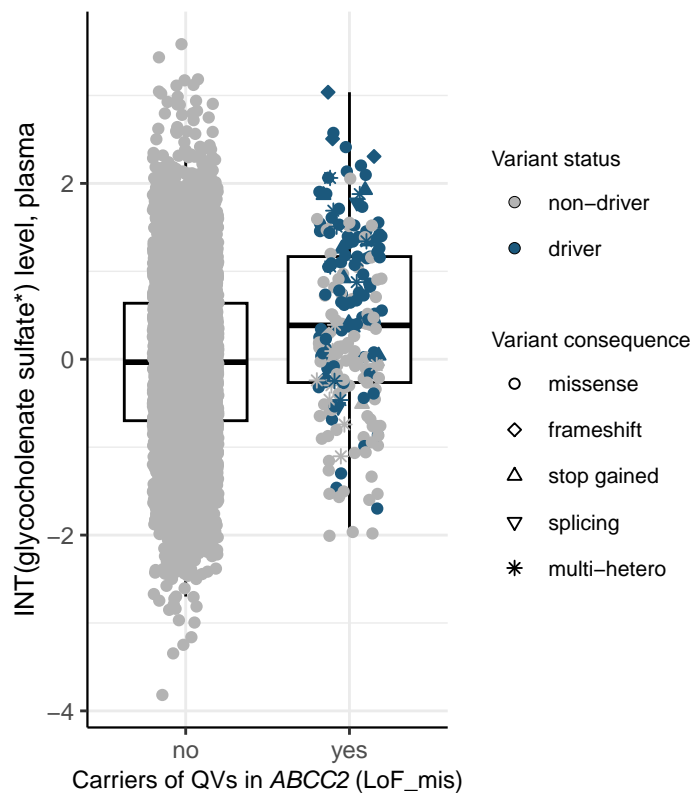
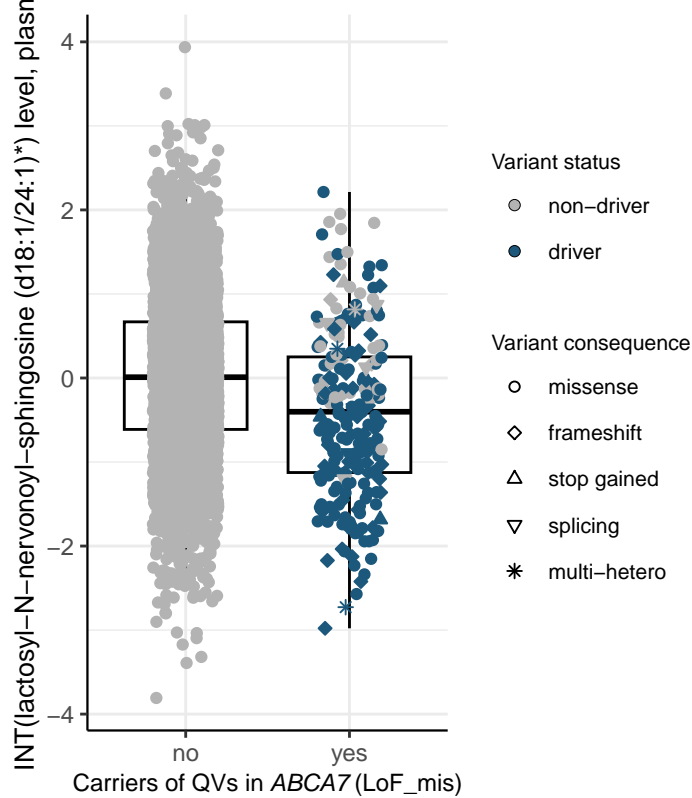
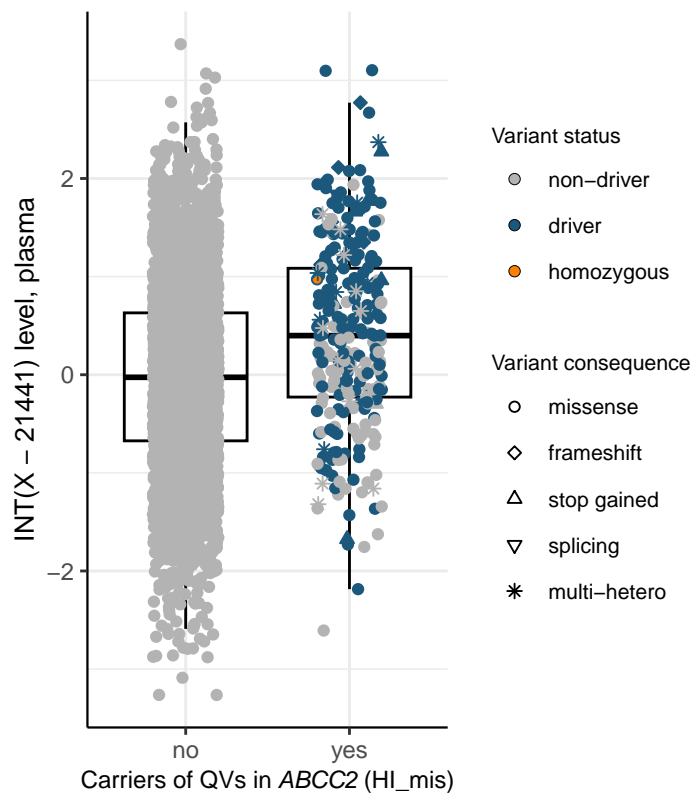
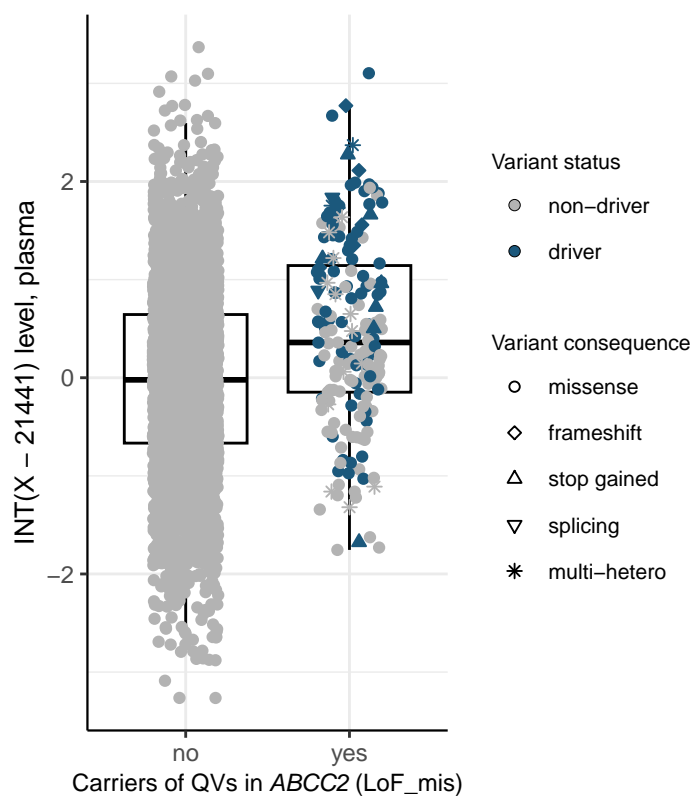
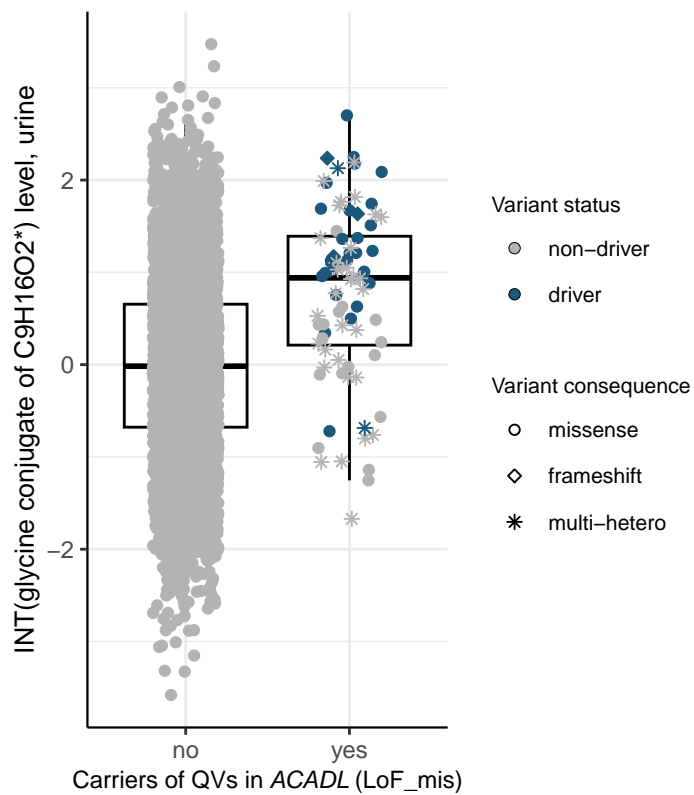
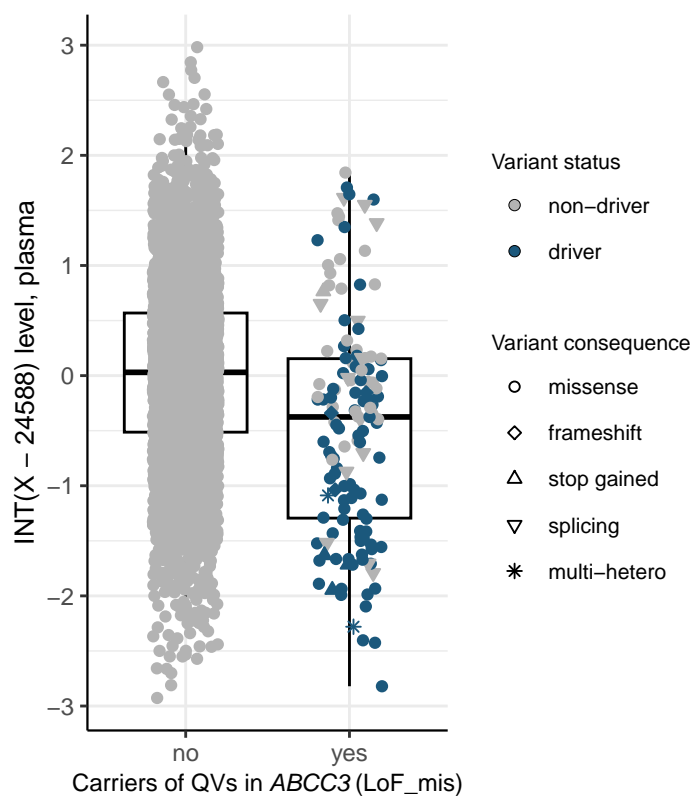


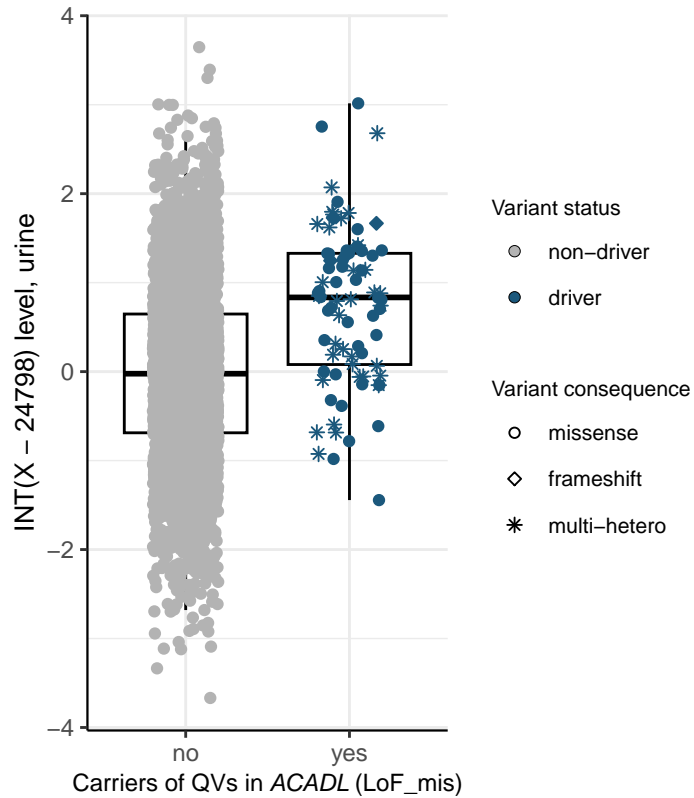
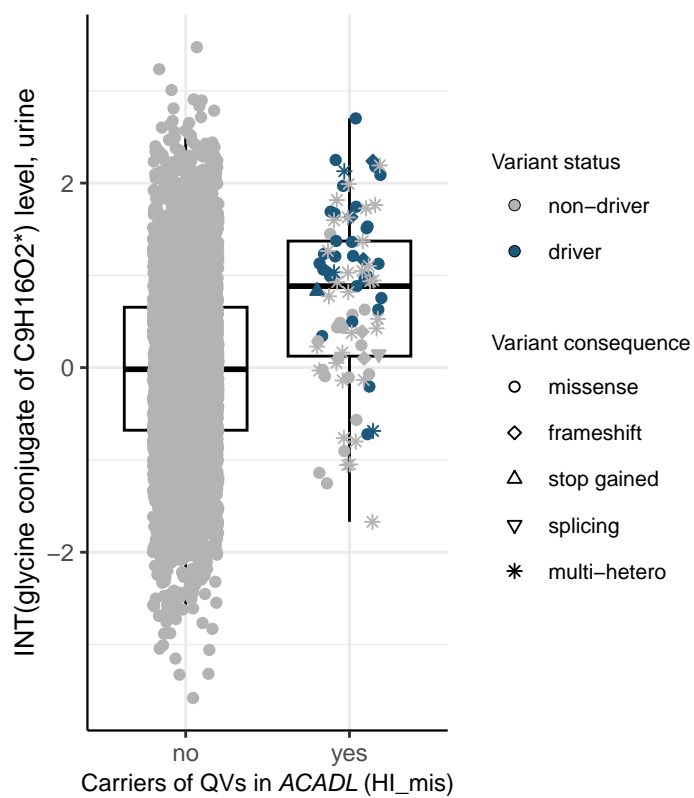
Supplementary Data 1: Plasma and urine metabolite levels among carriers and non-carriers of QVs in significantly associated genes.

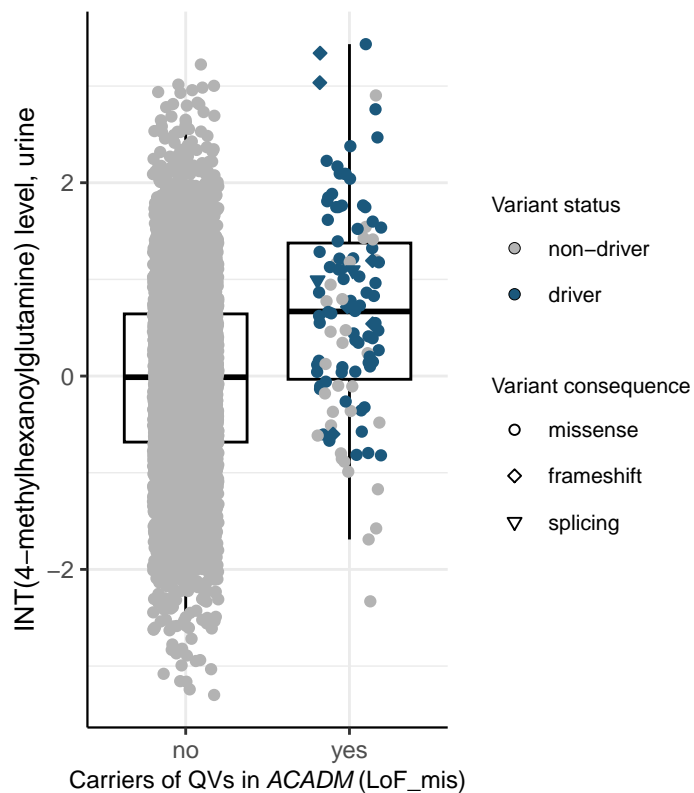
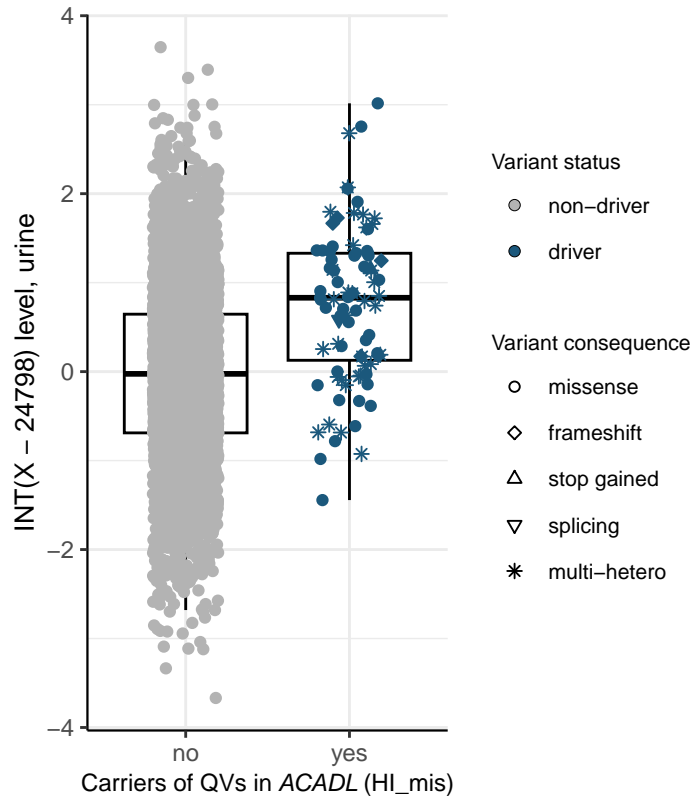
Metabolite levels after inverse normal transformation and covariate-adjustment are shown on the y-axis, among non-carriers and carriers of QVs in both masks (LoF_mis and HI_mis) on the x-axis for all significant gene-metabolite associations based on up to 4,713 individuals (**Supplementary Table 3**). Associations in plasma are shown on the left, in urine on the right. Plots are sorted alphabetically by gene name. Symbol color and shape indicate a variant's driver status and consequence, respectively. Carriers of multiple heterozygous QVs are denoted by an asterisk. Orange filling of symbols denotes homozygosity for the respective QV for autosomal genes, and hemizyosity for X-chromosomal genes. The boxes range from the 25th to the 75th percentile of metabolite levels, the median is indicated by a line, and whiskers end at the last observed value within 1.5*(interquartile range) away from the box.

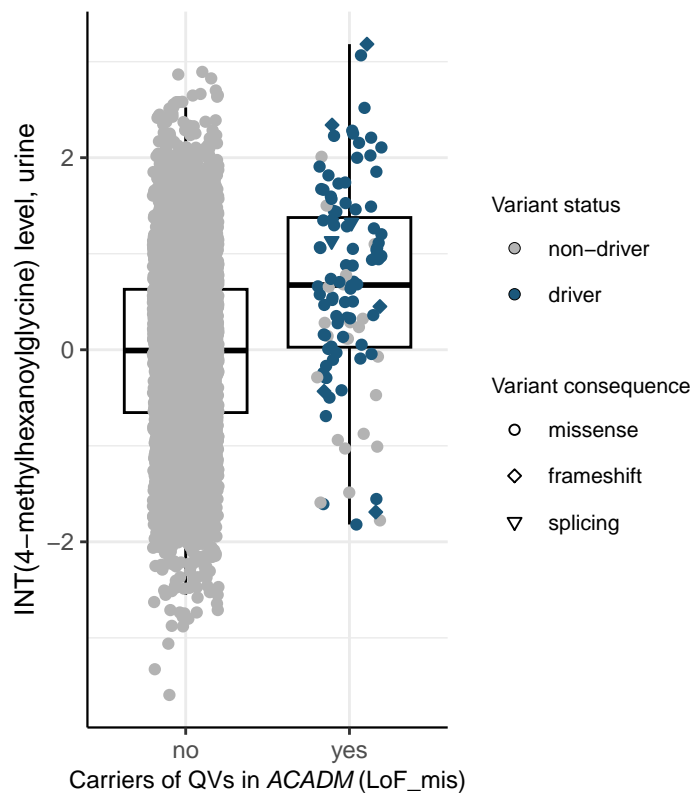
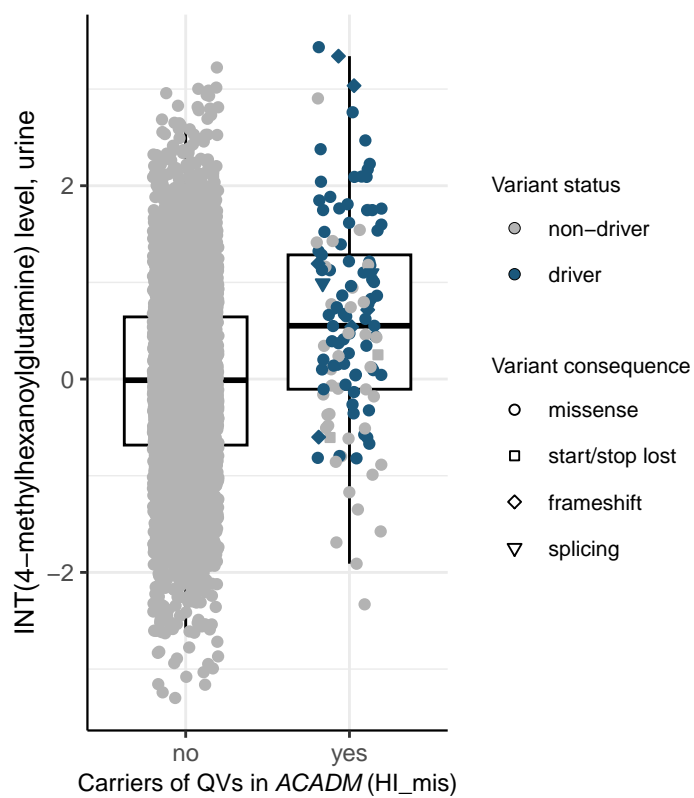


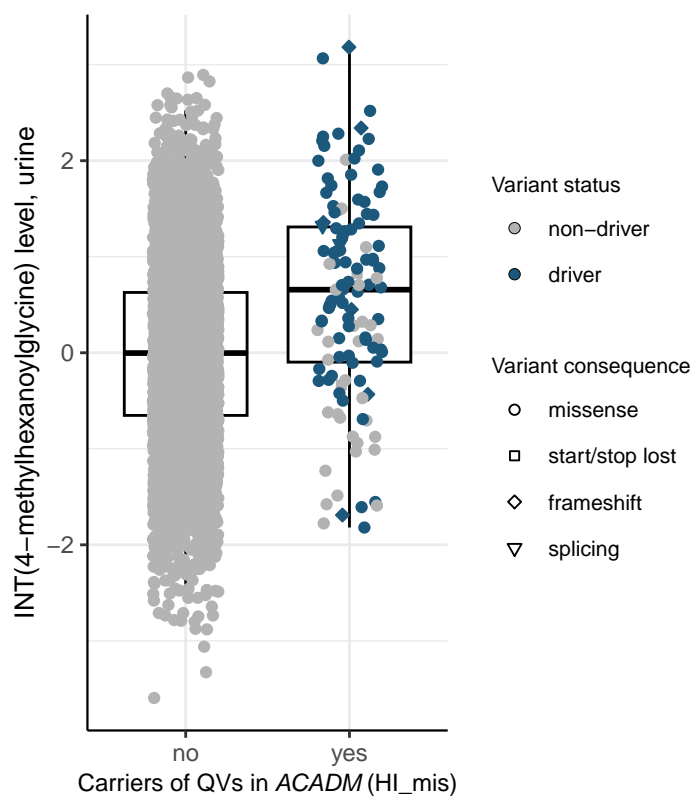
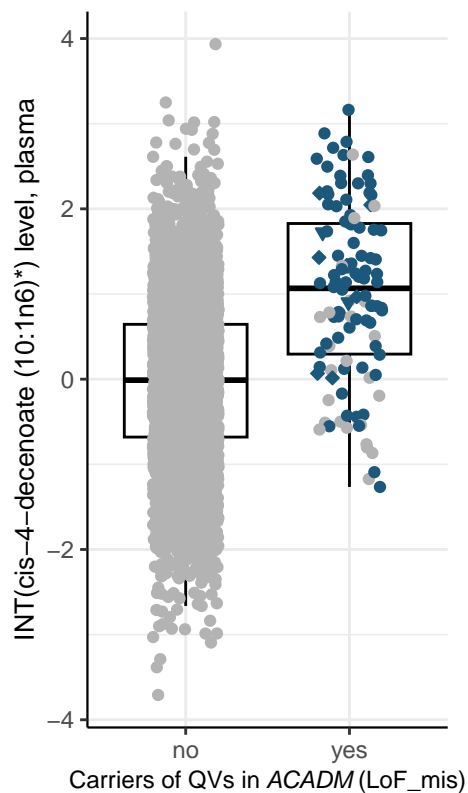


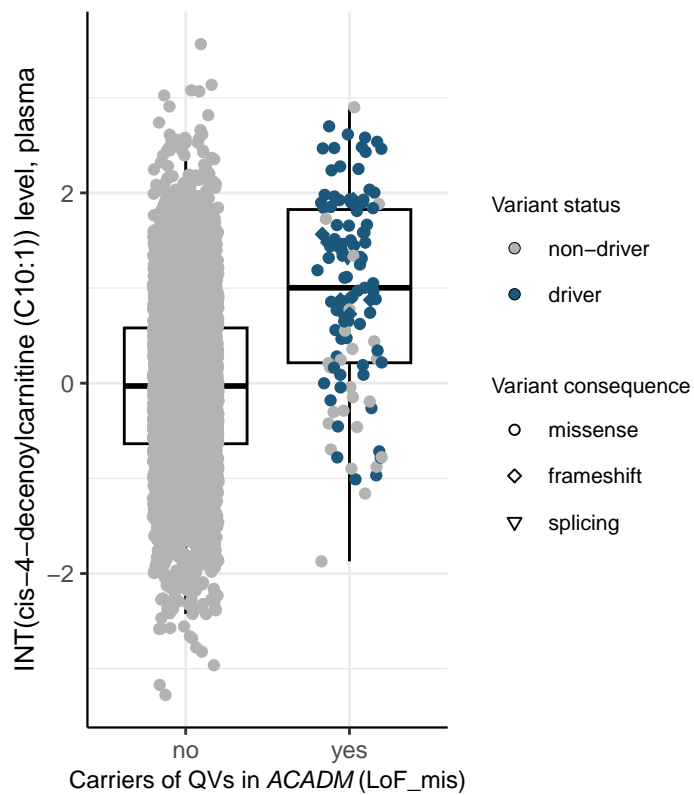
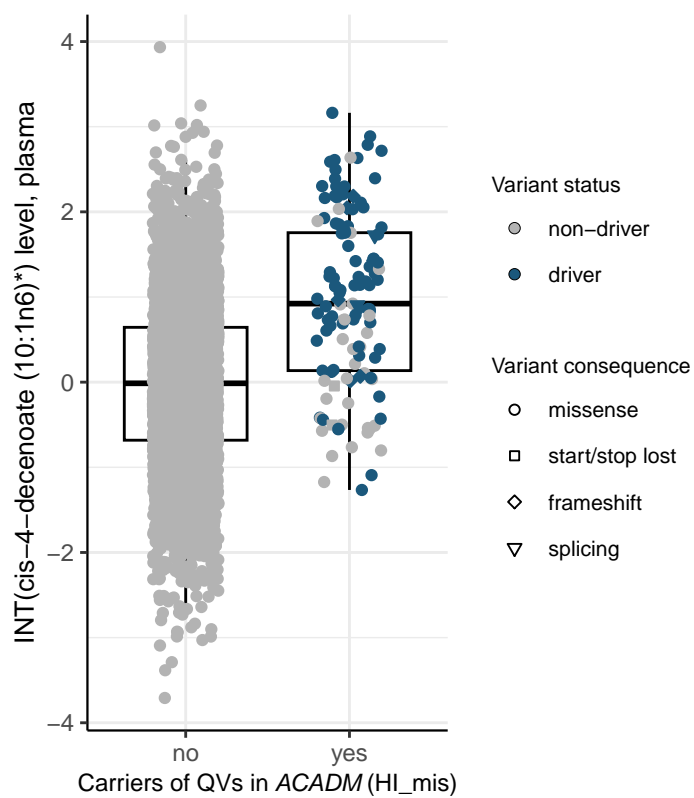


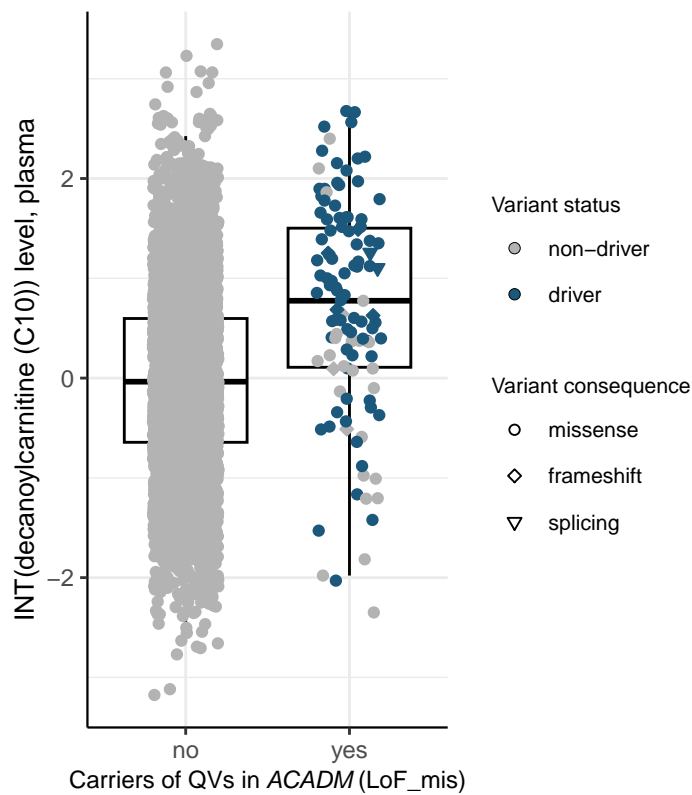
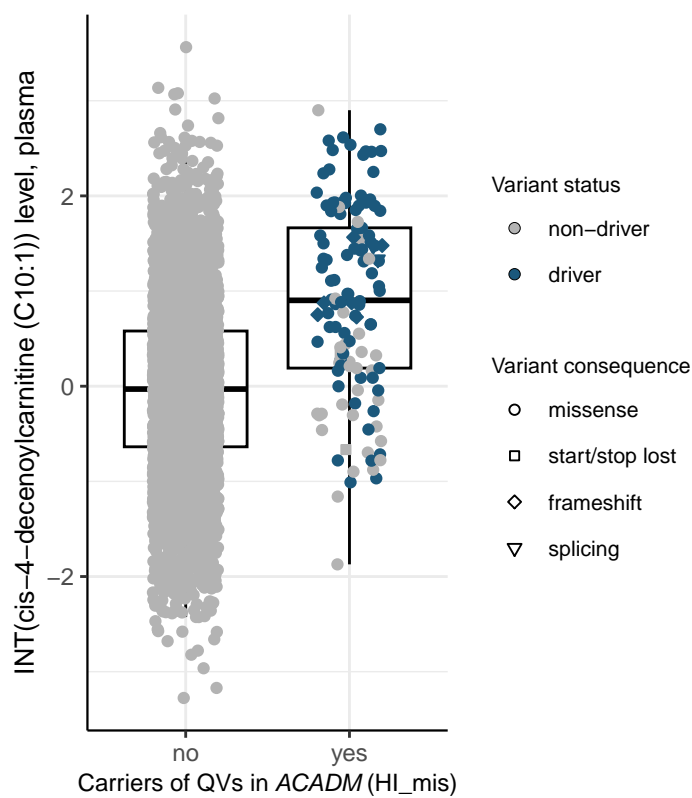


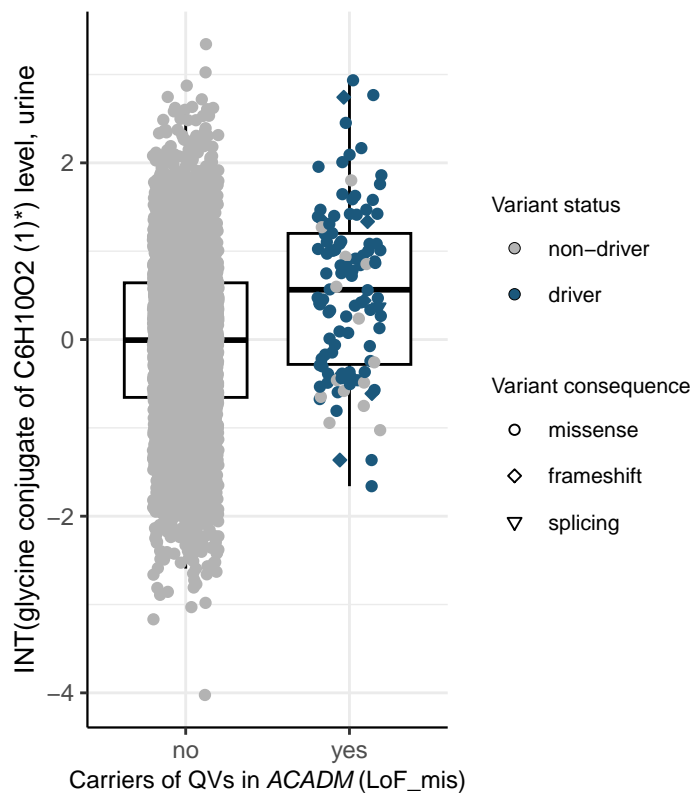
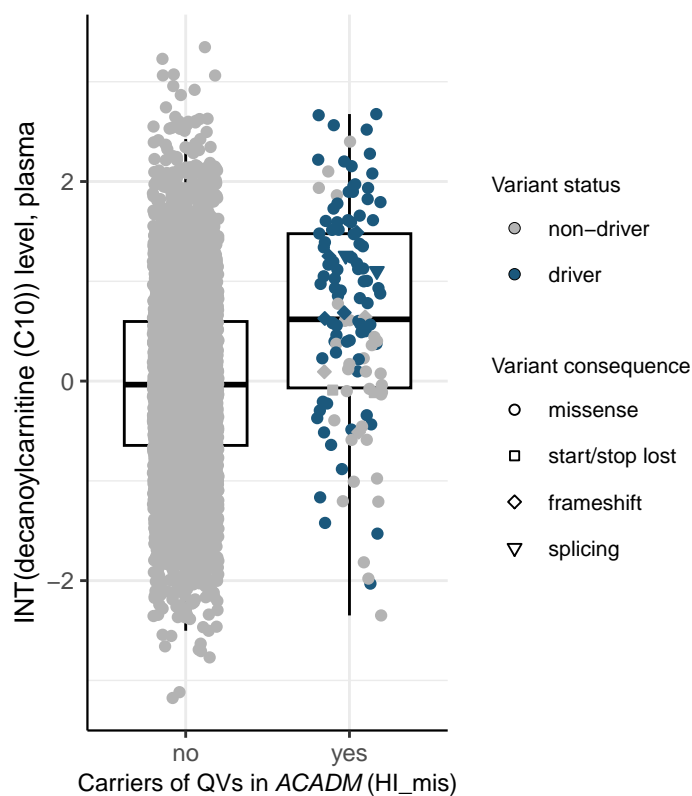


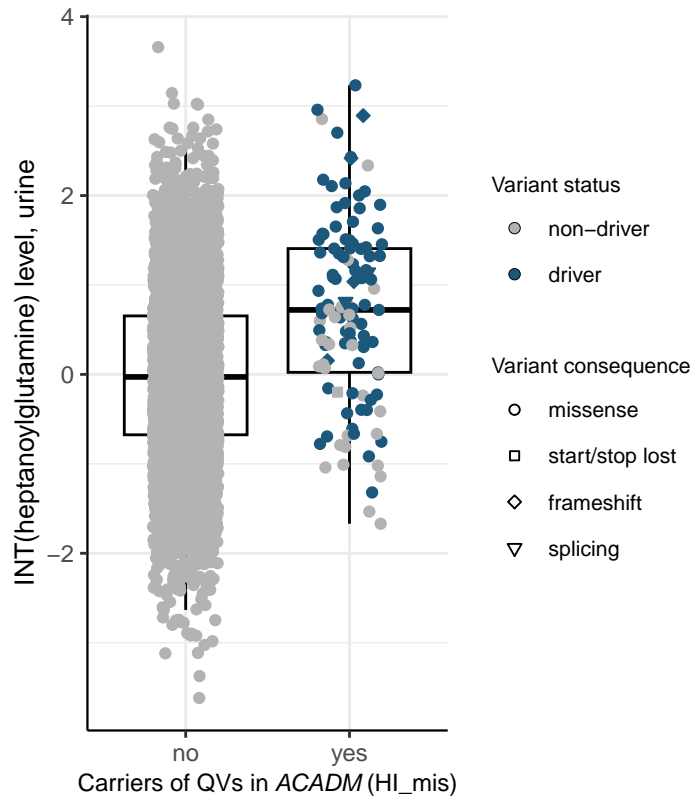
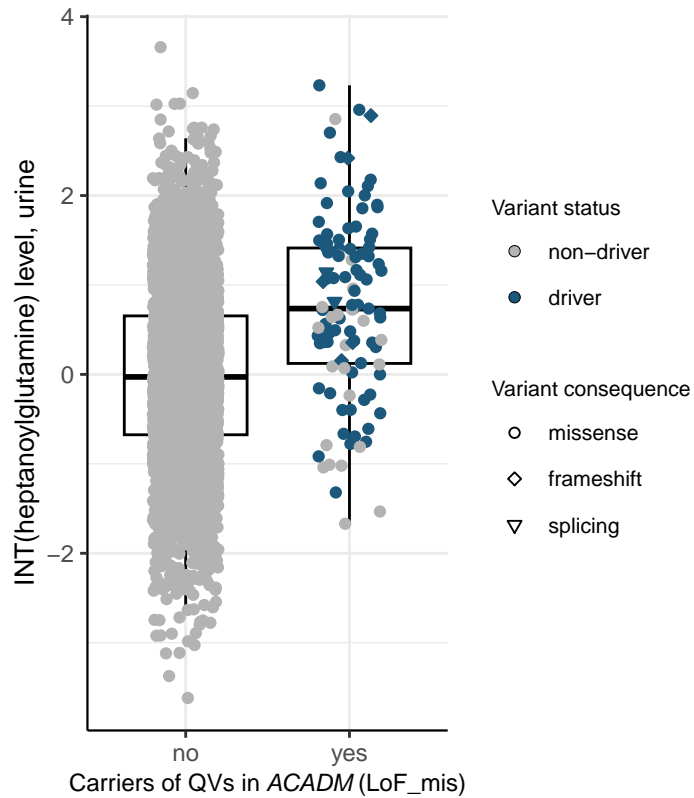


