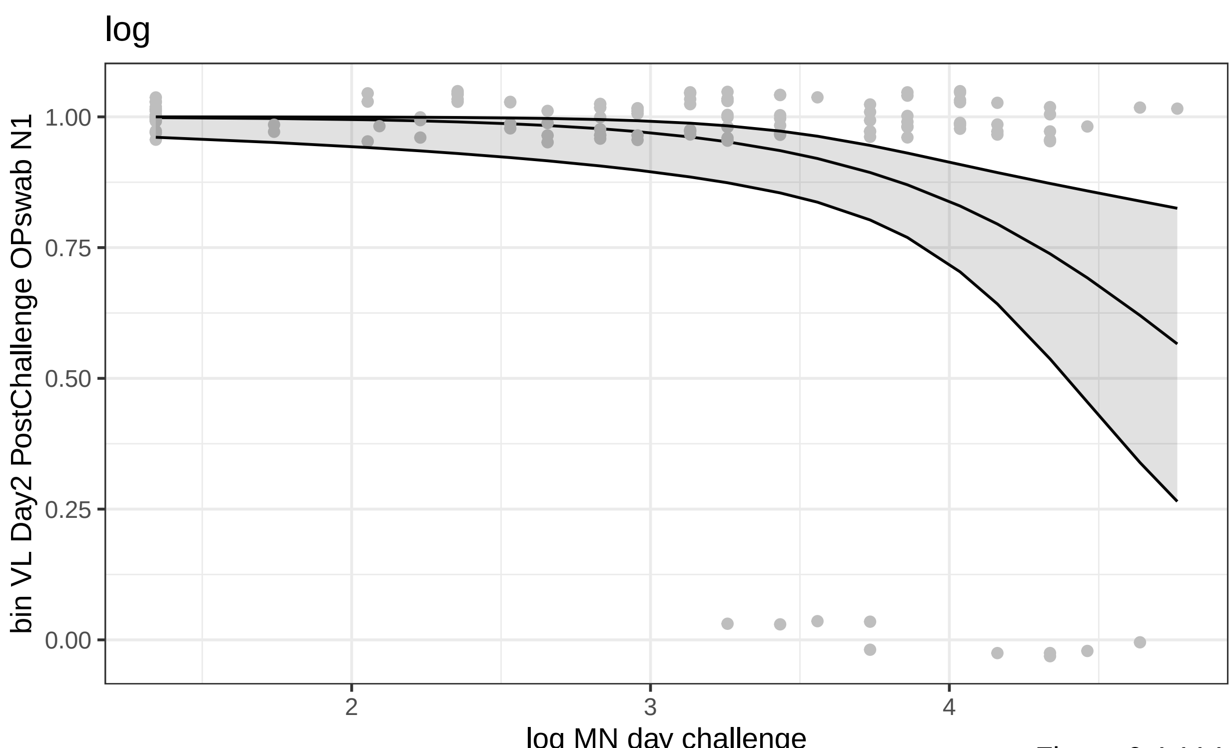

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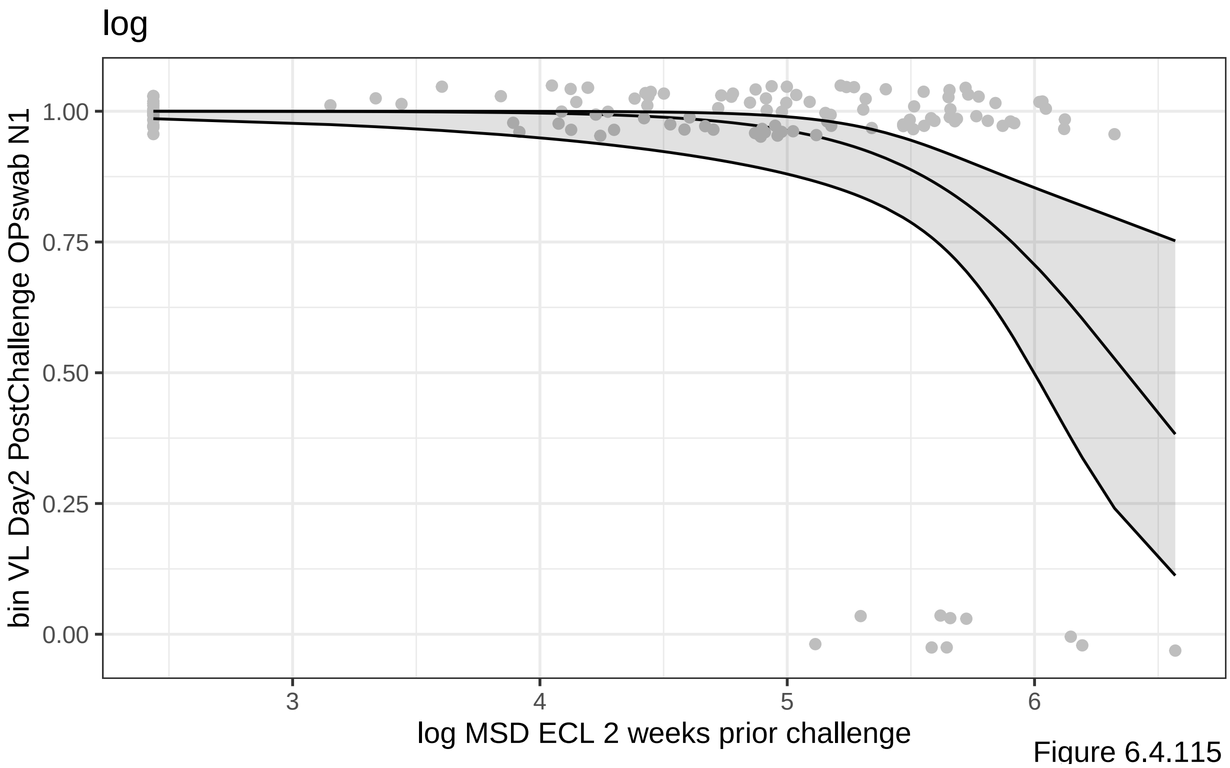

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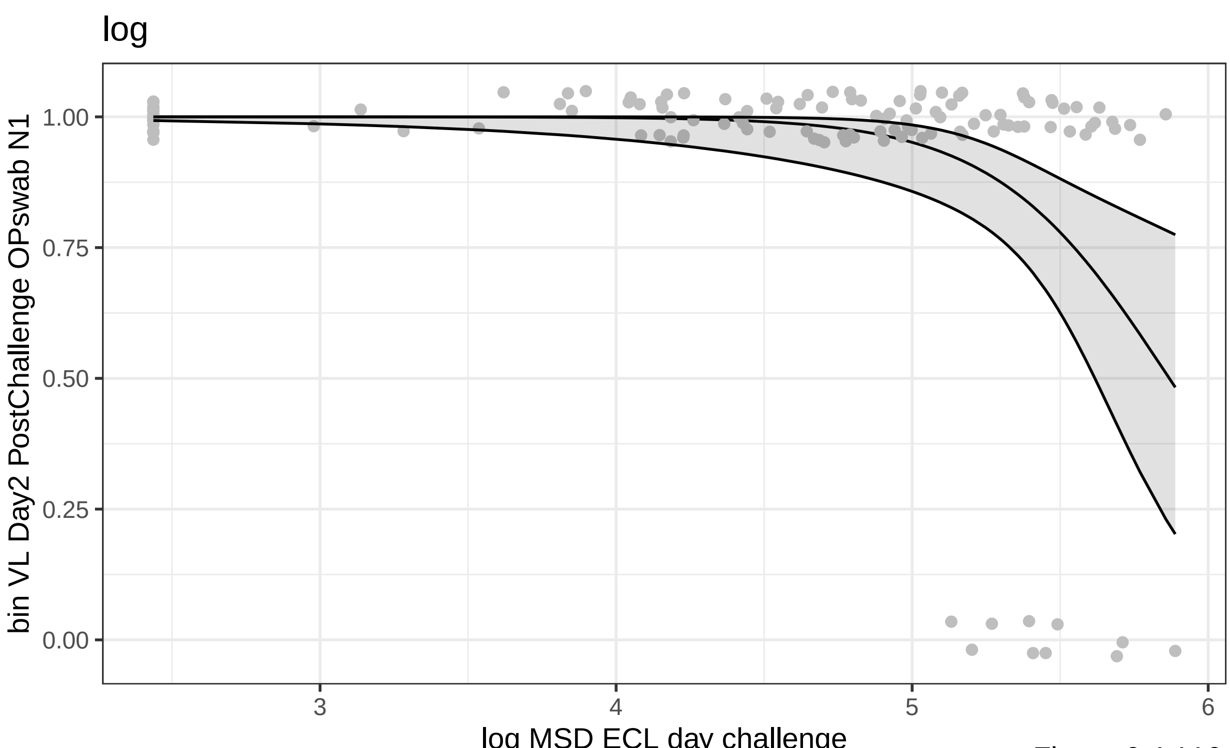

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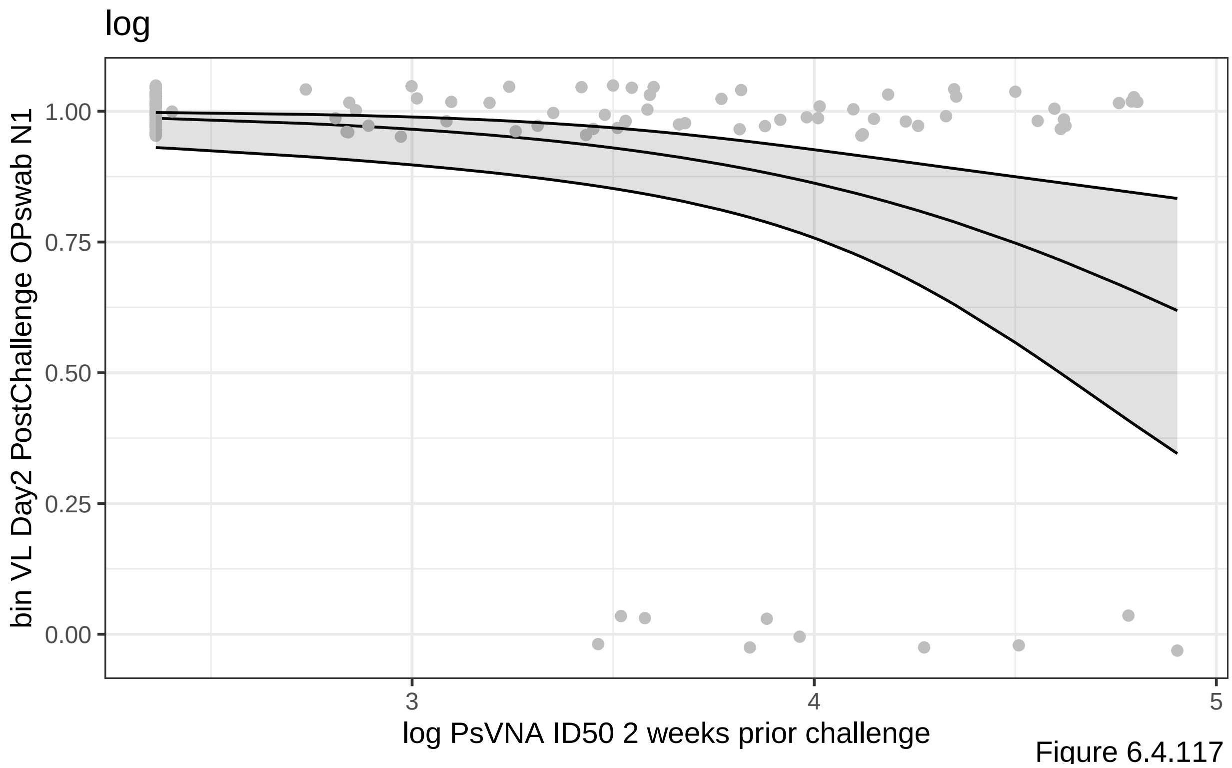

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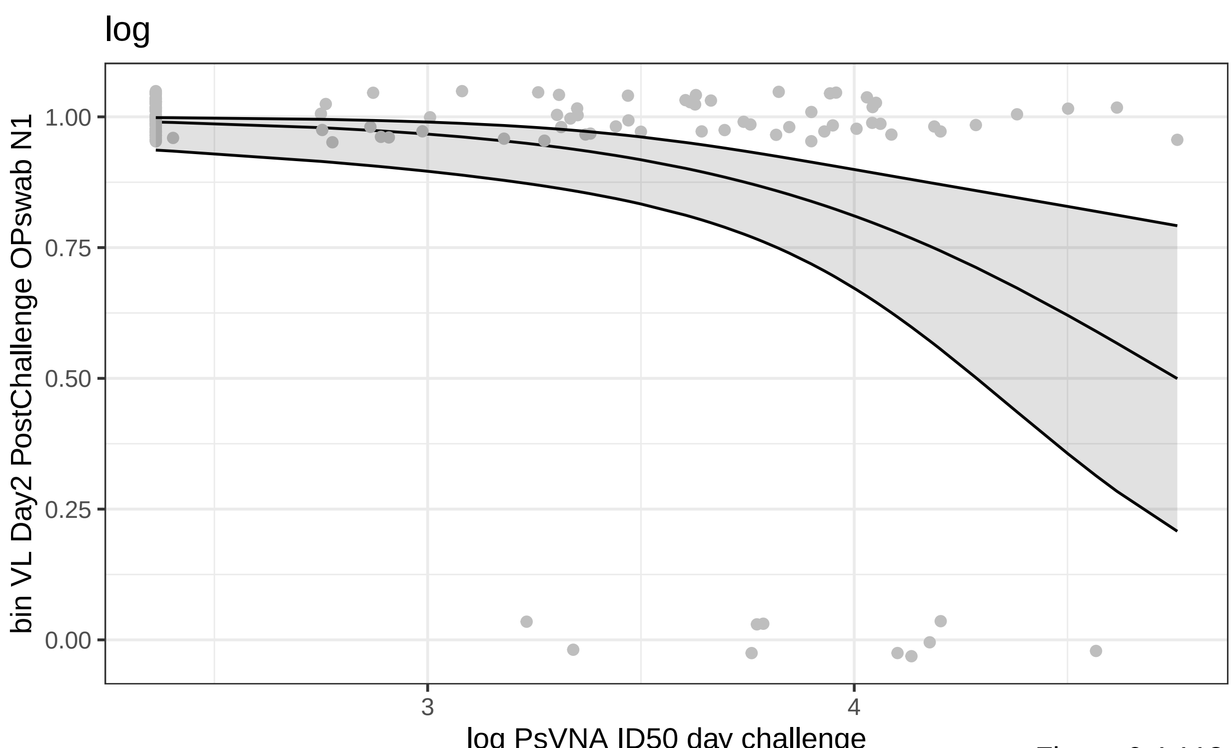

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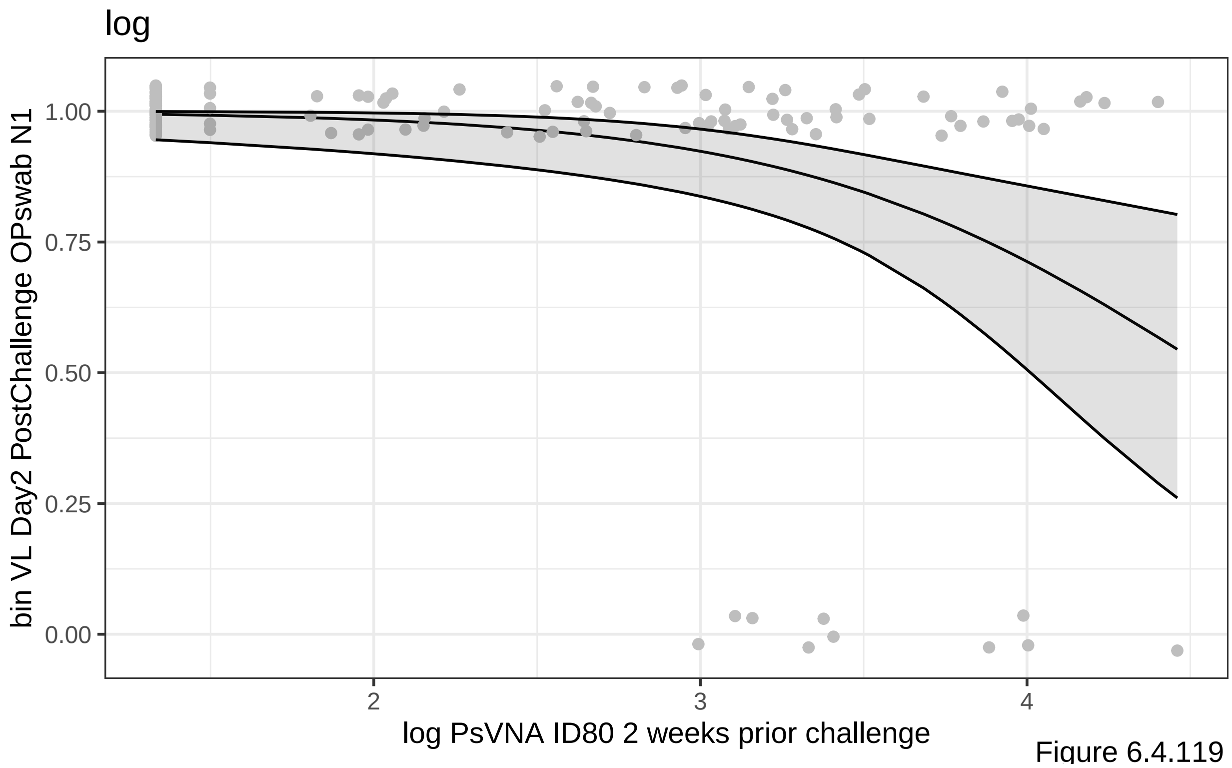

