## Bayesian models of longitudinal IFN resistance

To create a simple model of the longitudinal dynamics of IFN and IFN IC were each modeled using a Bayesian change point hierarchical model. The model is based on a segmented regression of the log IC where:

• each participant has an acute level of resistance at initial infection drawn from separate population distributions for typical, non- or fast progressors

• each participant has a drop (or rise) in resistance from acute levels drawn from separate population distributions for typical, non- or fast progressors

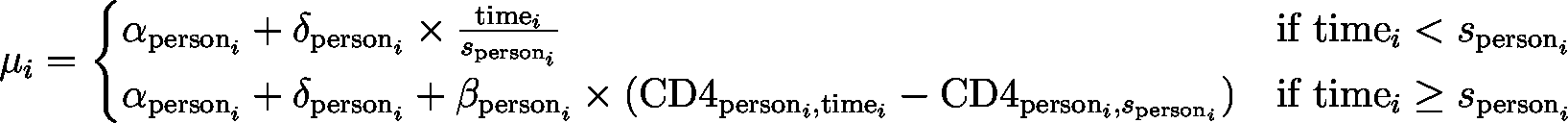
• each participant has a time to nadir (or zenith) drawn from a shared population distribution

• resistance changes linearly from onset of symptoms to time of nadir

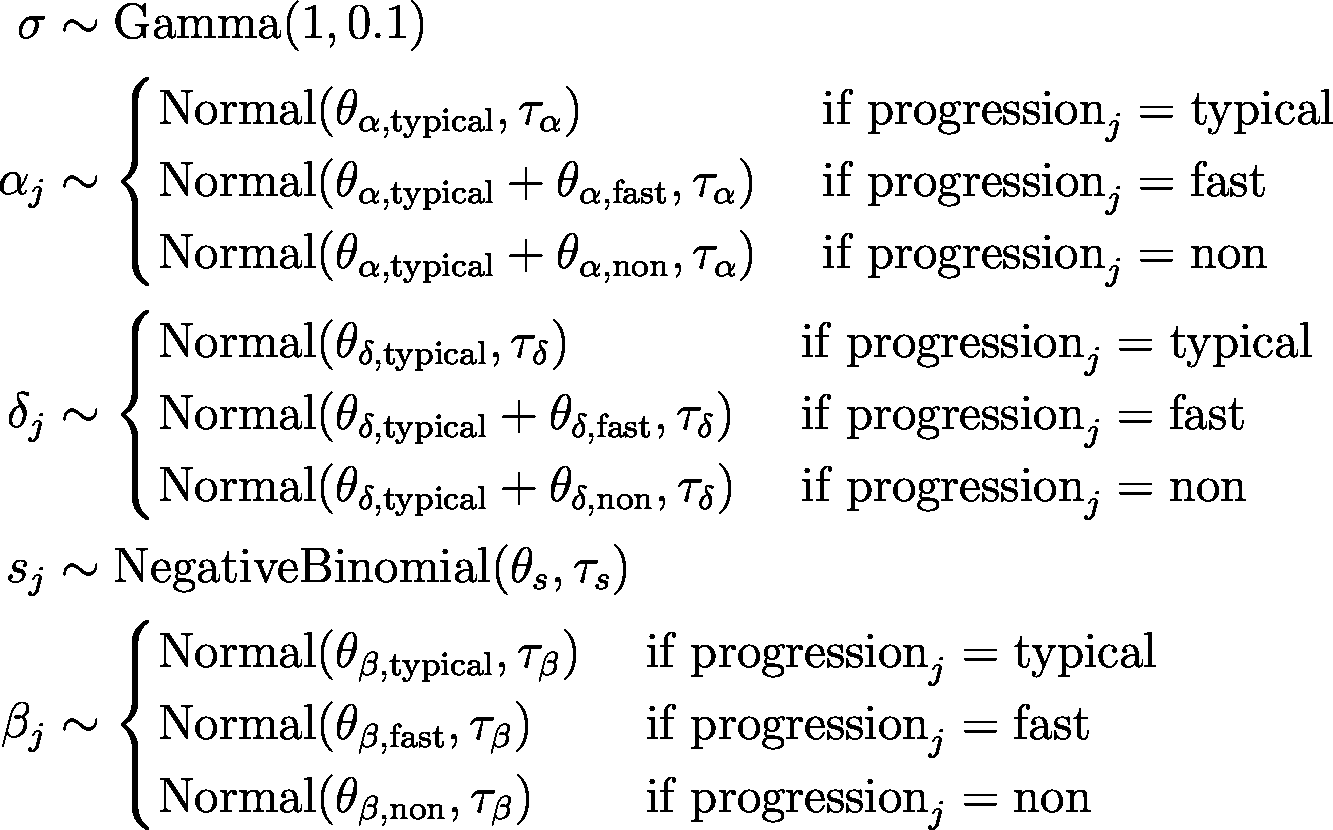
• after nadir, interferon resistance depends linearly on change in CD4 count from the level found at nadir with the effect of CD4 for each participant drawn from separate population distributions for typical, non- or fast progressors