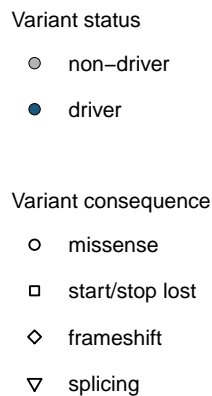
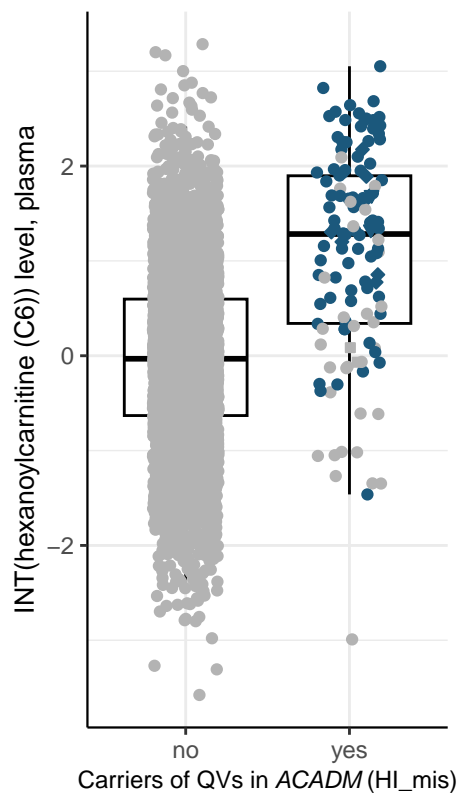
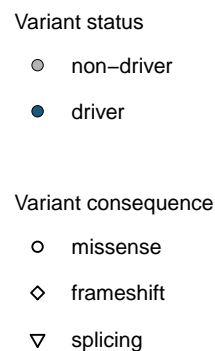
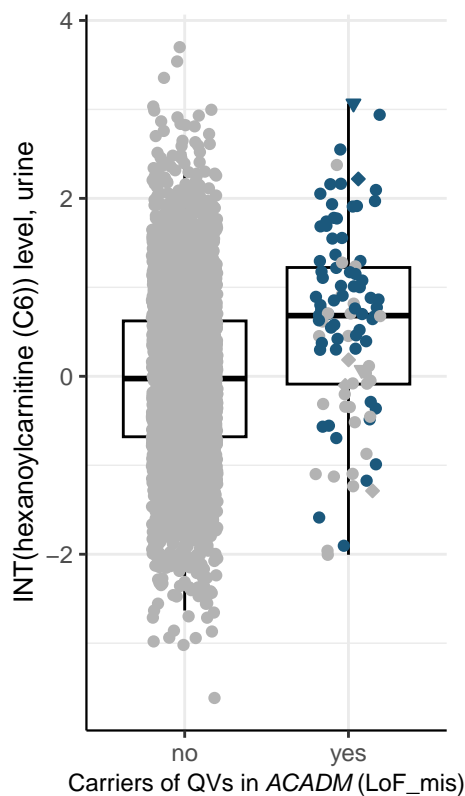
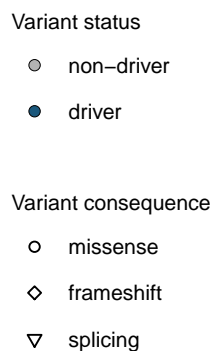
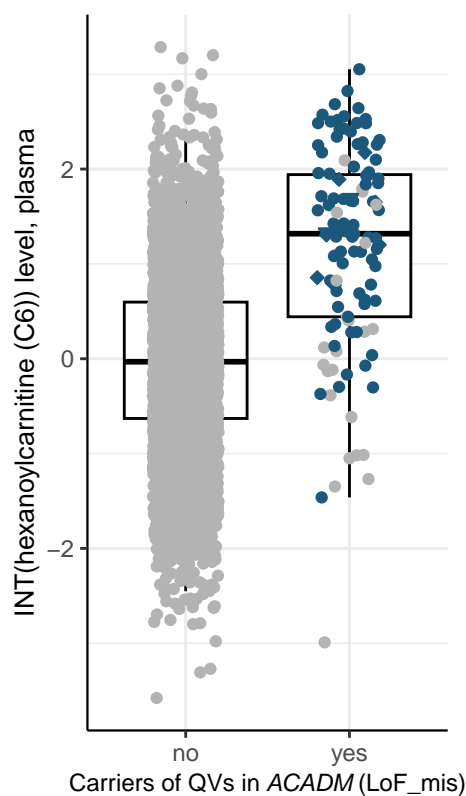


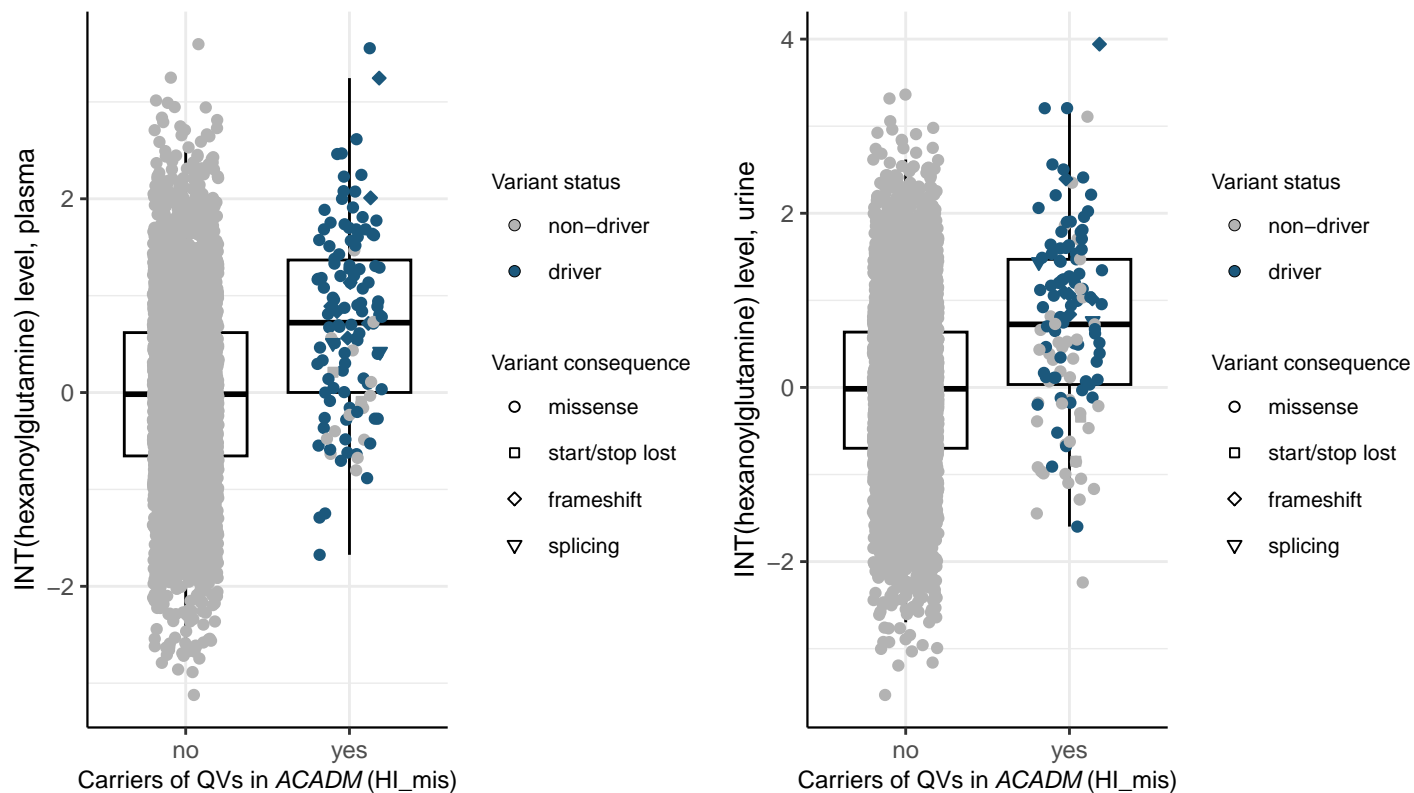
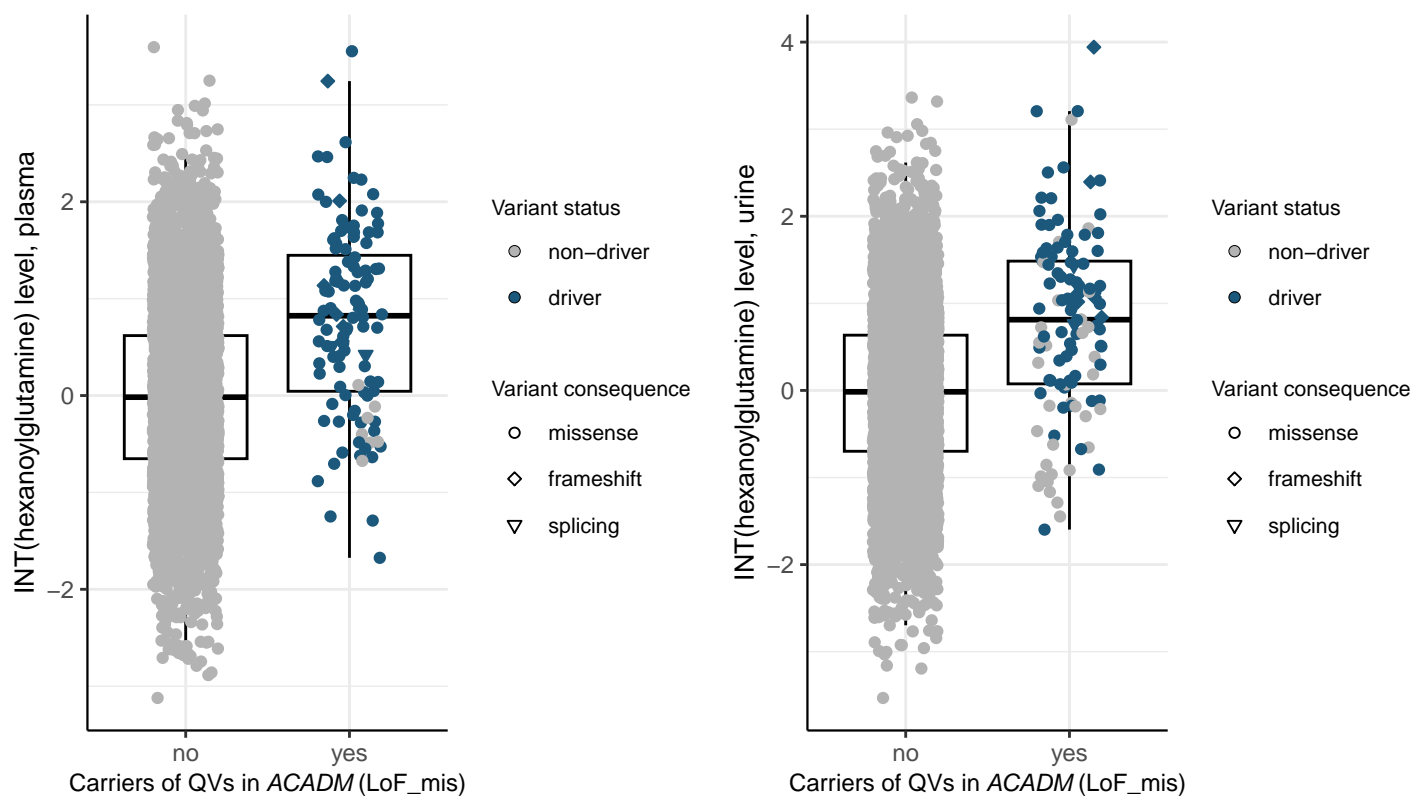


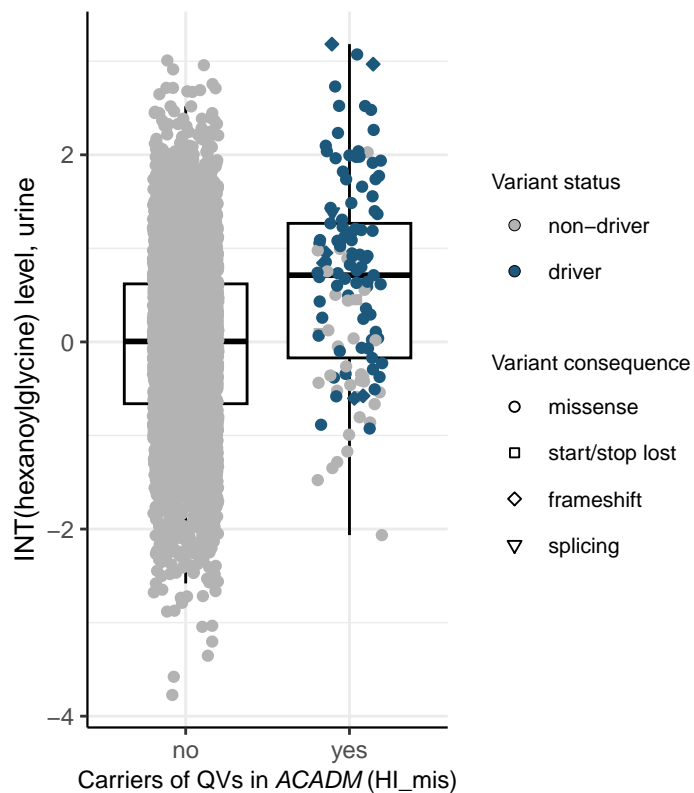
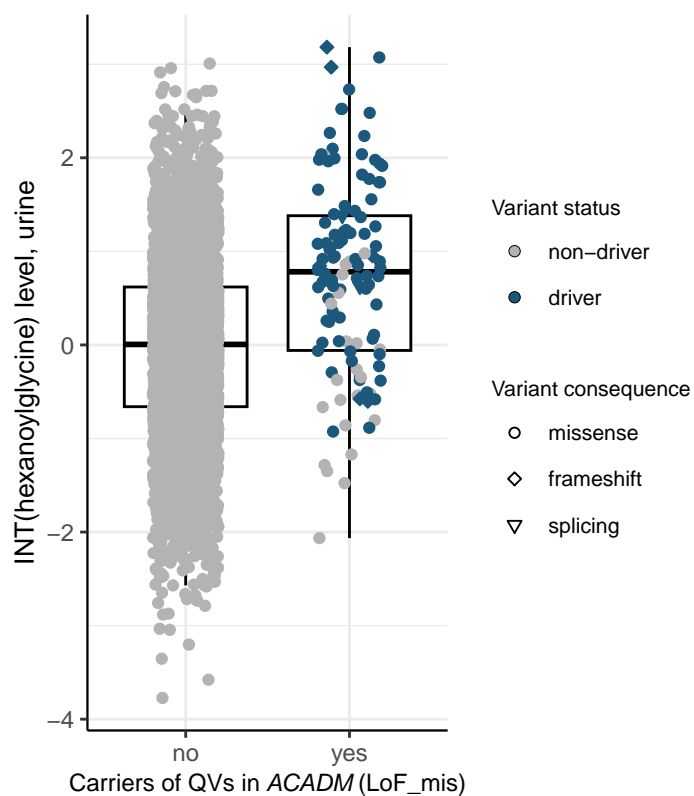


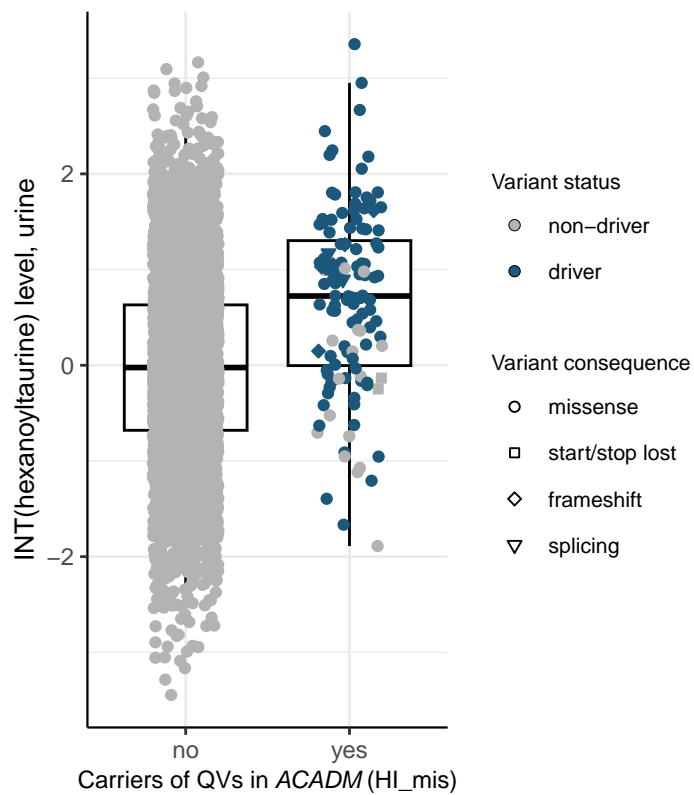
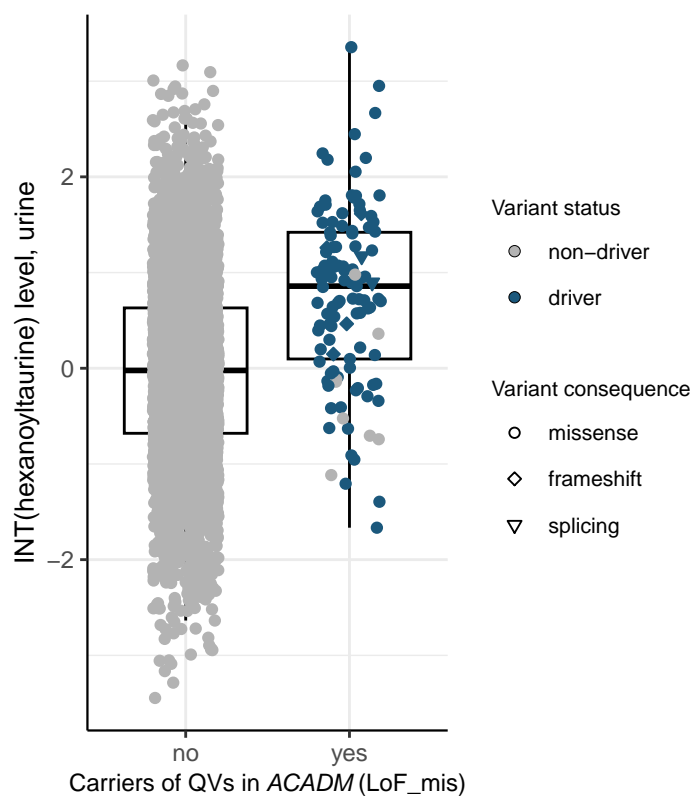


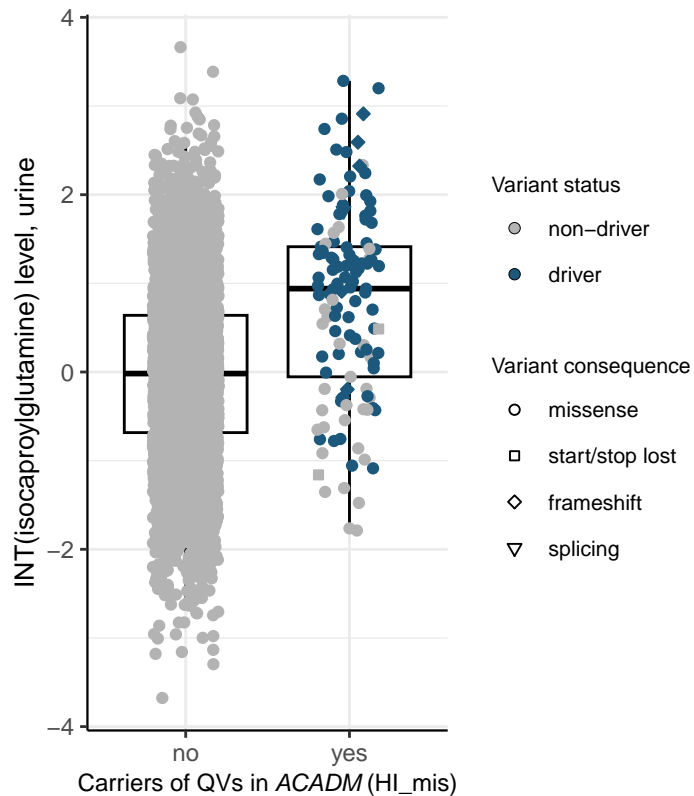
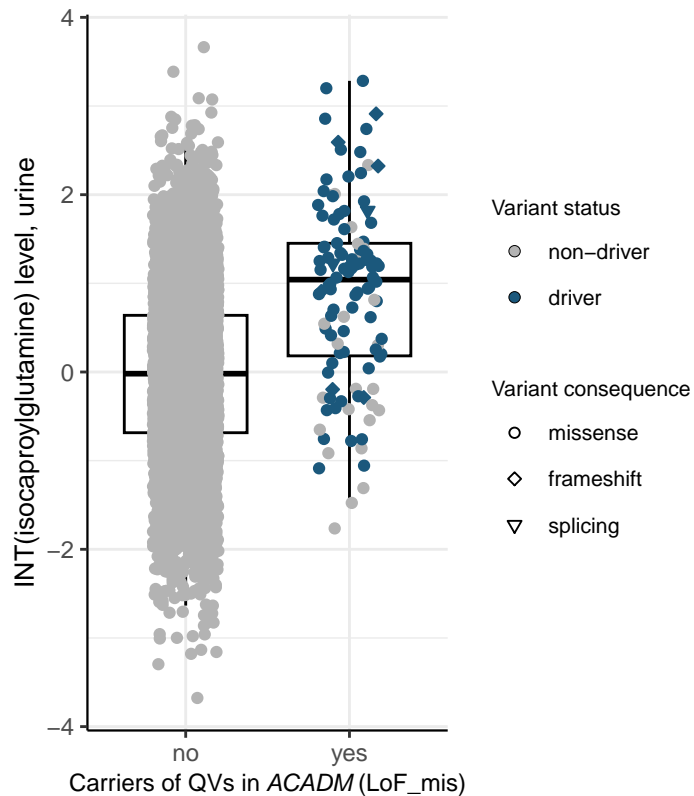


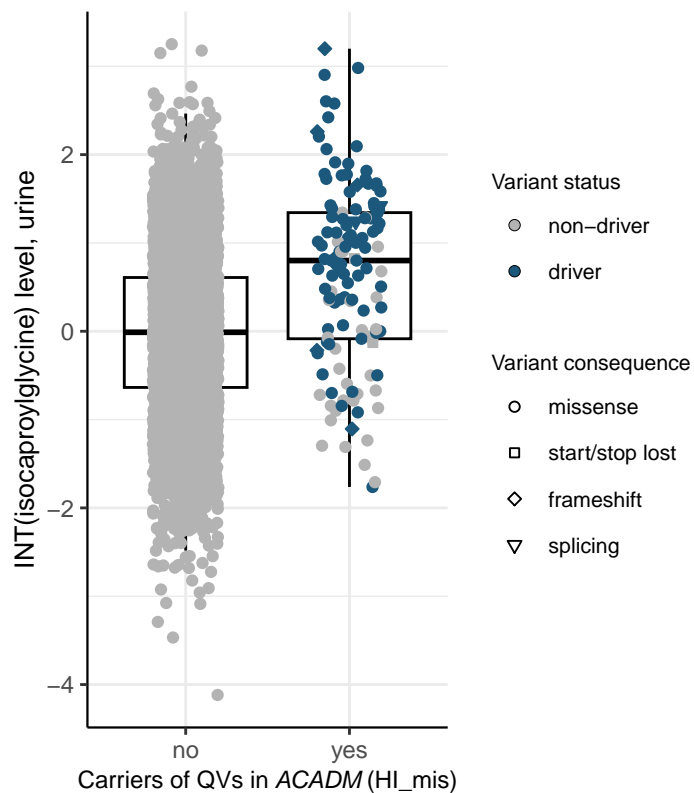
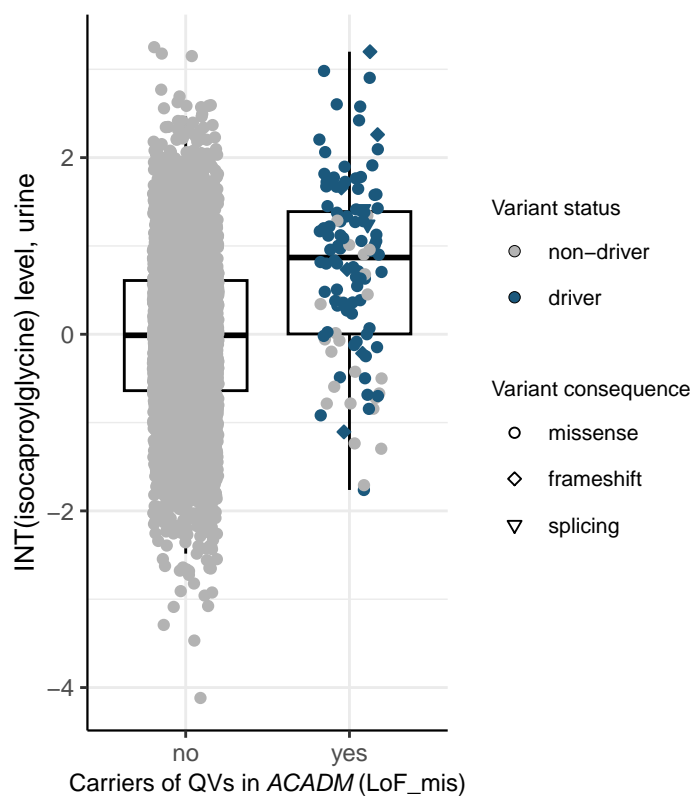


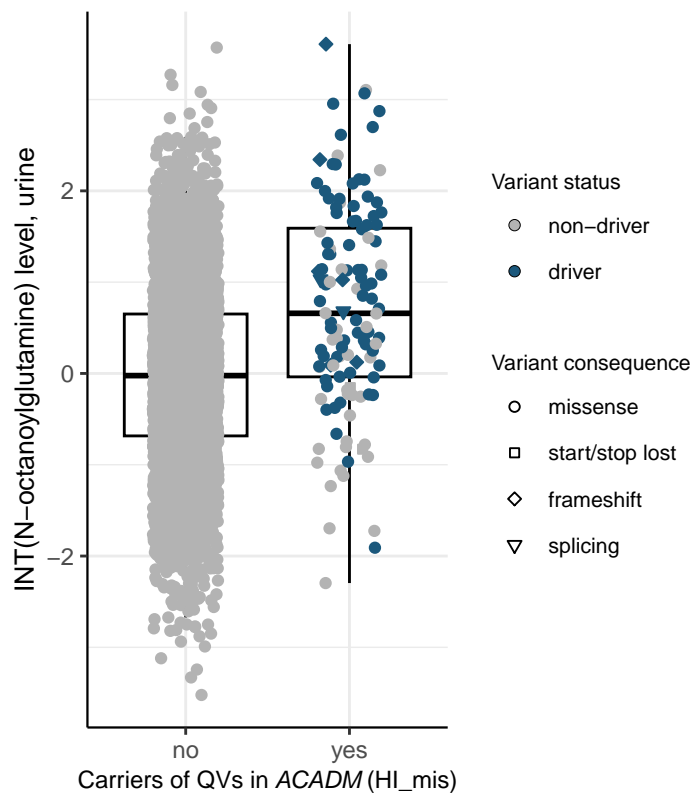
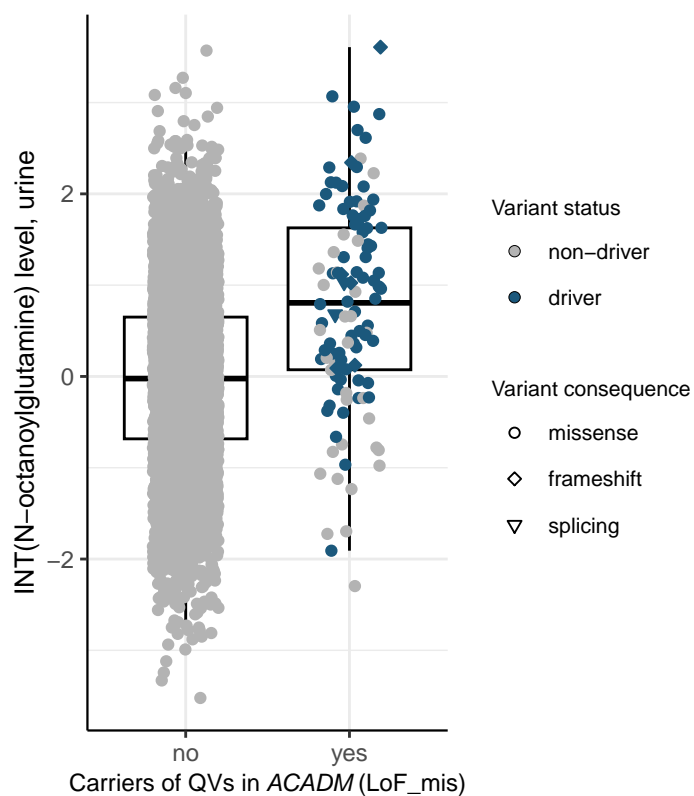


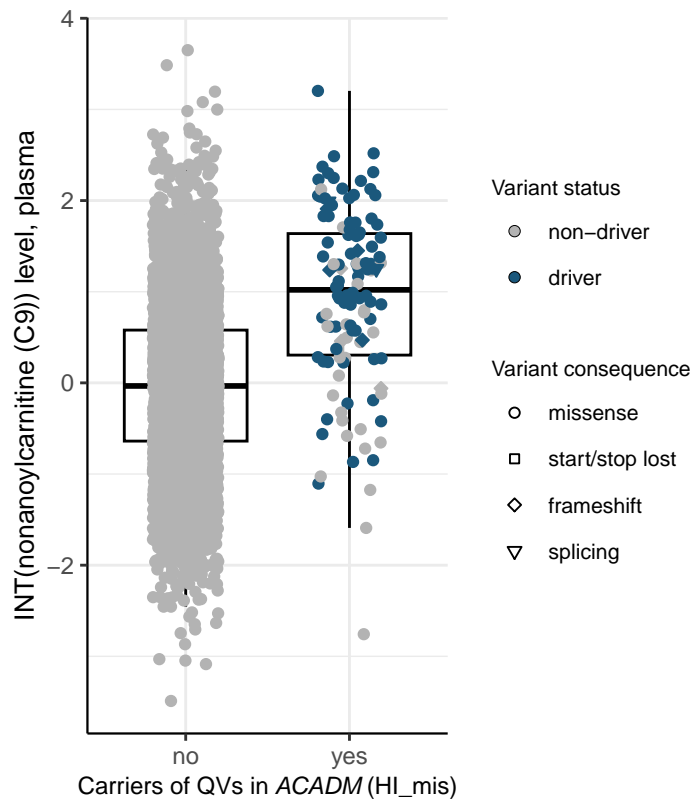
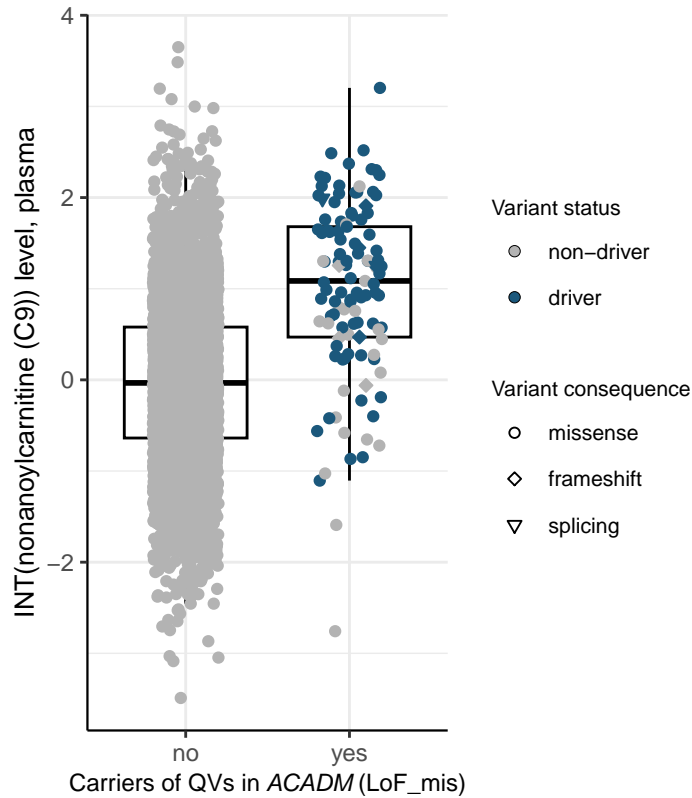


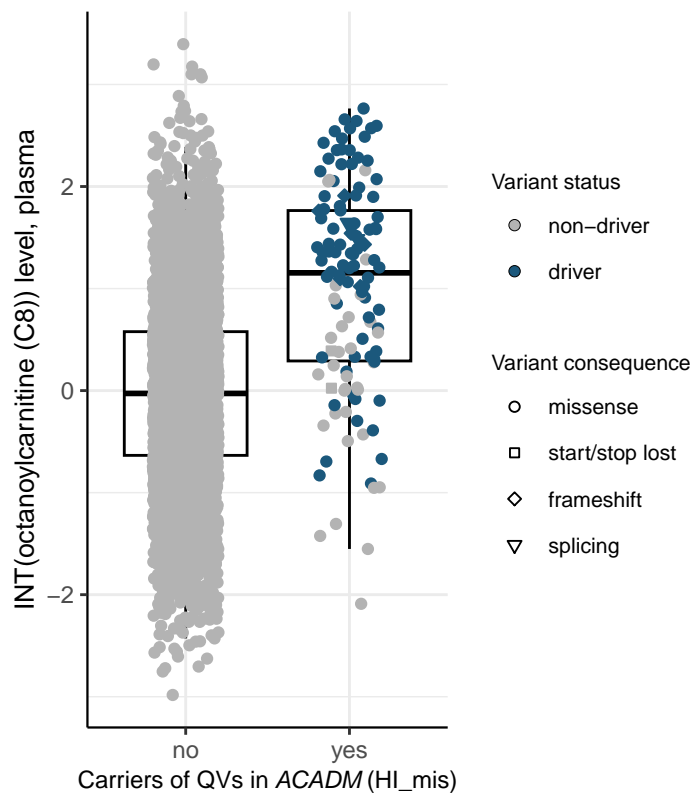
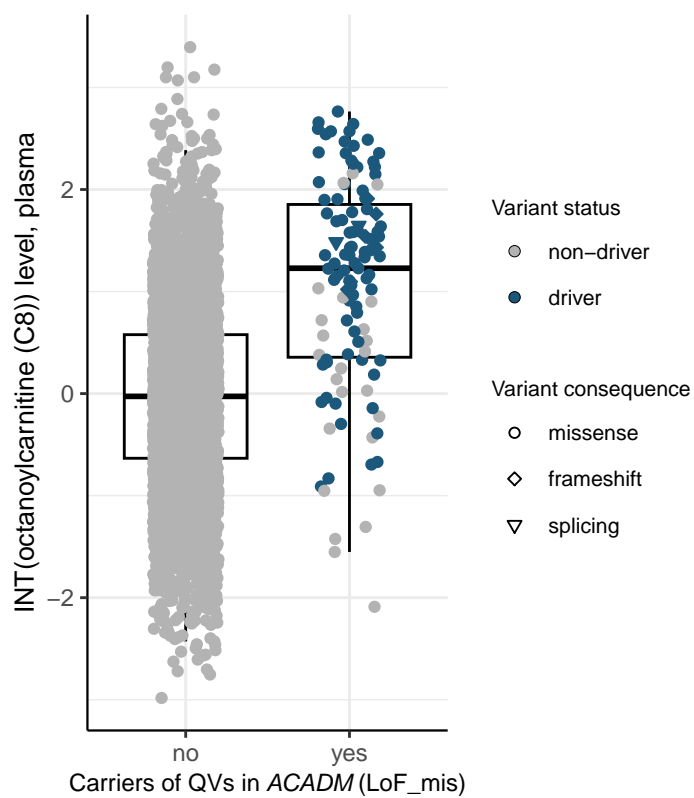


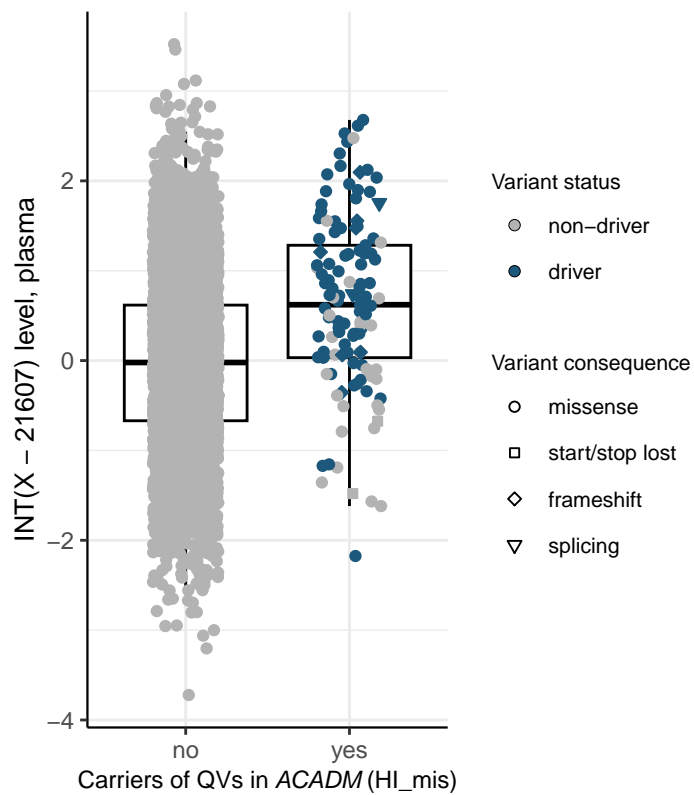
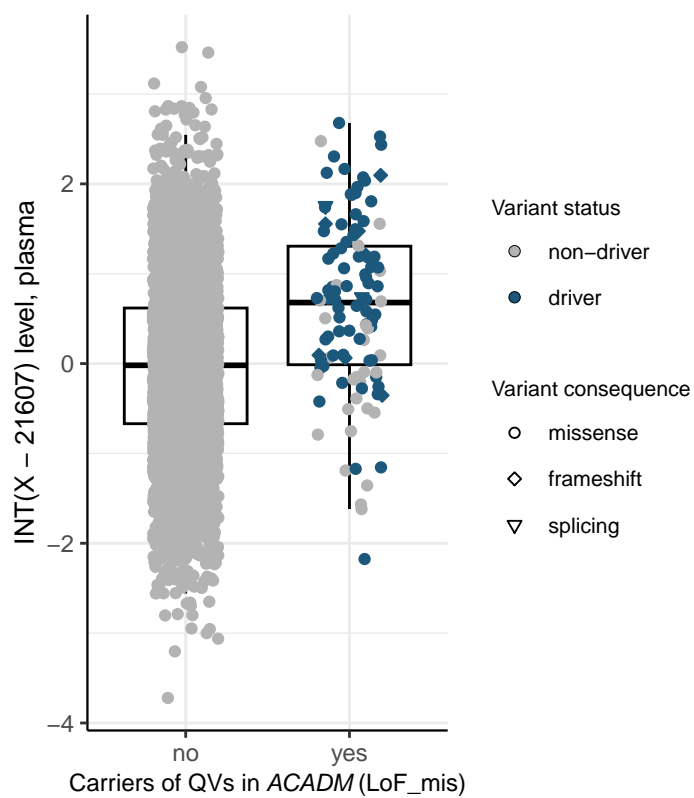