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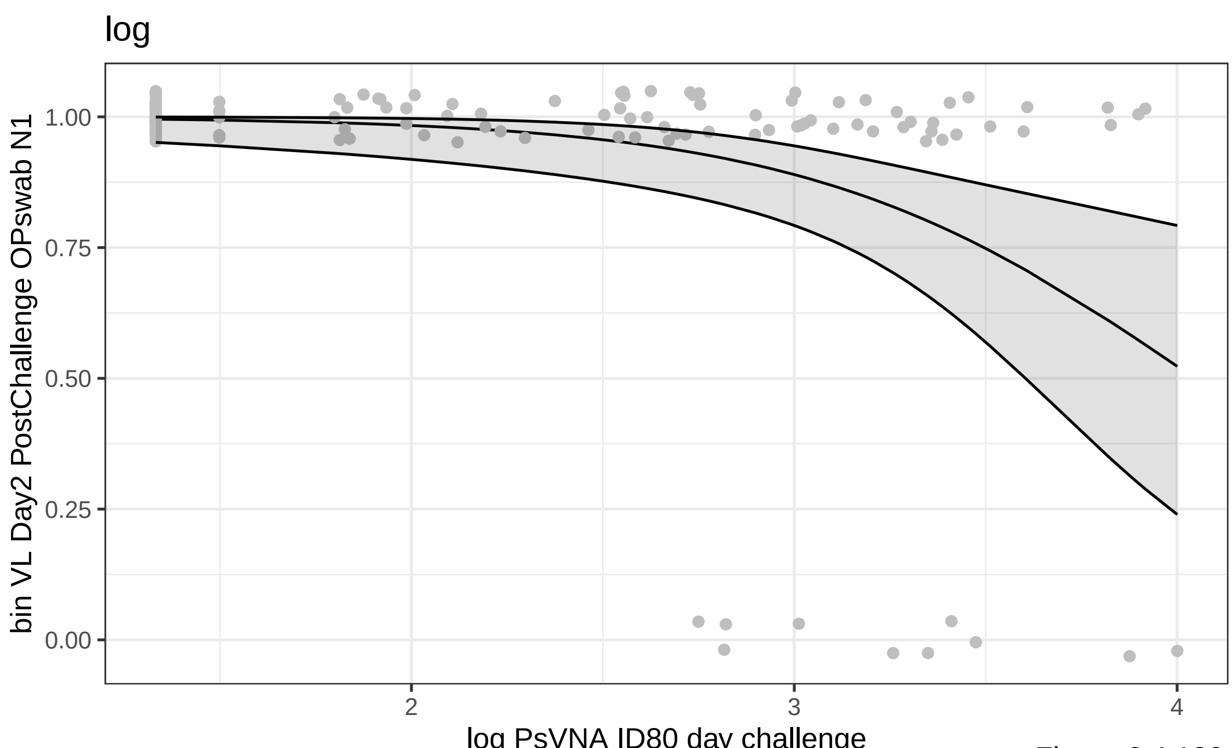

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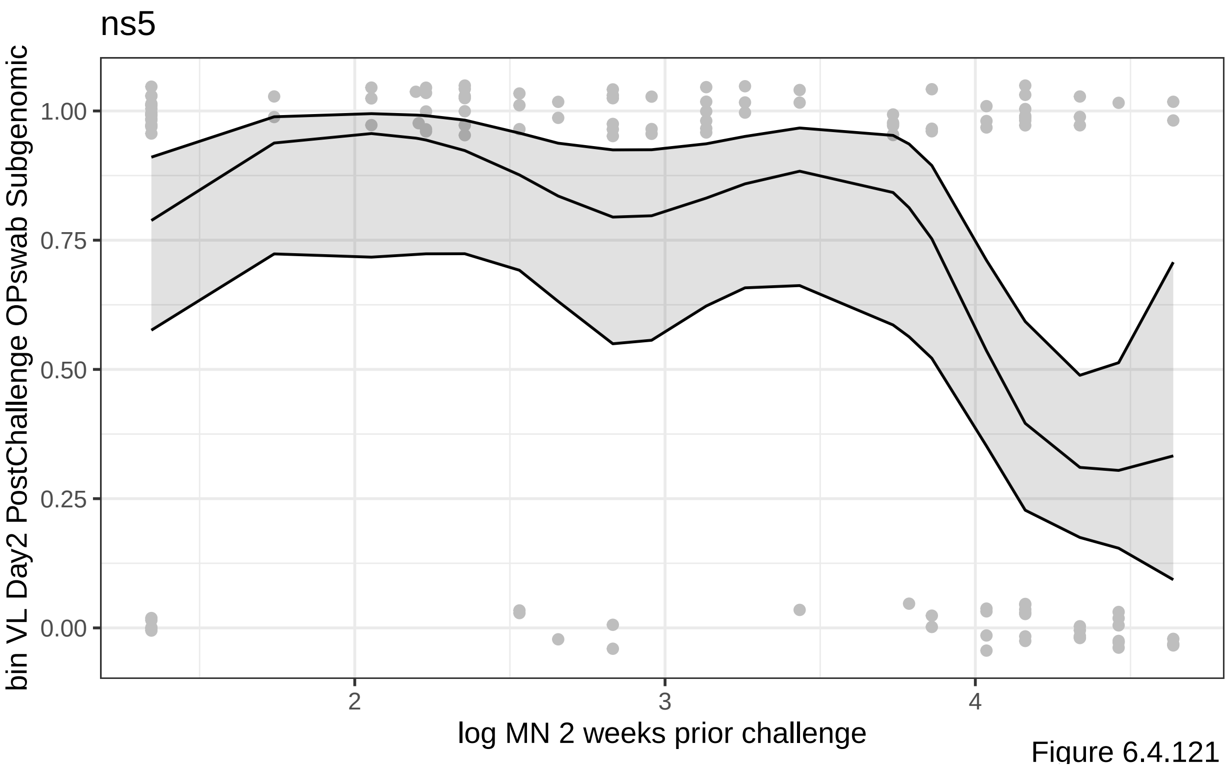

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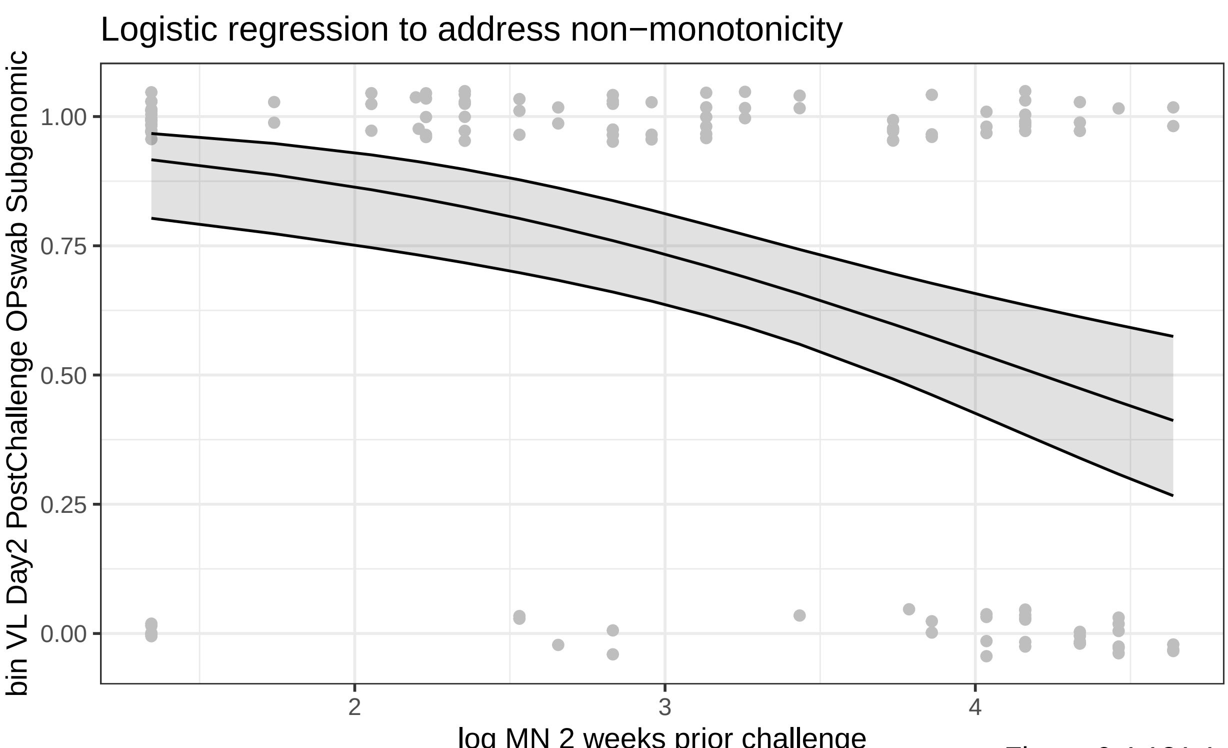

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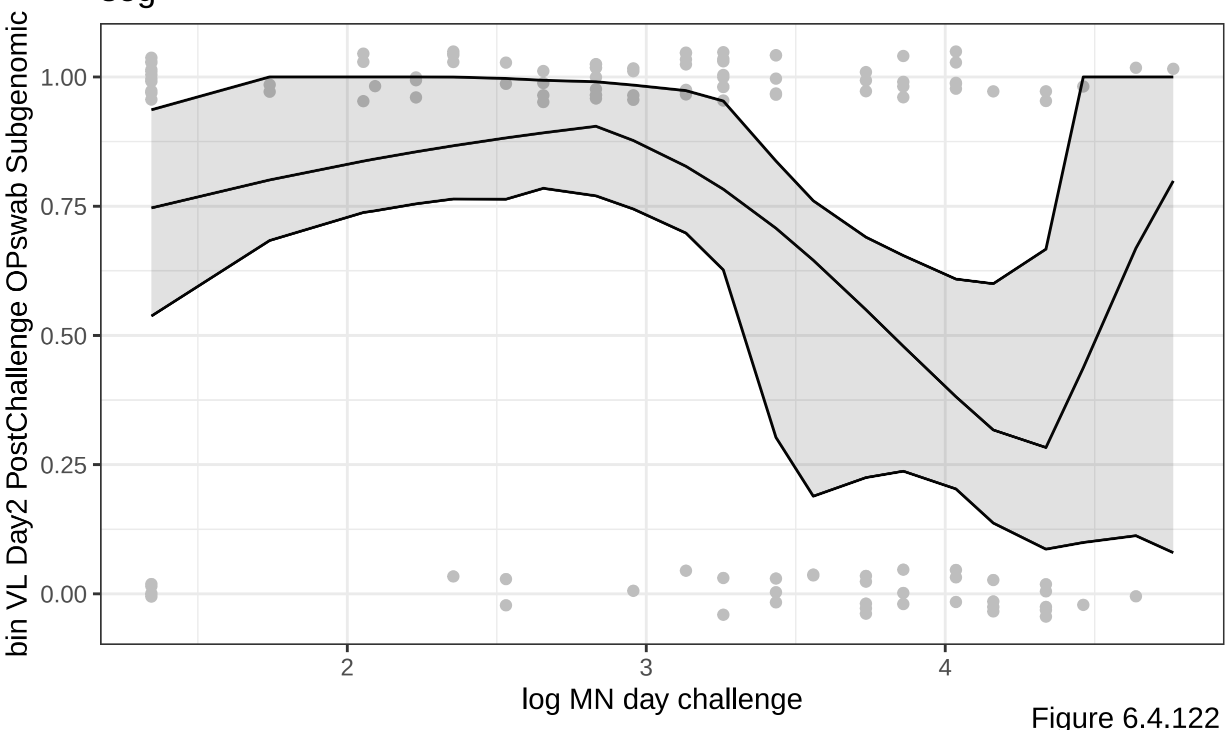
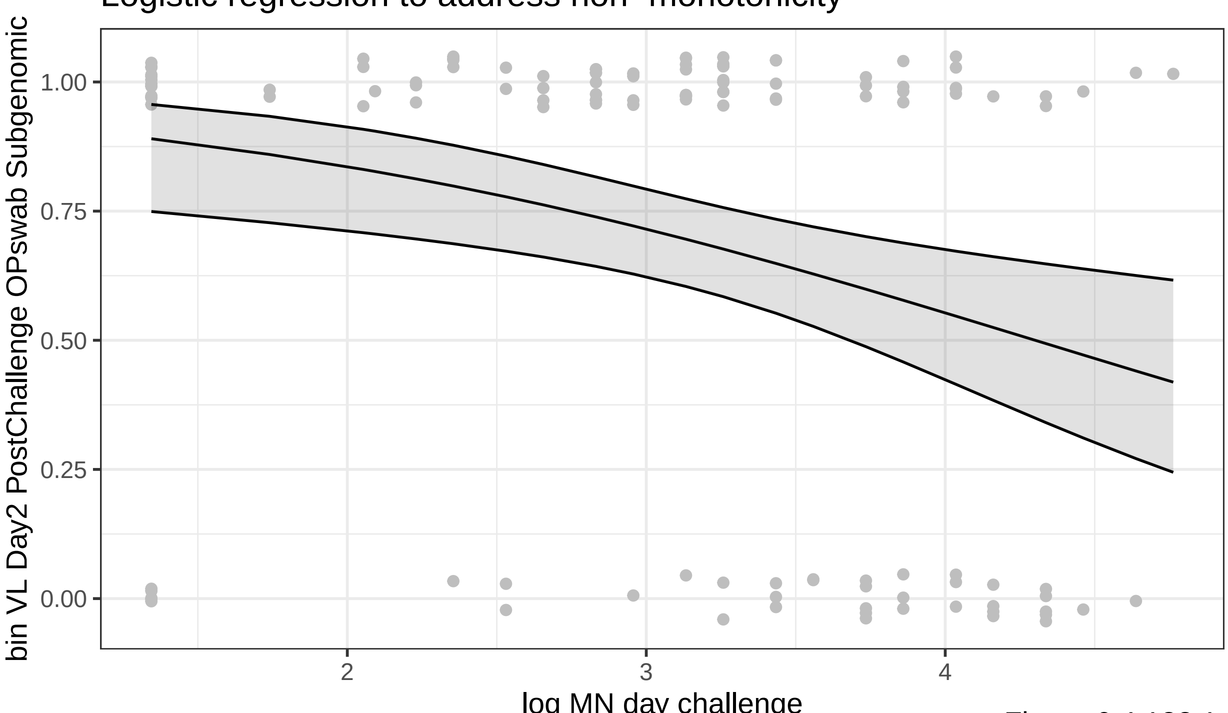