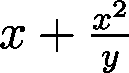
• CD4 count was linearly interpolated between observations

The log IC observation from each viral isolate  was modeled as a normal distribution  with mean  where:

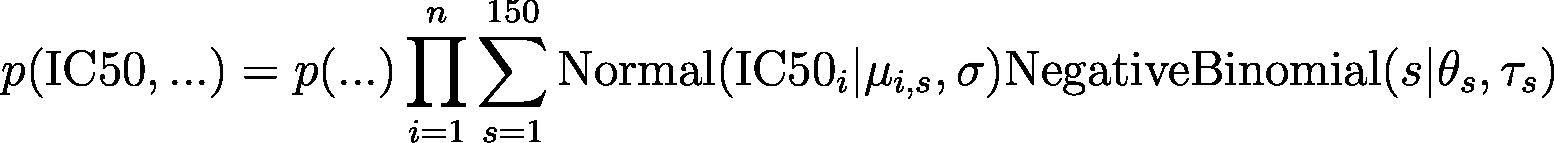


where the parameters  represent the level of interferon resistance at symptom onset,  represents the change from syptom onset to nadir and  represents the time of nadir in person . Study participant data is represented by  and  corresponding to respectively the time and participant from which isolate  was collected,  containing the estimated CD4 count for person  at time  and  is the progression type (fast/non/typical) for participant . The hierarchical probabilities for these parameters were:

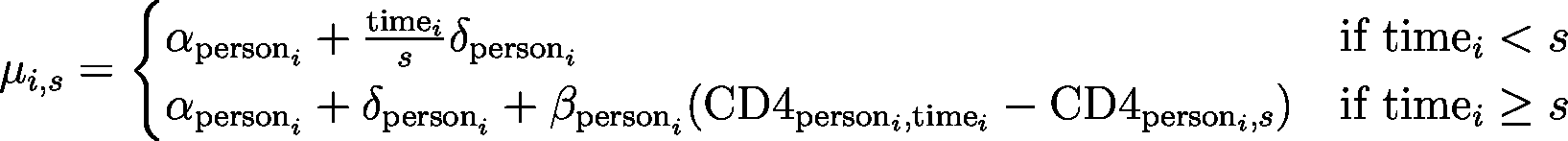


where  indicates each participant and  represents a negative binomial distribution parameterized such that the expected value is  and the variance is . All hyperparameters were given prior probabilities of  for parameters representing the means of a distribution and  for parameters representing standard deviations other than  and  which were given a flat prior and .

For computational efficiency, the nadir time parameter  was discretized to weekly intervals, assumed to fall within 1 to 150 weeks after symptom onset and marginalized out of the joint probability:



where  represents all parameters other than  and  is defined the same as :



## Bayesian models of outgrowth and rebound resistance

To compare virus isolated during rebound, ART-suppressed (QVOA), acute and chronic stages of infection, difference between the IFN and IFN IC were modeled using a Bayesian hierarchical model. The model is based on the assumptions that:

• Isolates within a person were assumed to share some similarity in IFN resistance.

• The mean IC level within each person for a given virus type was assumed to be drawn from a shared population distribution for that type.

• QVOA virus were separated into to two populations; “pre” a group composed of QVOA viruses isolated from study participants without treatment interruptions (ATI) or prior to ATI and “post” QVOA viruses isolated from participants following ATI.