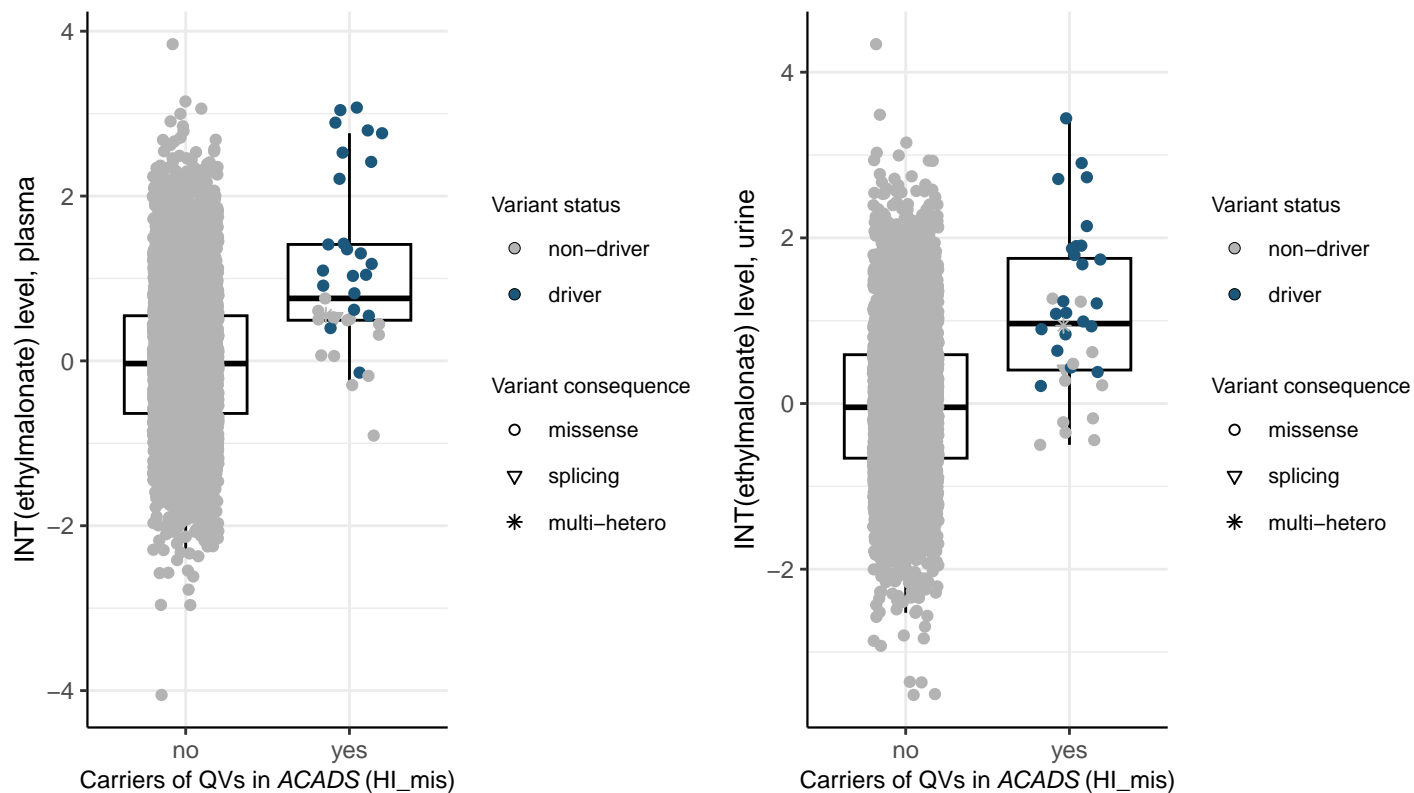
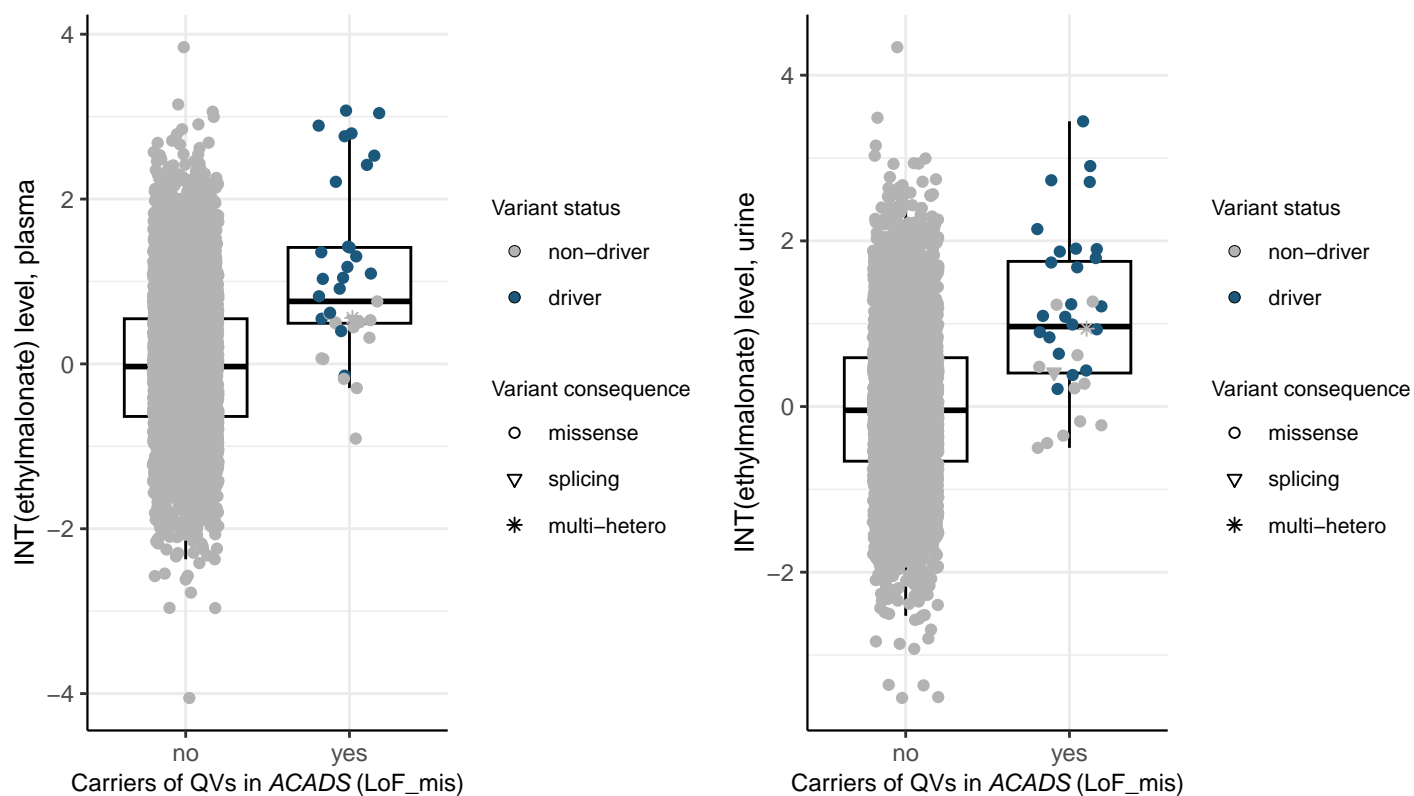


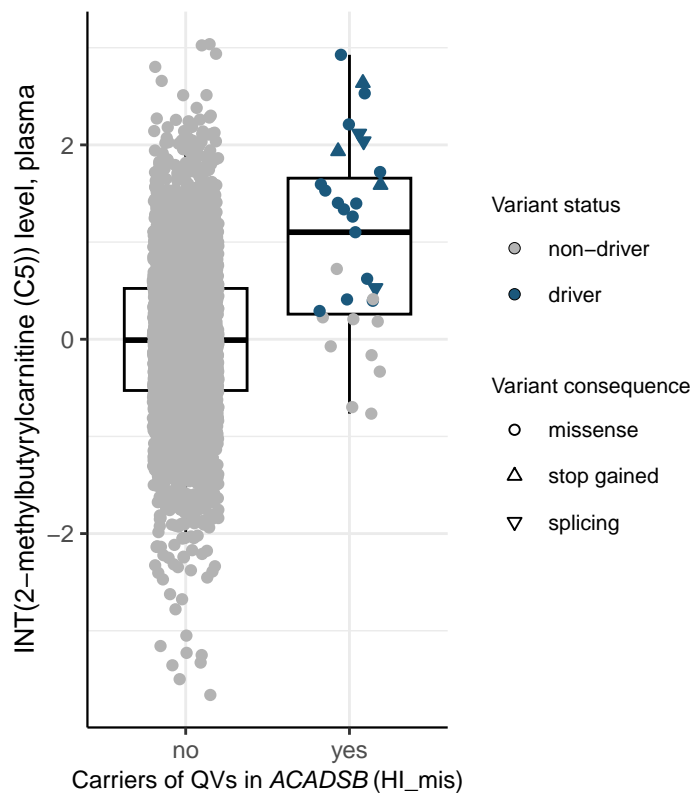
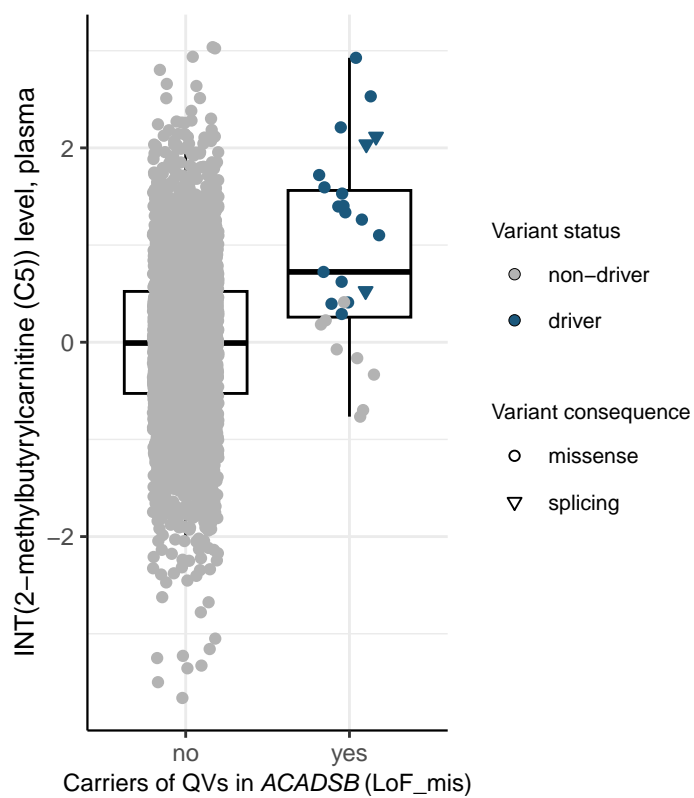


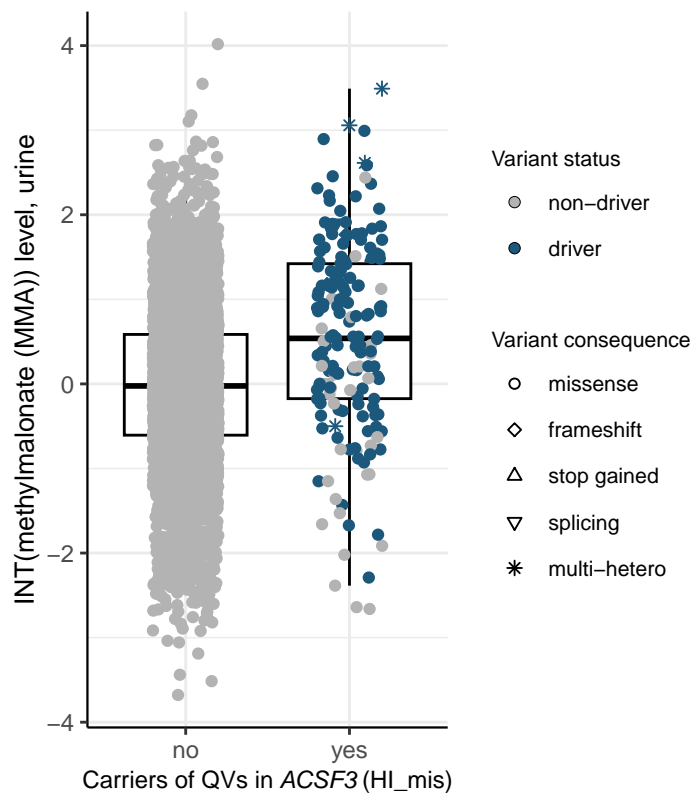
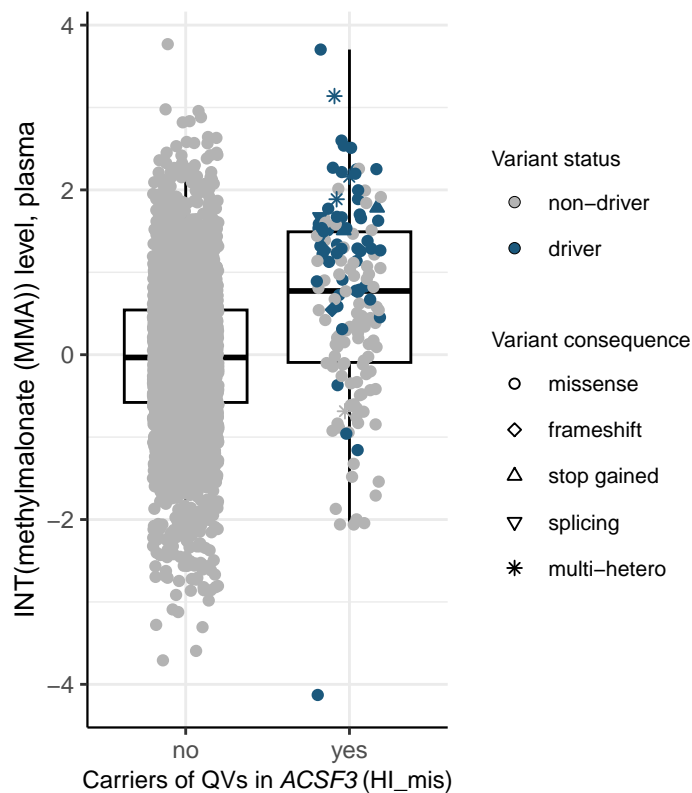
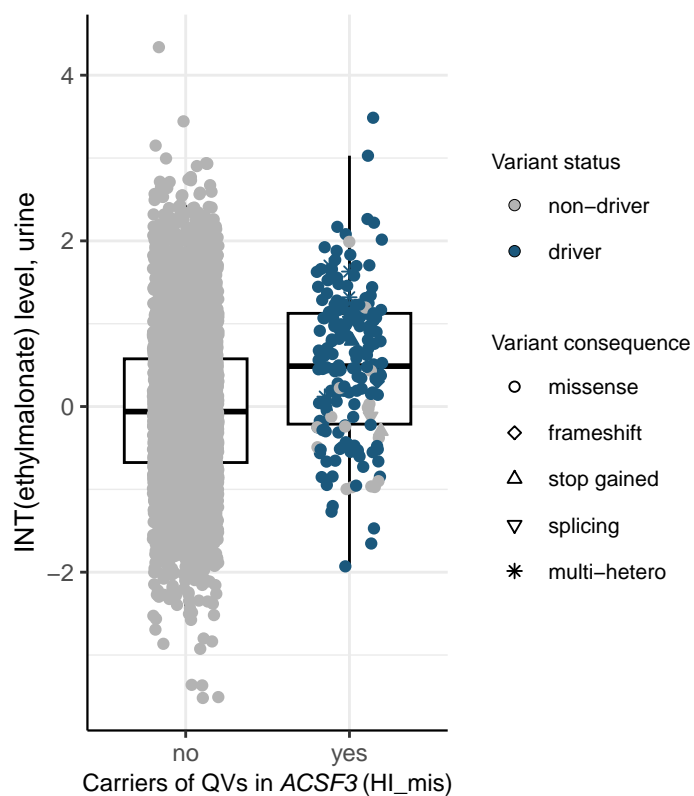


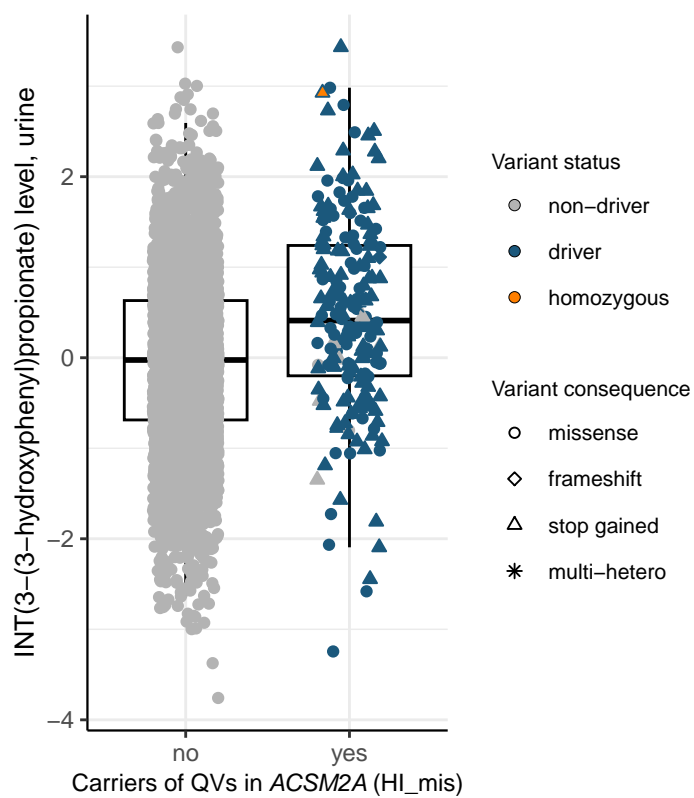
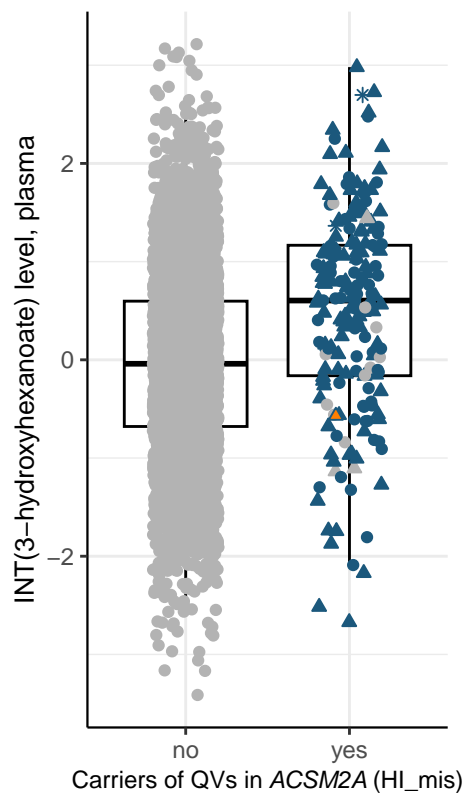


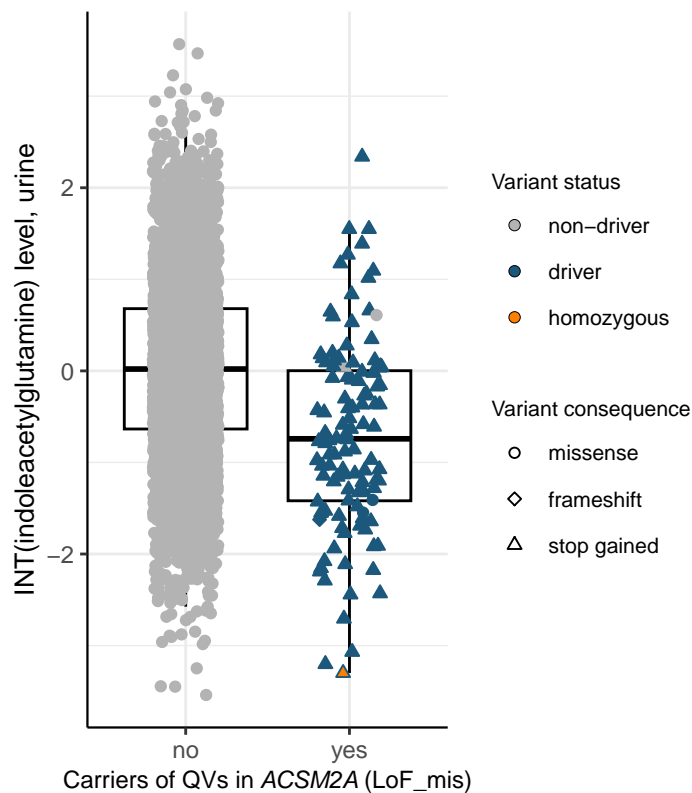
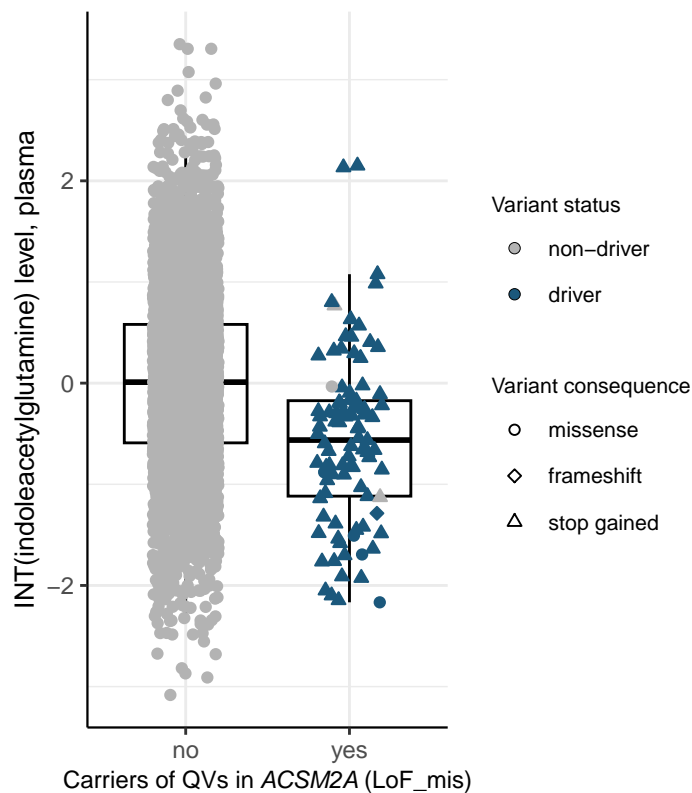
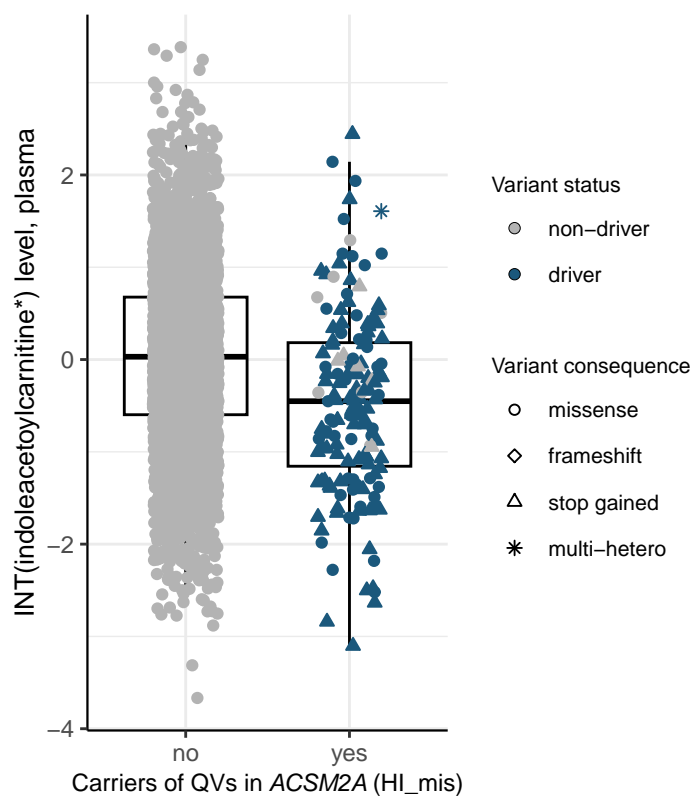


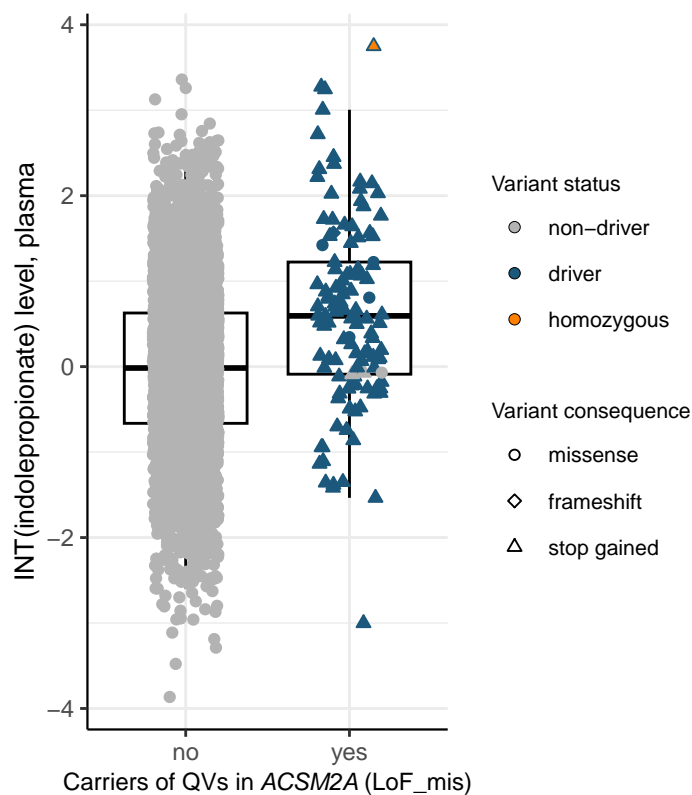
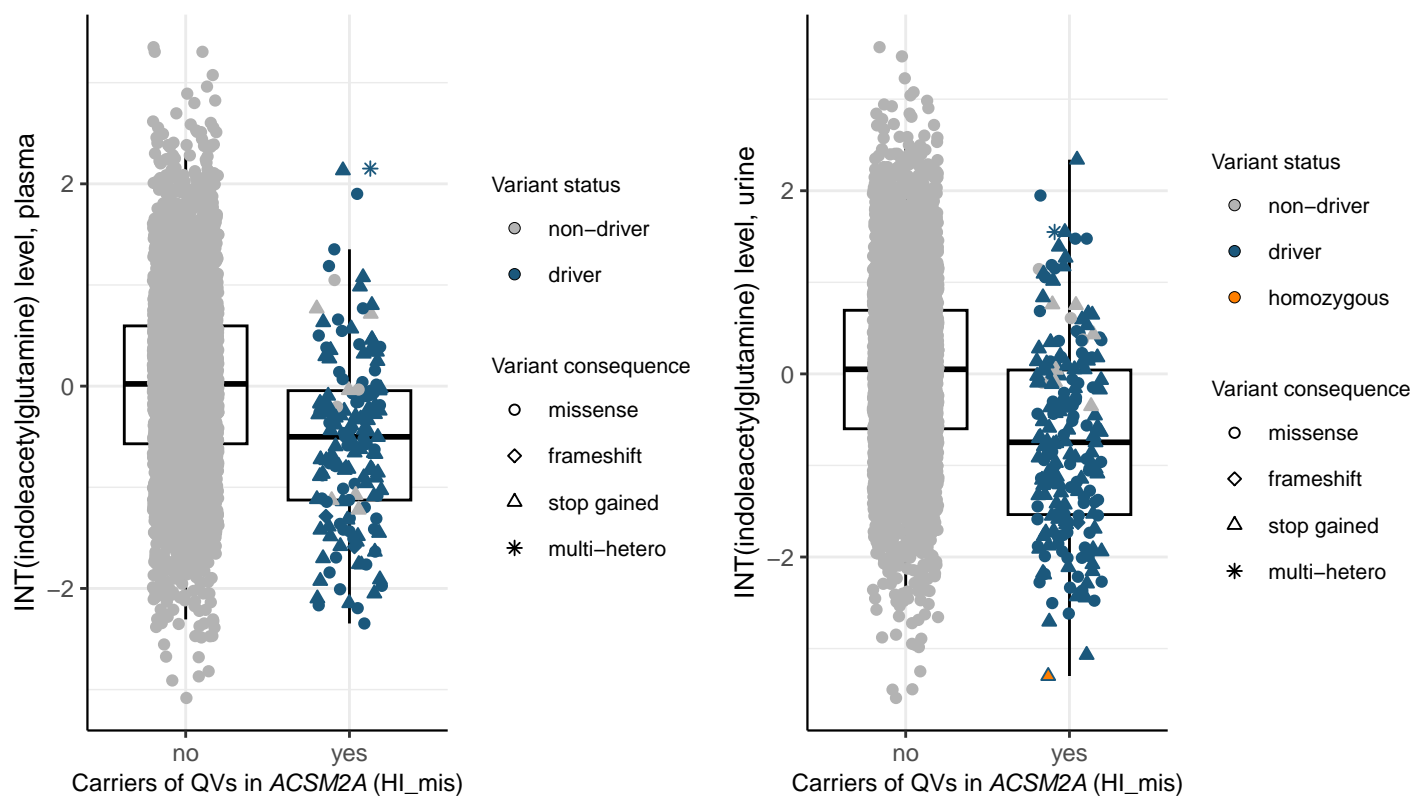


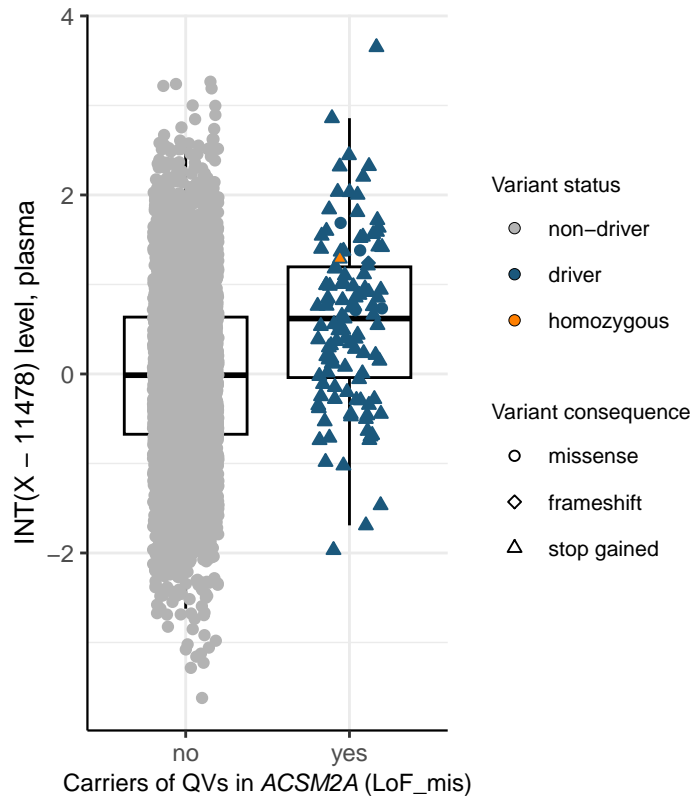
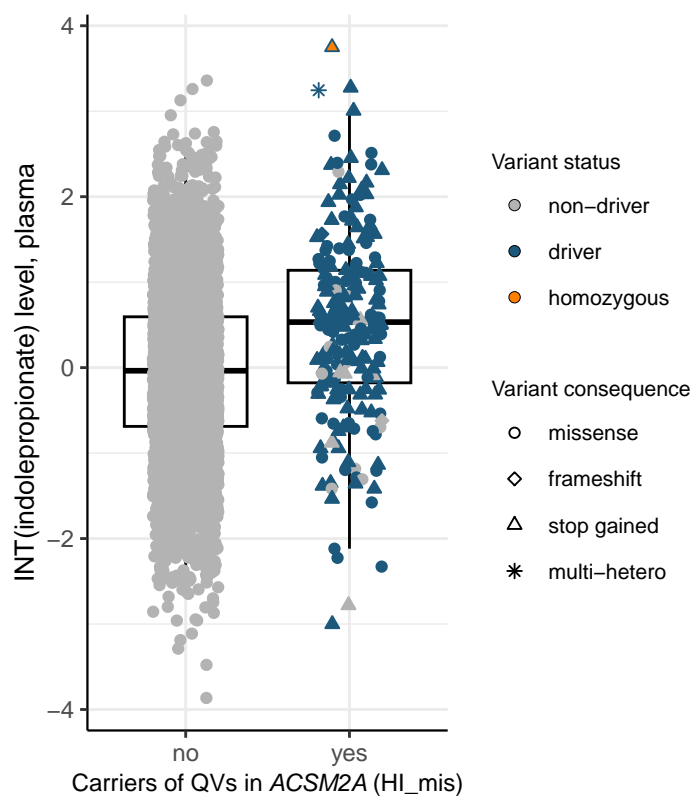


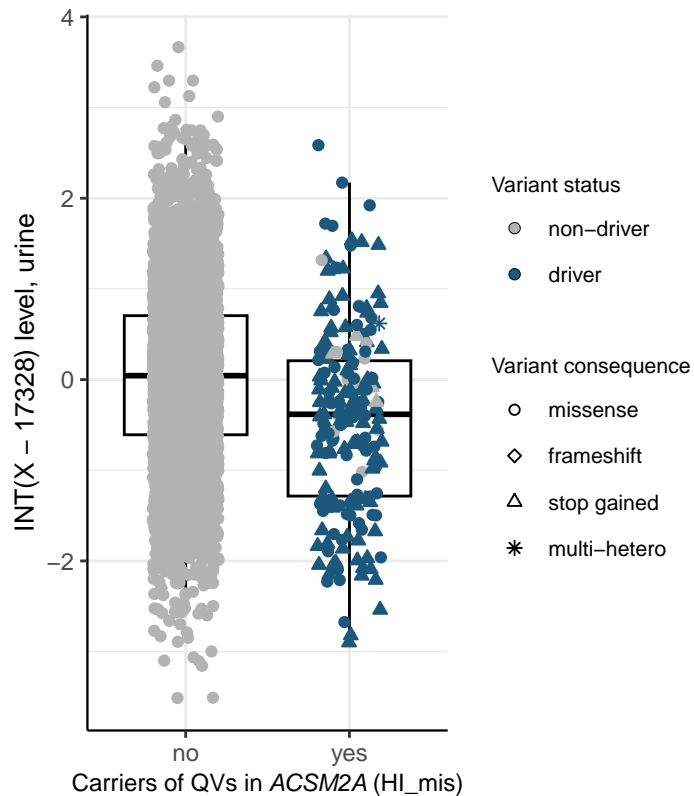
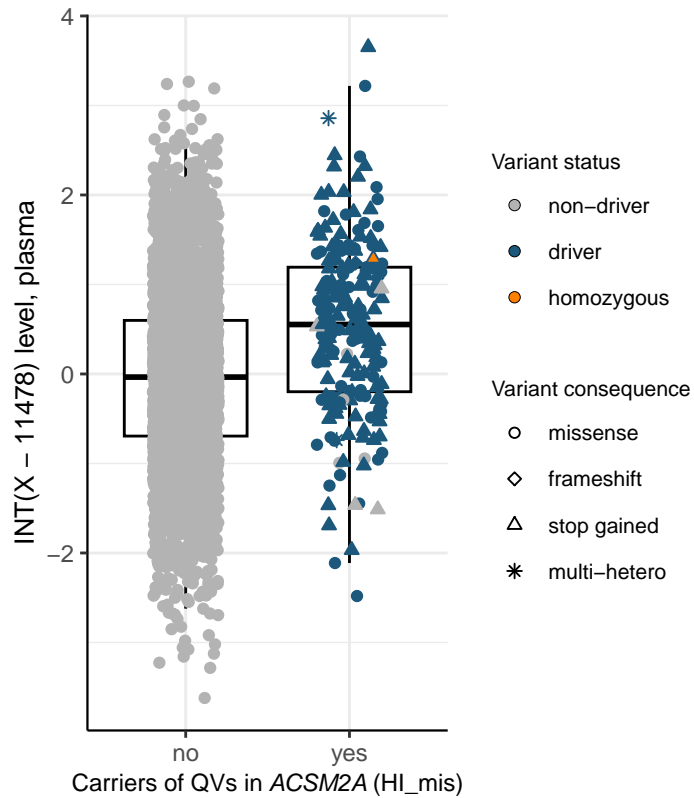


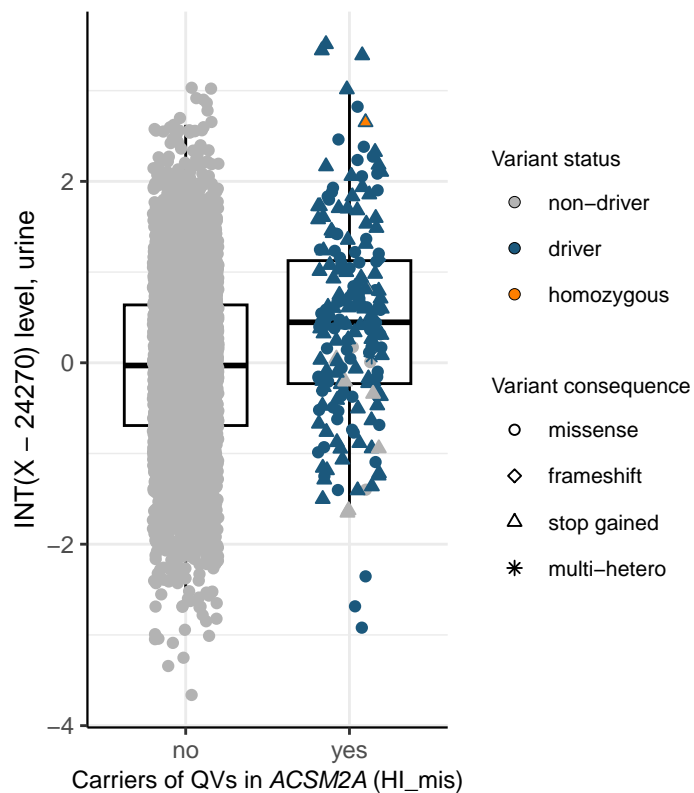
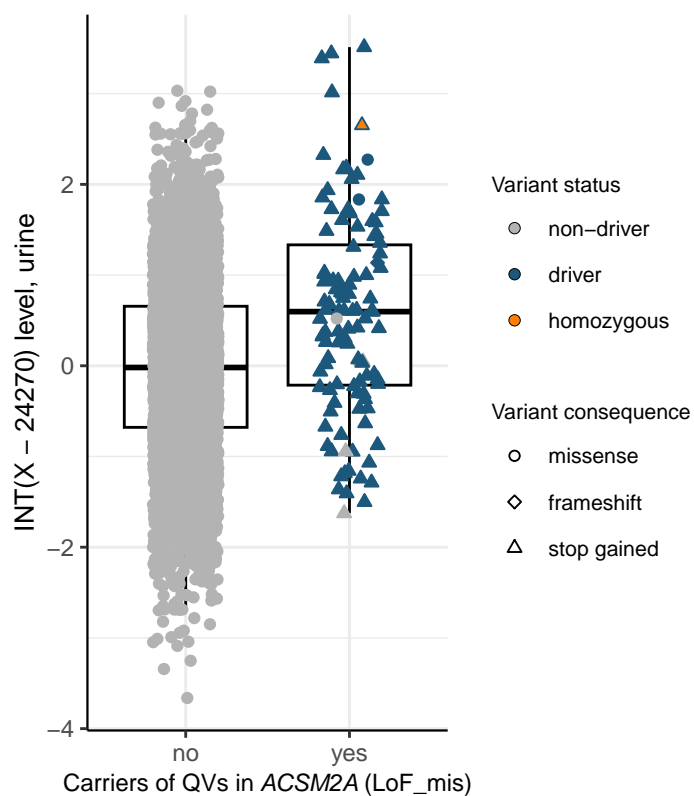