Figure 6.4.122

Logistic regression to address non−monotonicity



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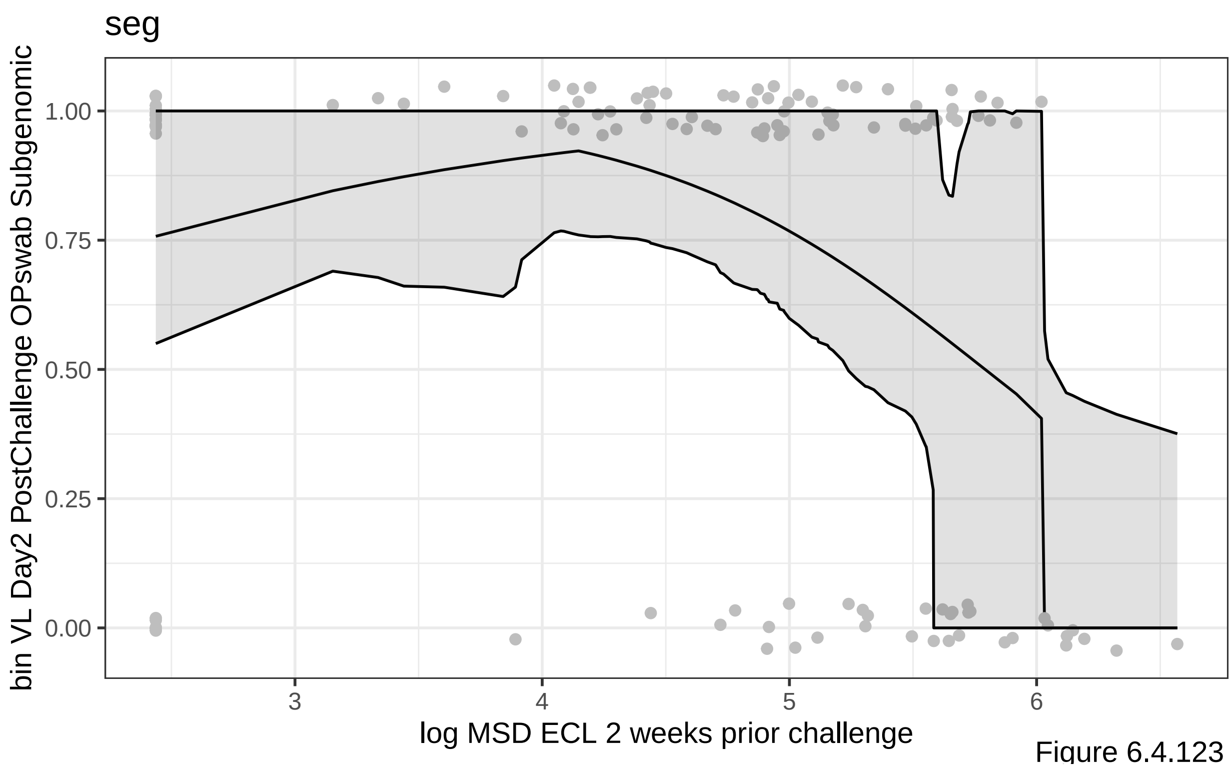

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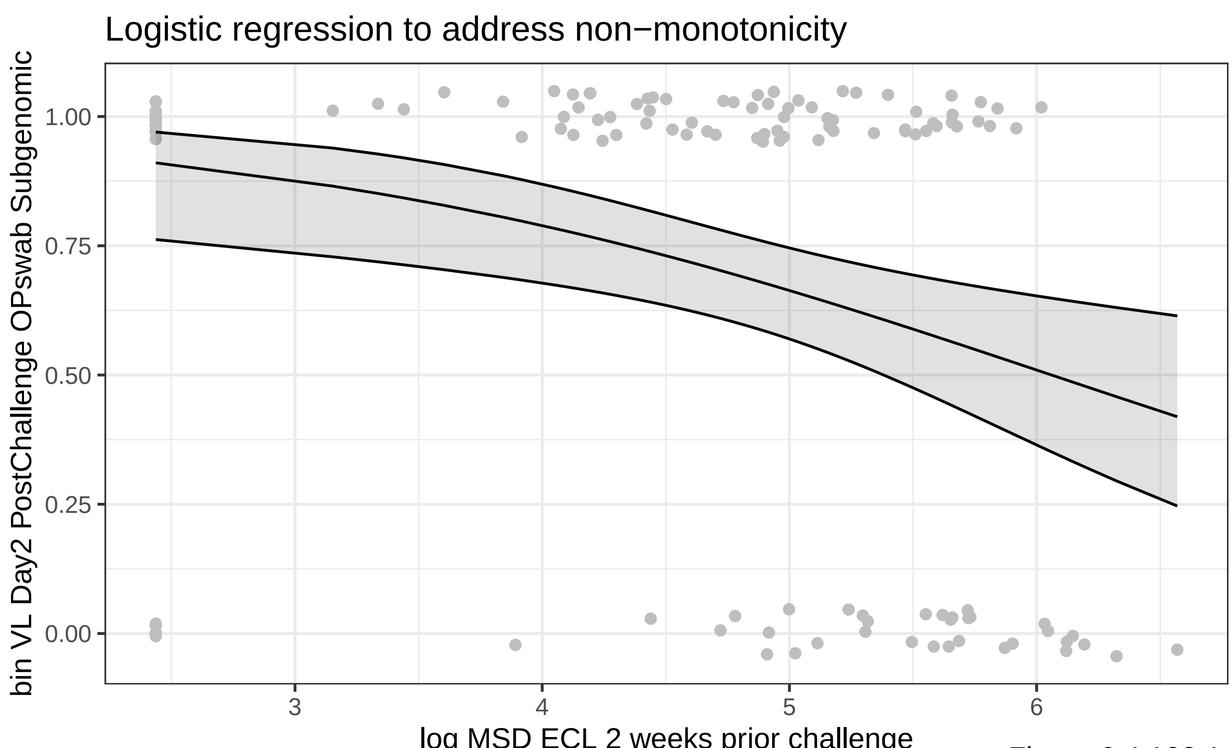

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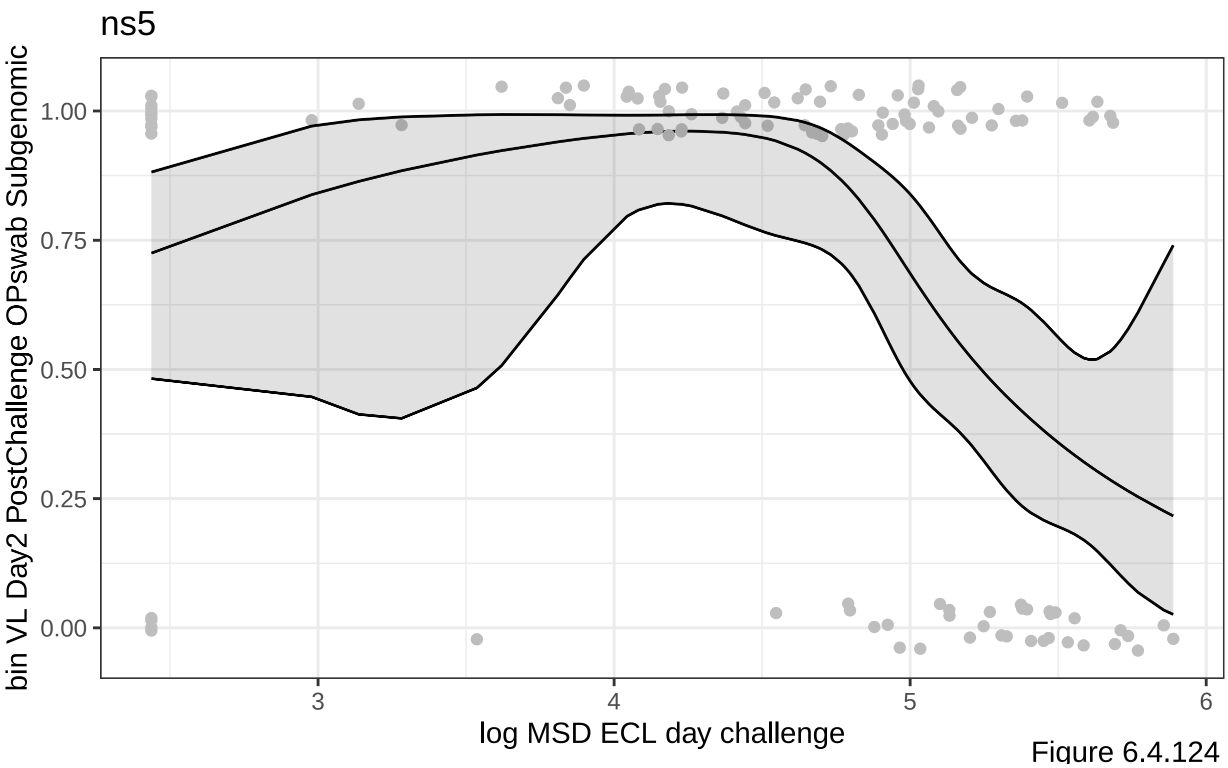

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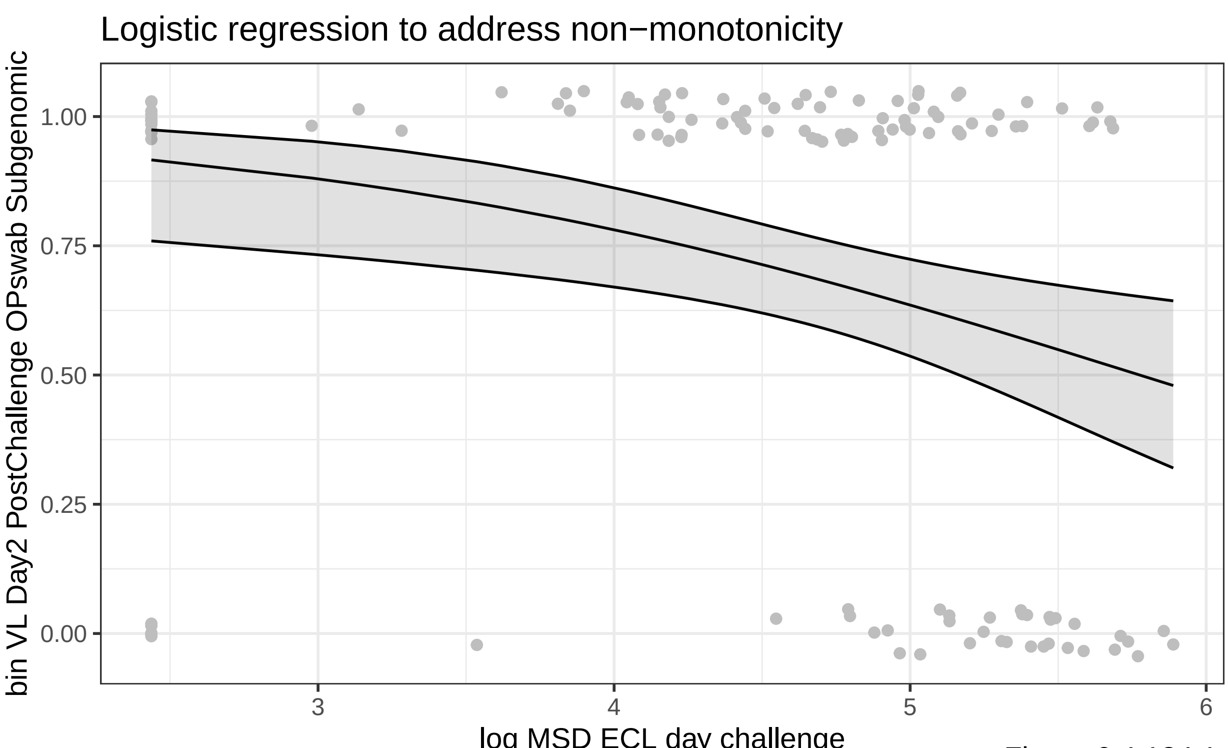

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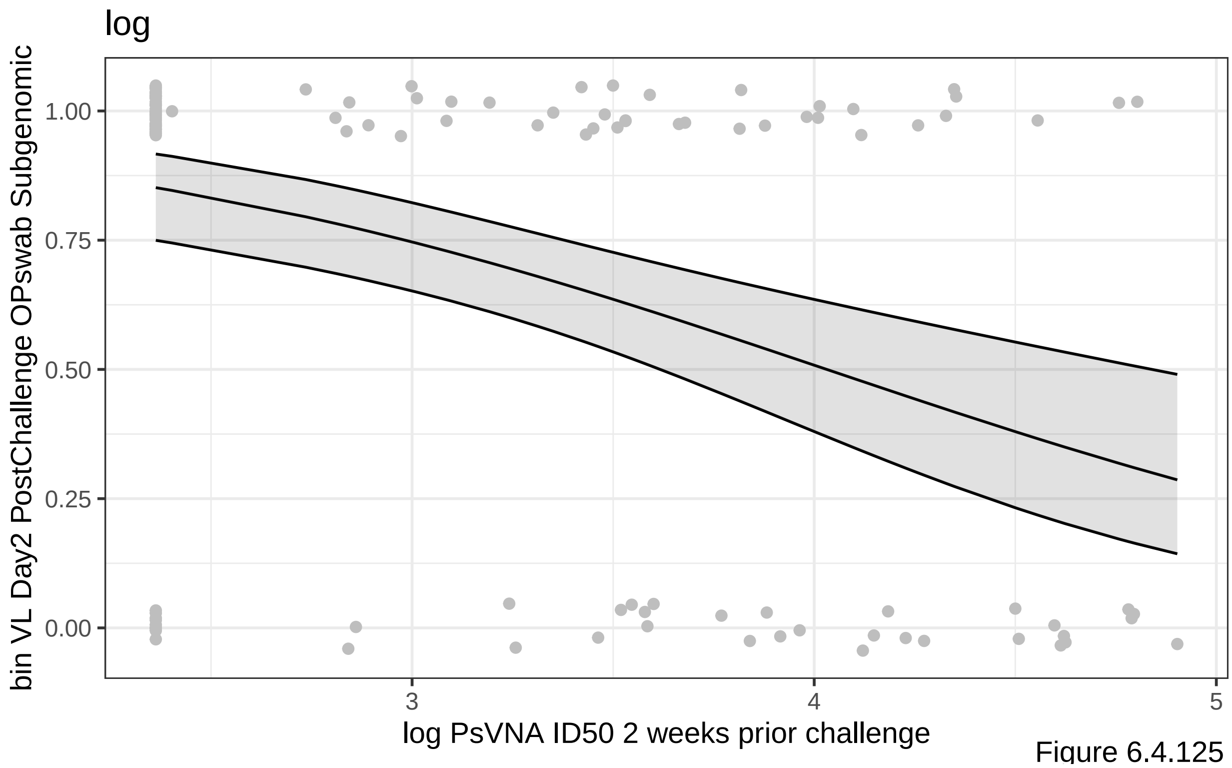

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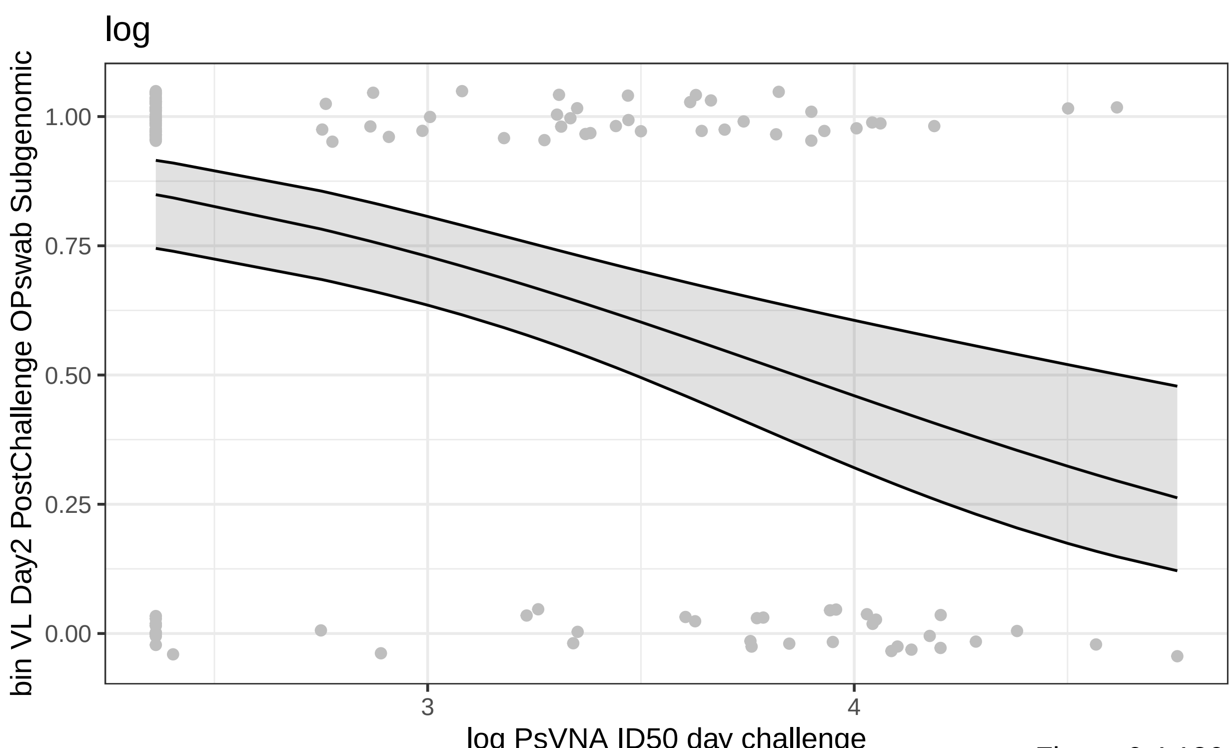