• In both QVOA populations, the viruses may be composed of a population found in QVOAs plus an additional admixture of virus similar to those observed during rebound i.e. potential reseeding after ATI. We model a mixture in both pre- and post-treatment so that we can assess differences in inferred mixture proportion between the two populations.

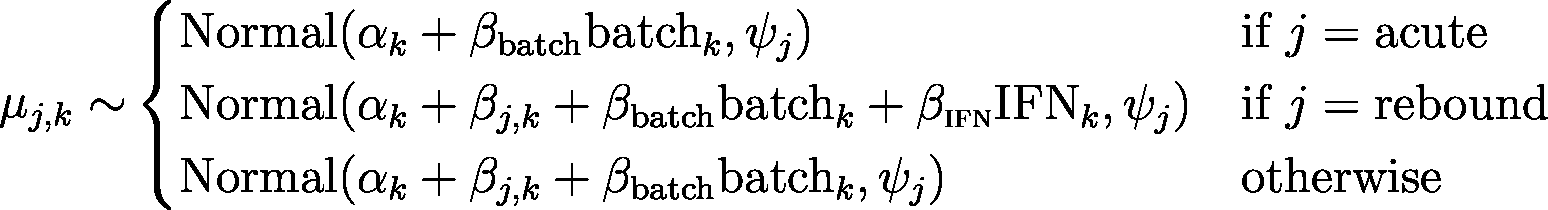
• A difference due to batch to batch variability in reagent strength may exist between isolates tested in Iyer et al. 2017 and the current study.

• A difference may exist in virus isolated from patients treated with exogenous IFN.

The log IC observation from each viral isolate  from acute, chronic and rebound isolates was modeled as a normal distribution:

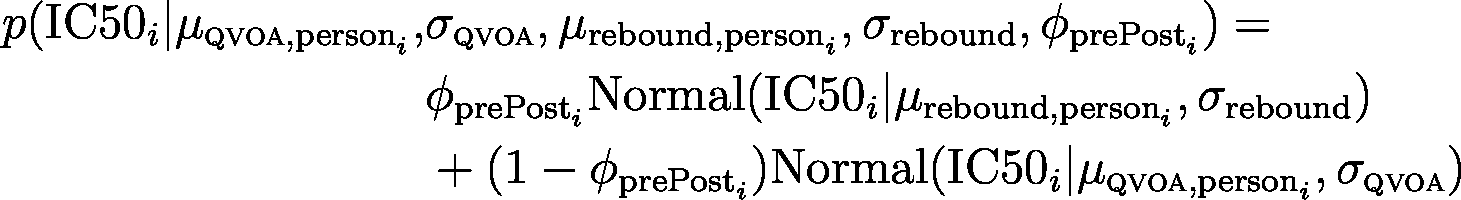


with the mean resistance for isolate type  from person :



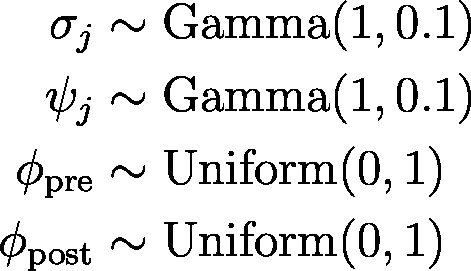
where  indicates whether isolate  was isolated during acute, chronic, QVOA or rebound infection from participant ,  indicates when isolates from person  were tested in Iyer et al. 2017 (to account for variation in IFN batches from this study) and  indicates when person  was given exogenous IFN during treatment interruption. Parameters are included for the mean resistance level during acute infection for each person , standard deviation of isolates of type  within a person , standard deviation of mean resistance for type  isolates among people , change from acute levels in isolates of type  in a given participant , the effects of exogenous IFN treatment  and batch to batch variation in IFN in isolates previously assayed by Iyer et al. 2017 .

For QVOA isolates, the IC was modeled as a mixture of two populations such that:



where  indicates whether isolate  was isolated pre- or post-ATI and and  and  represent the proportion of rebound-like virus present in pre- and post-ATI QVOA isolates.

The hierarchical parameter priors were modeled as:



where  indicates the isolate type (acute, chronic, QVOA, rebound). , ,  and  were all given flat priors.