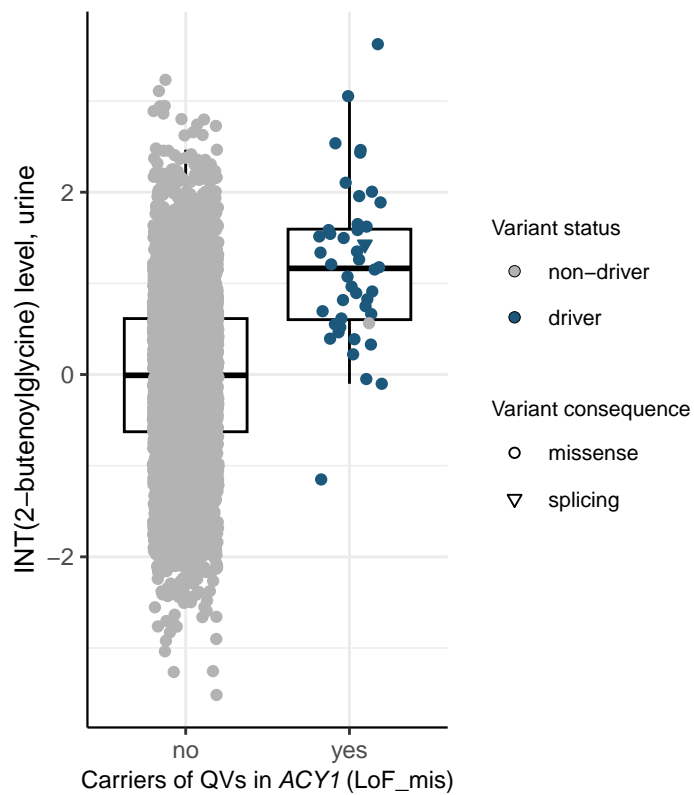
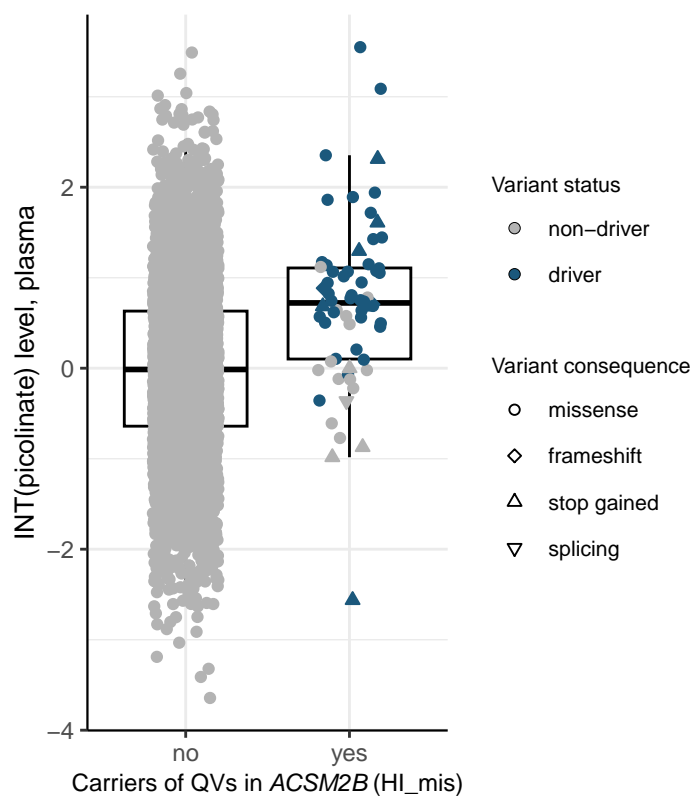


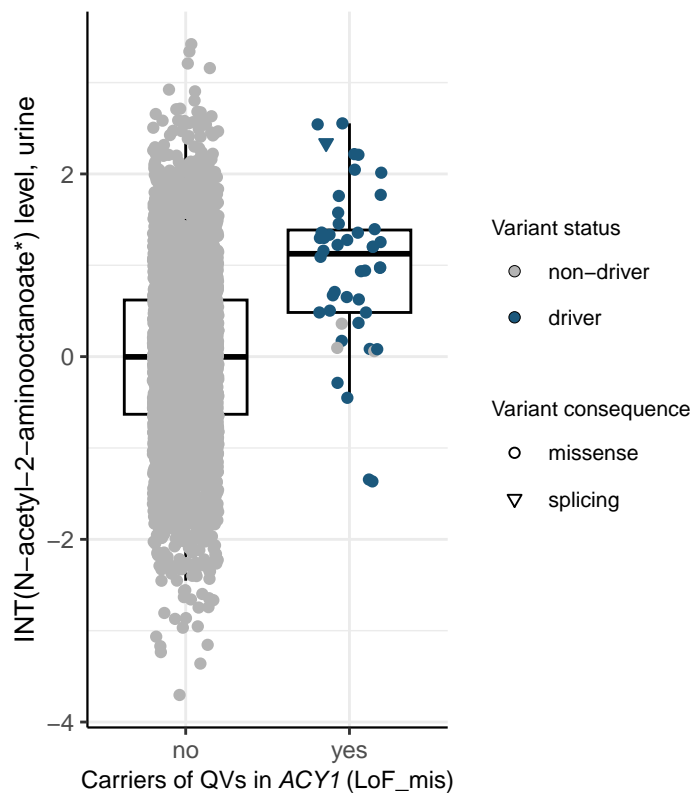
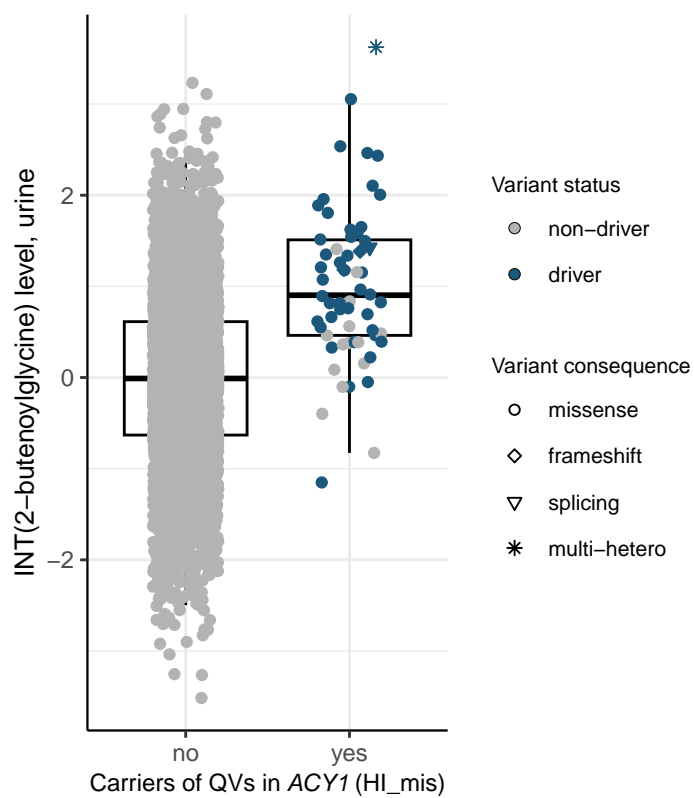


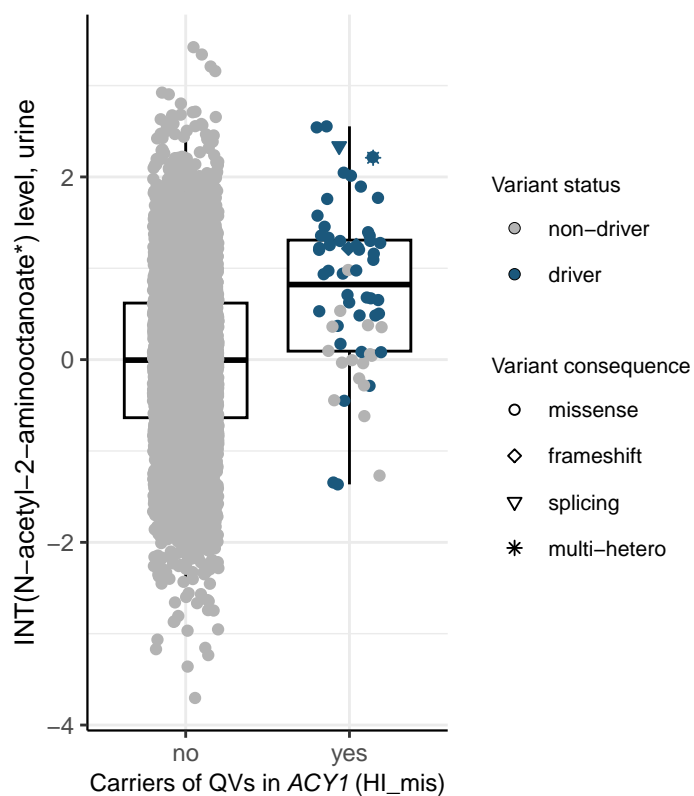
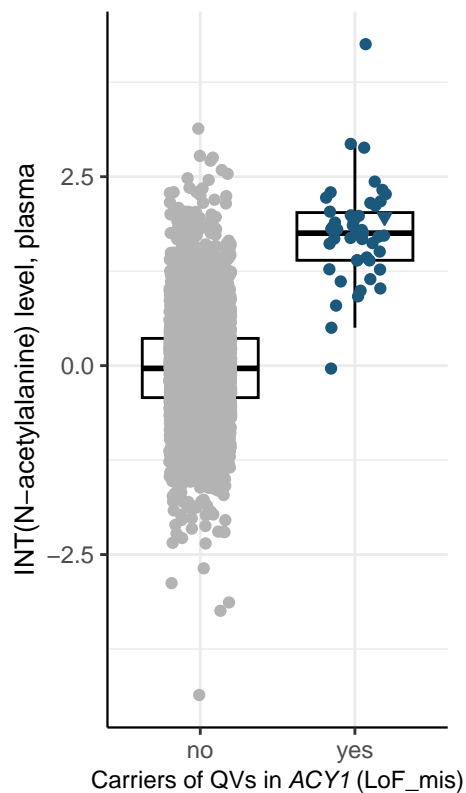


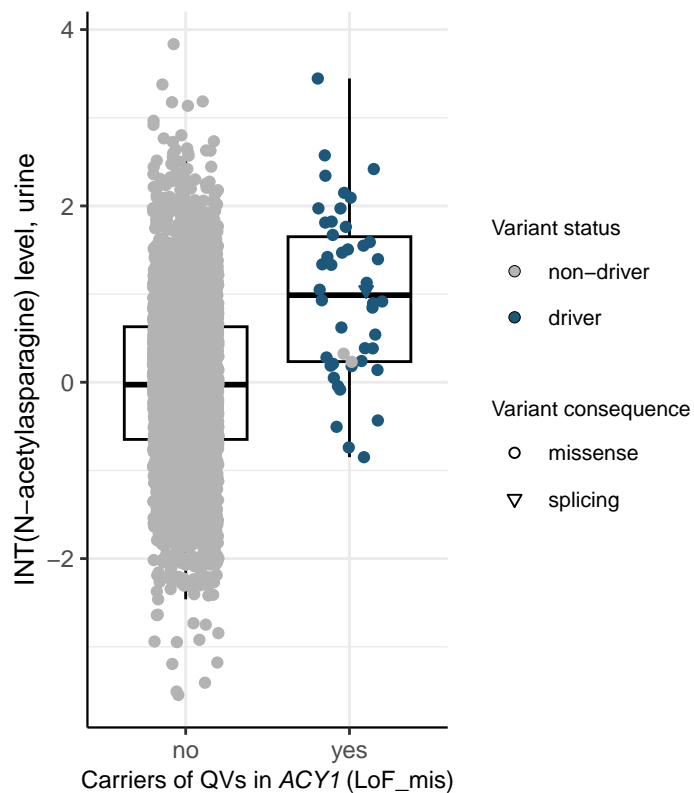
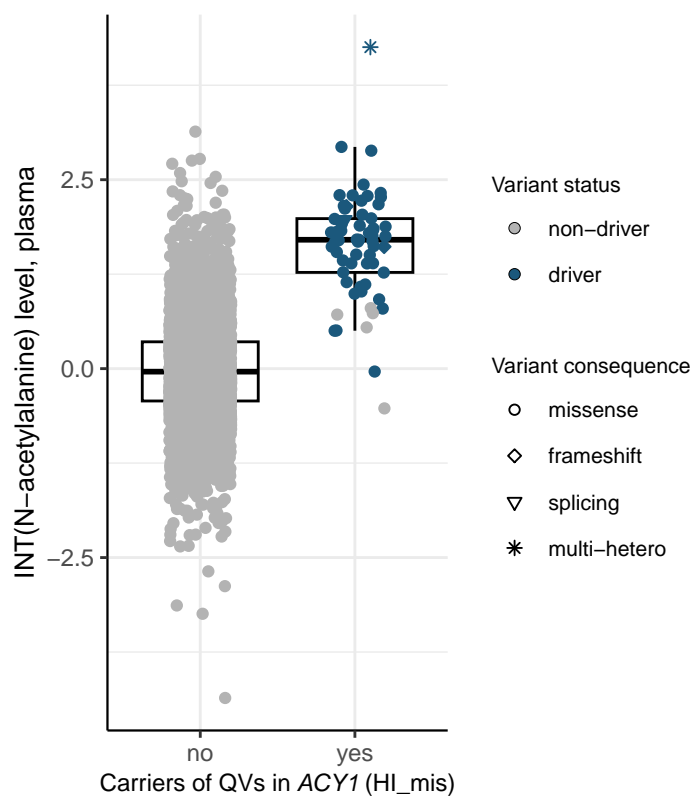


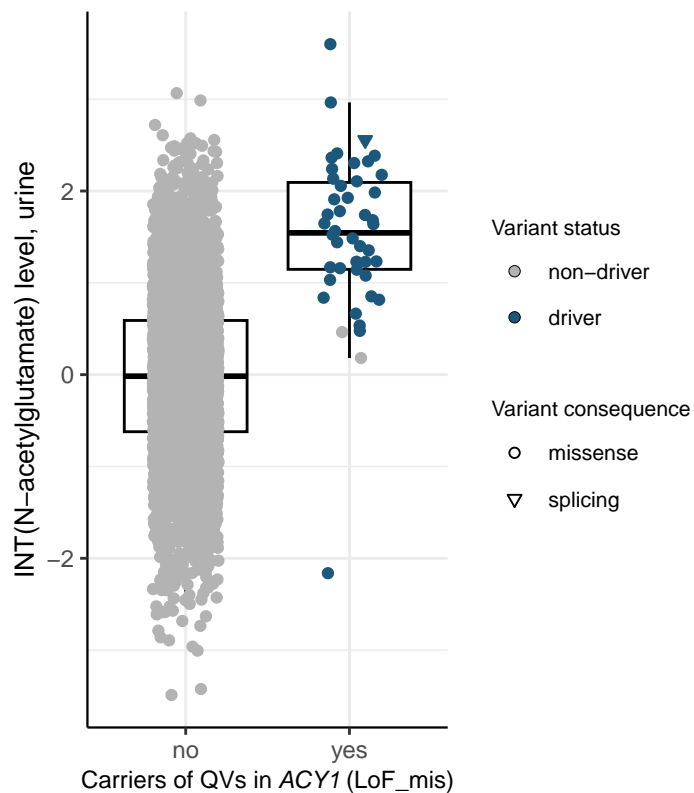
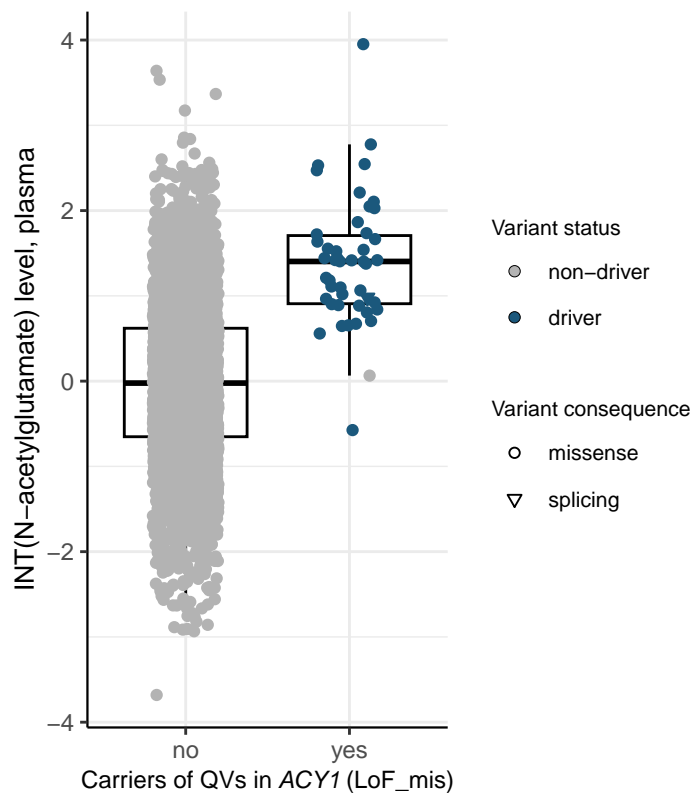
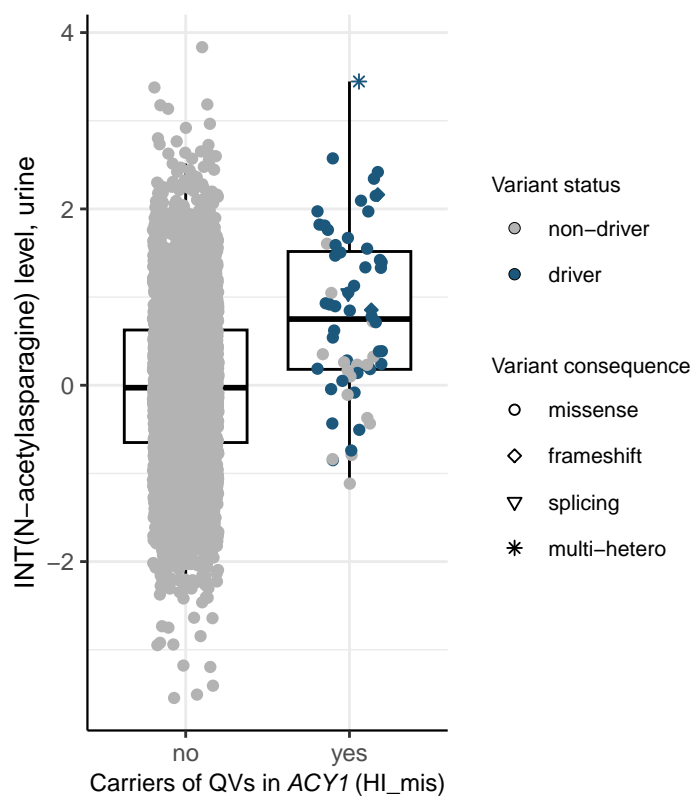


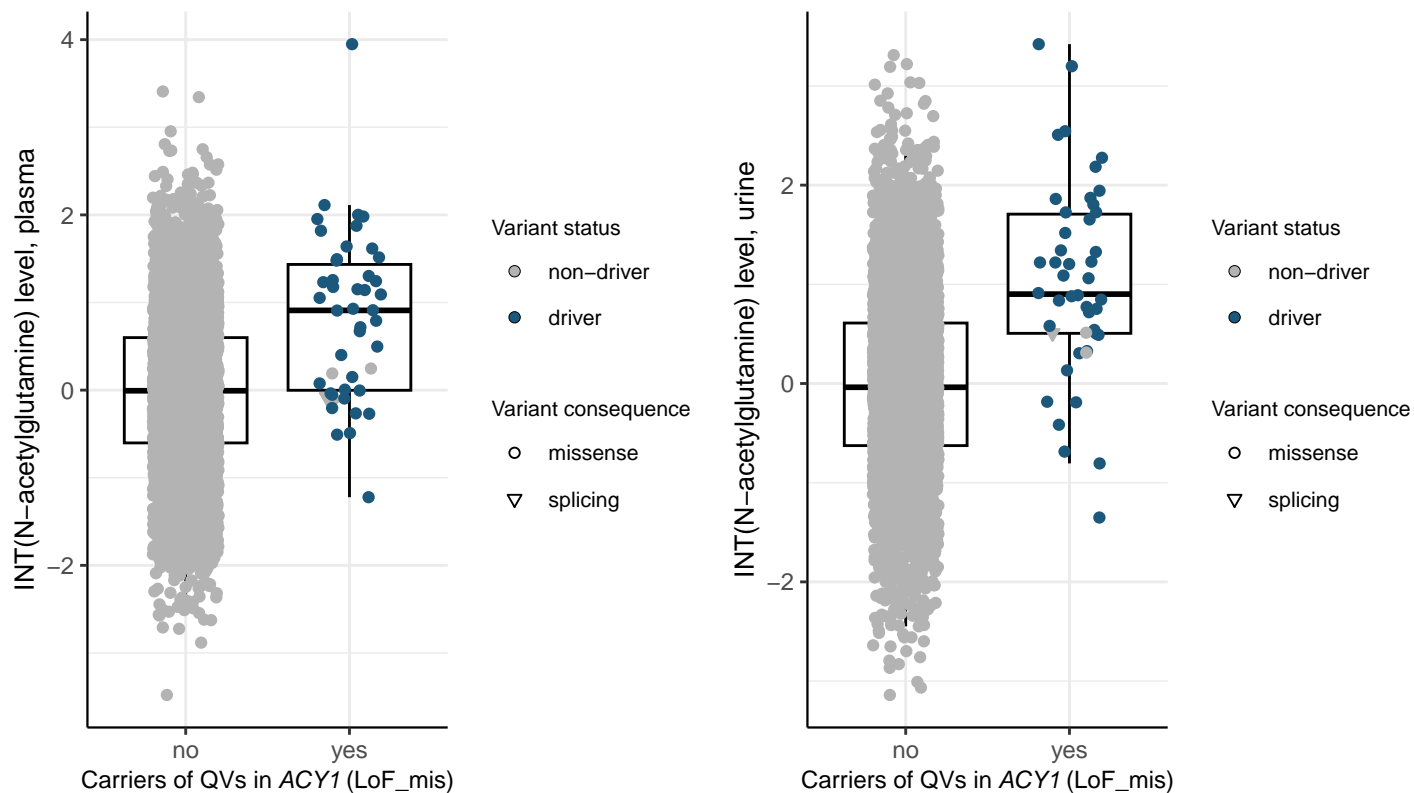
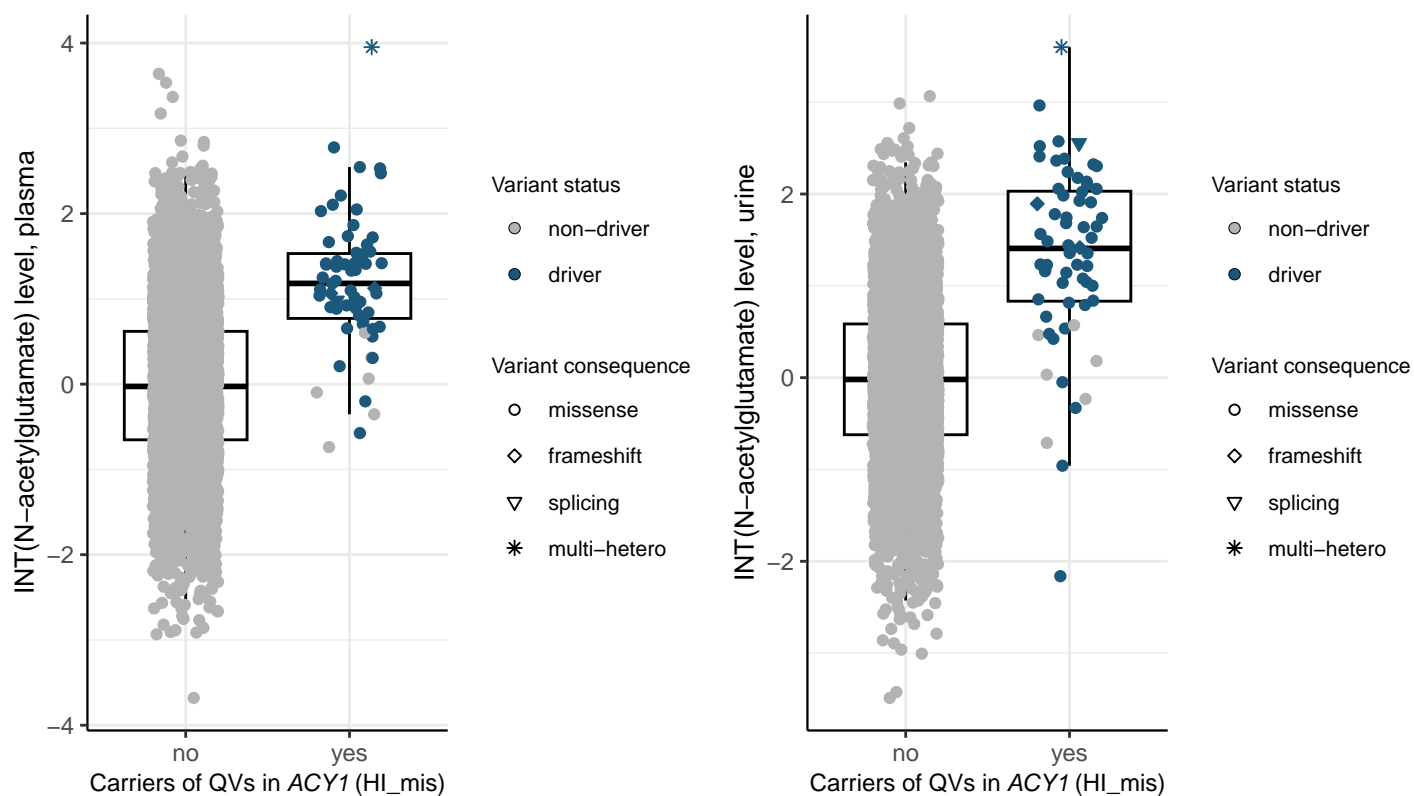


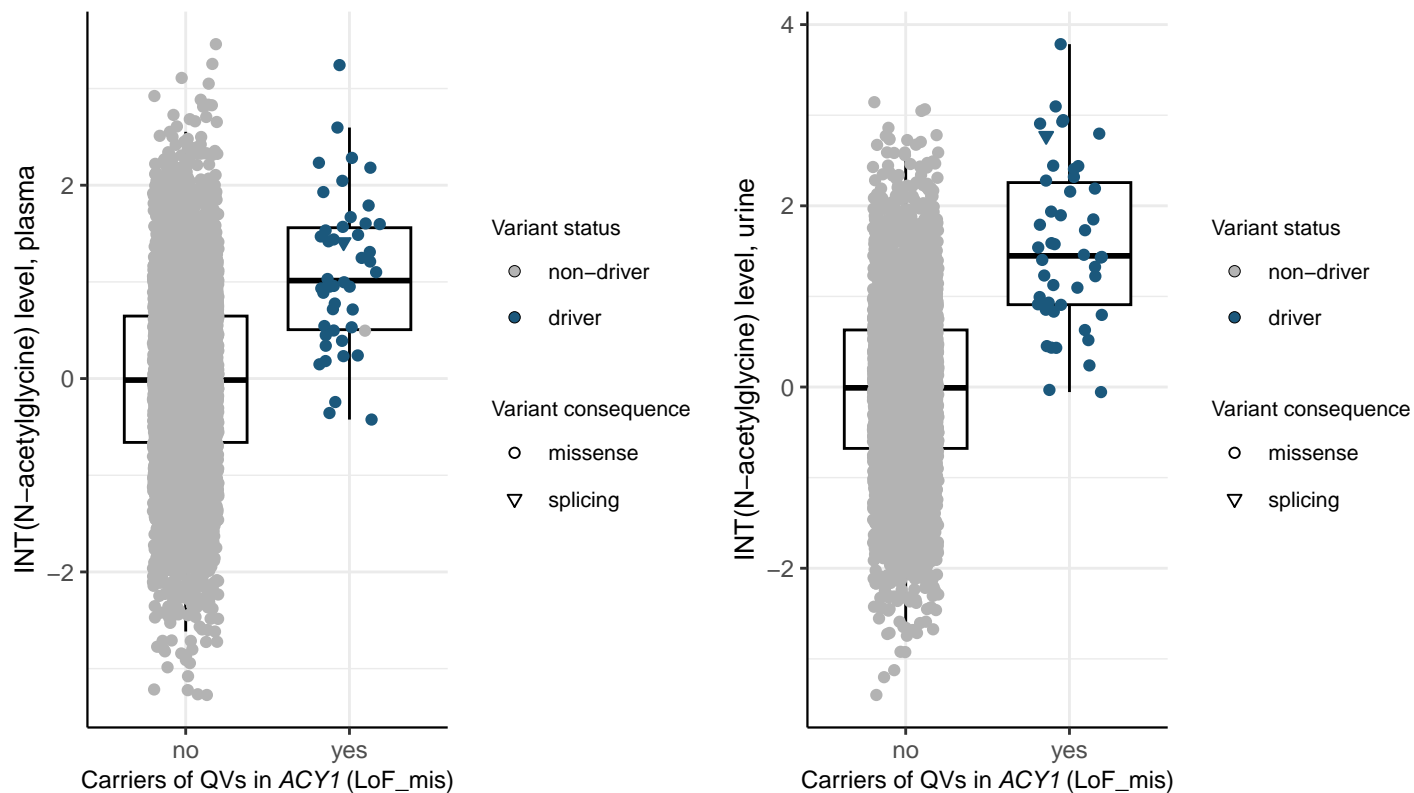
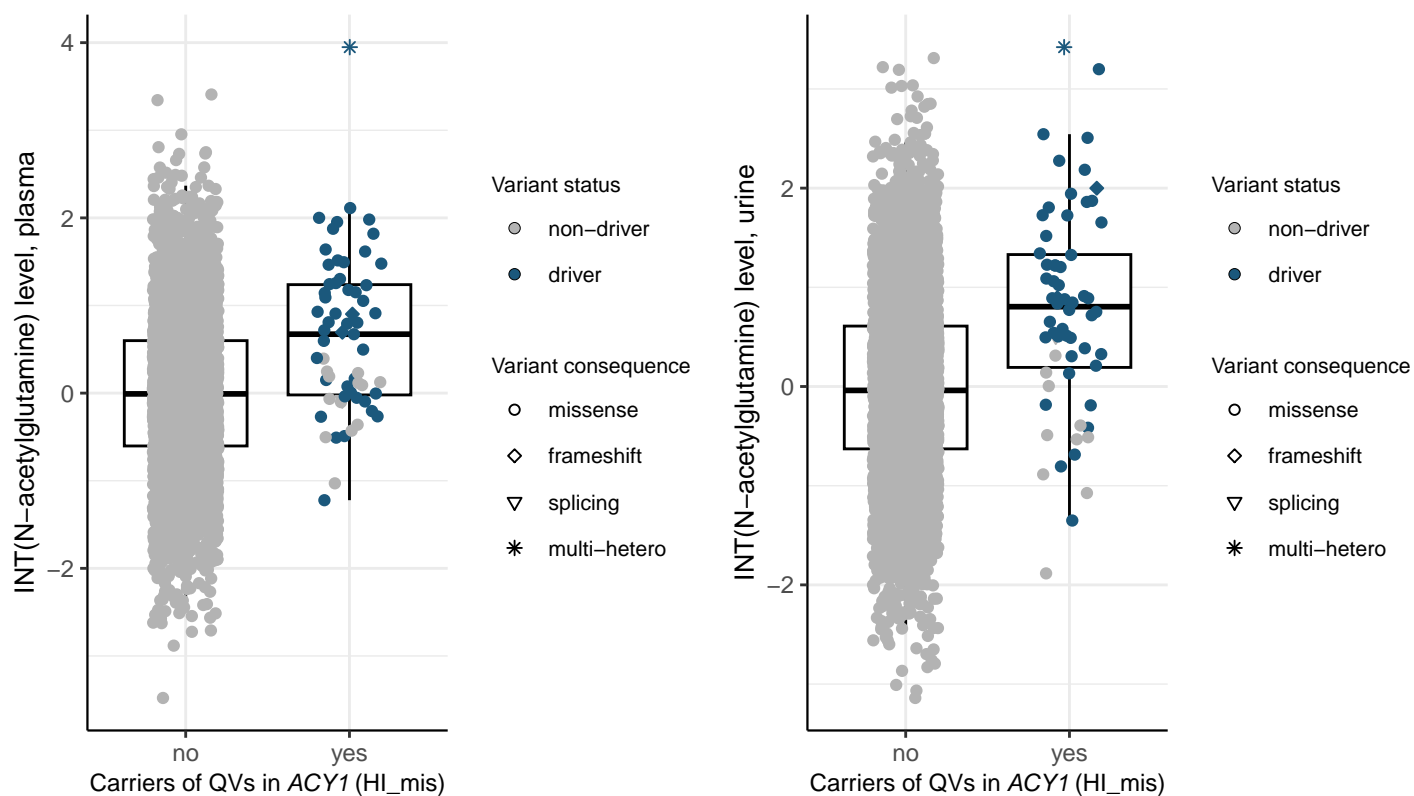


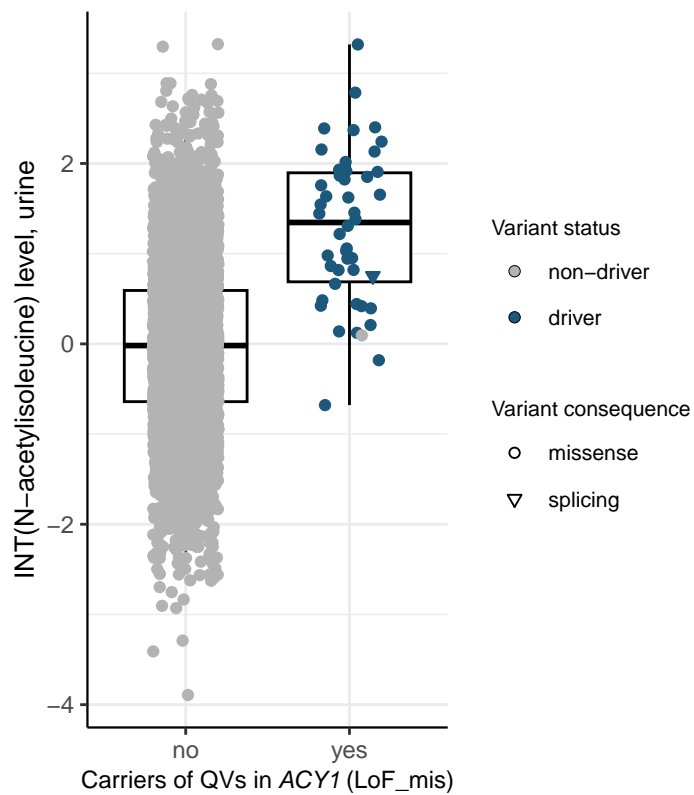
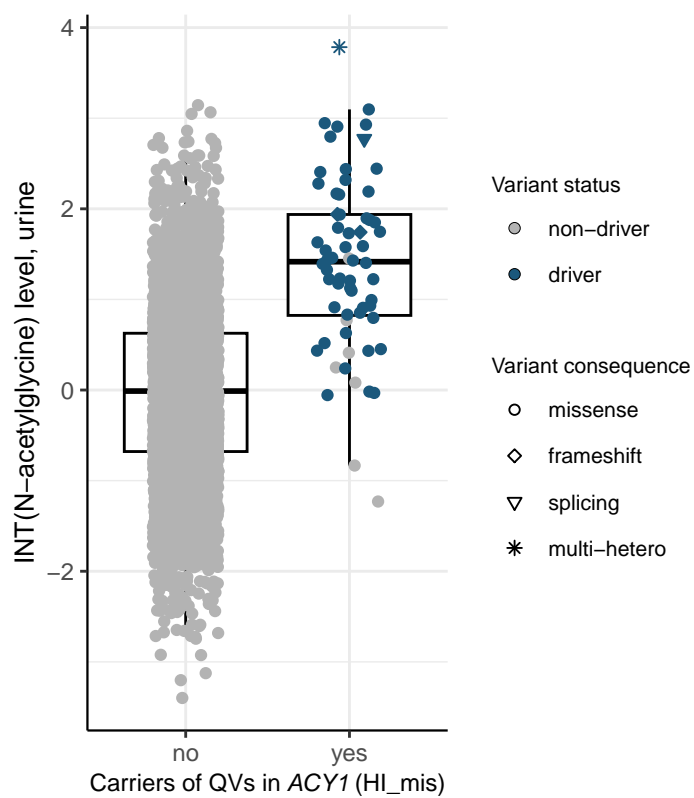
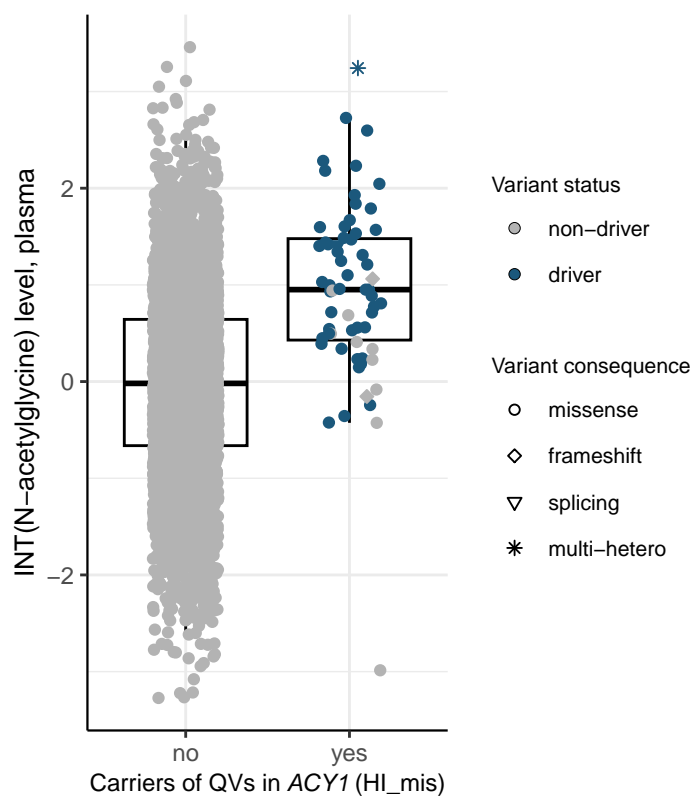


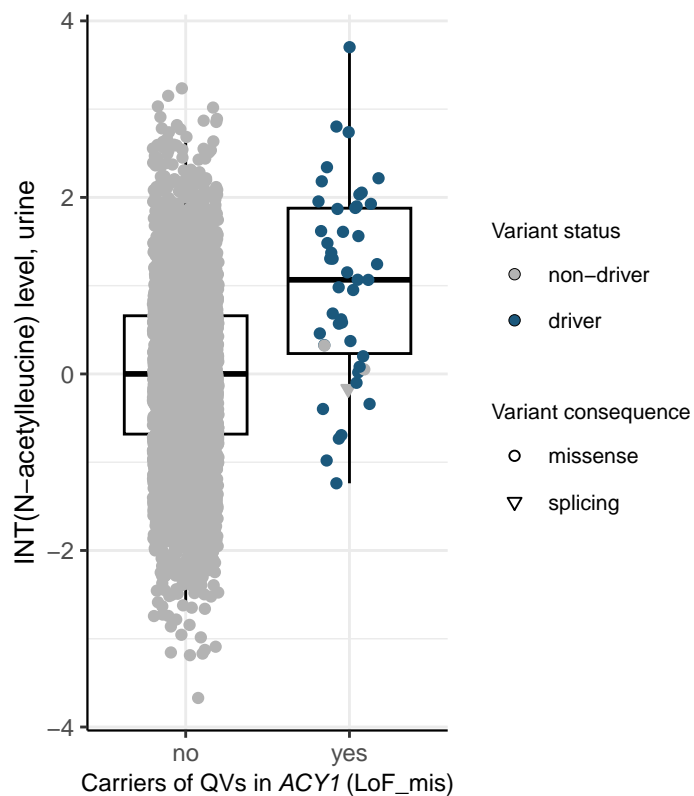
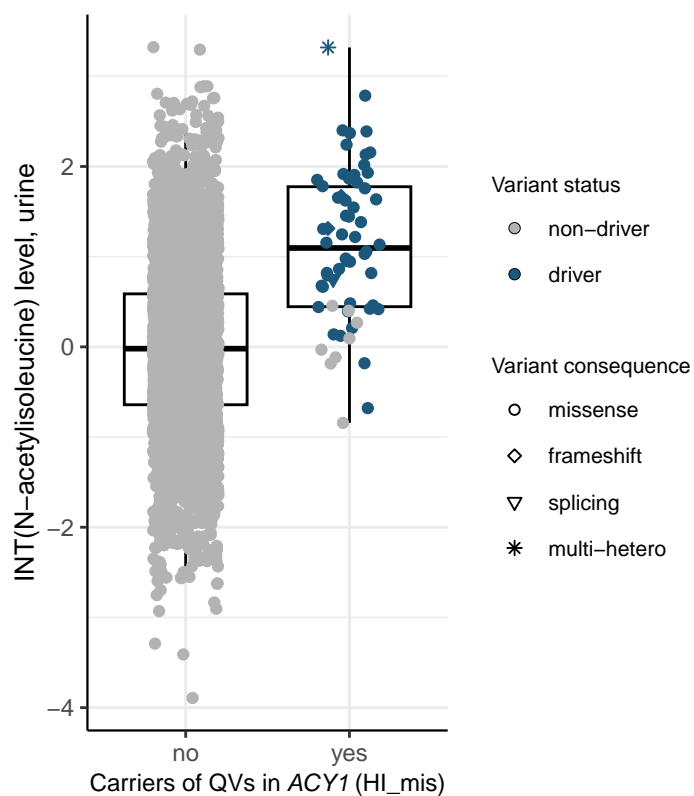