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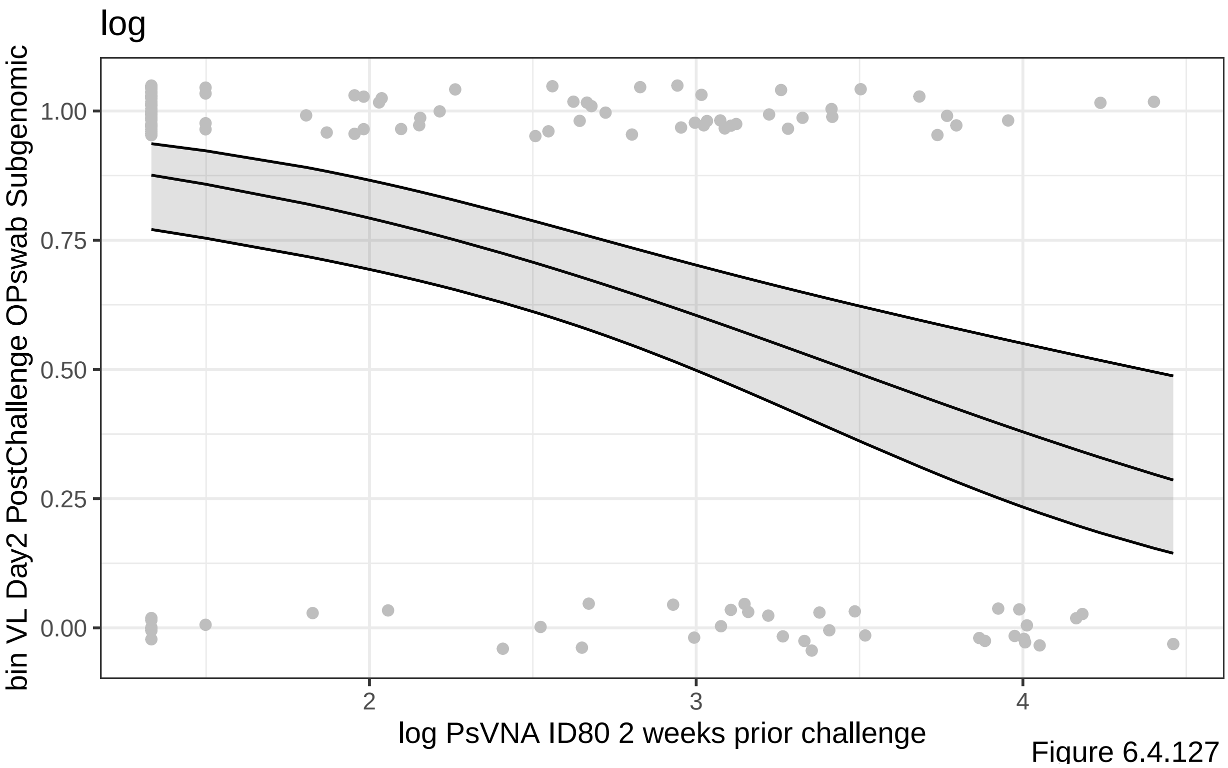

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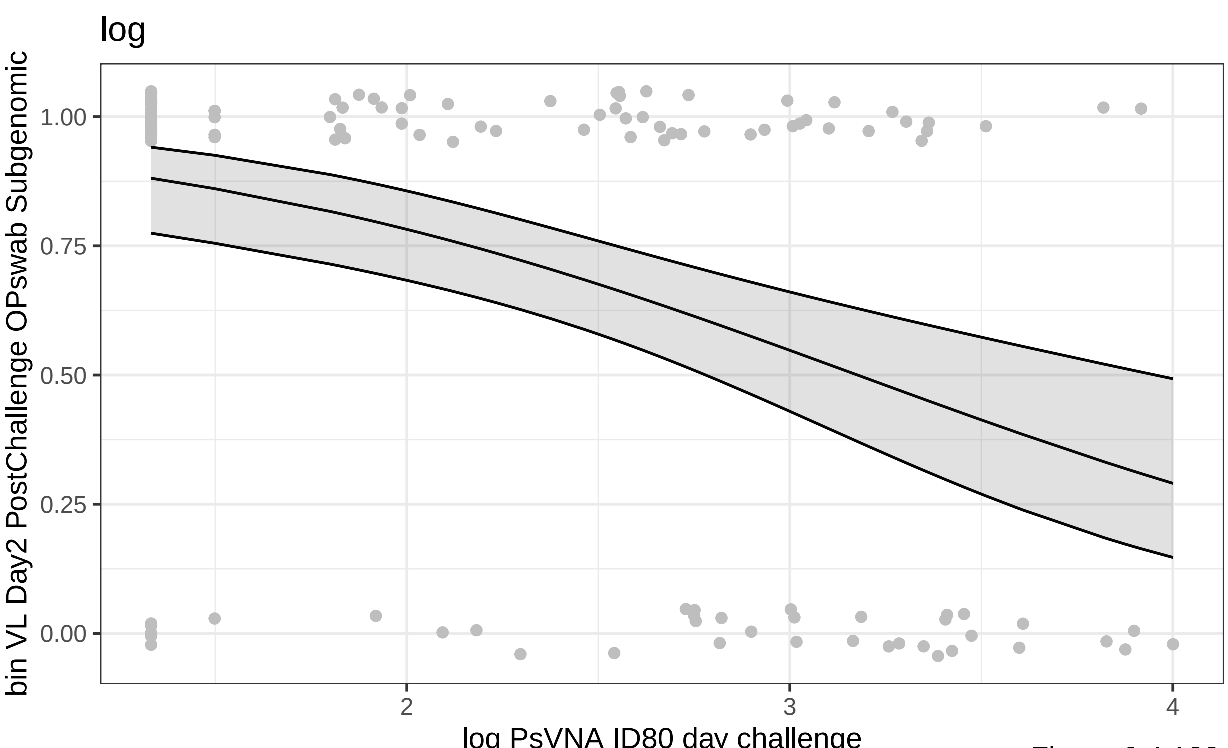

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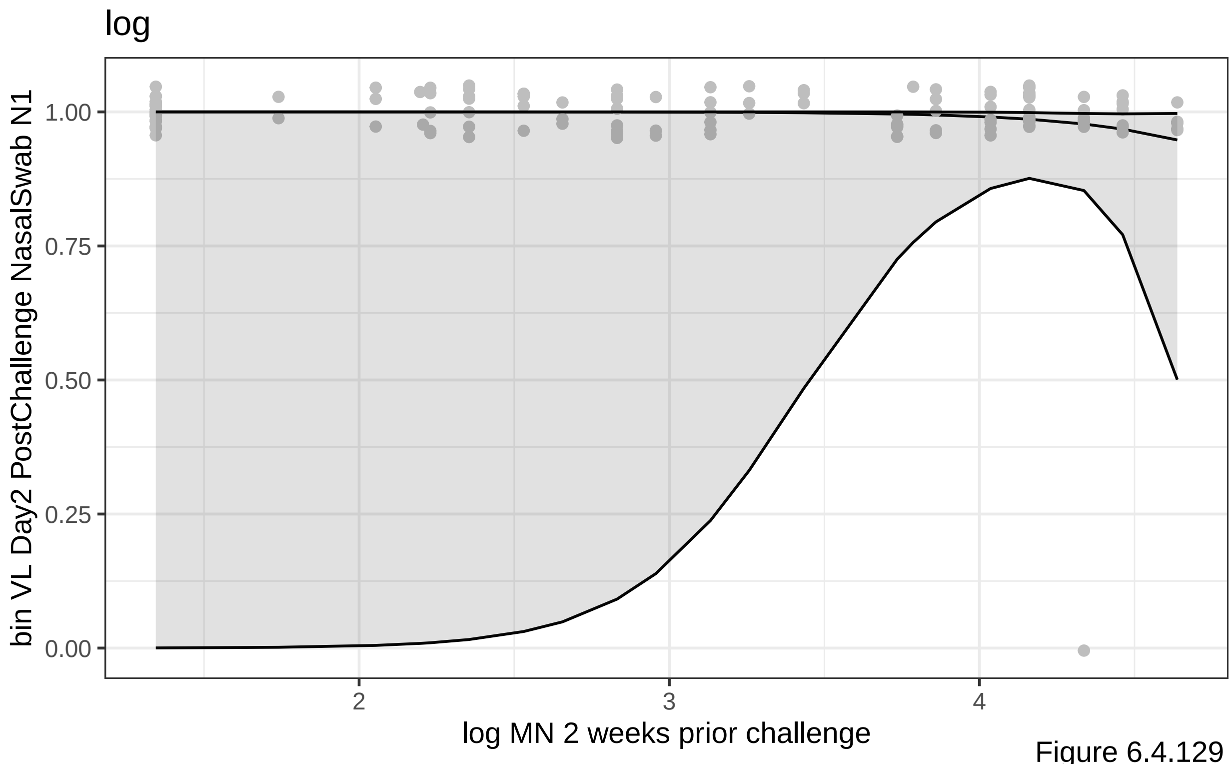

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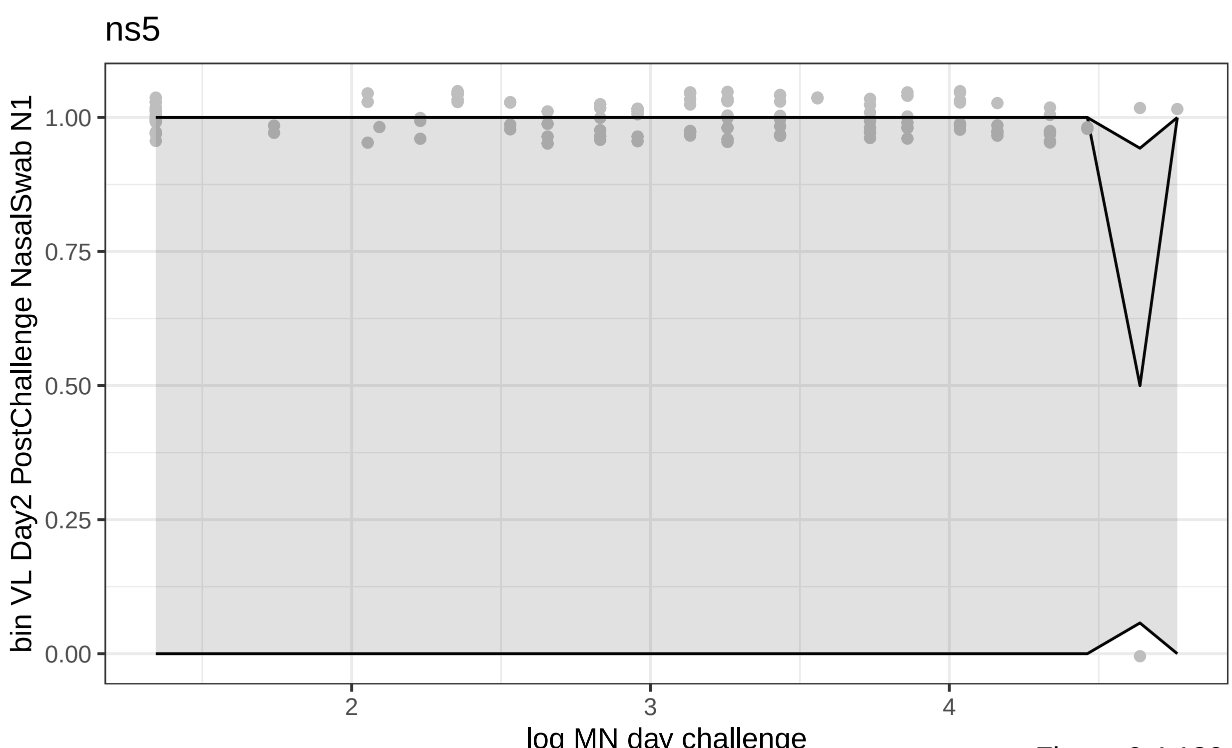

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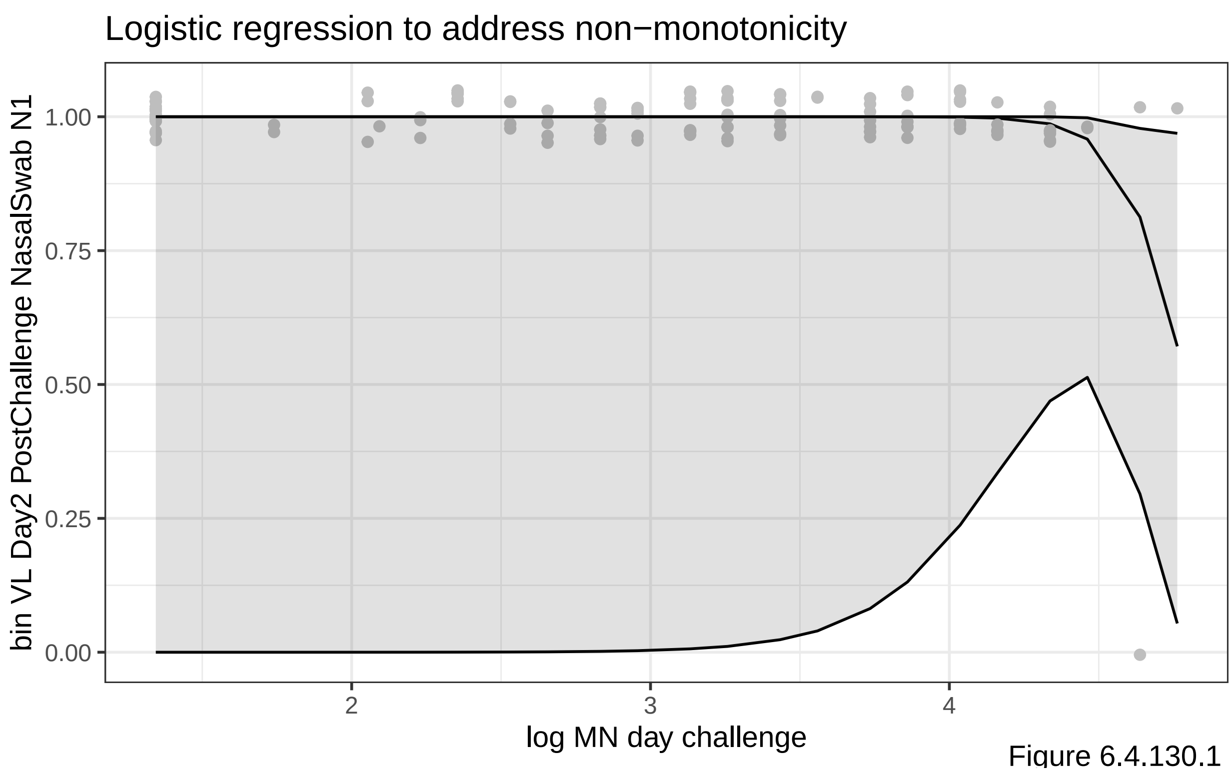

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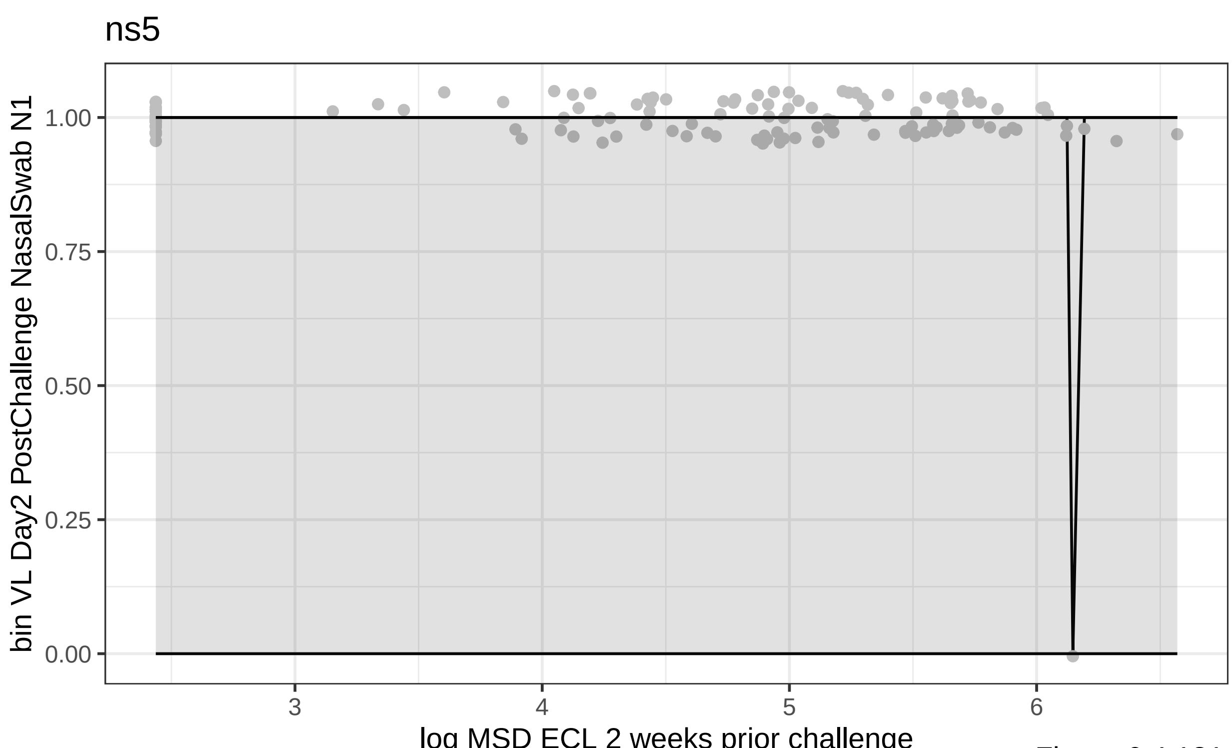

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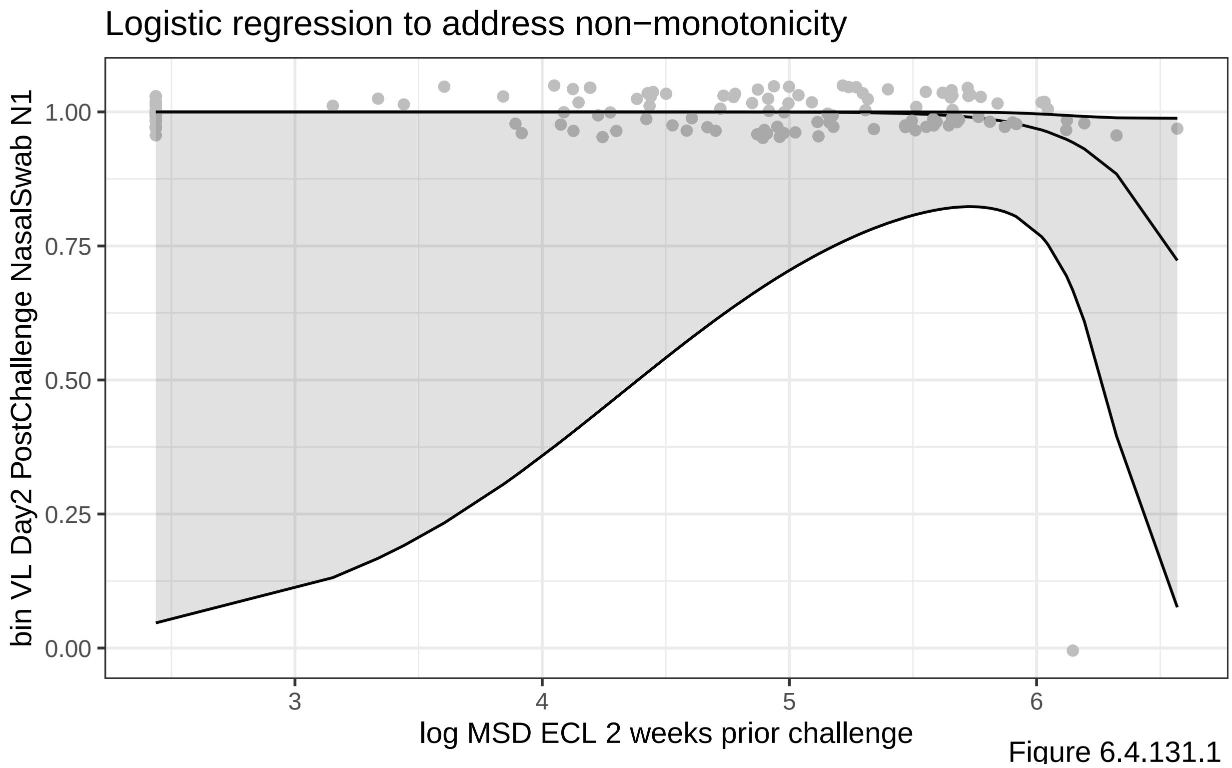

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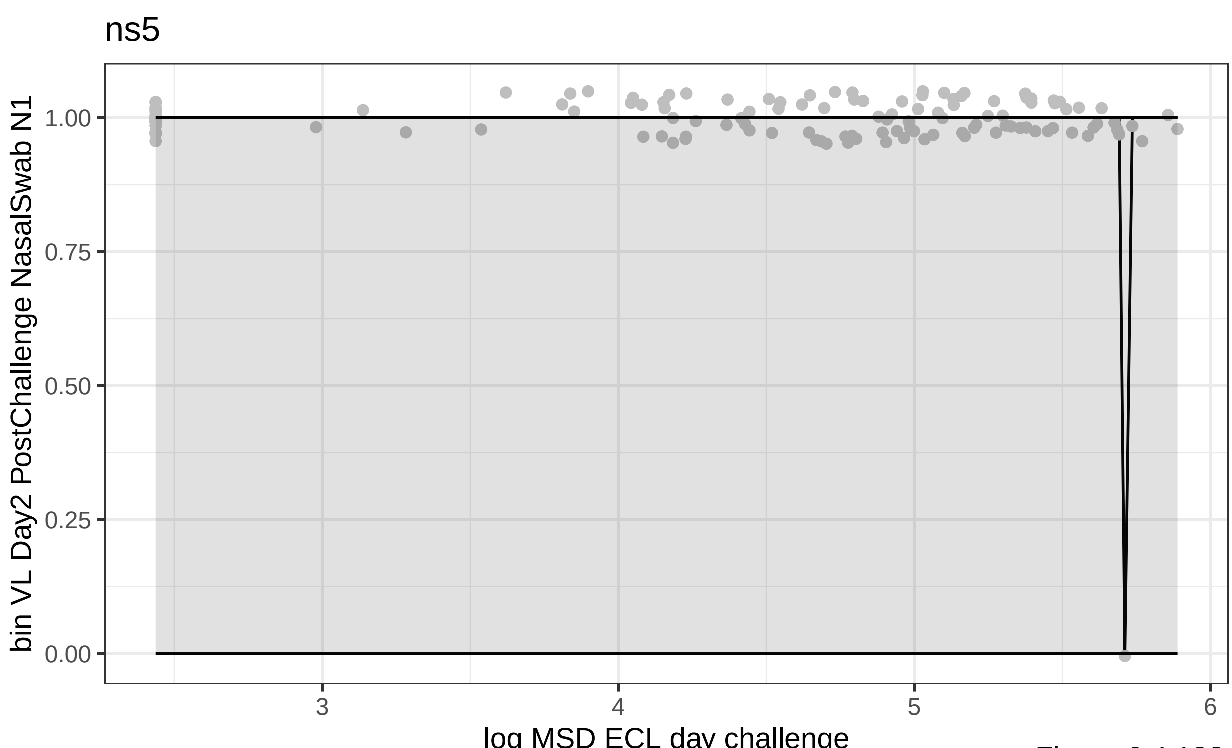
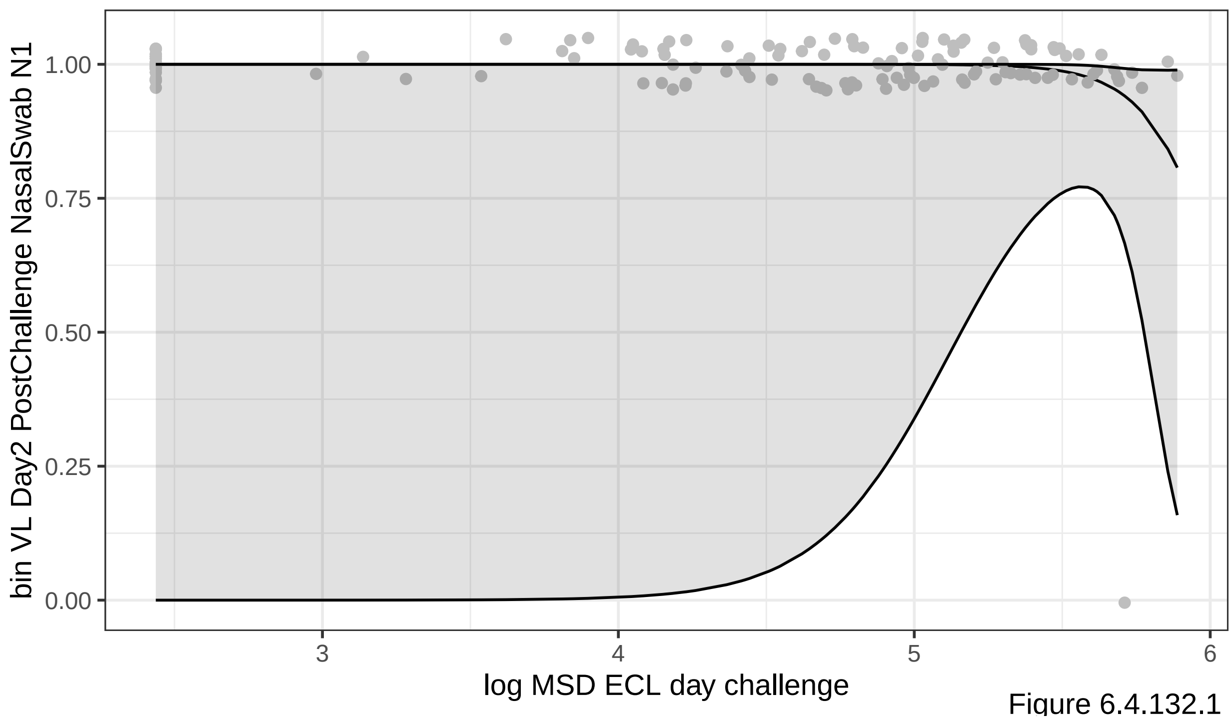


Figure 6.4.132

Logistic regression to address non−monotonicity



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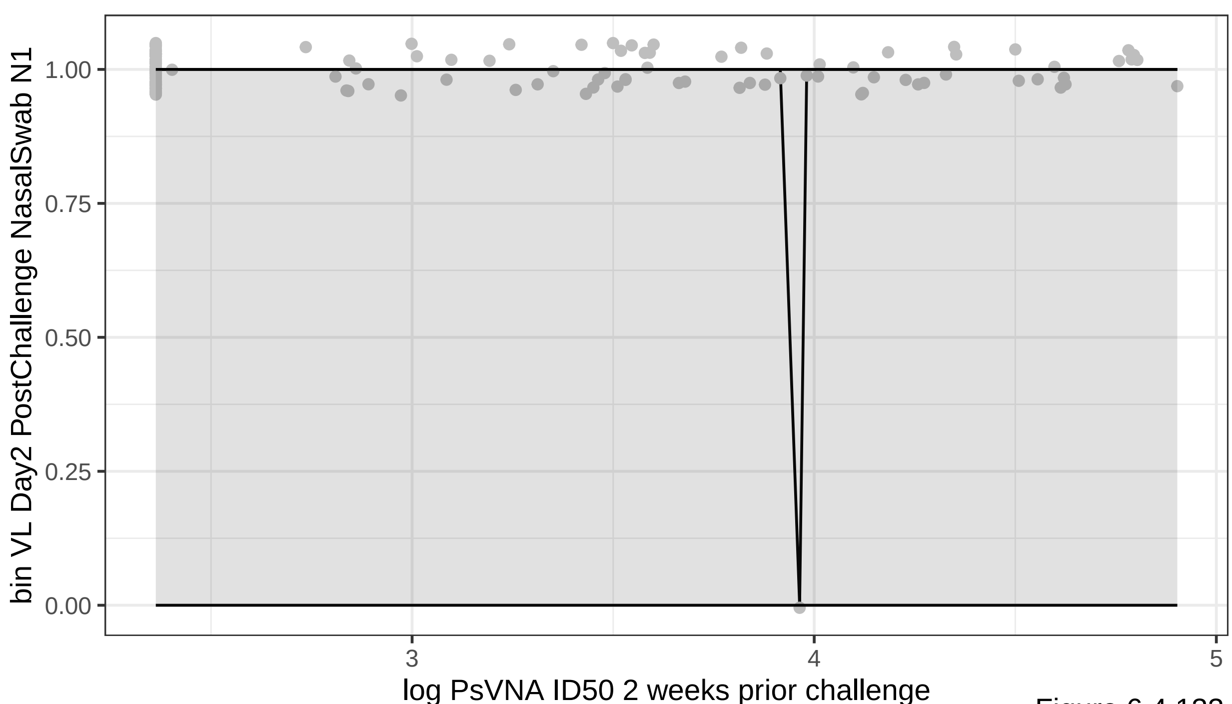
ns5



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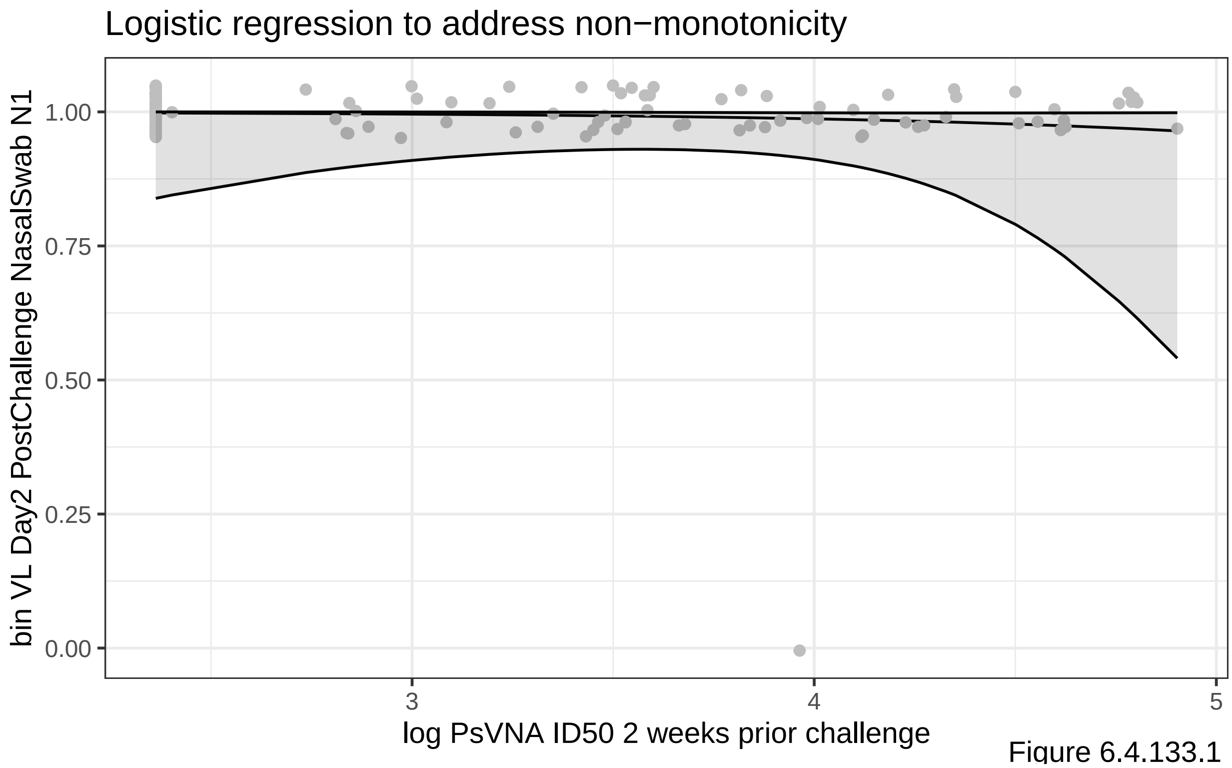