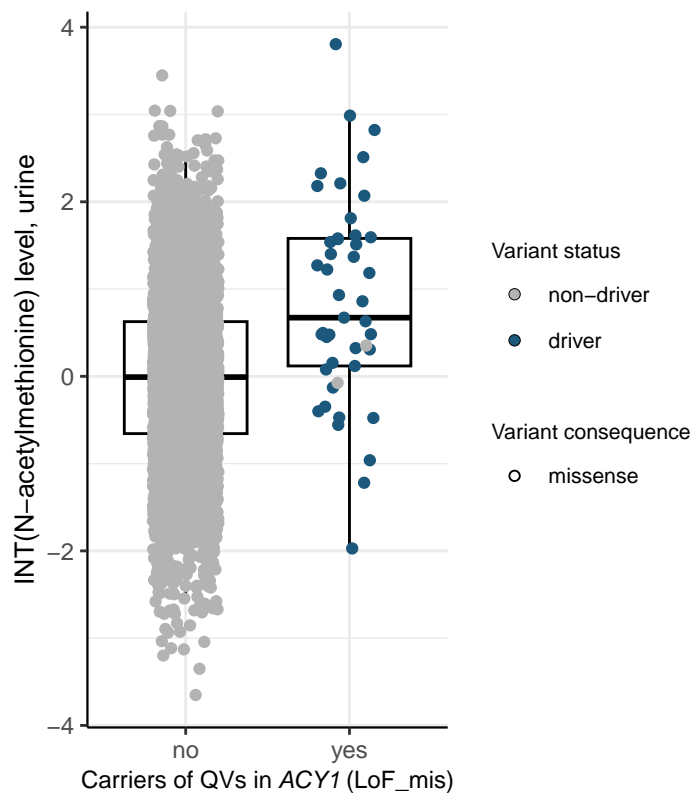
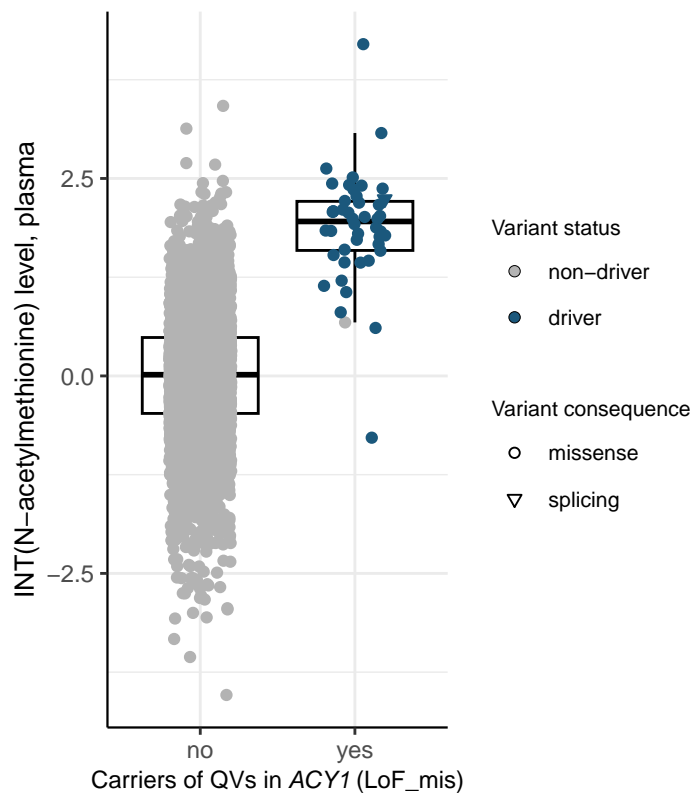
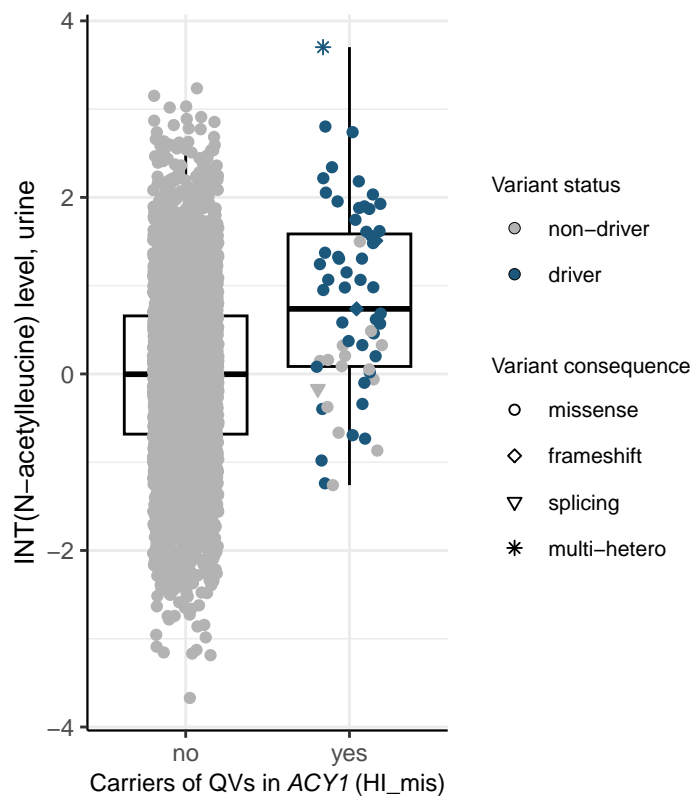


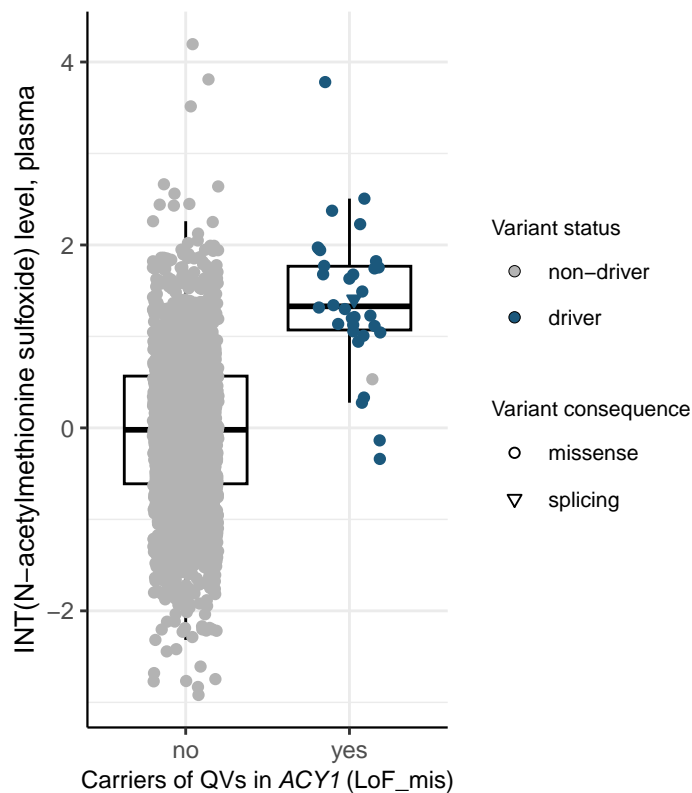
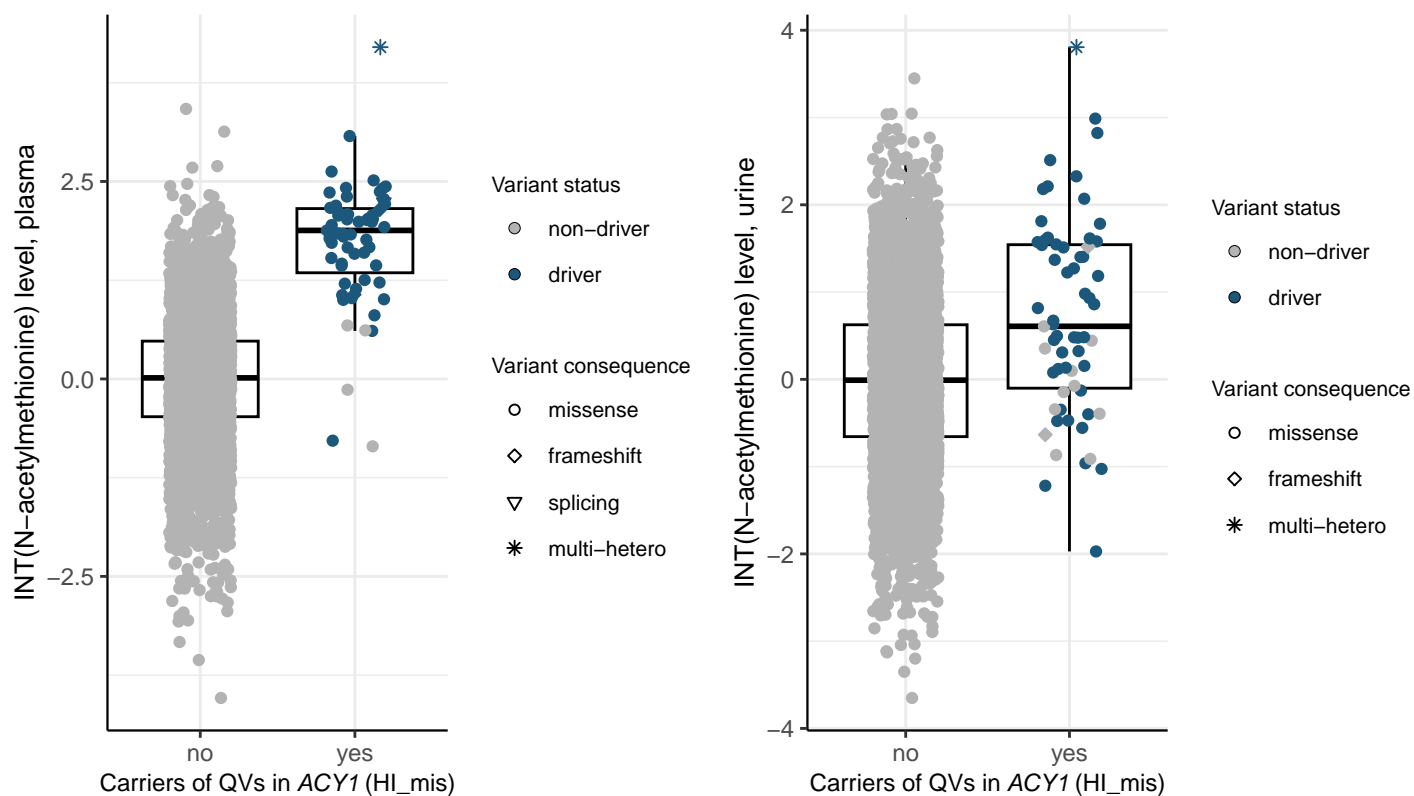


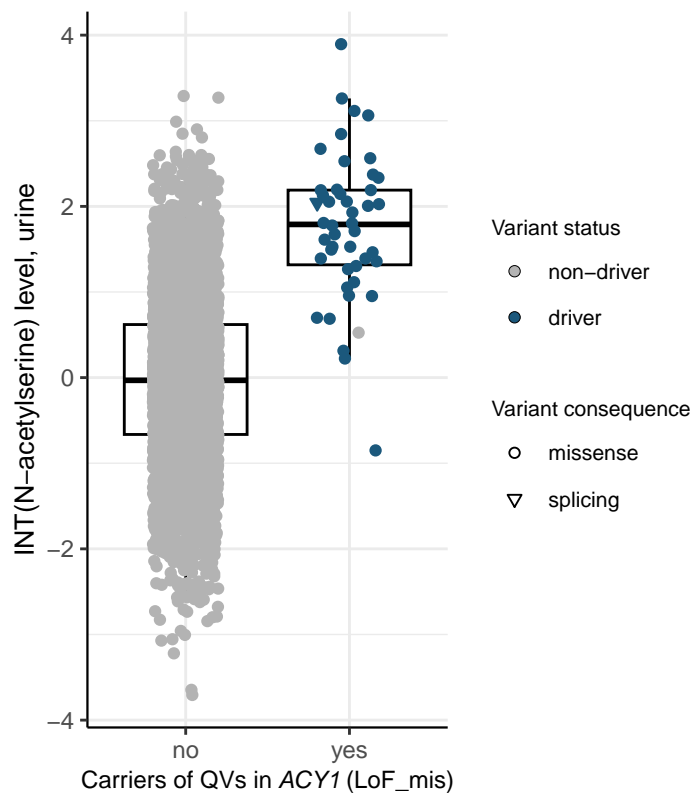
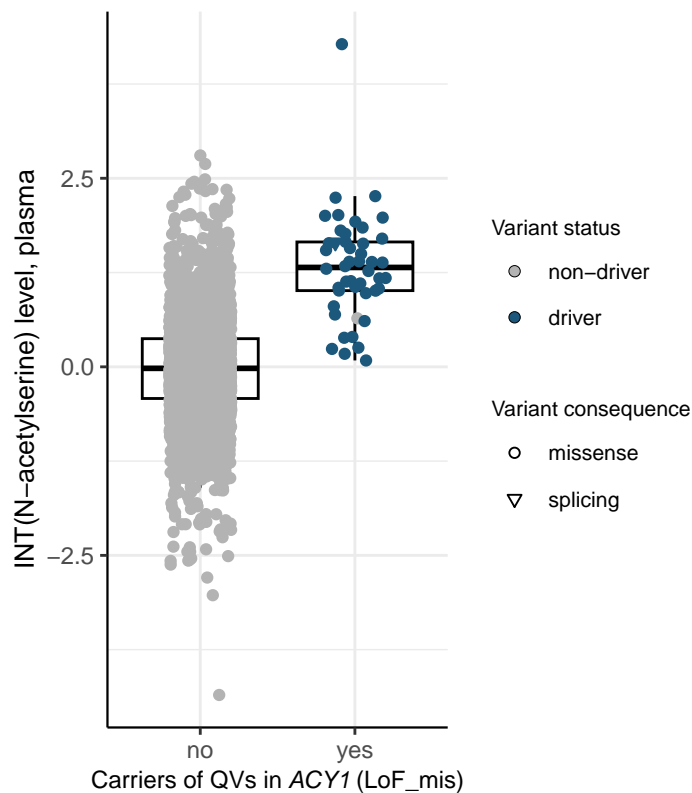
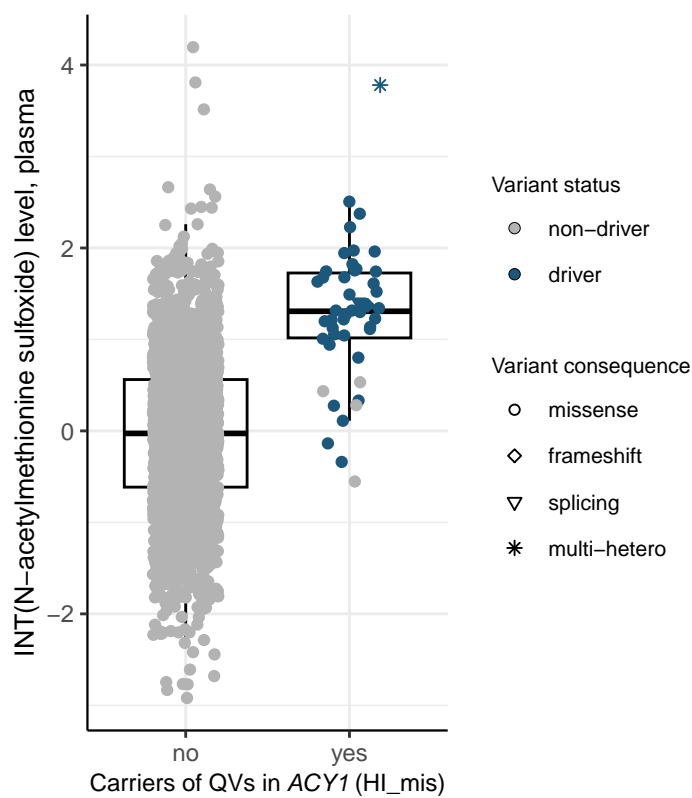


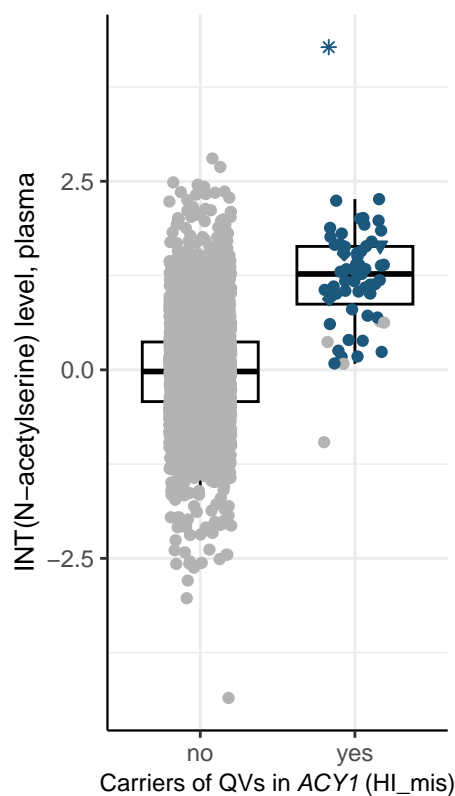










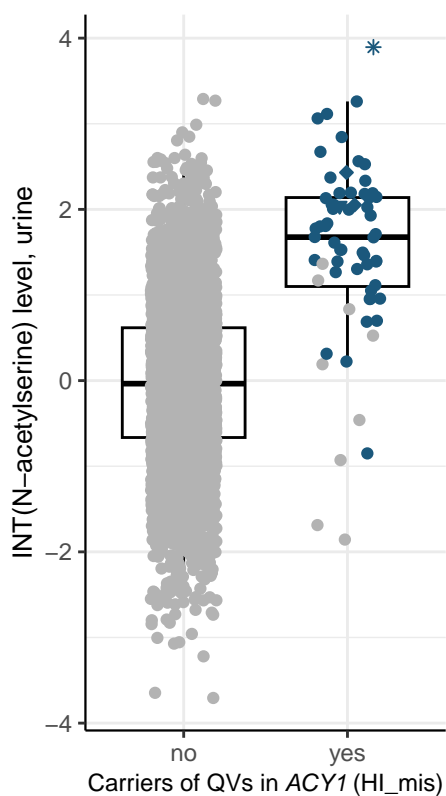


Variant status

- non-driver
- driver

Variant consequence

- missense
- frameshift
- splicing
- multi-hetero

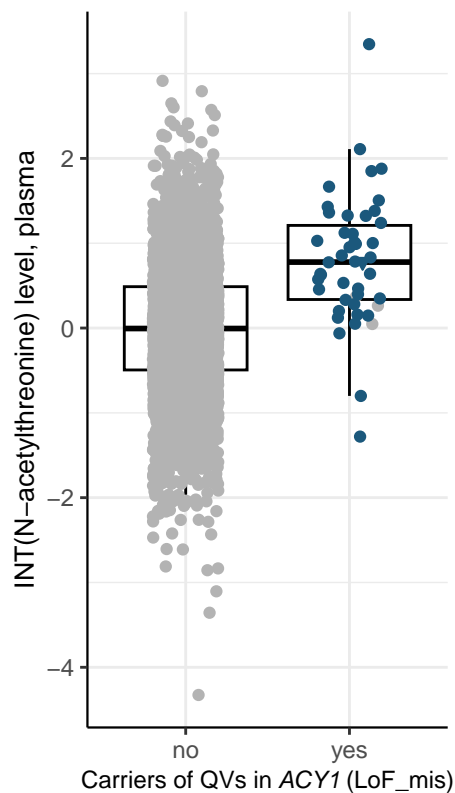


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- splicing
- multi-hetero

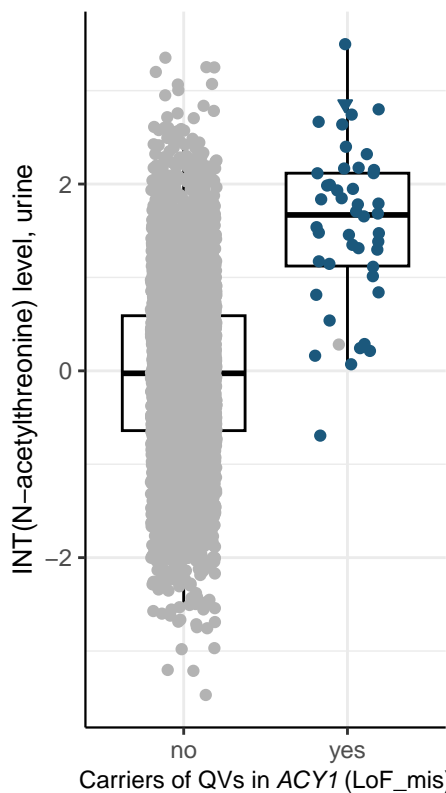


Variant status

- non-driver
- driver

Variant consequence

- missense
- splicing

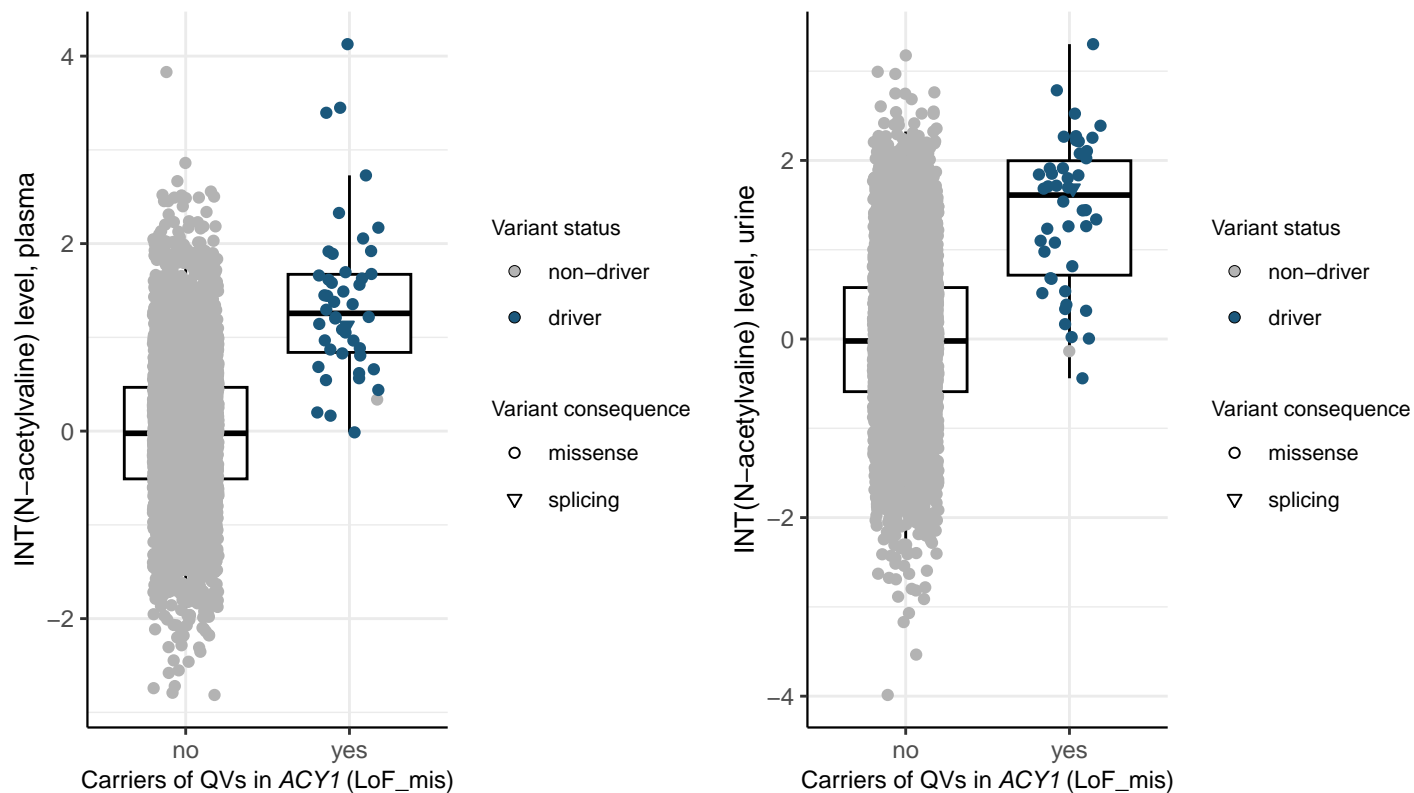
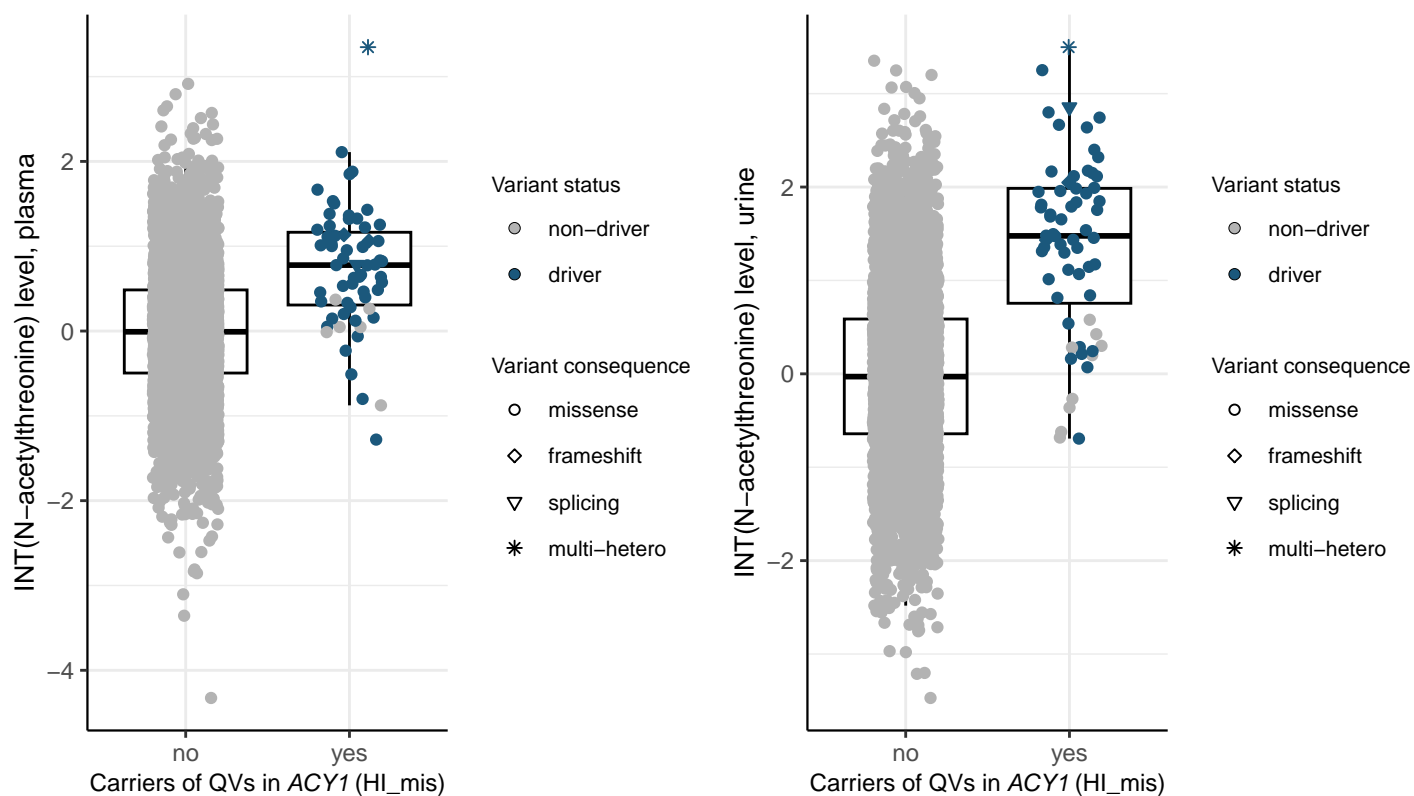


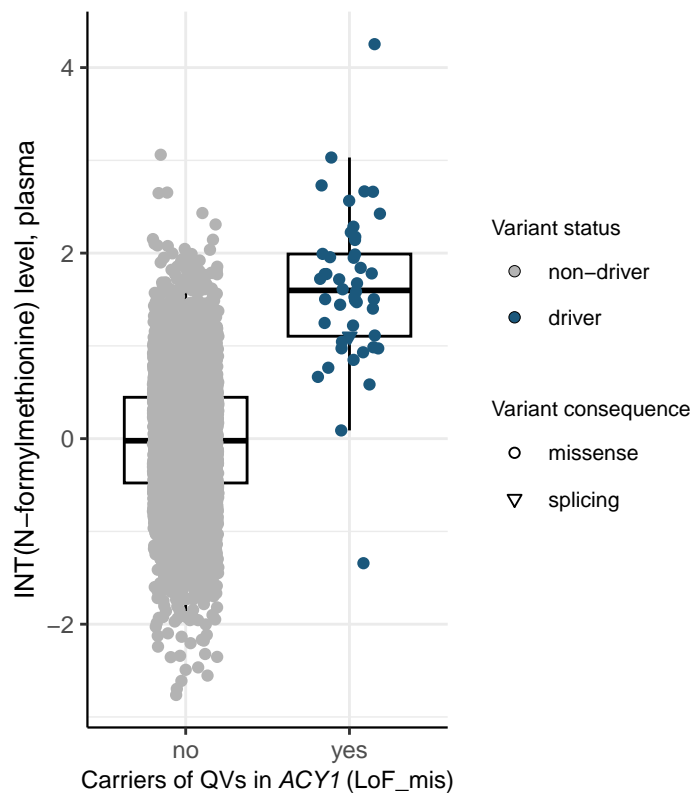
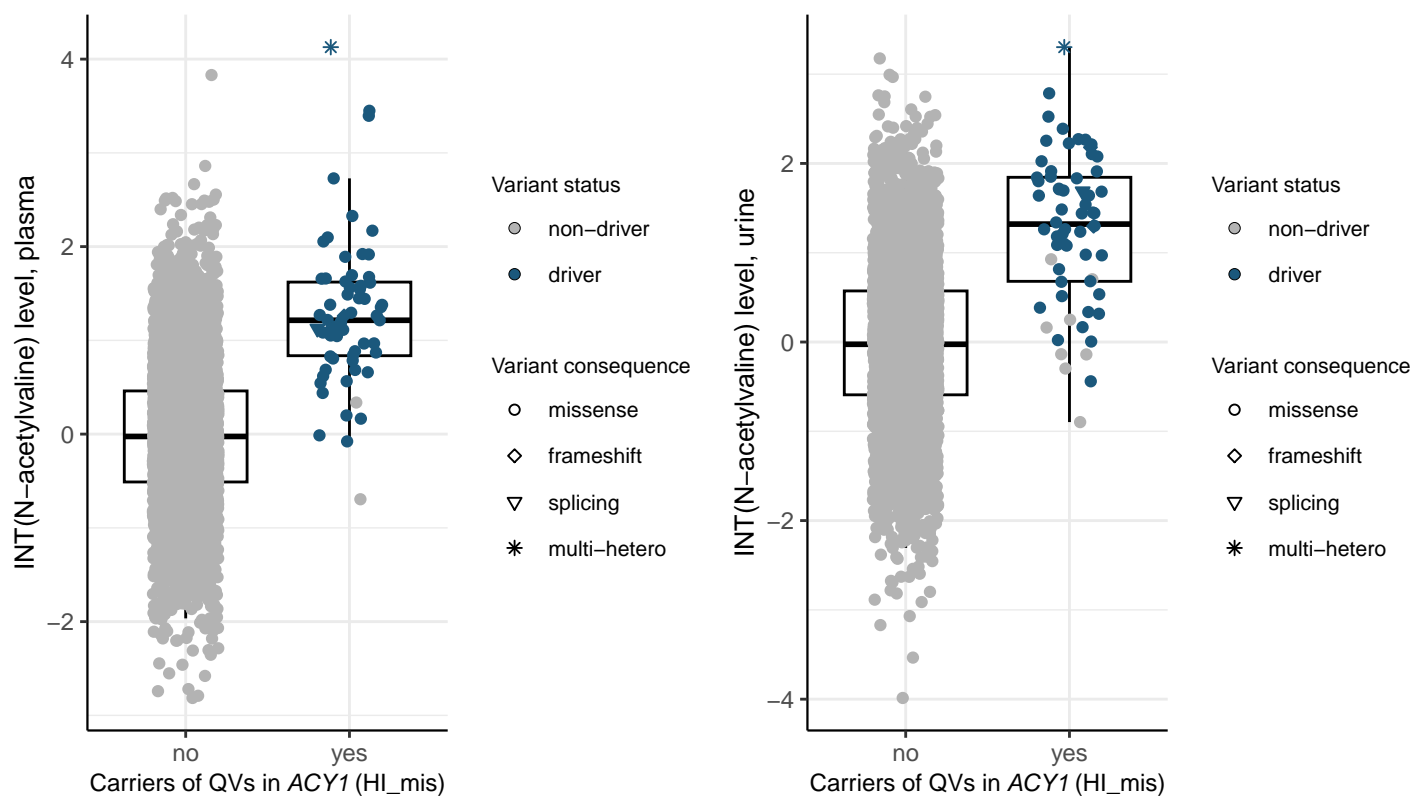
Variant status

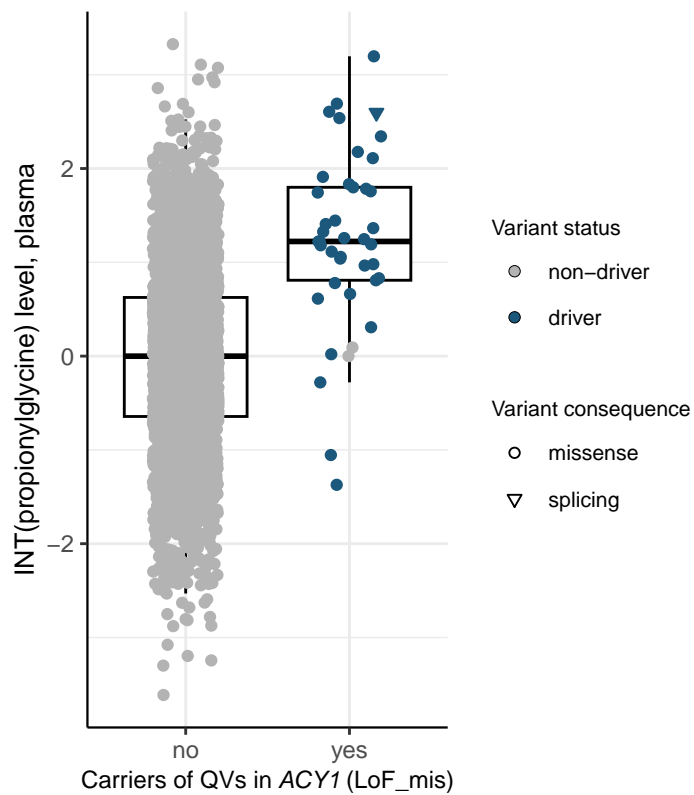
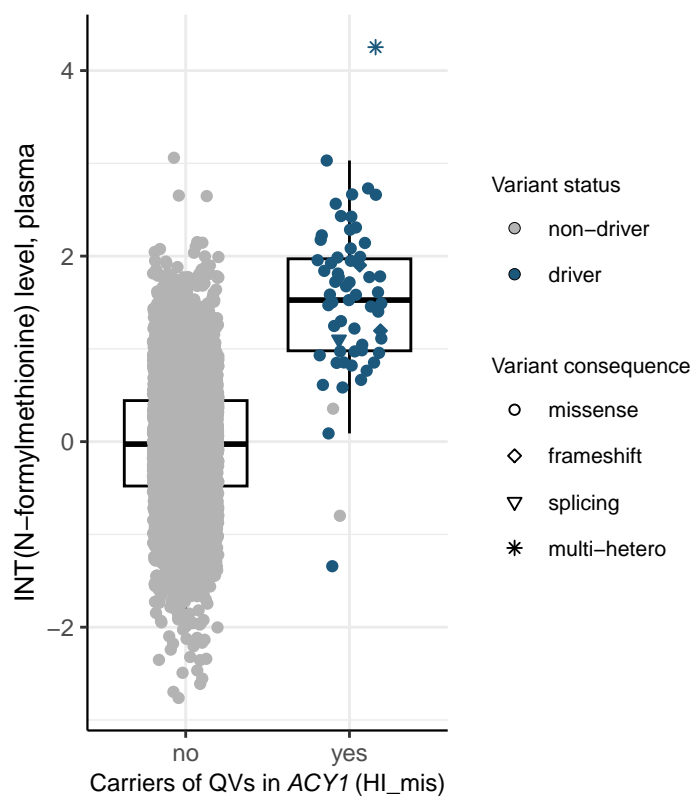
- non-driver
- driver