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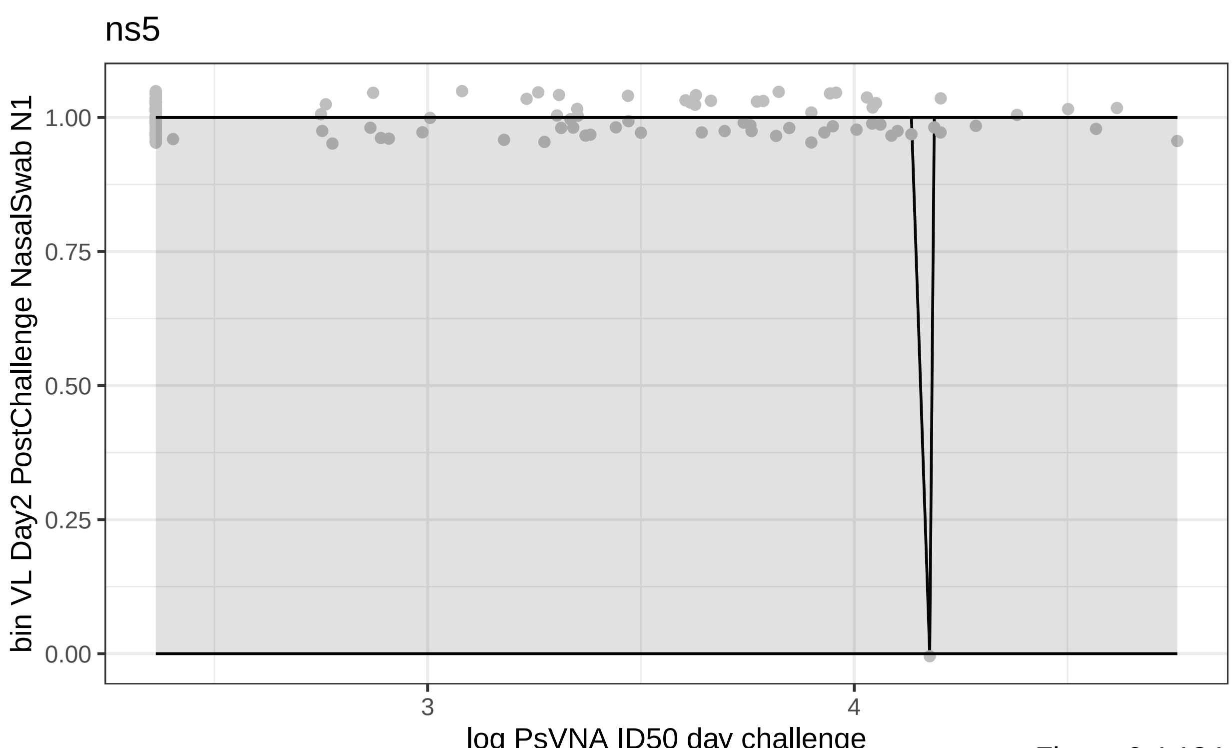

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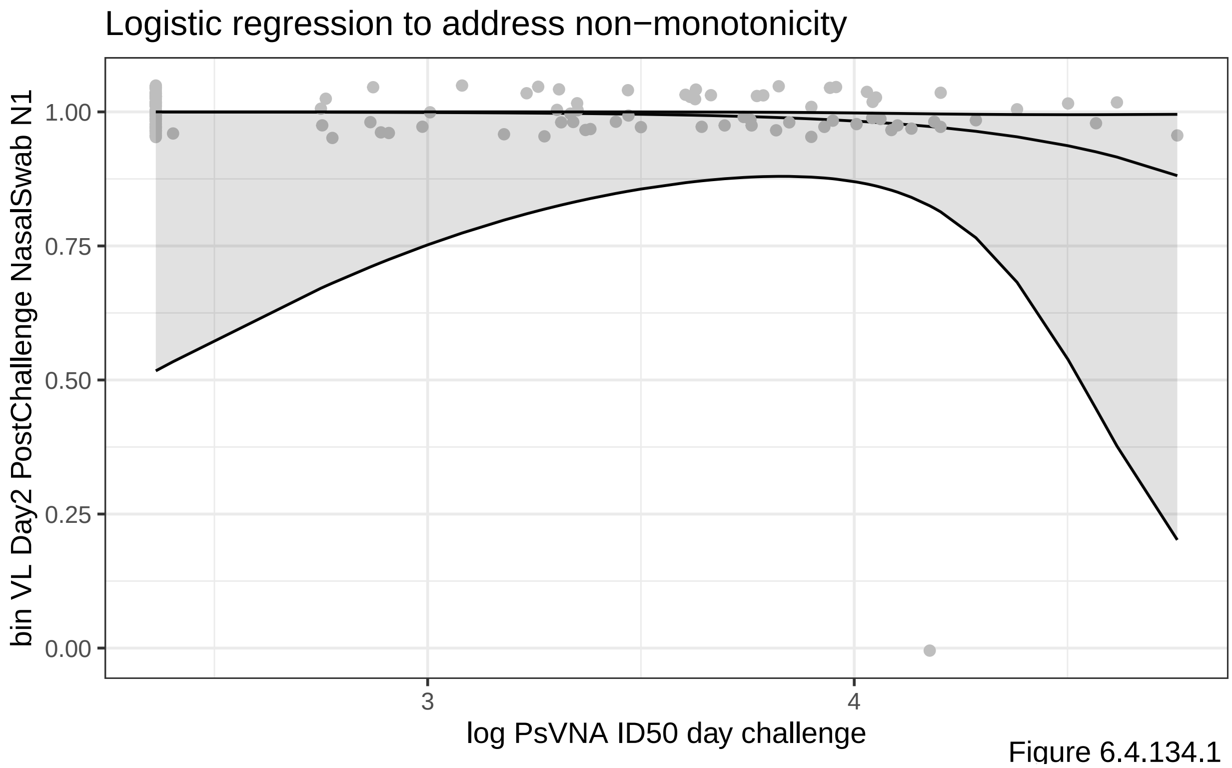

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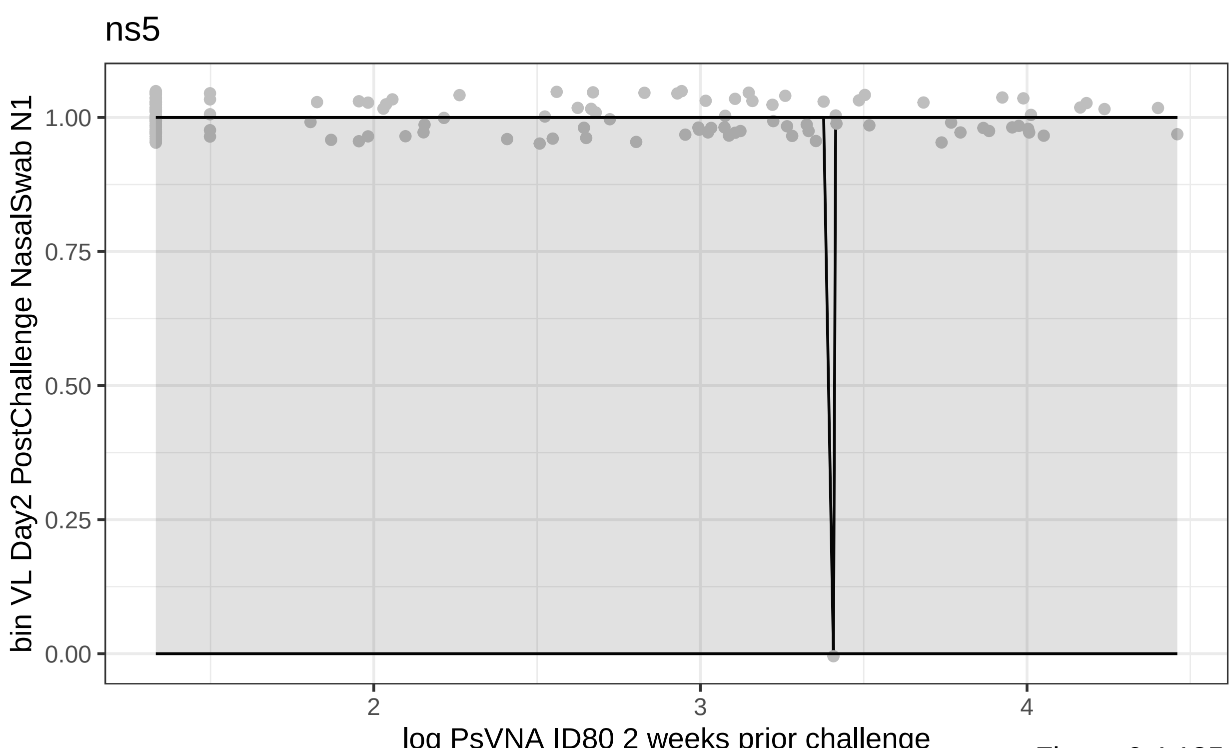

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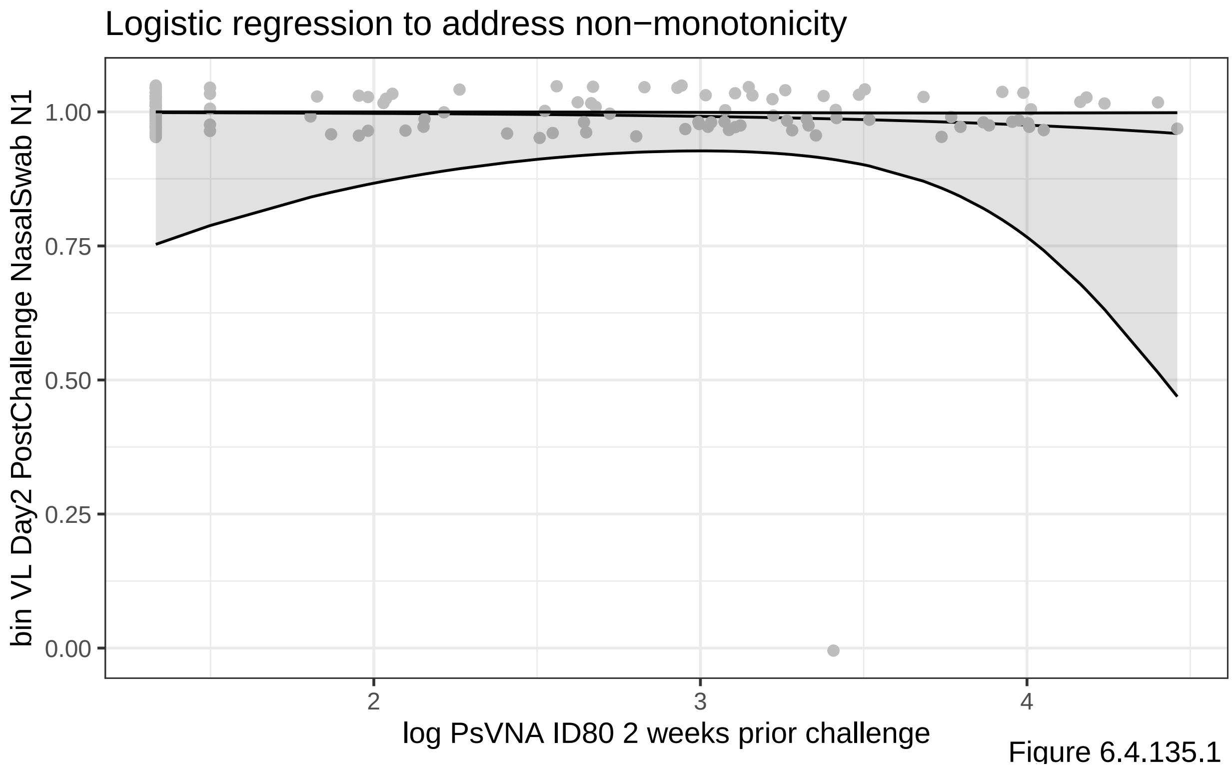

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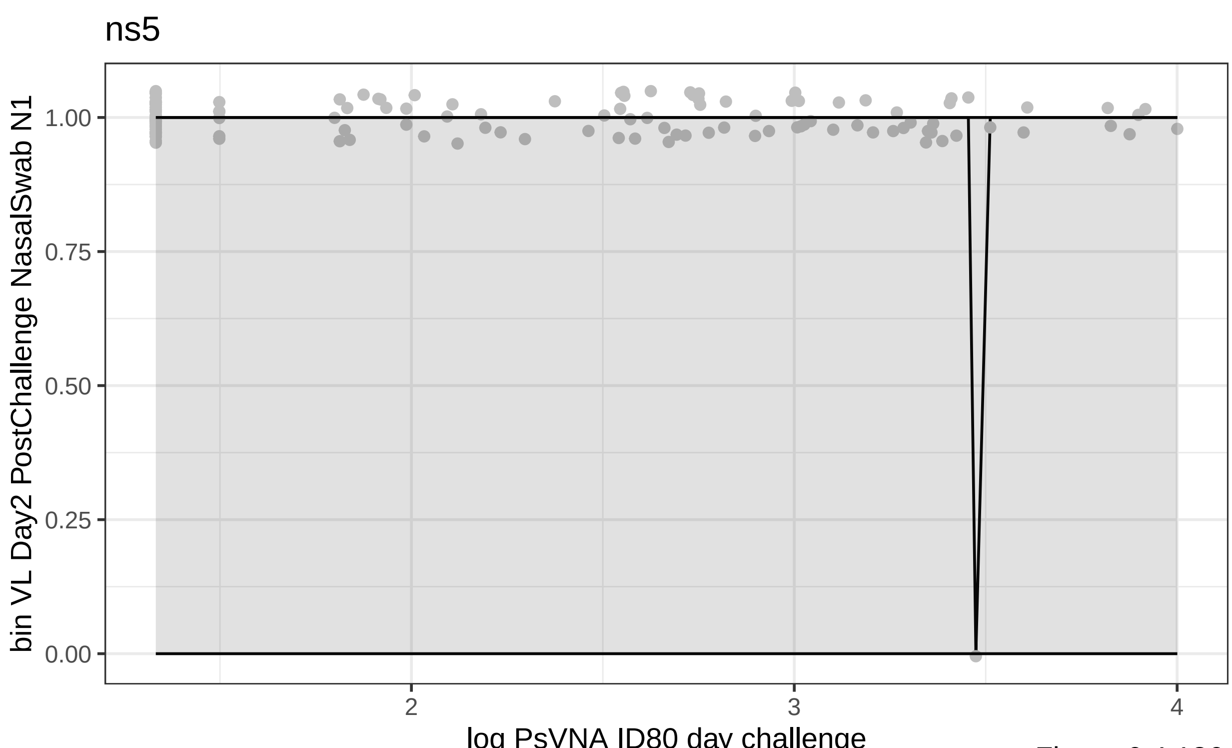

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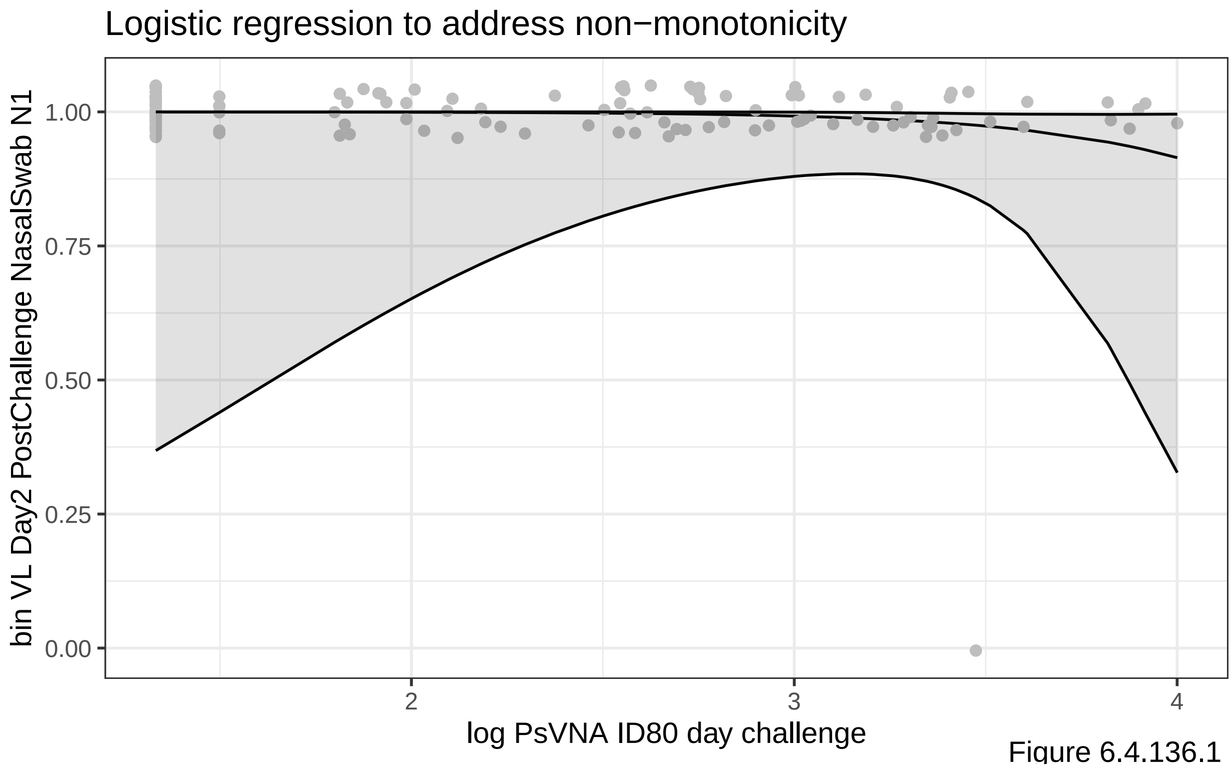