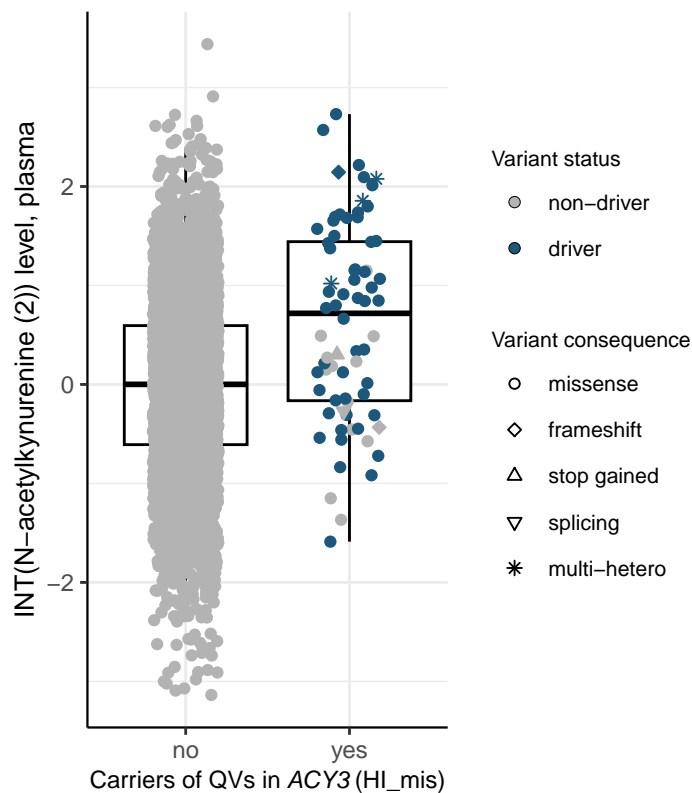
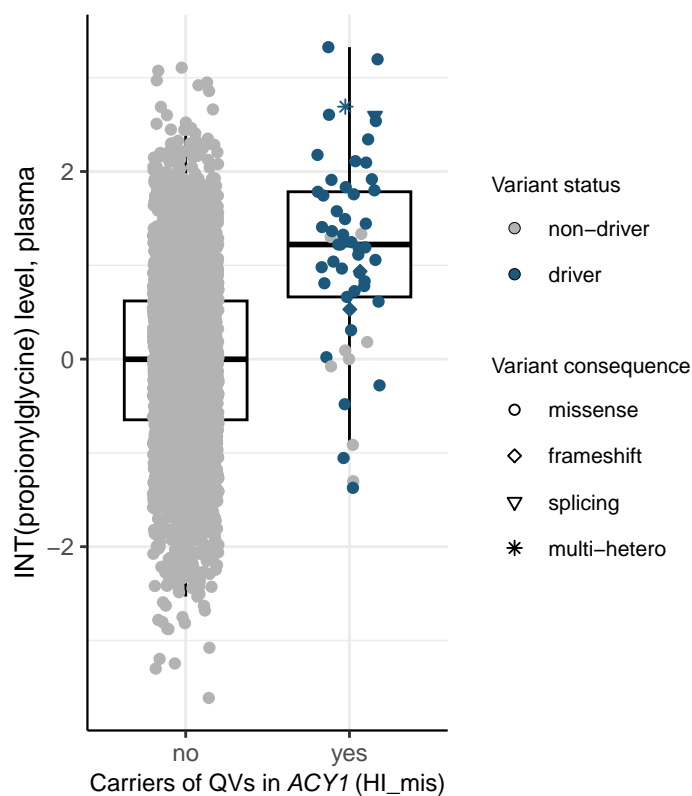
Variant consequence

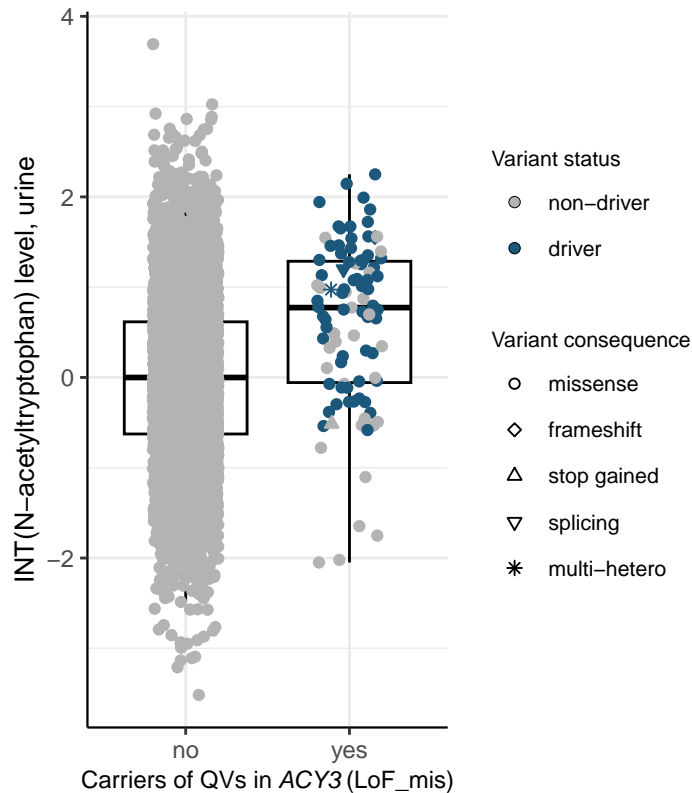
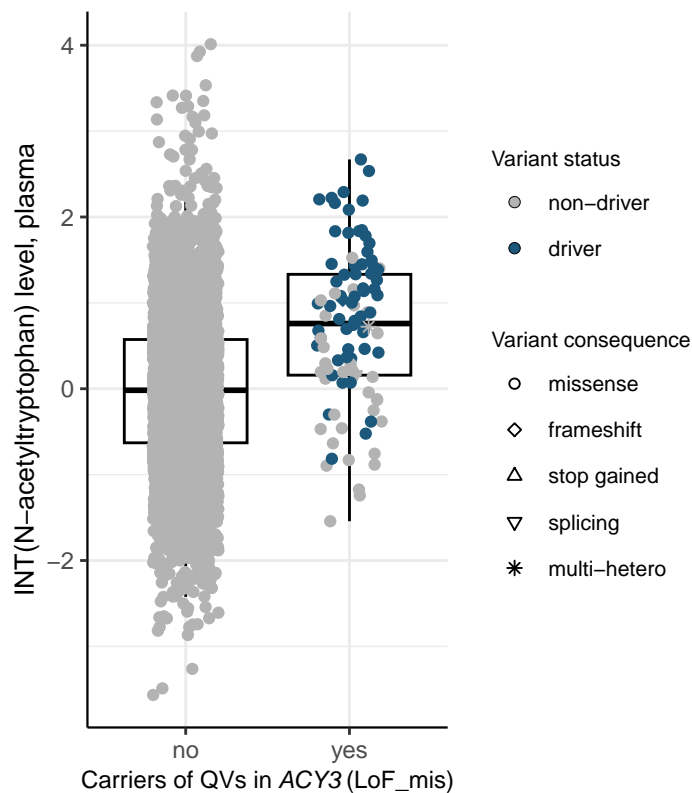
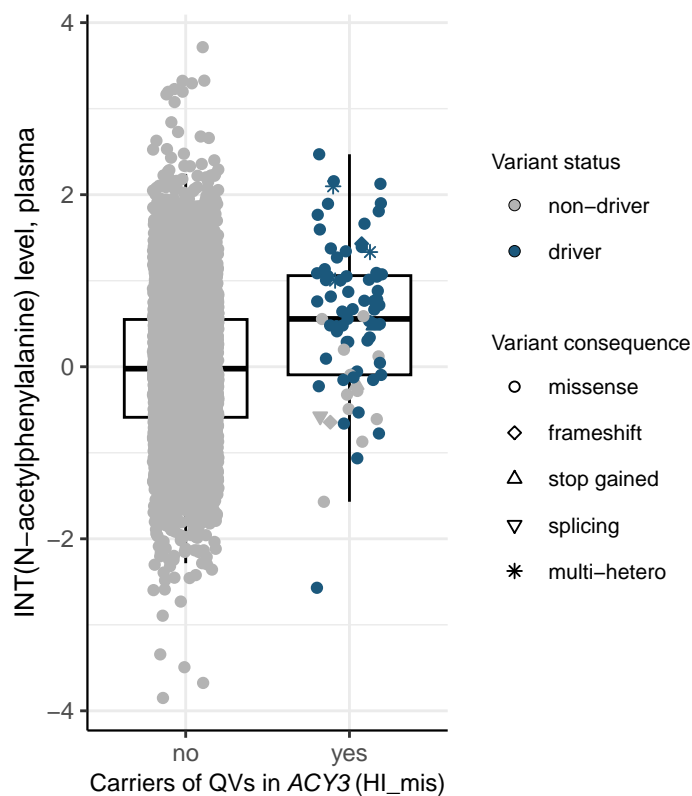
- missense
- splicing

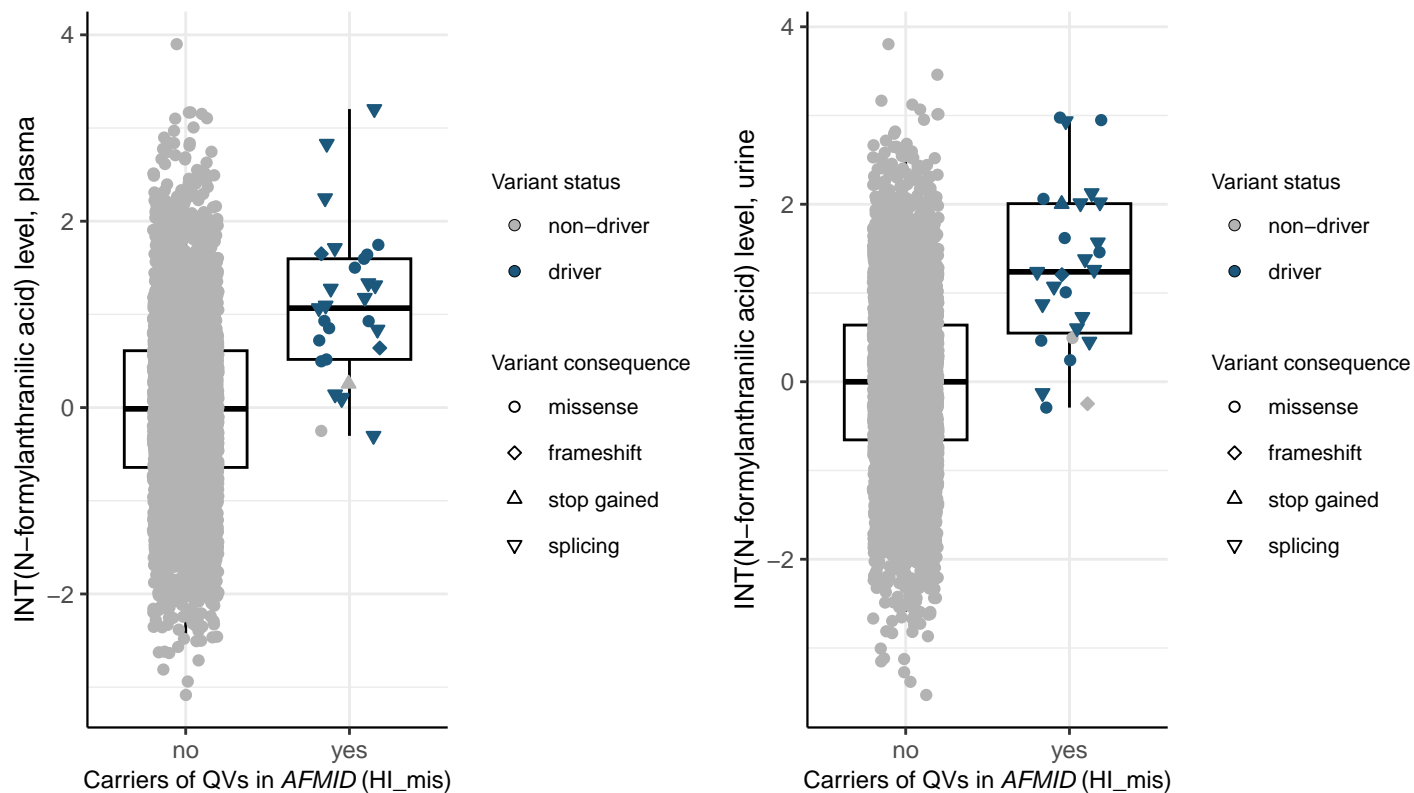
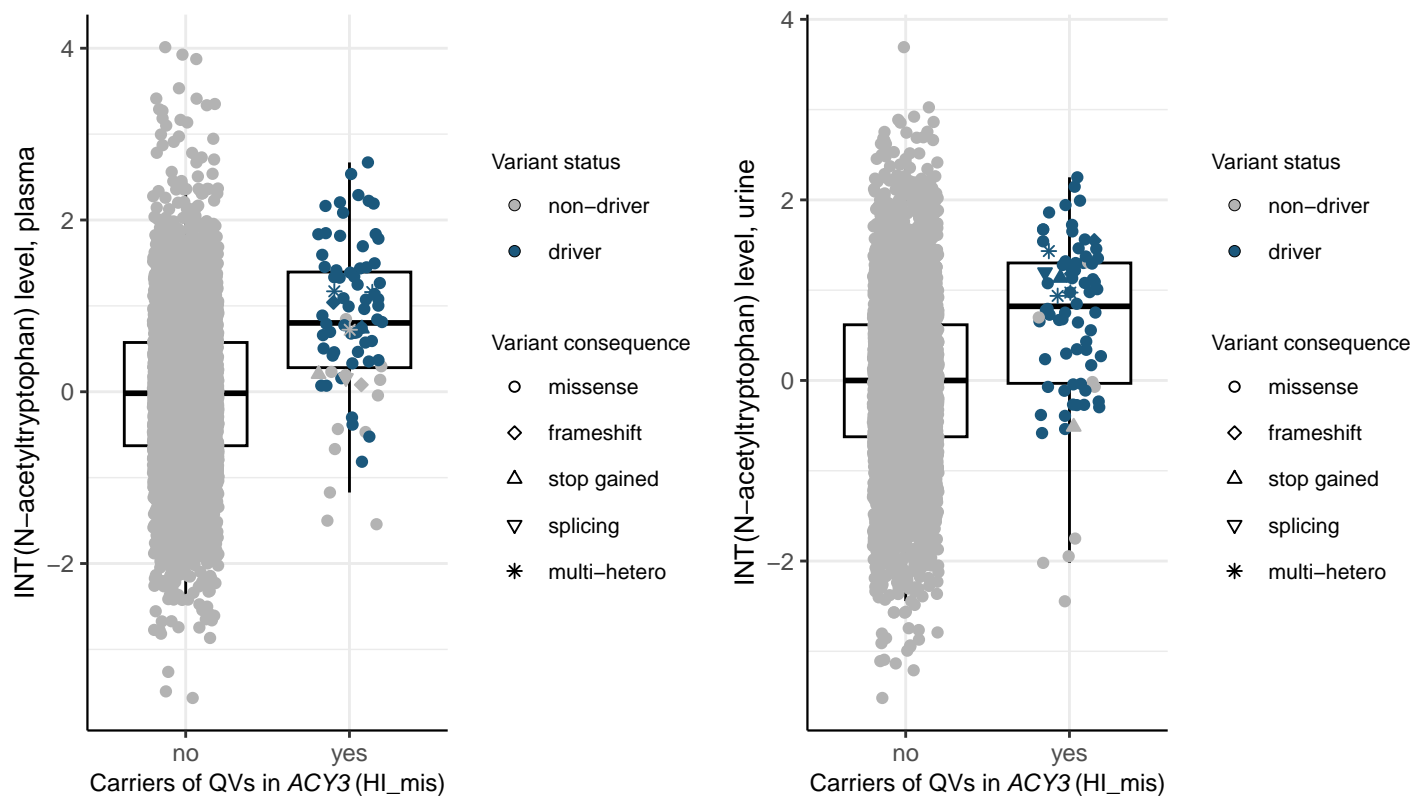


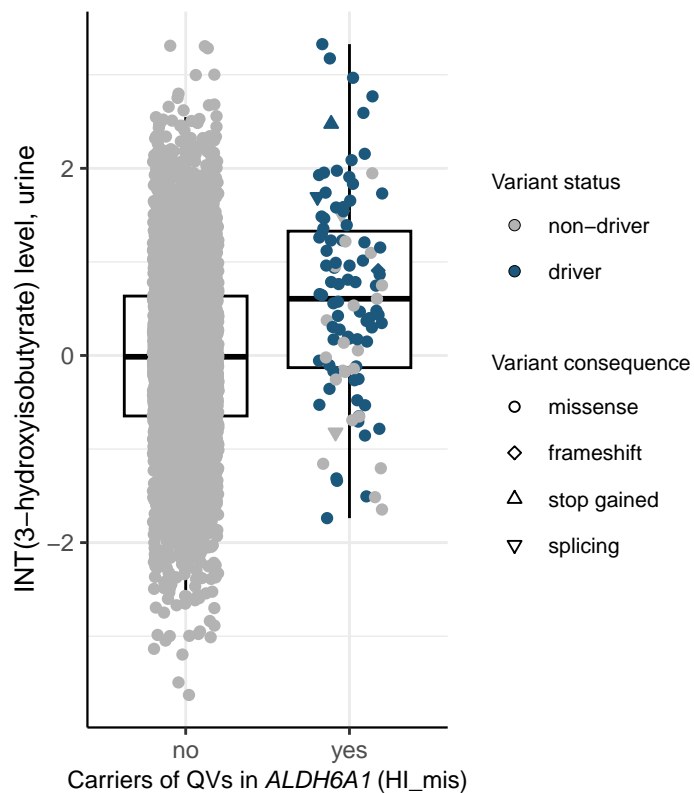
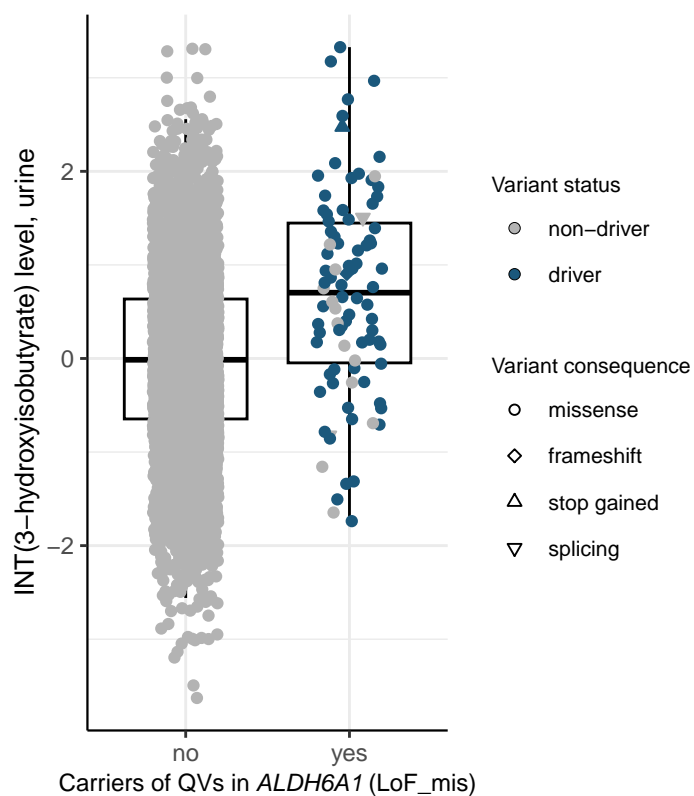


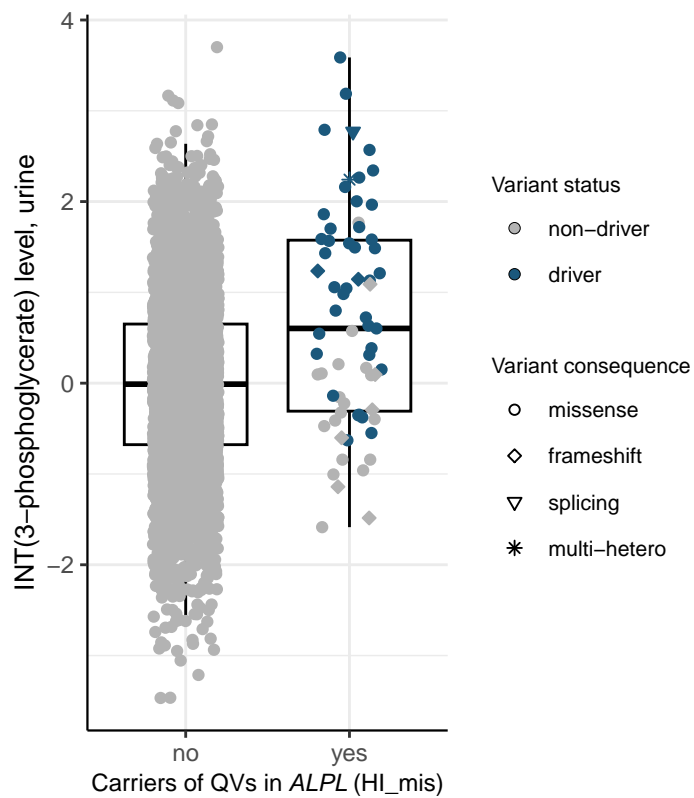
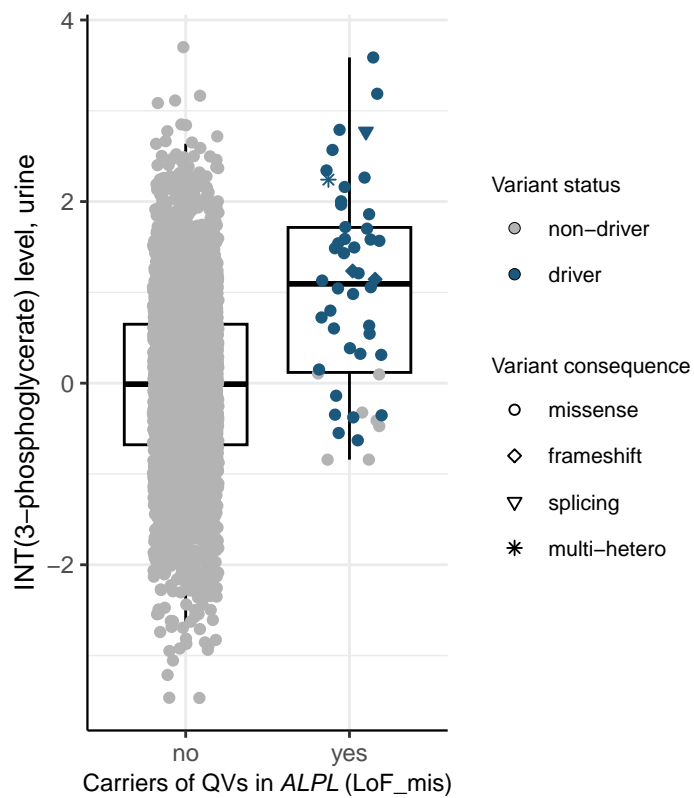


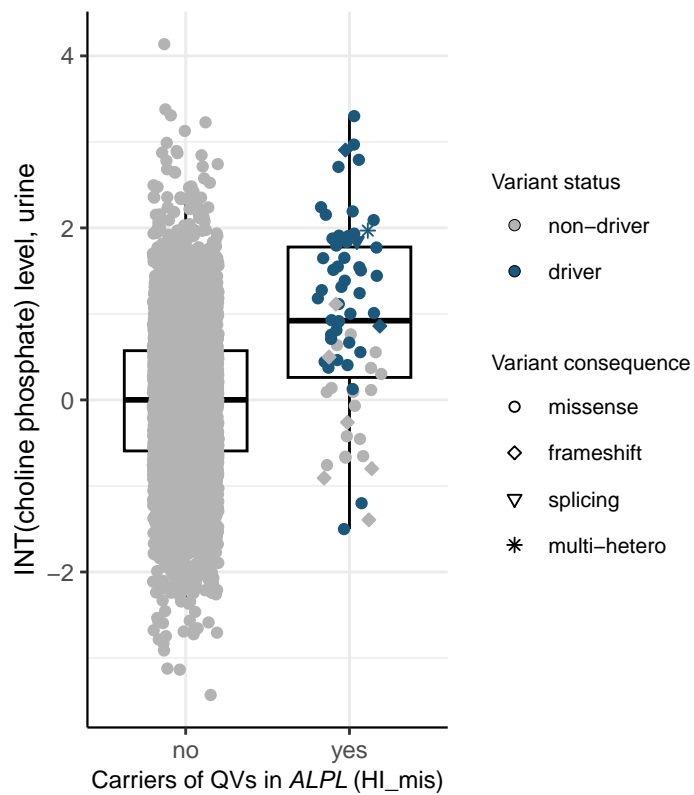
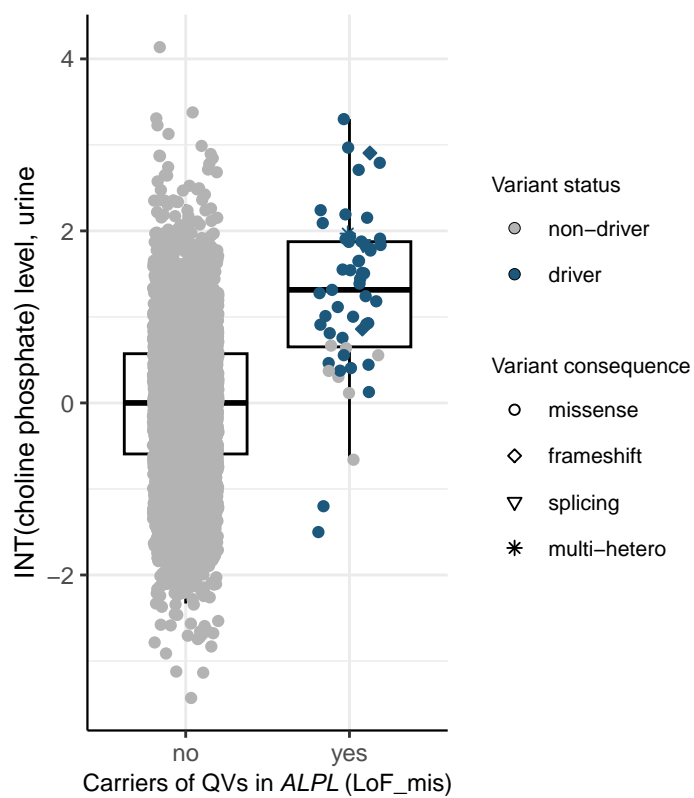


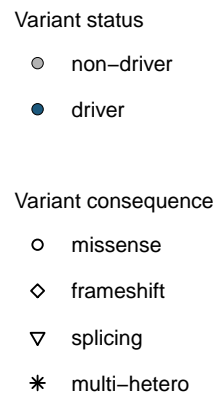
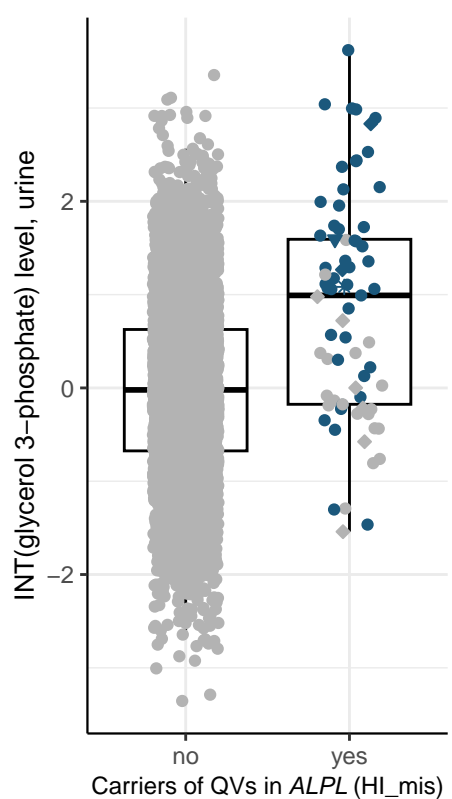
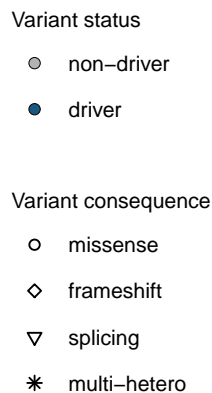
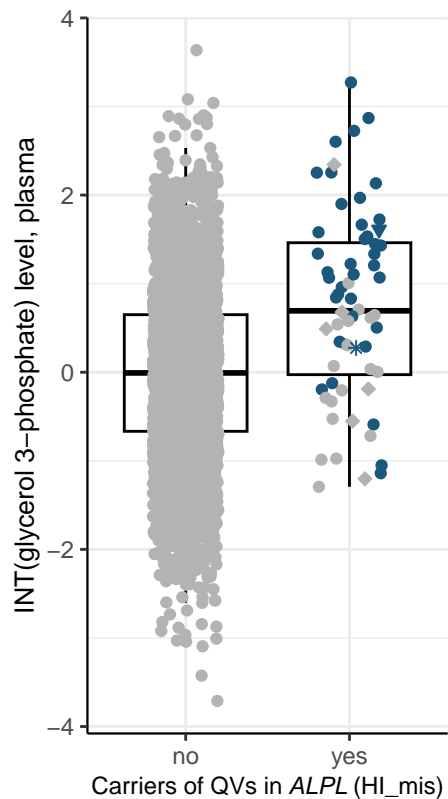
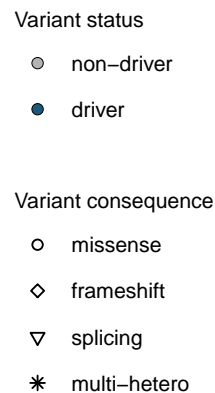
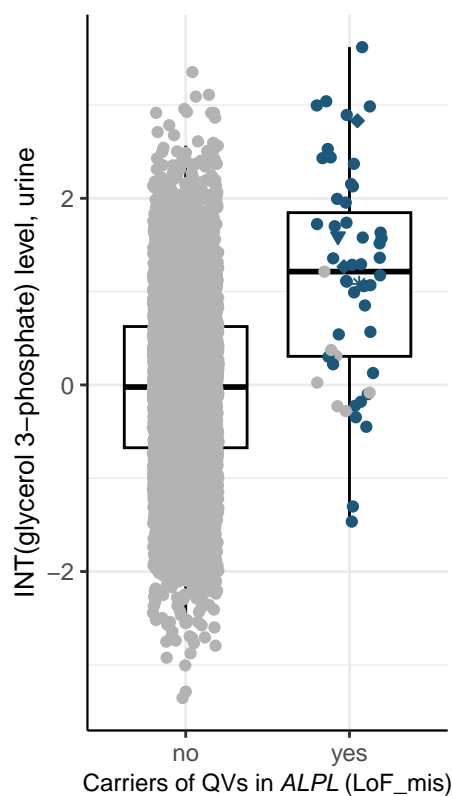
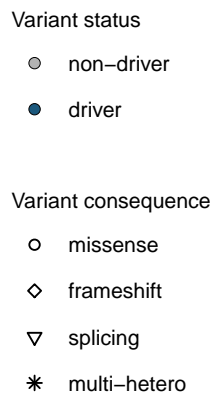
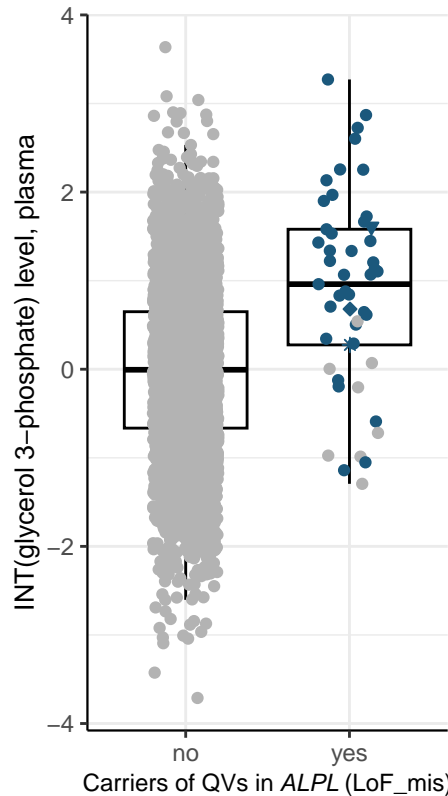


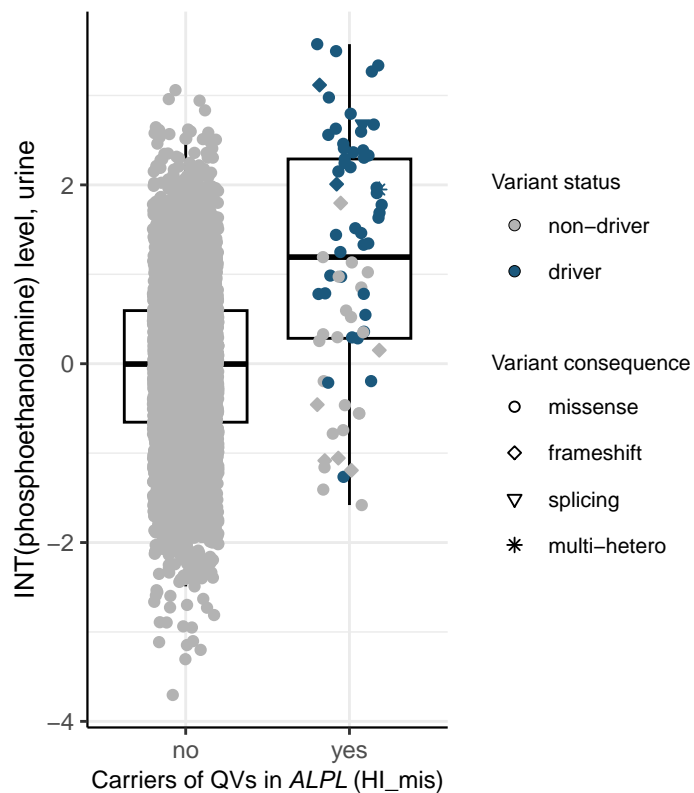
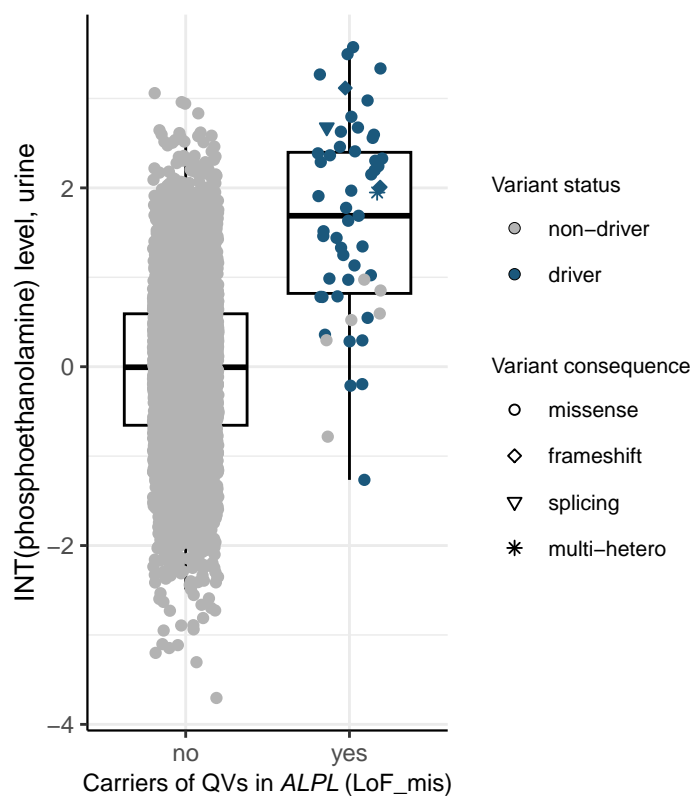


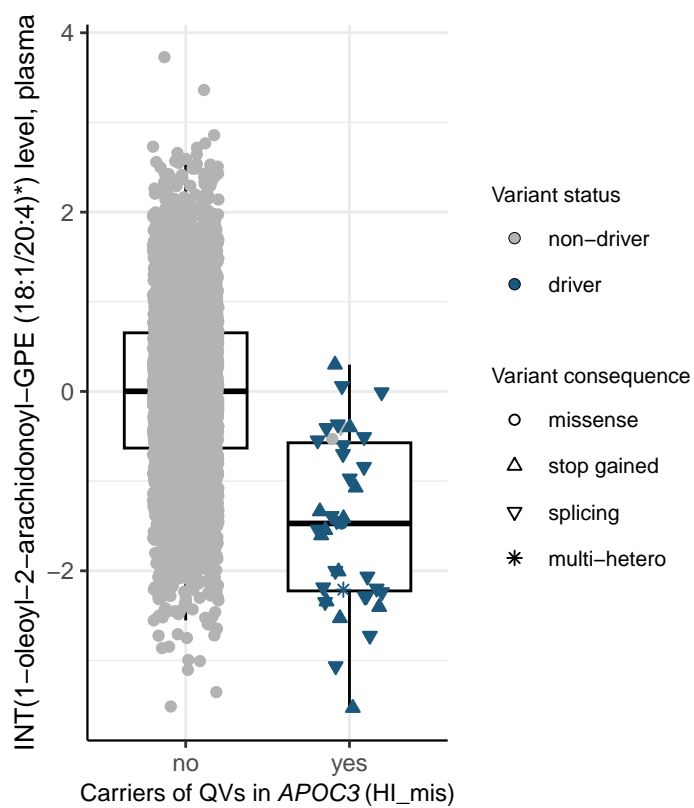
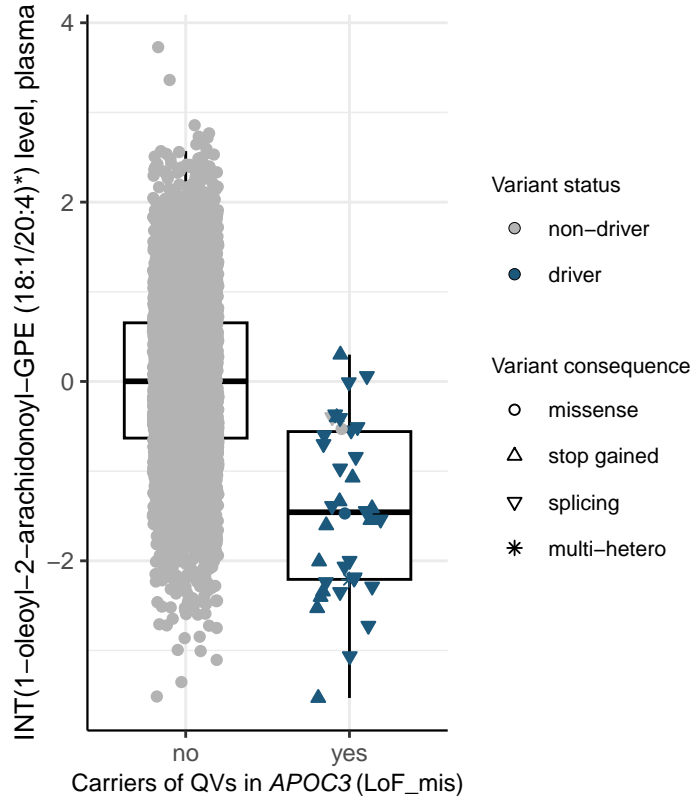


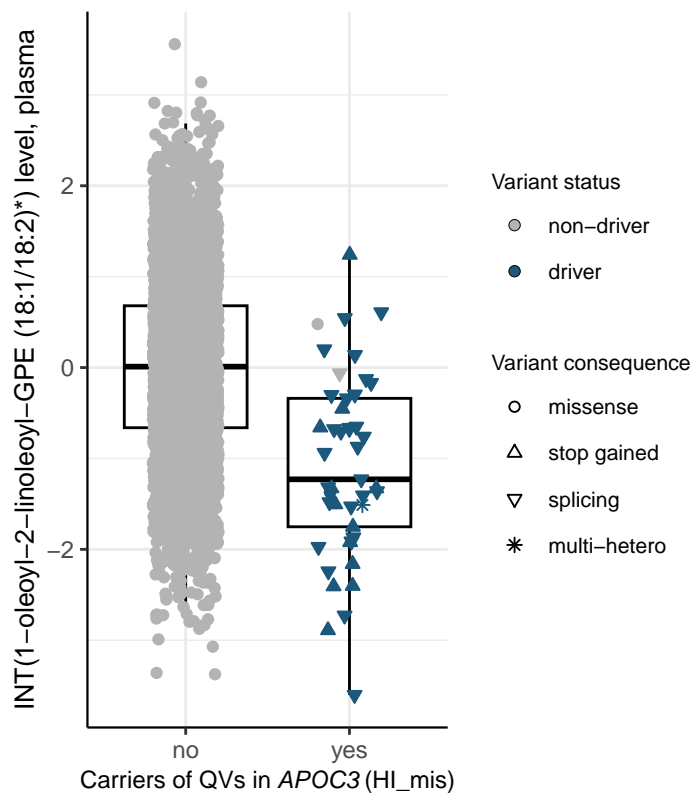
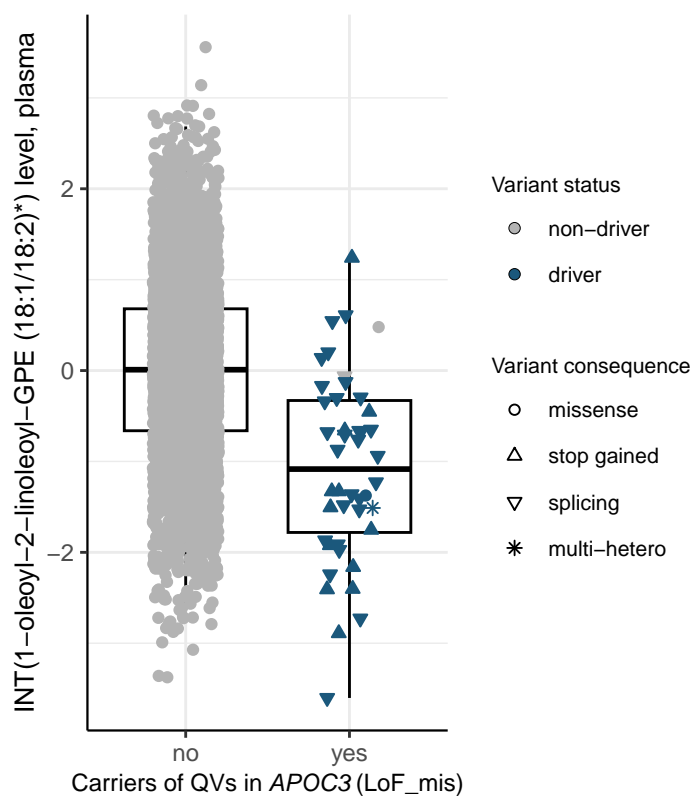


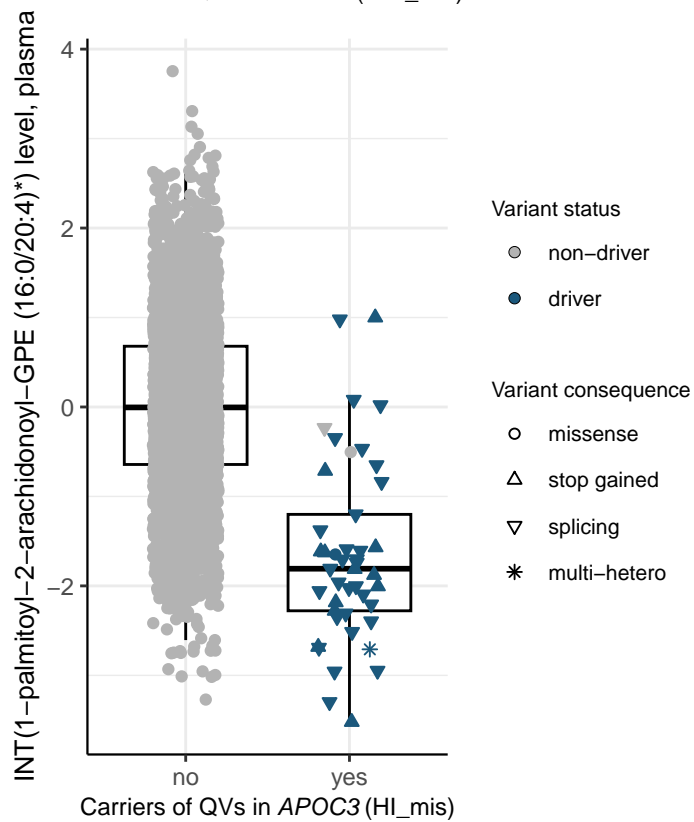
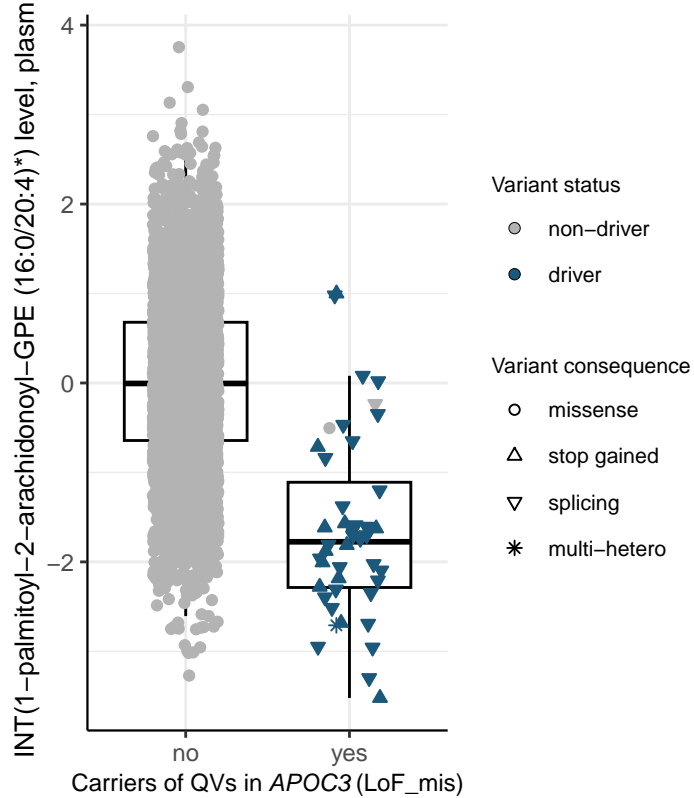


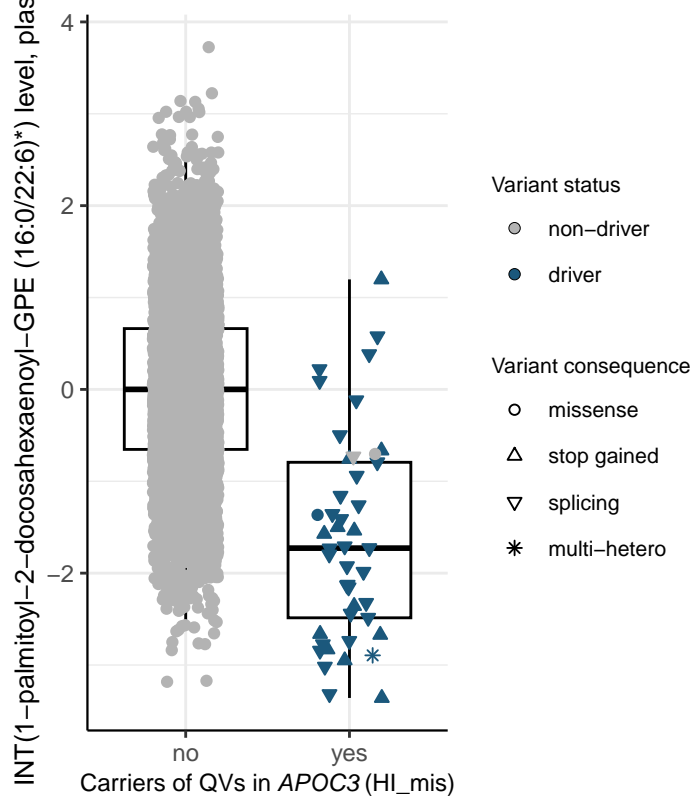
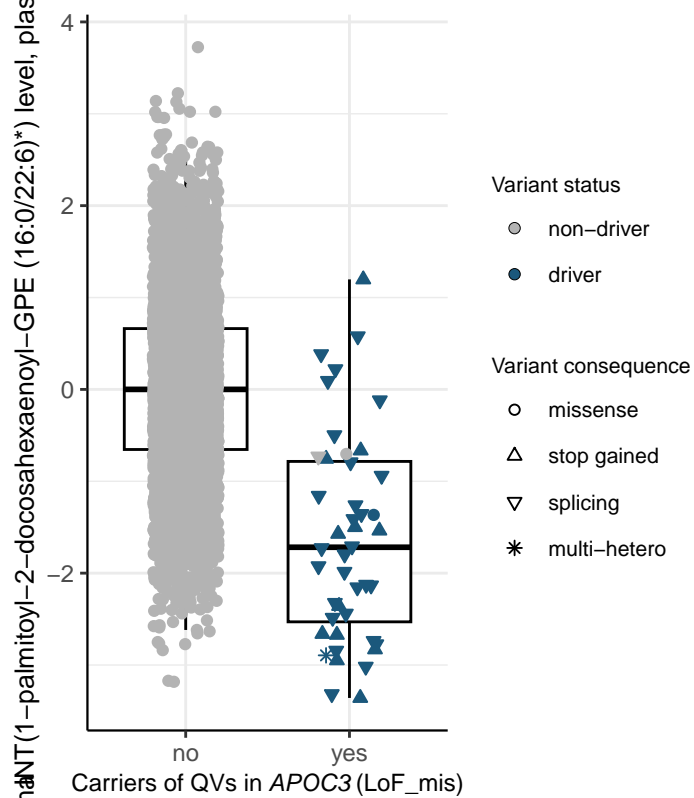


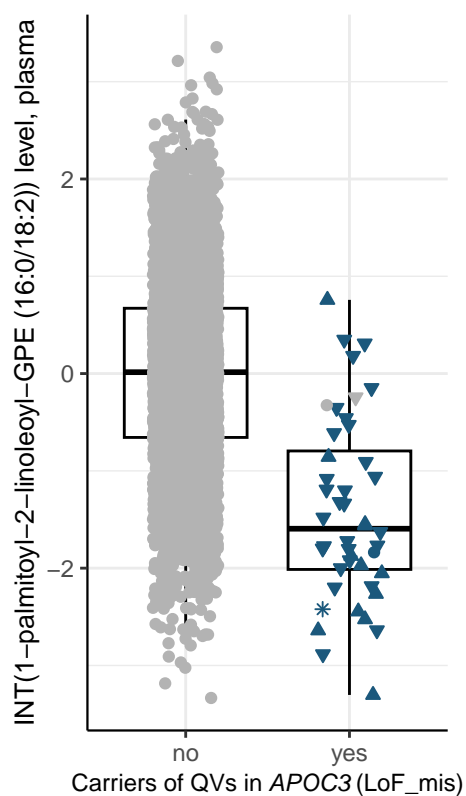












Variant status

○ non-driver

● driver

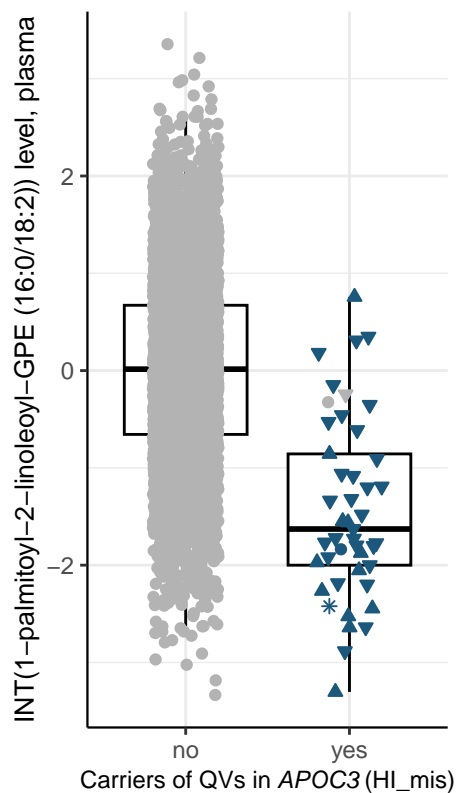
Variant consequence

○ missense

△ stop gained

▽ splicing

* multi-hetero



Variant status

○ non-driver

● driver

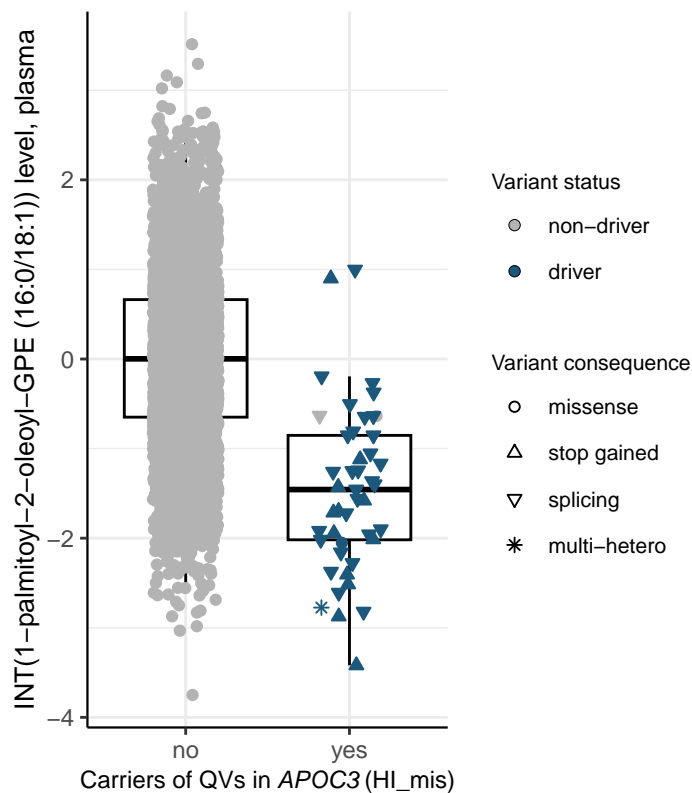
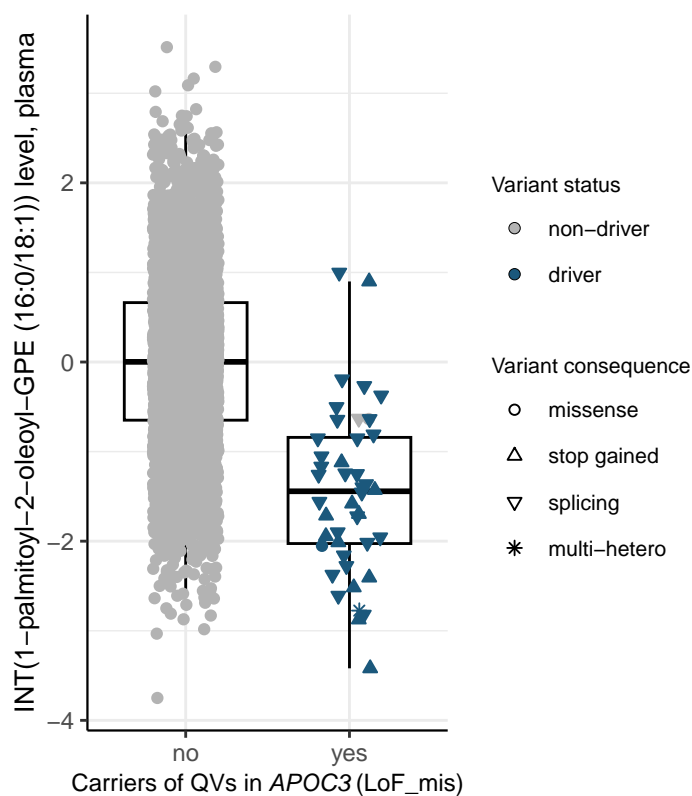
Variant consequence

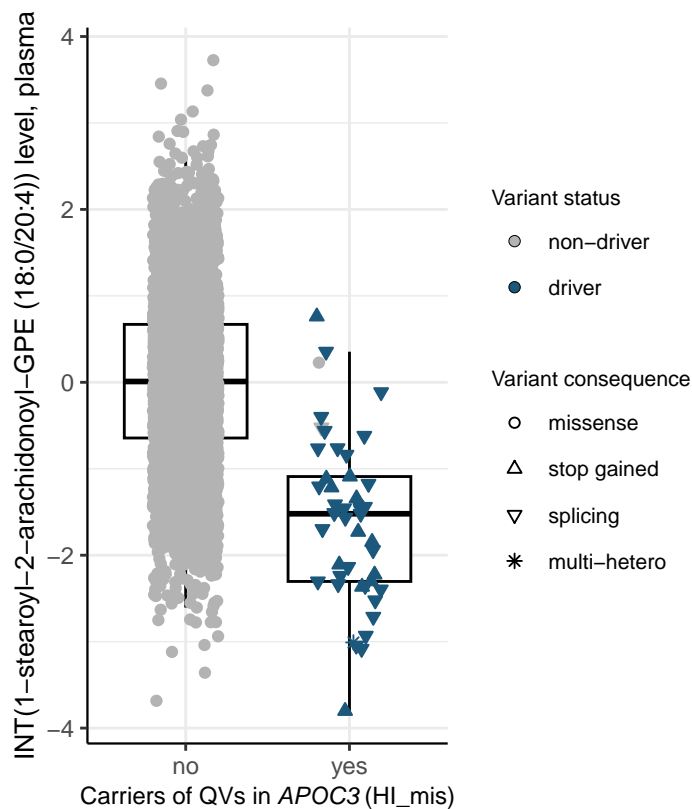
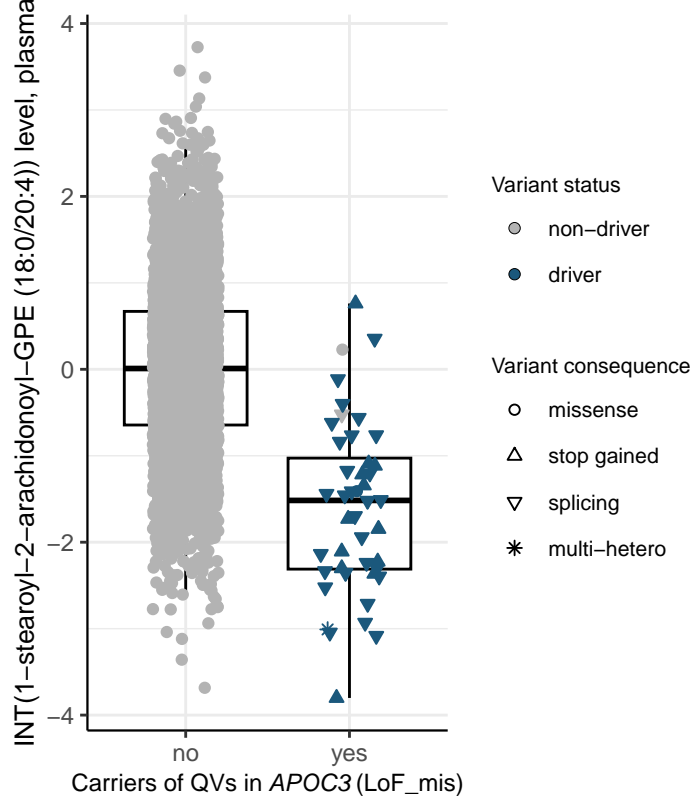
○ missense

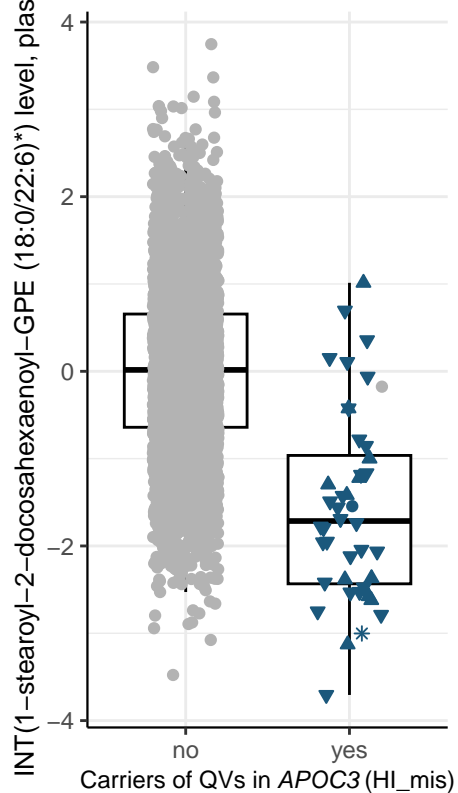
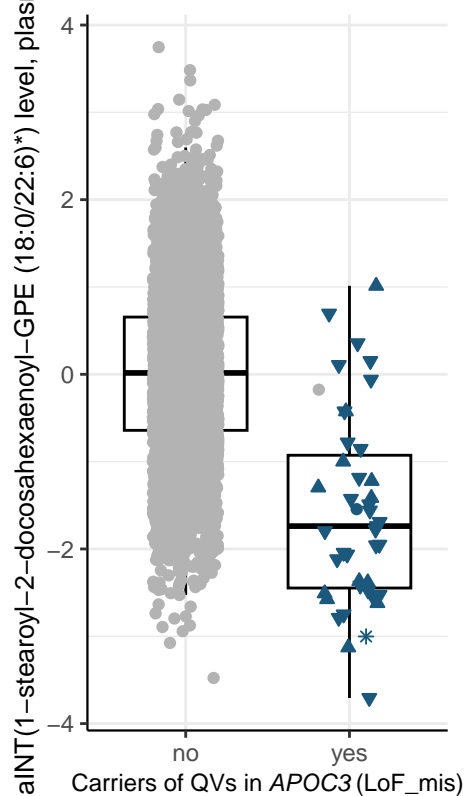
△ stop gained

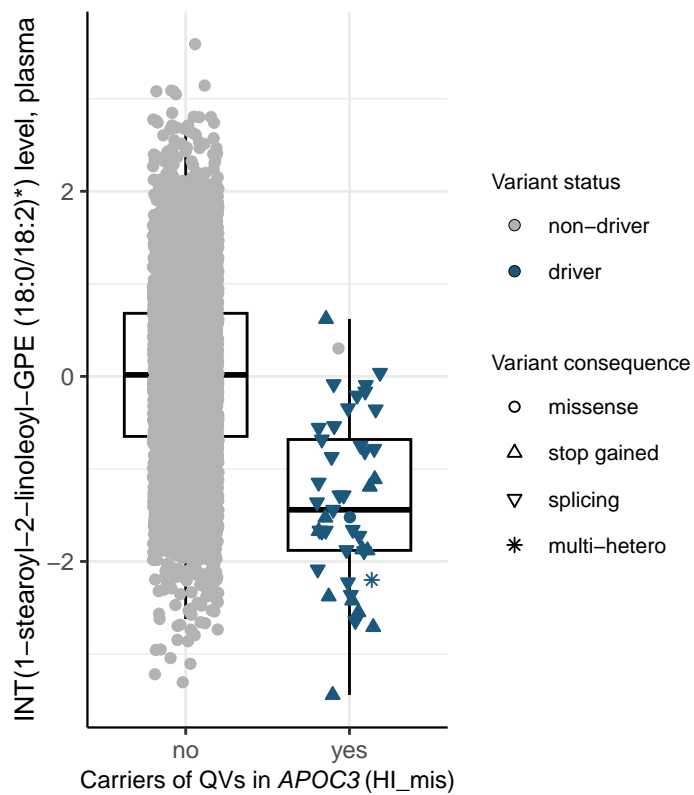
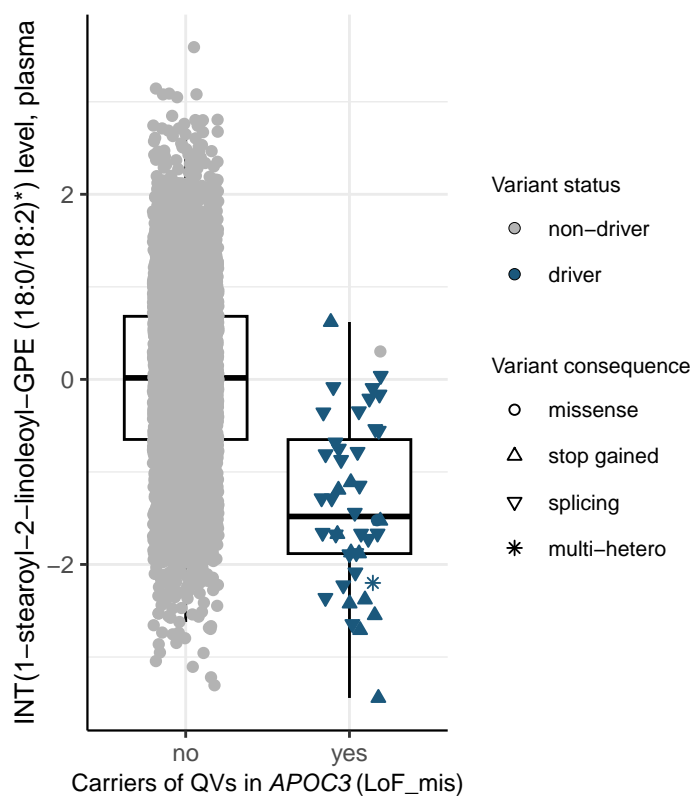
▽ splicing

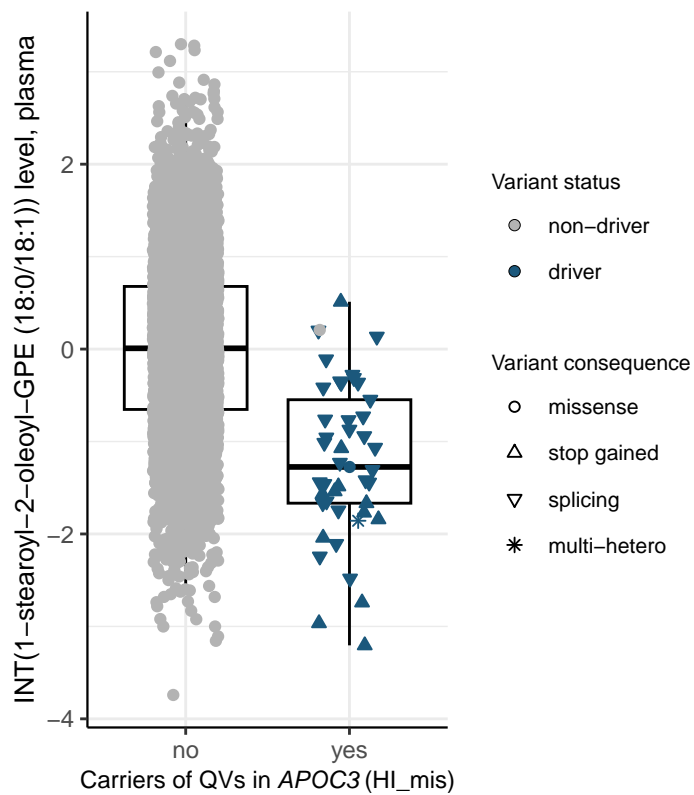
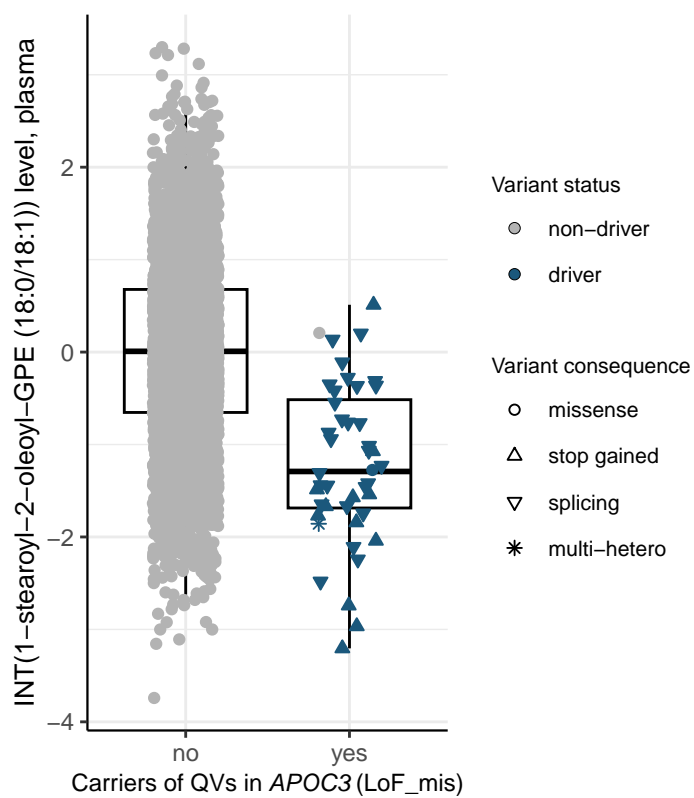
* multi-hetero

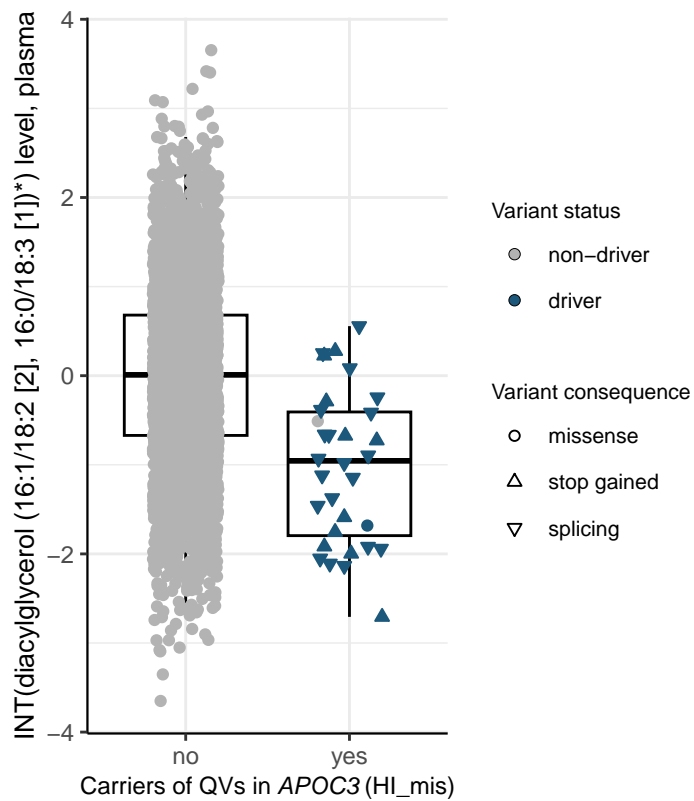
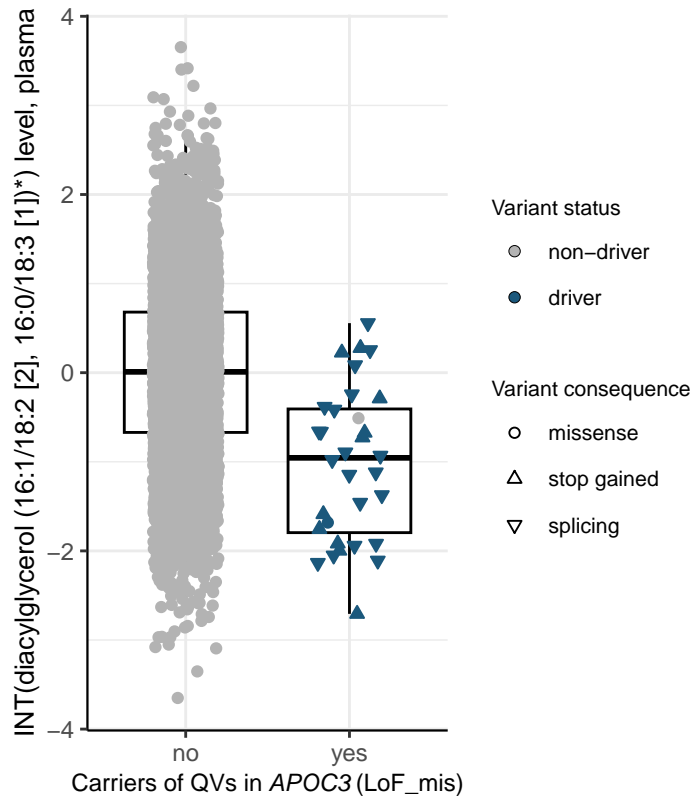


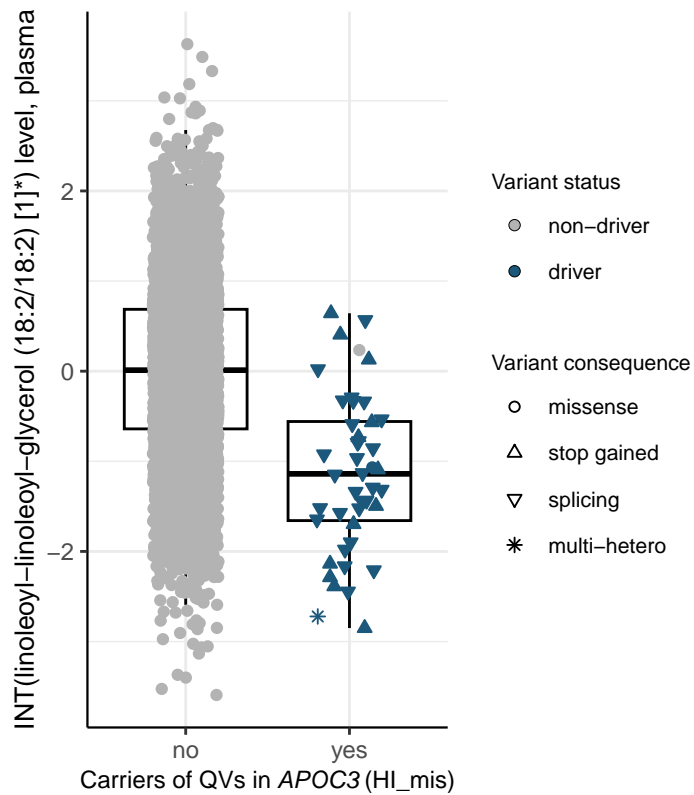
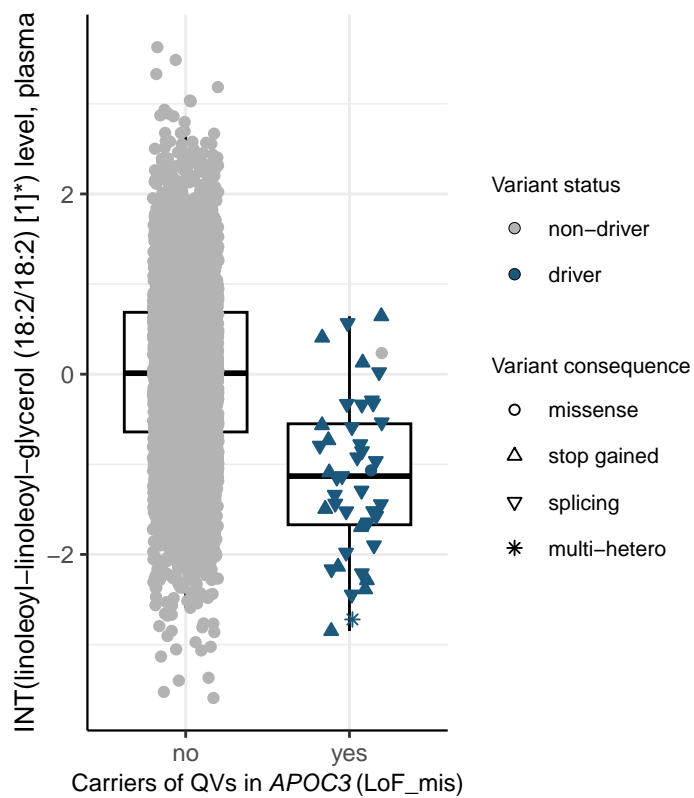


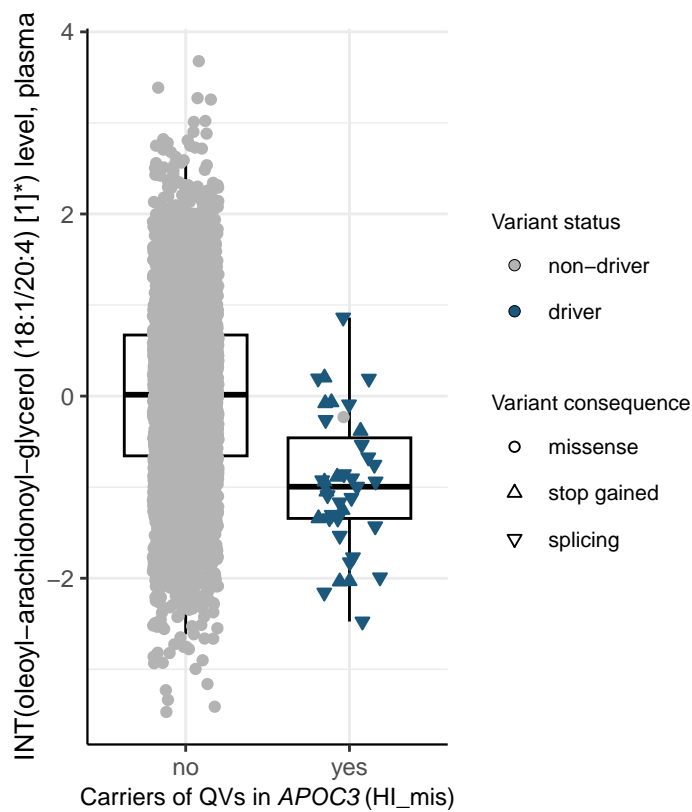
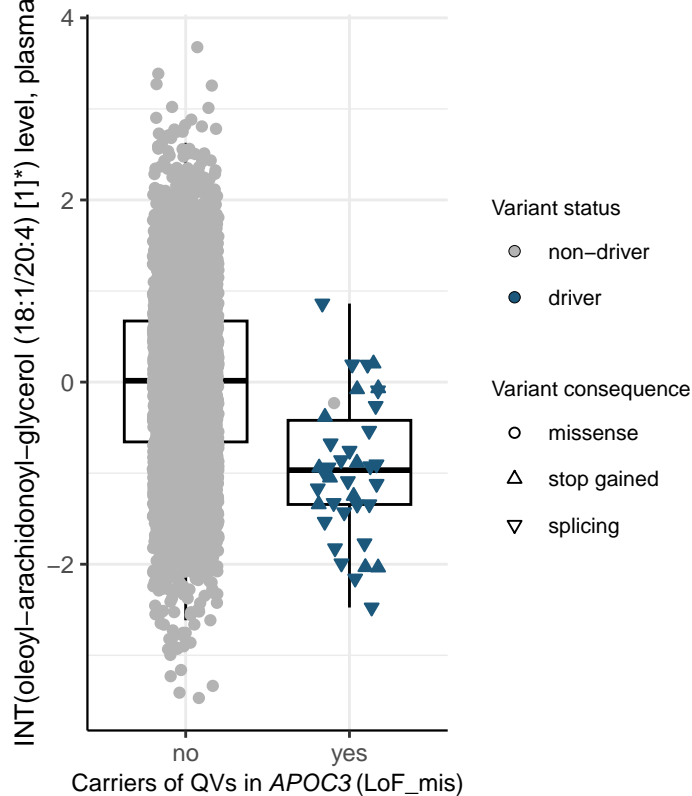