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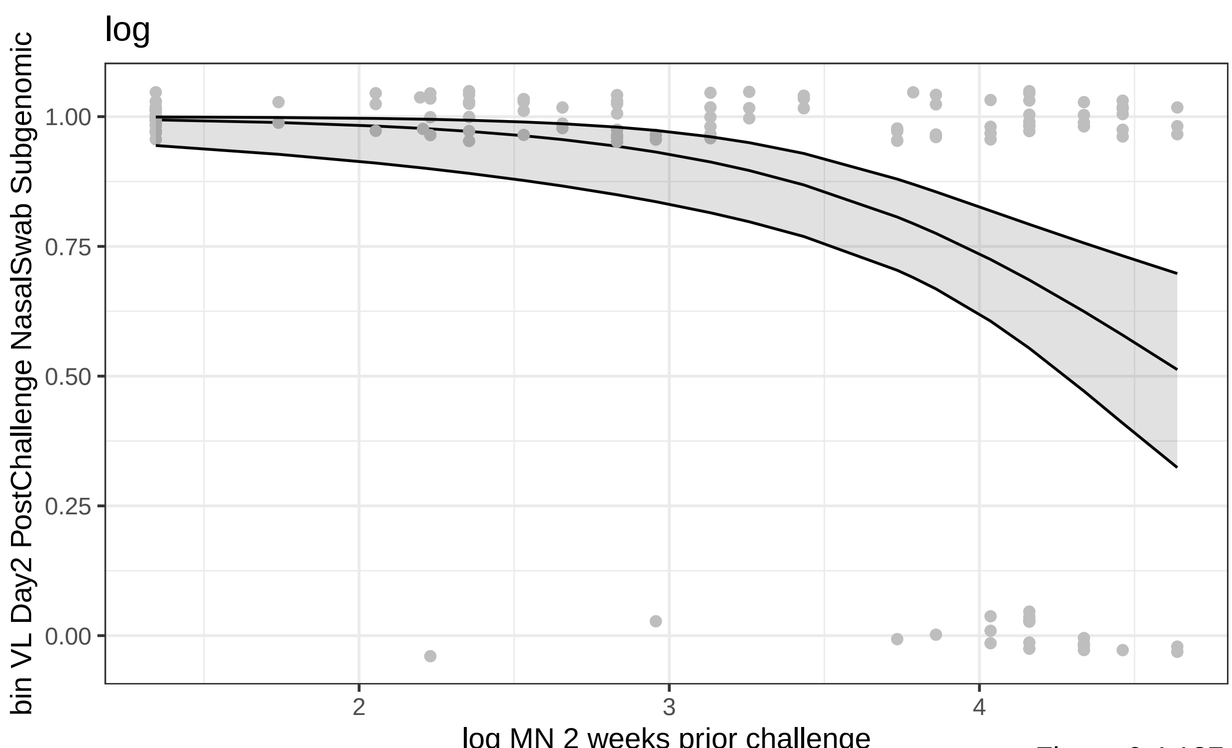

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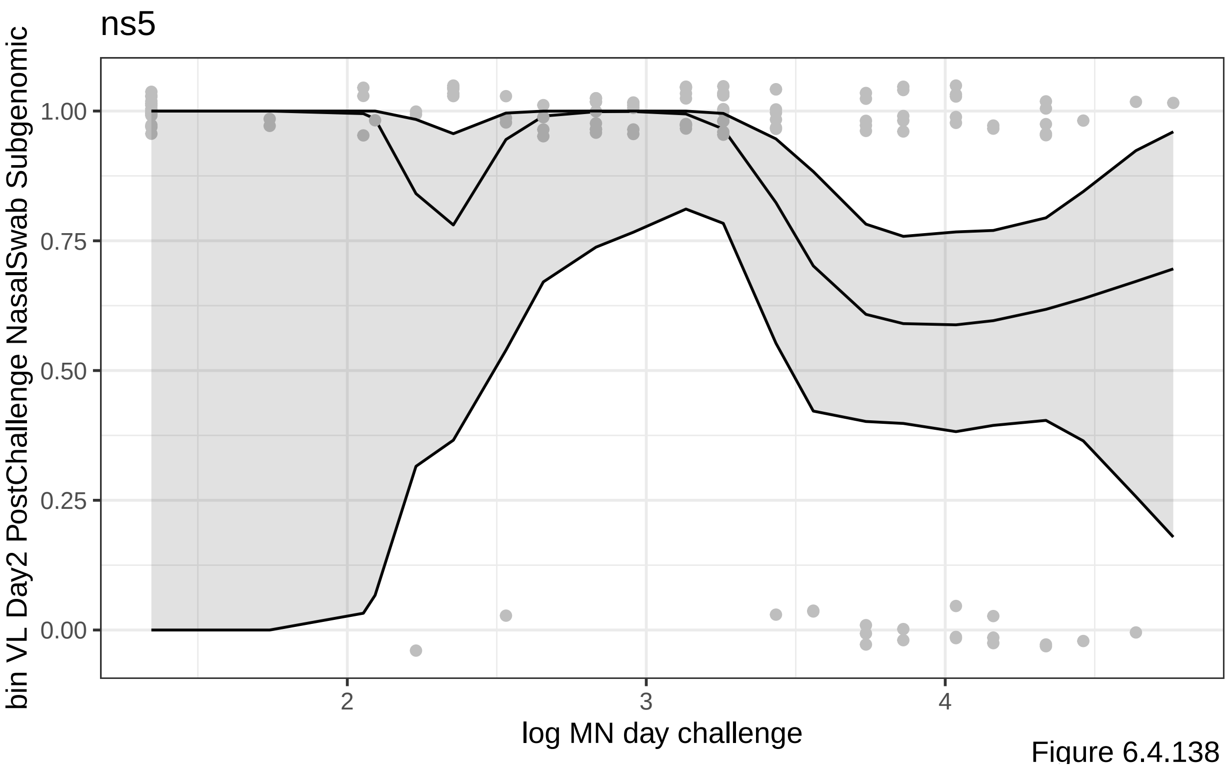

Figure 6.4.138

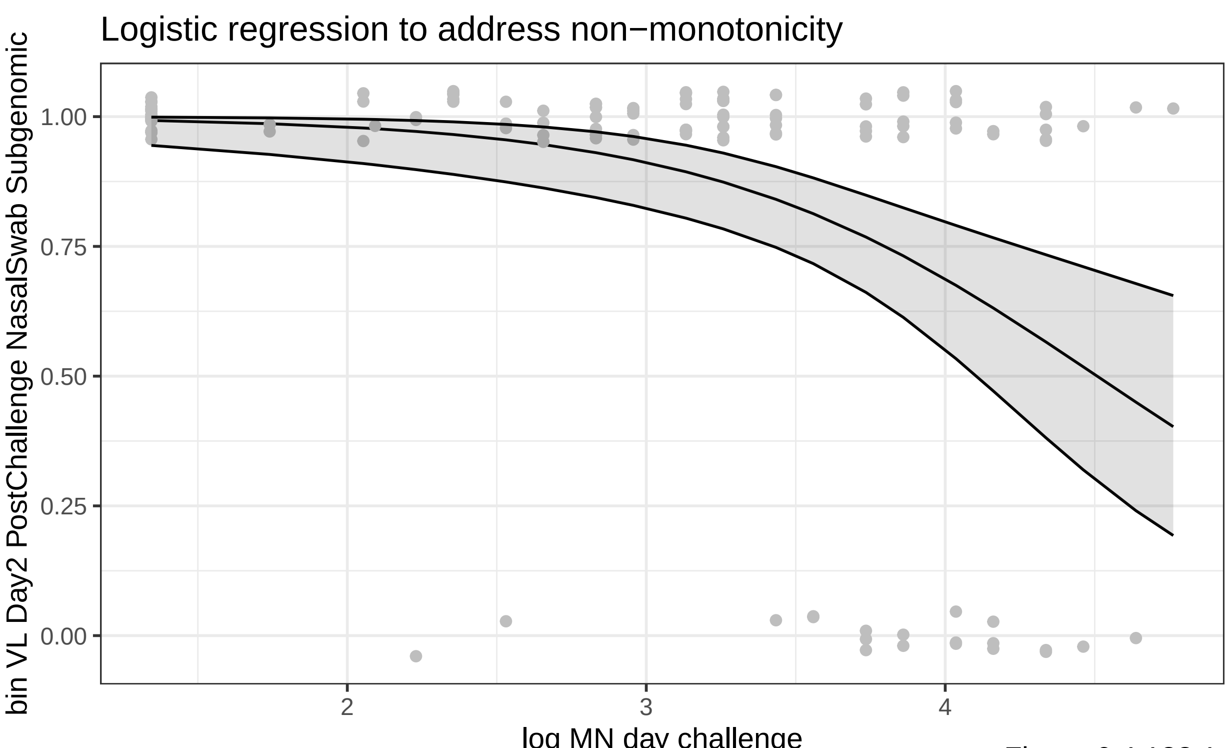

Figure 6.4.138.1

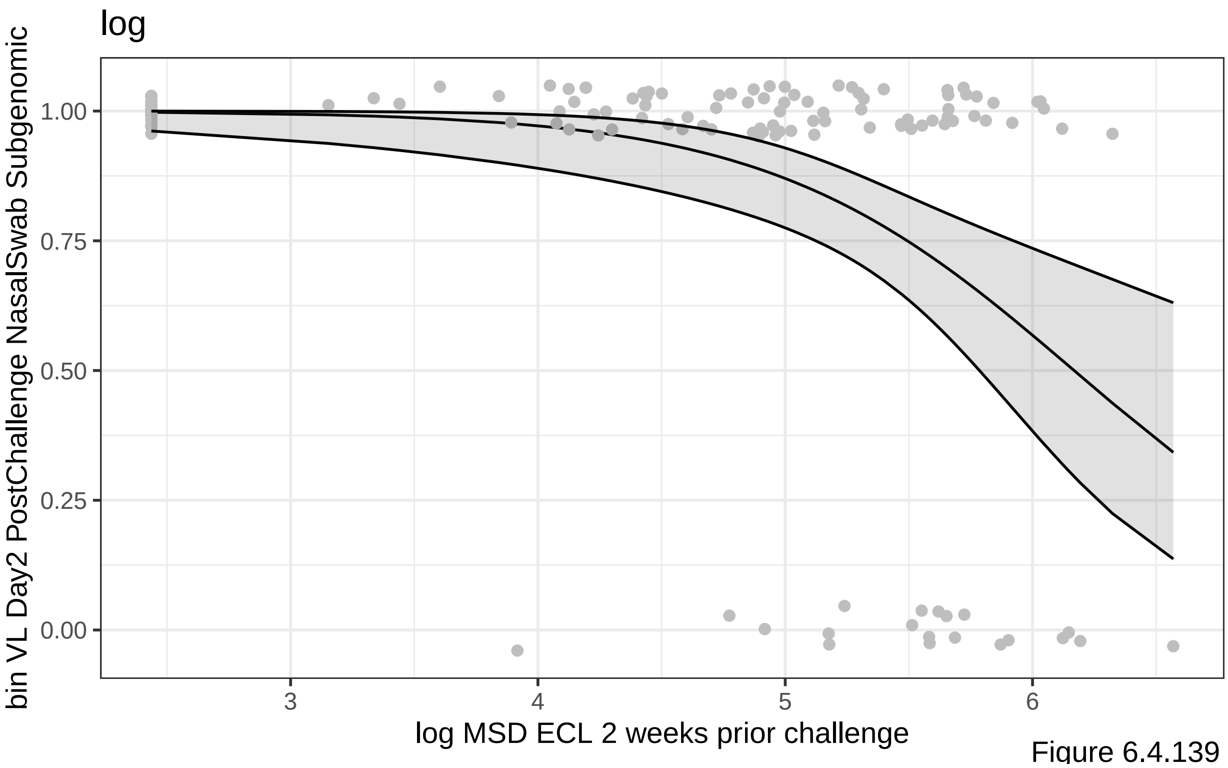

Figure 6.4.139

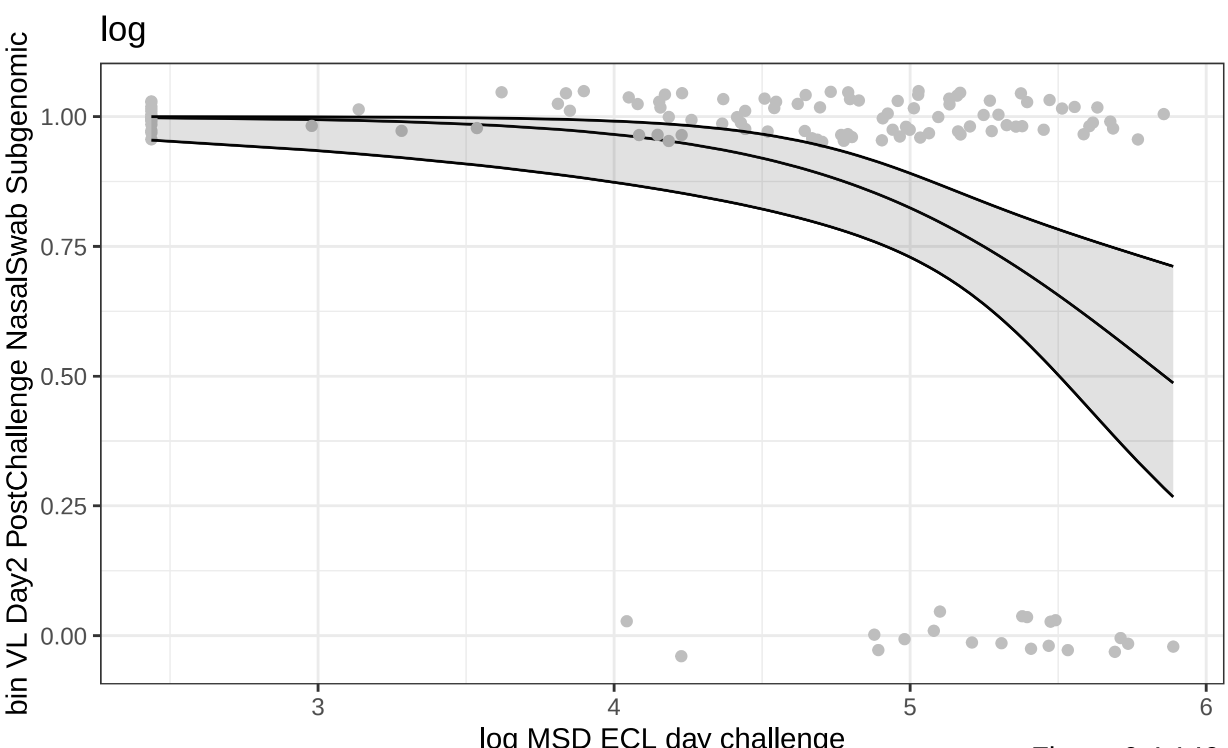

Figure 6.4.140

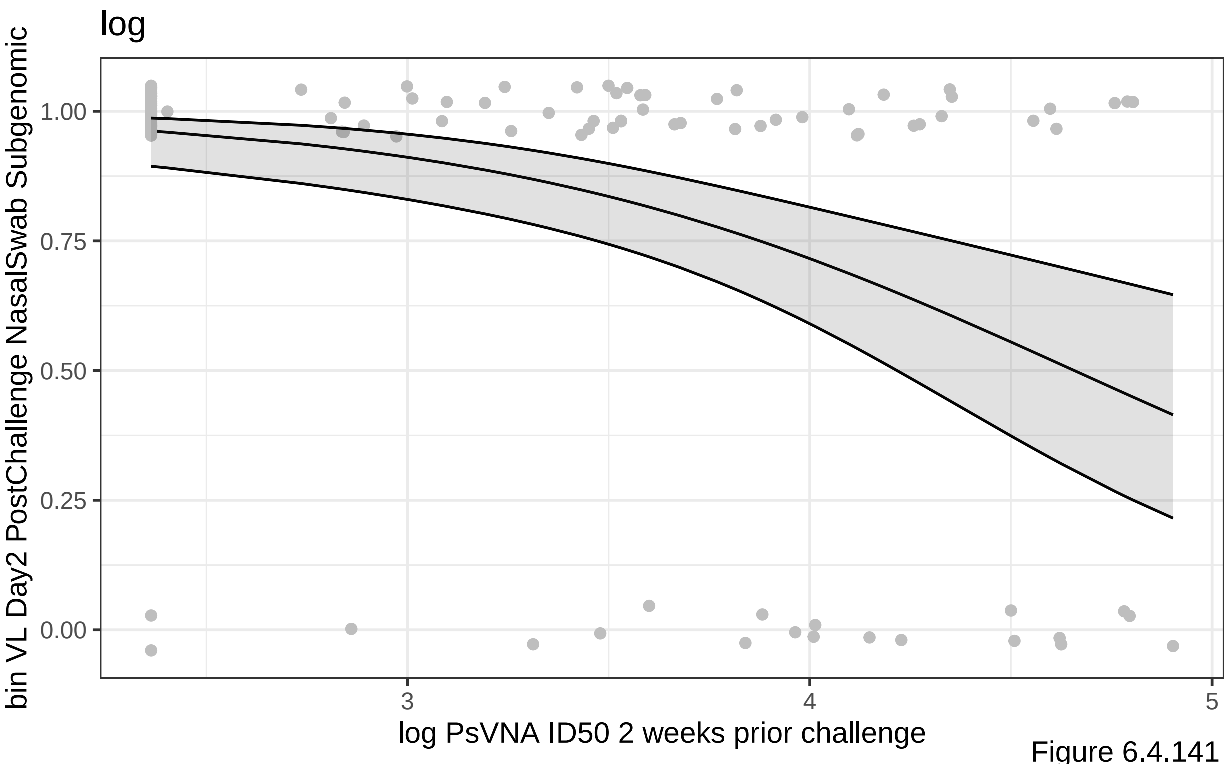

Figure 6.4.141

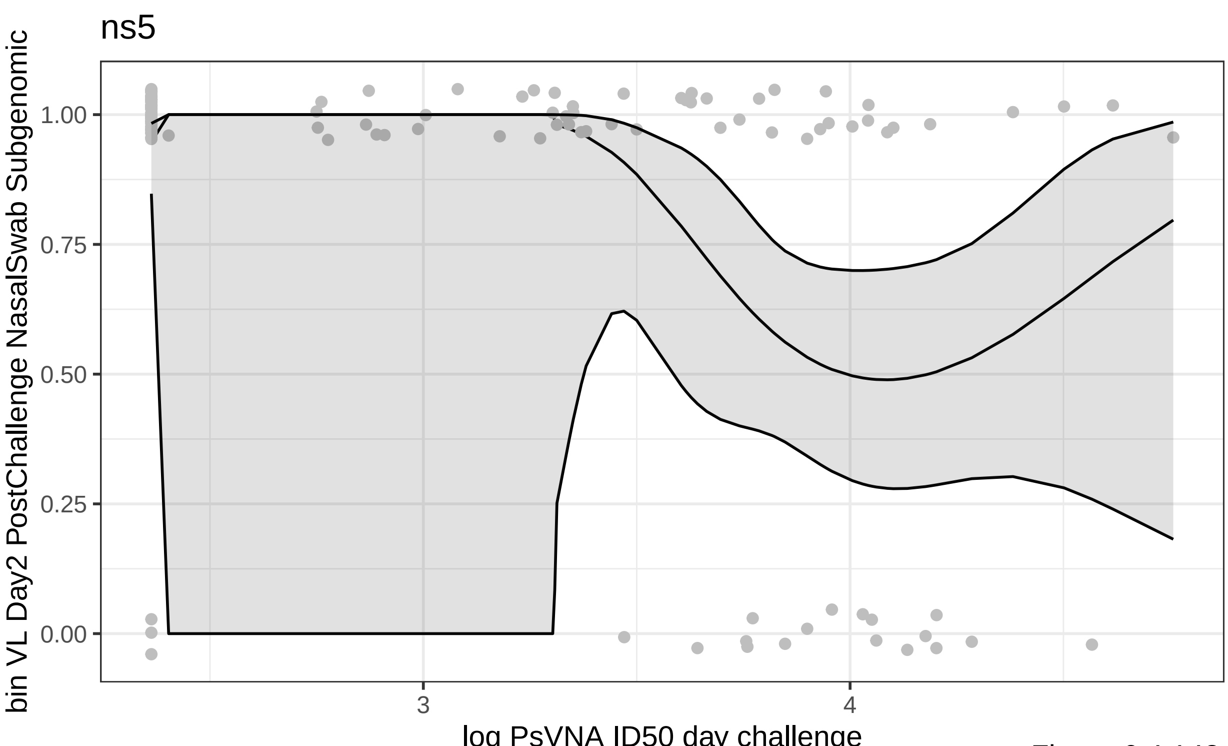

Figure 6.4.142

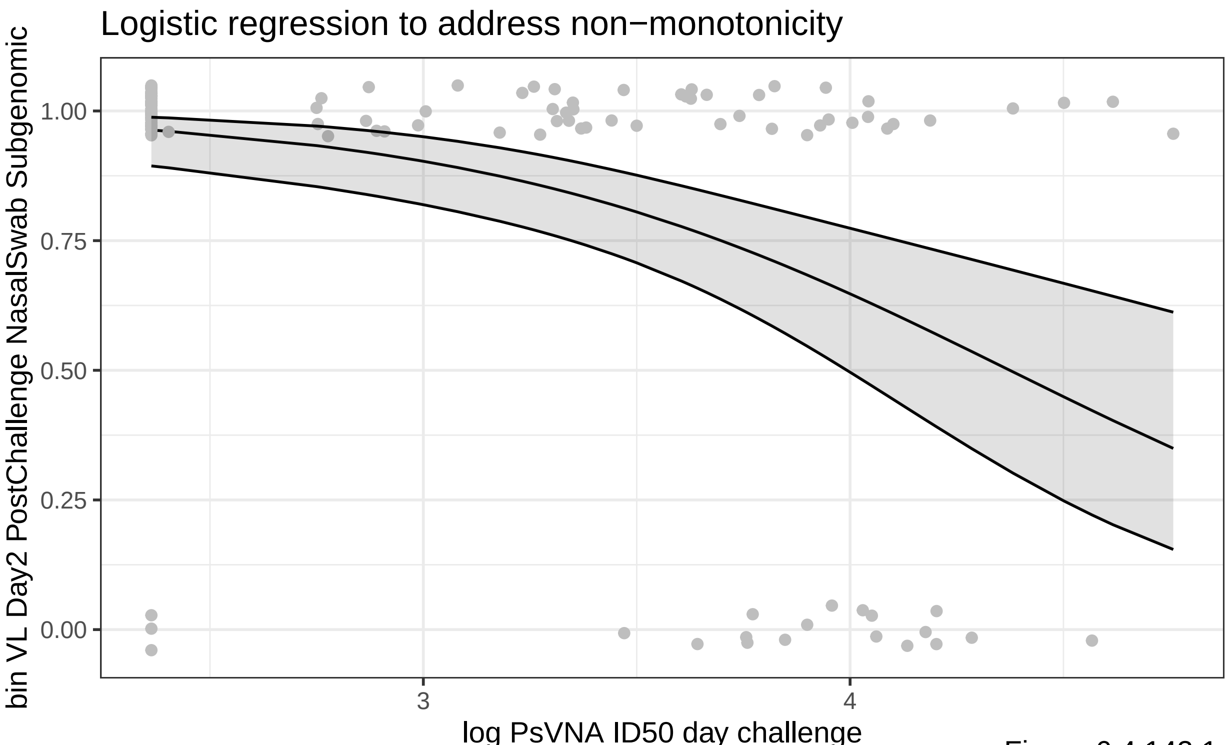

Figure 6.4.142.1

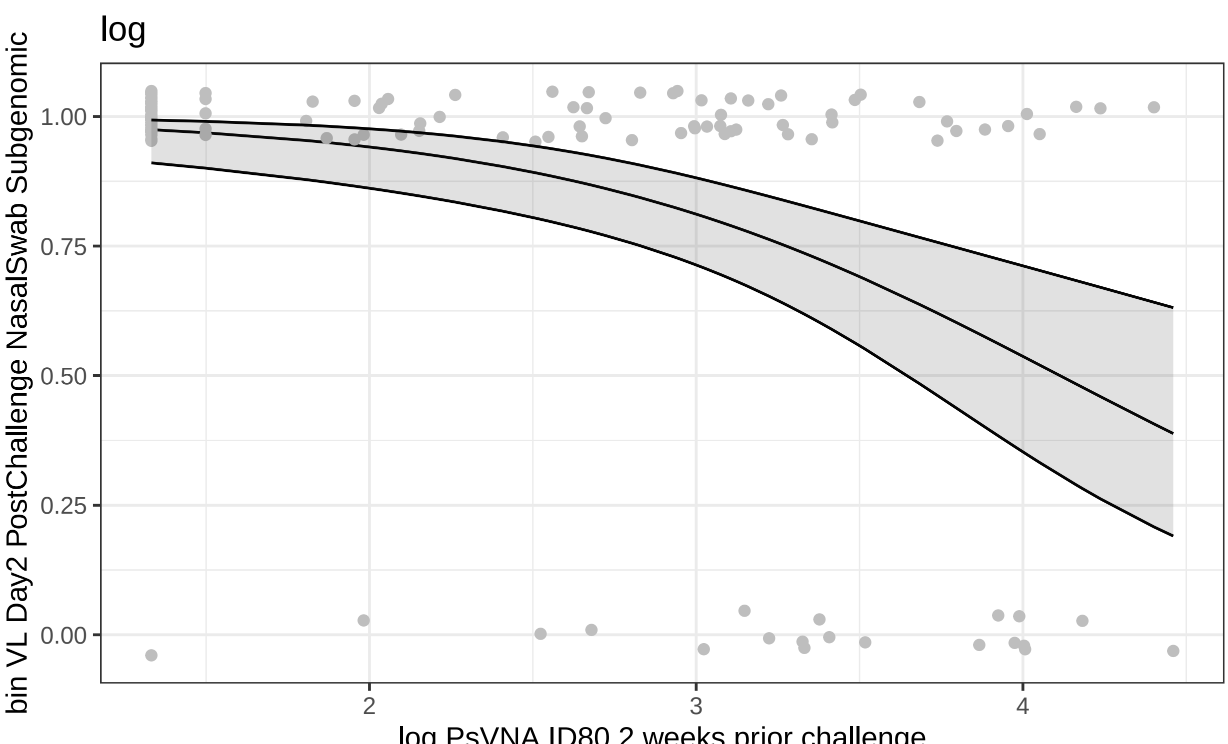

Figure 6.4.143

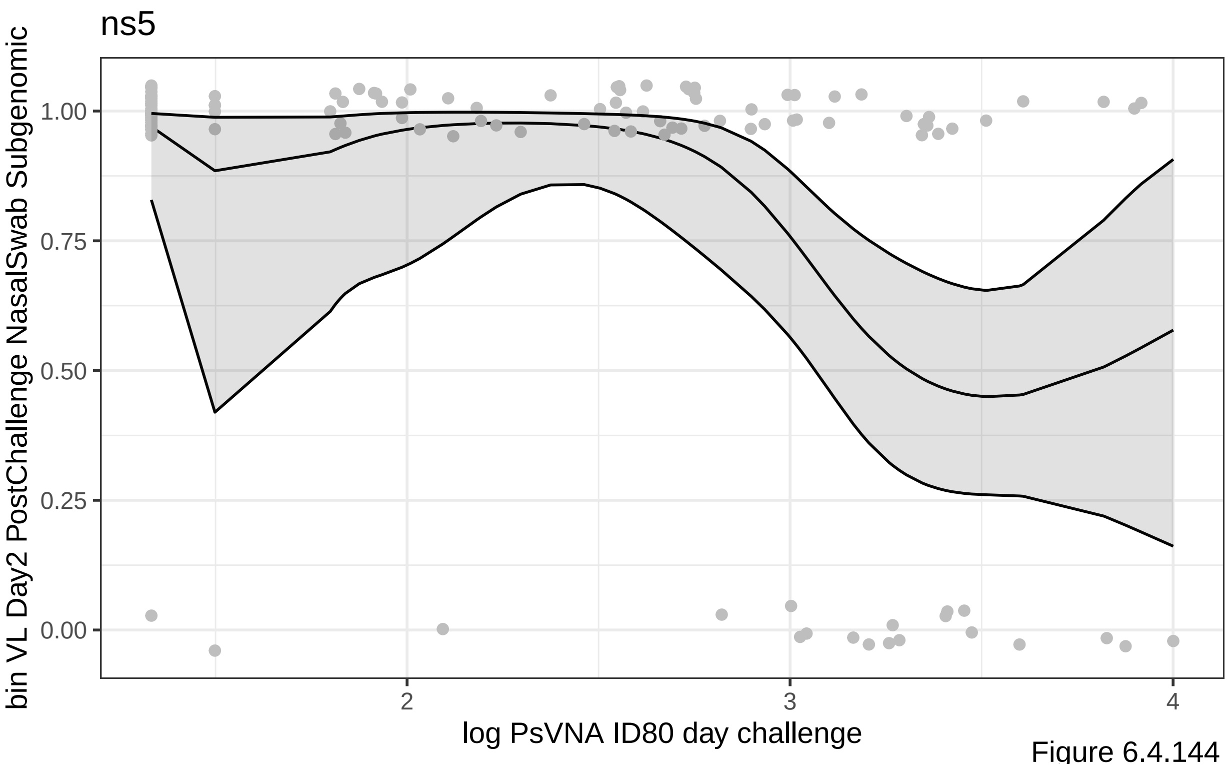

Figure 6.4.144

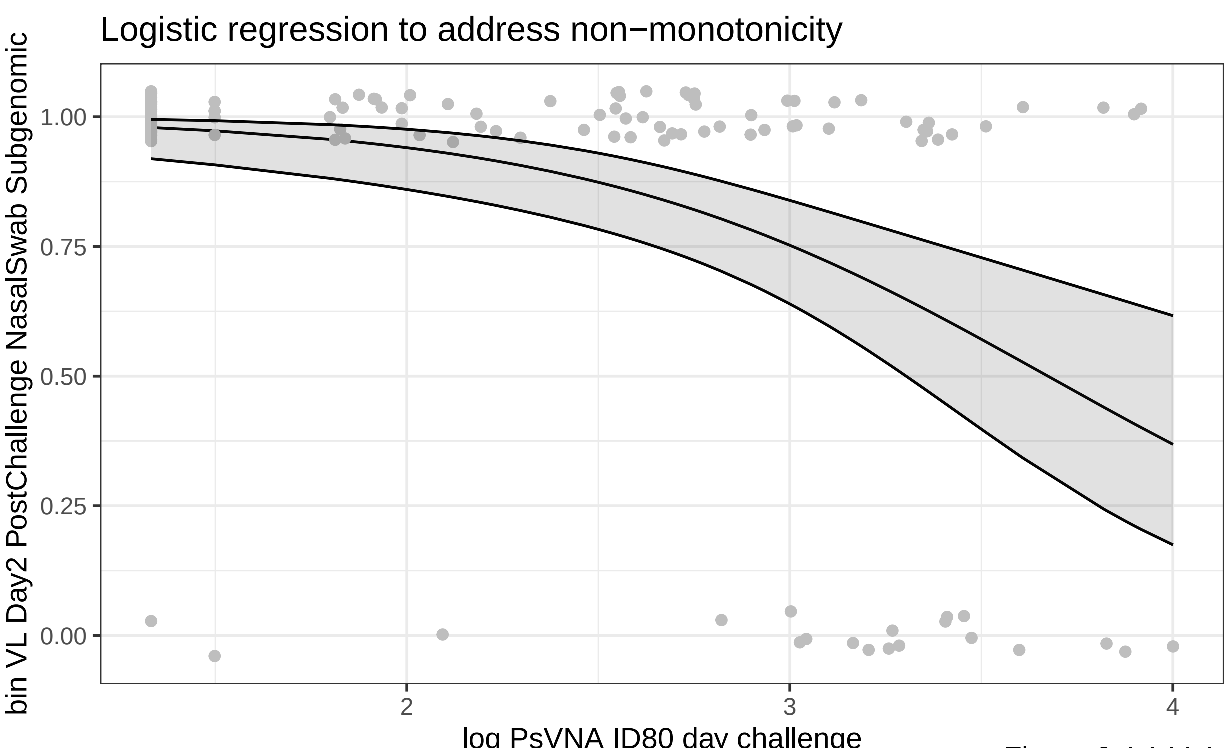

Figure 6.4.144.1