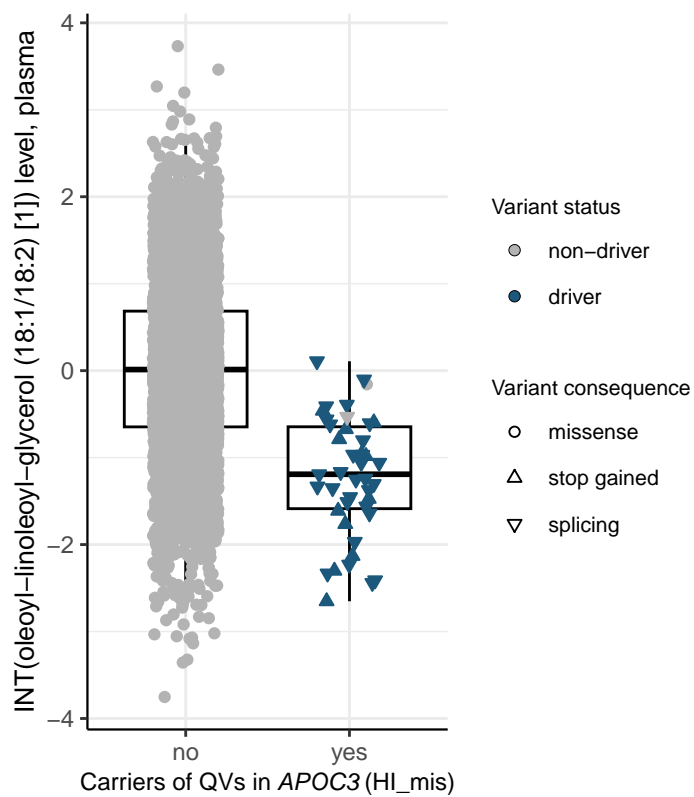
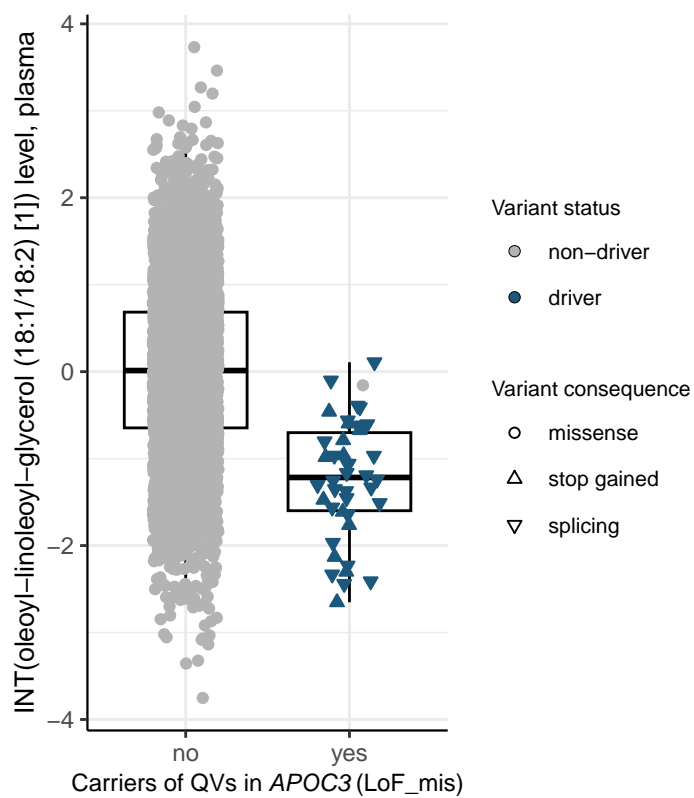


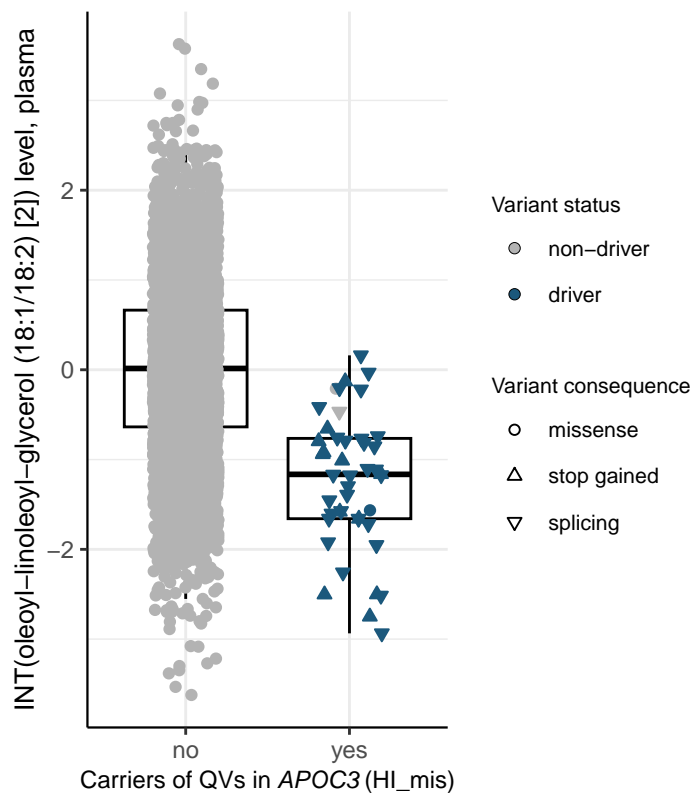
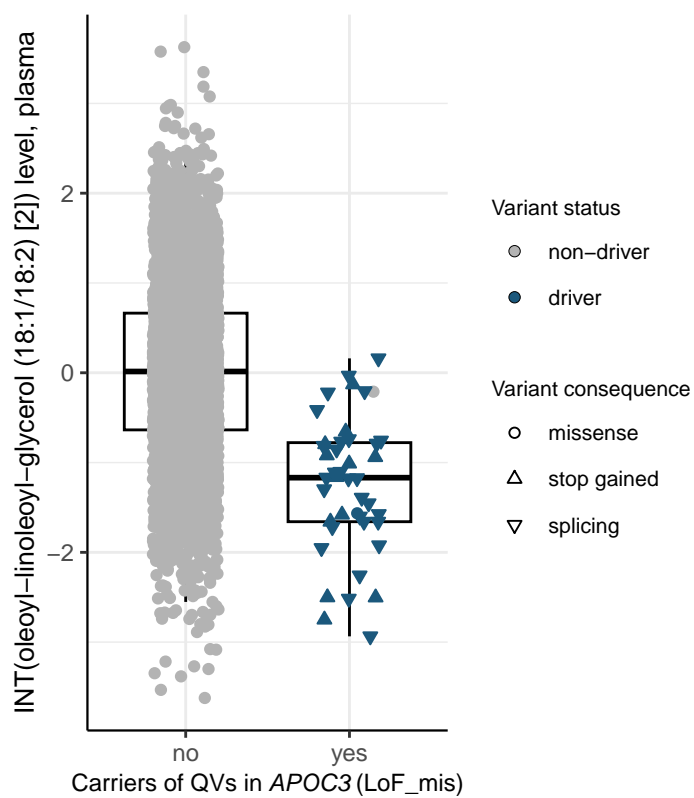


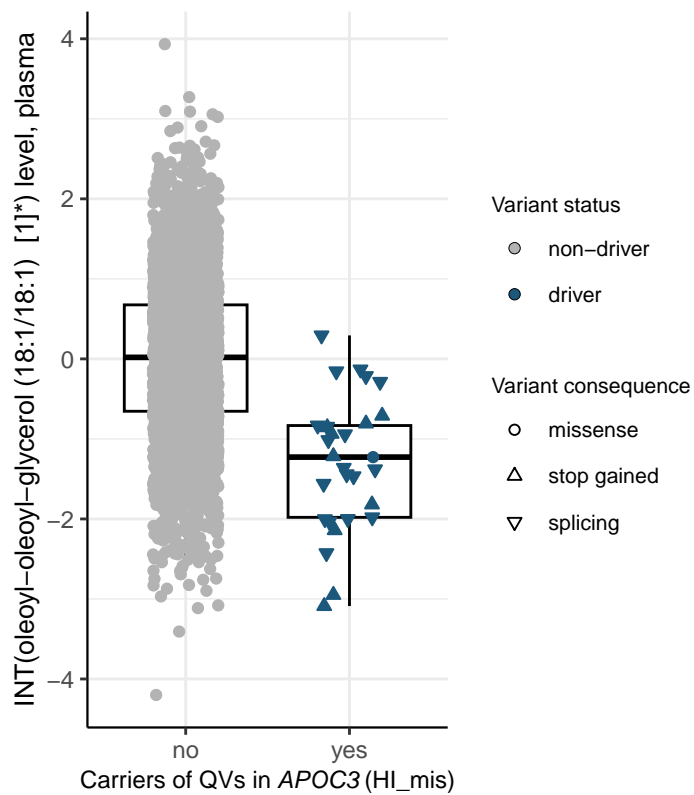
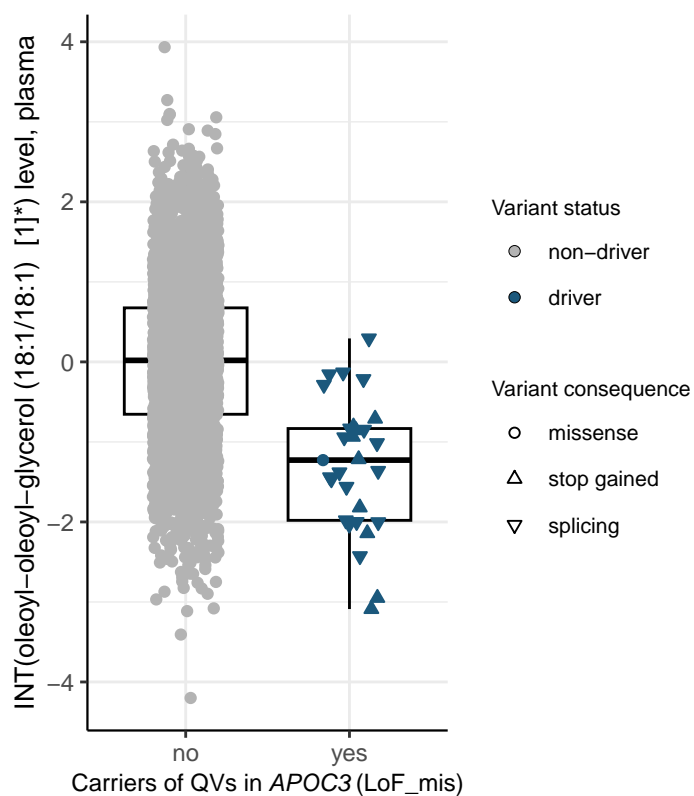


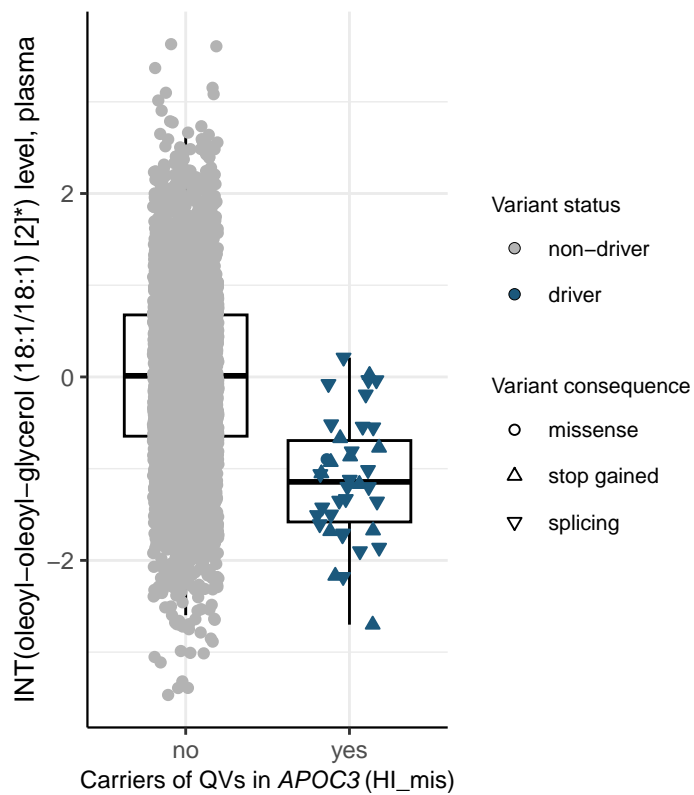
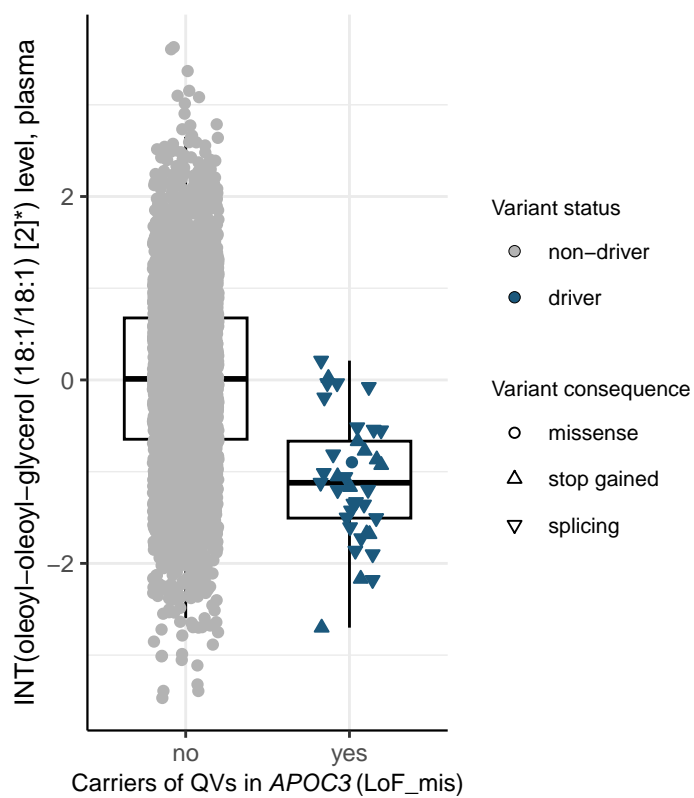


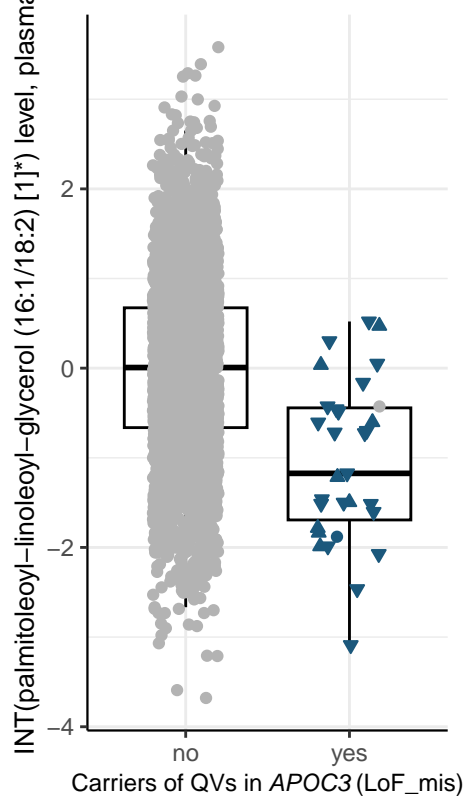










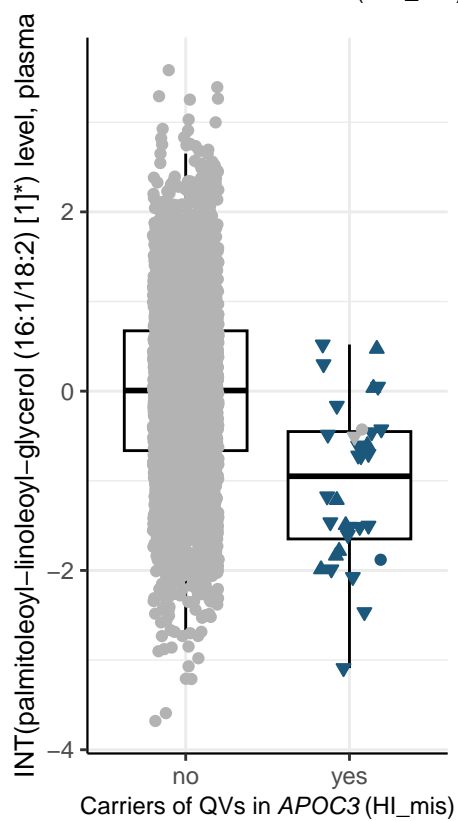


Variant status

- non-driver
- driver

Variant consequence

- missense
- stop gained
- splicing

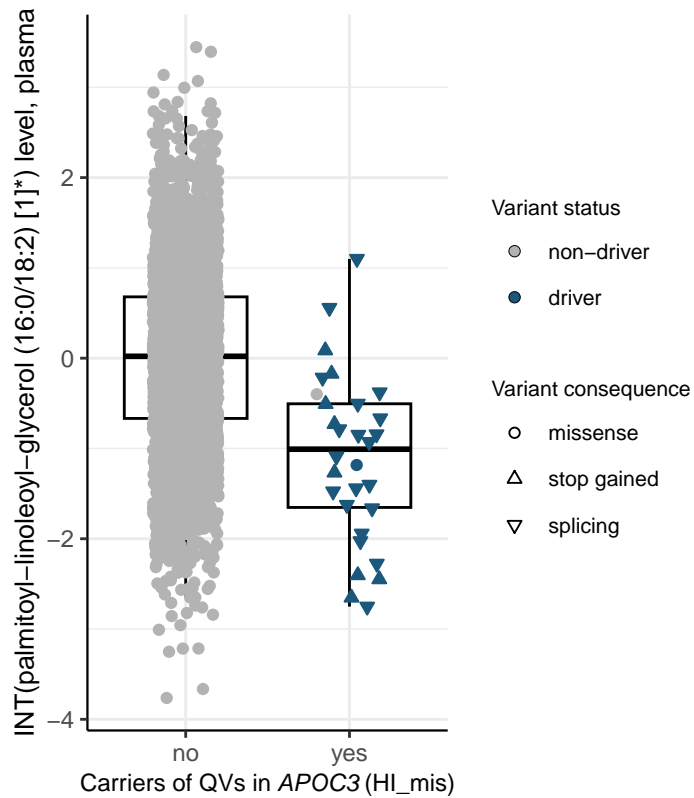
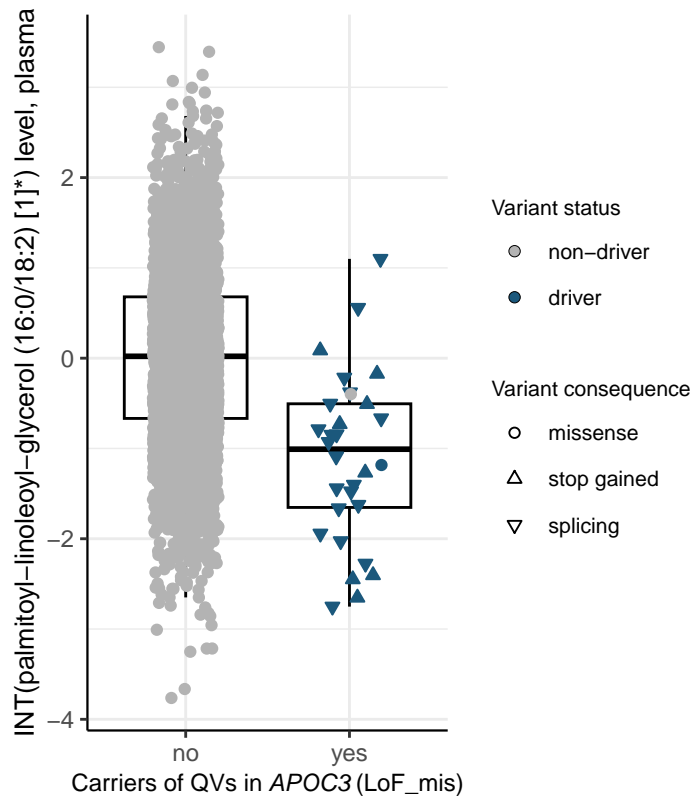


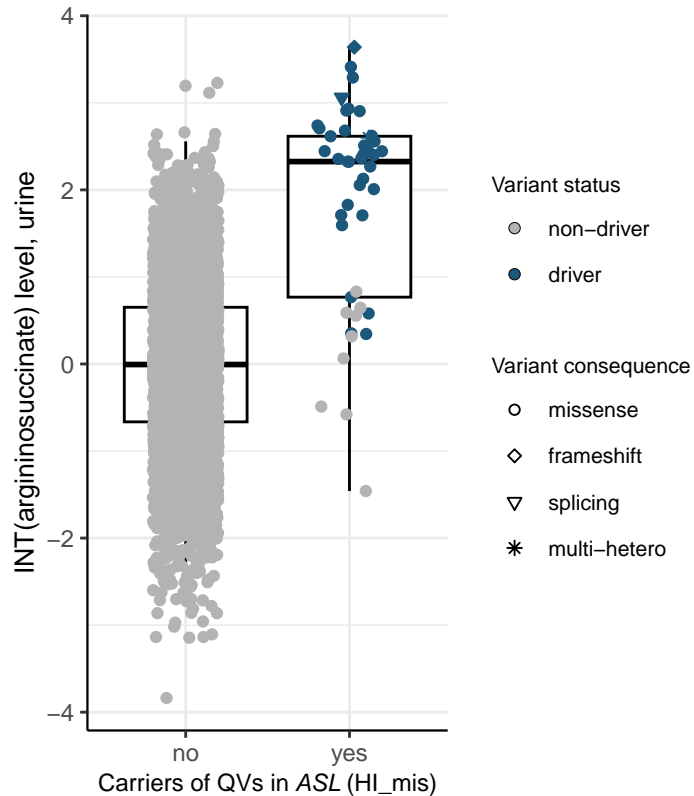
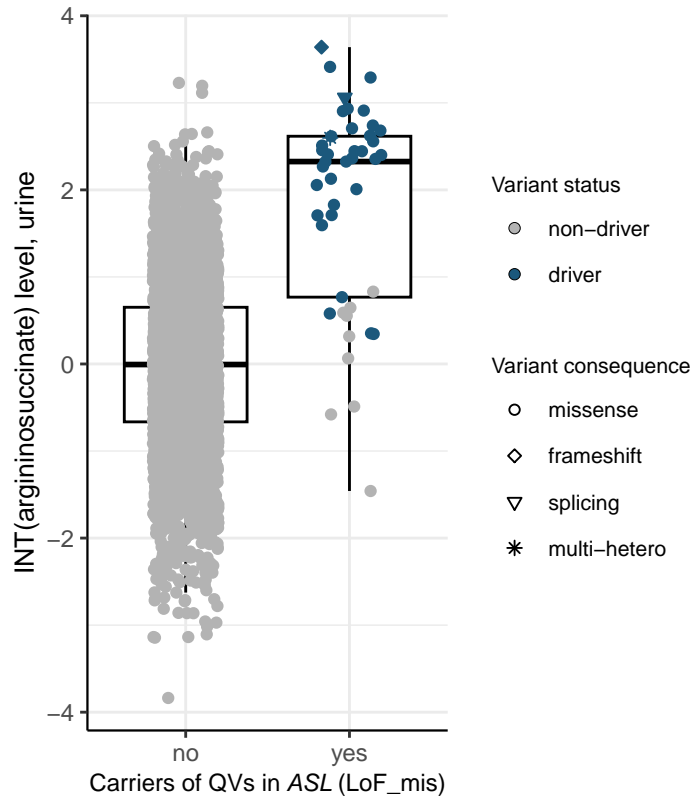
Variant status

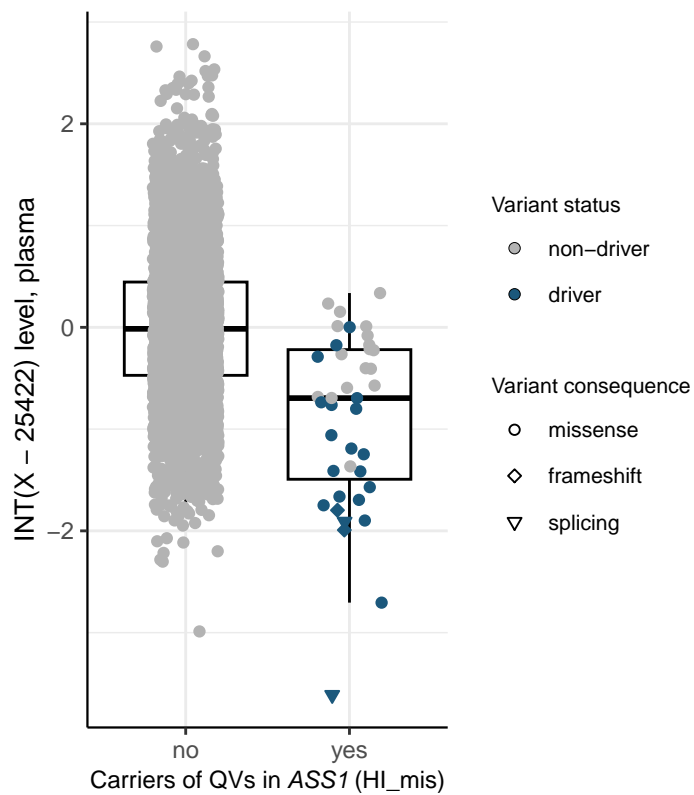
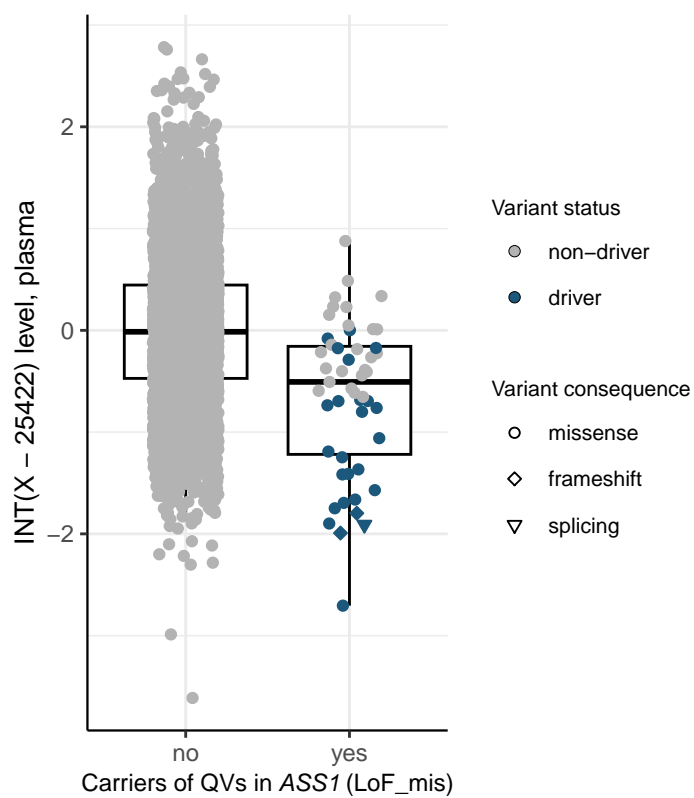
- non-driver
- driver

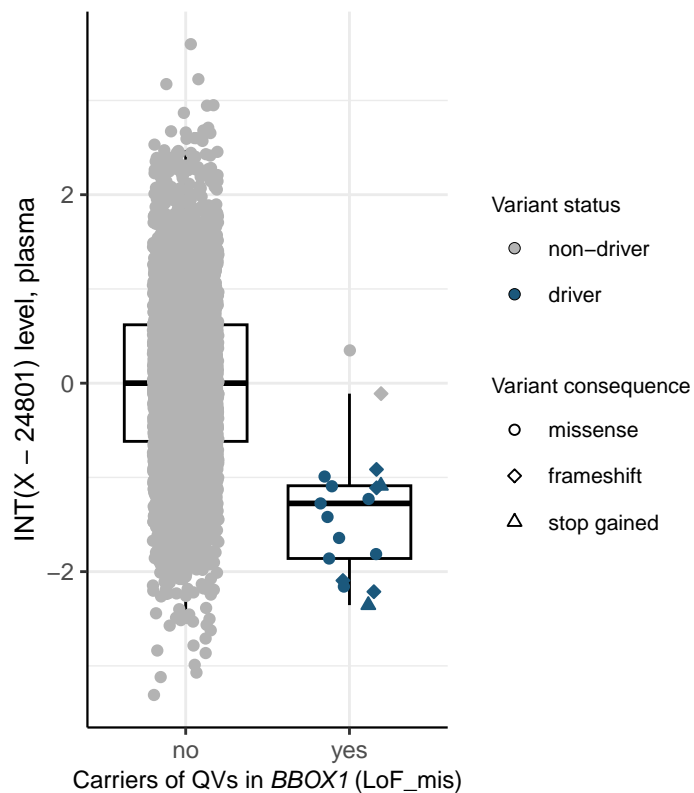
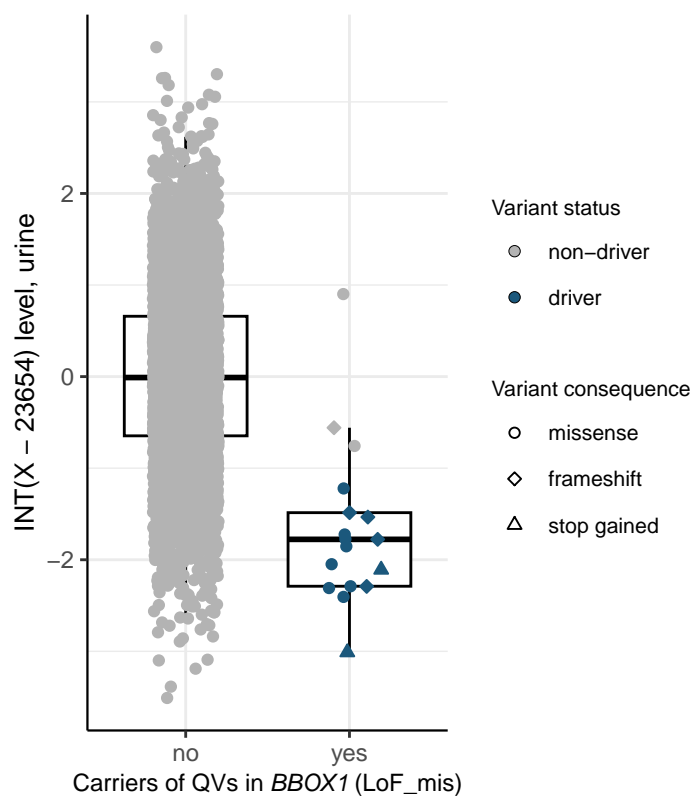
Variant consequence

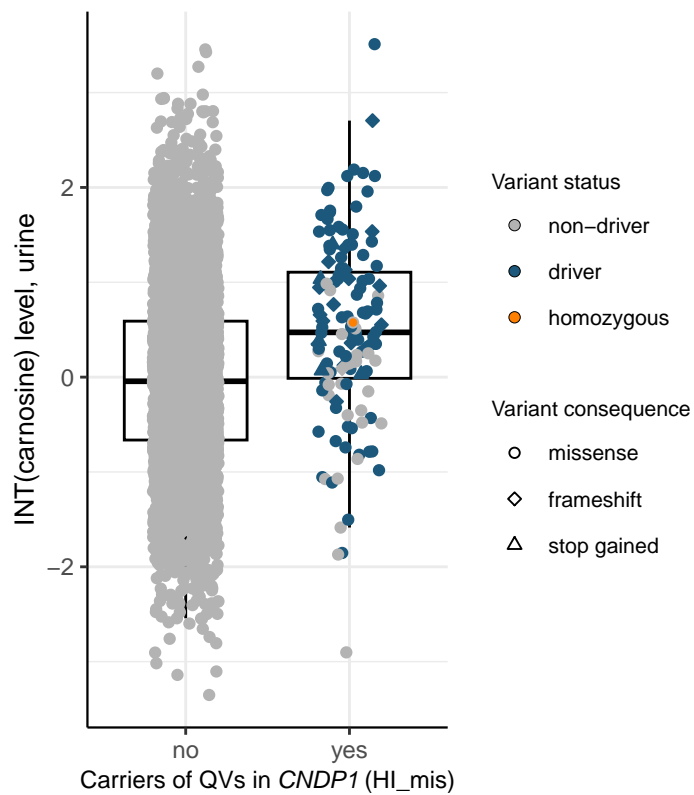
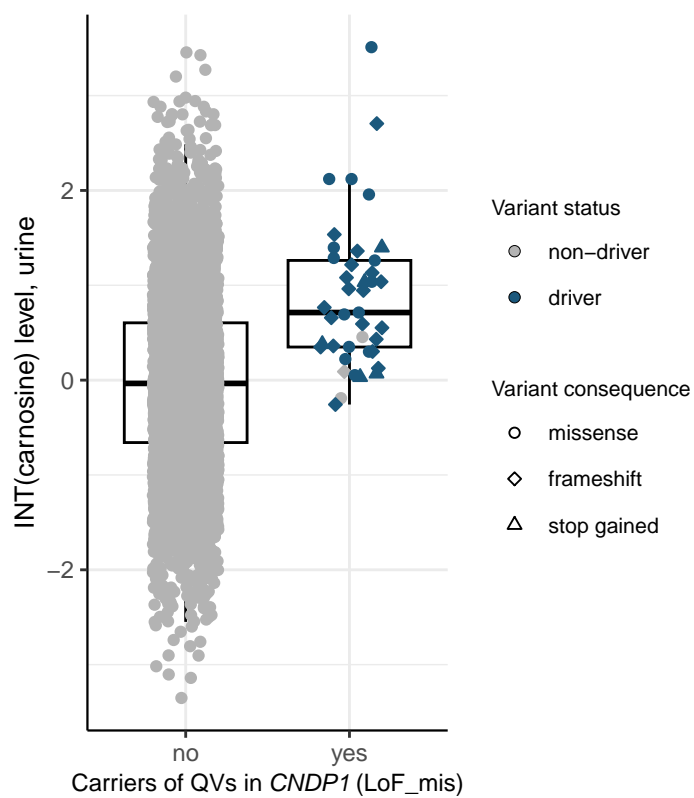
- missense
- stop gained
- splicing

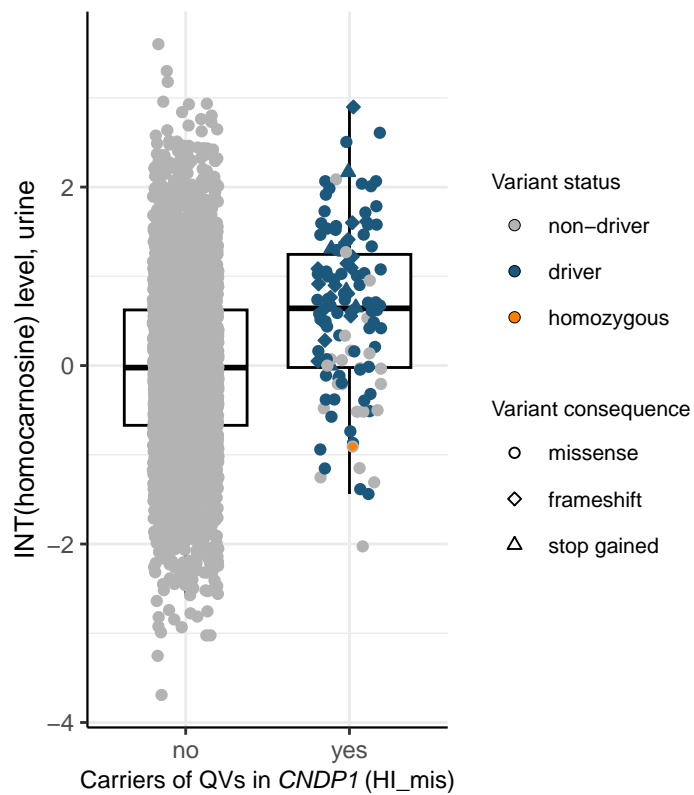
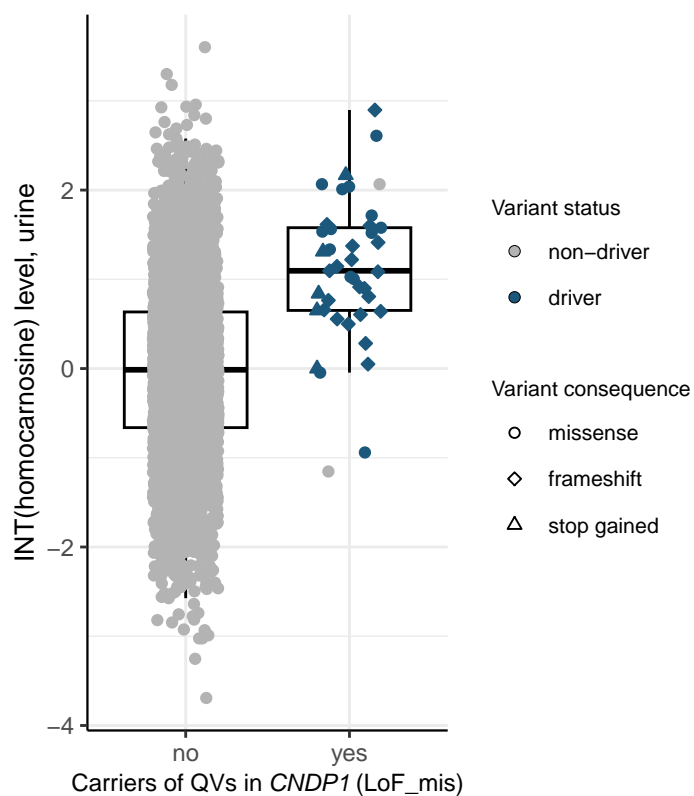


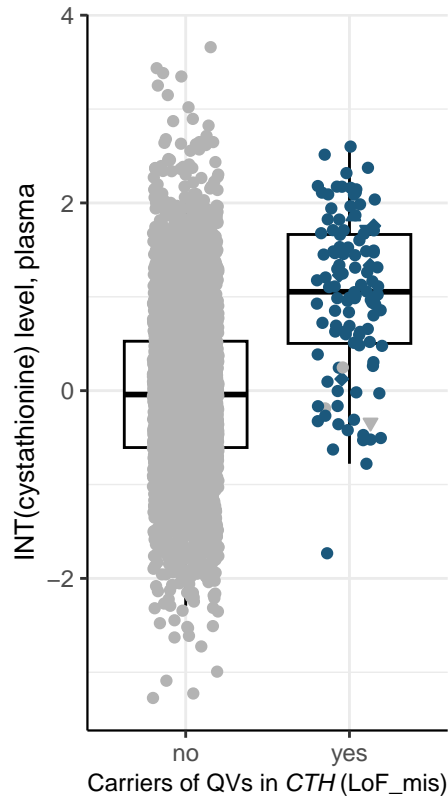










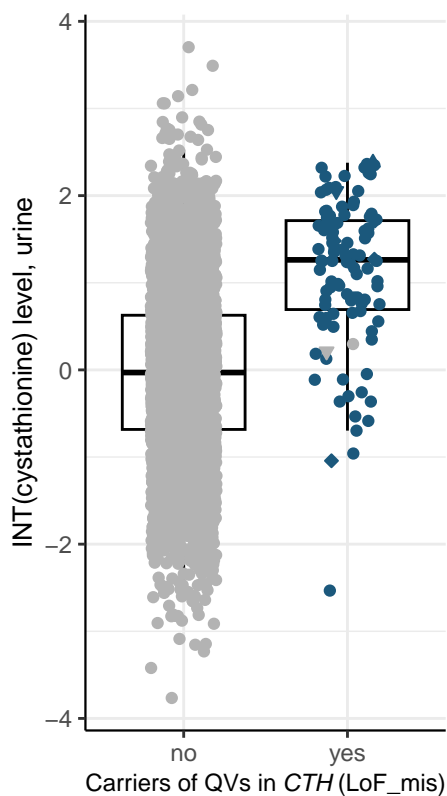


Variant status

- non-driver
- driver

Variant consequence

- missense
- frameshift
- stop gained
- splicing

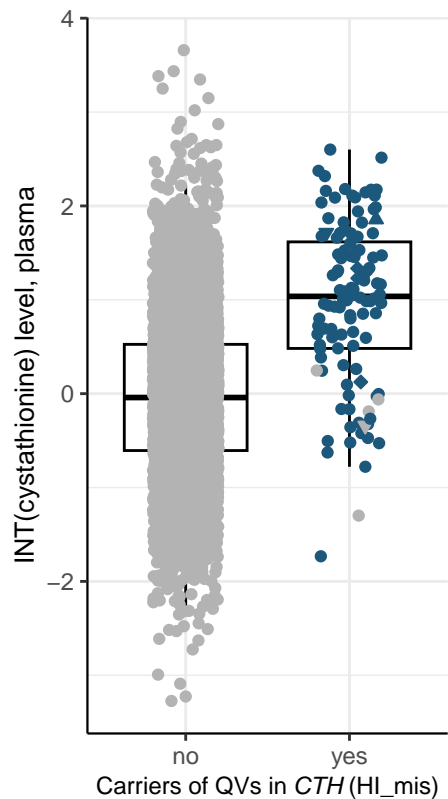


Variant status

- non-driver
- driver

Variant consequence

- missense
- frameshift
- stop gained
- splicing

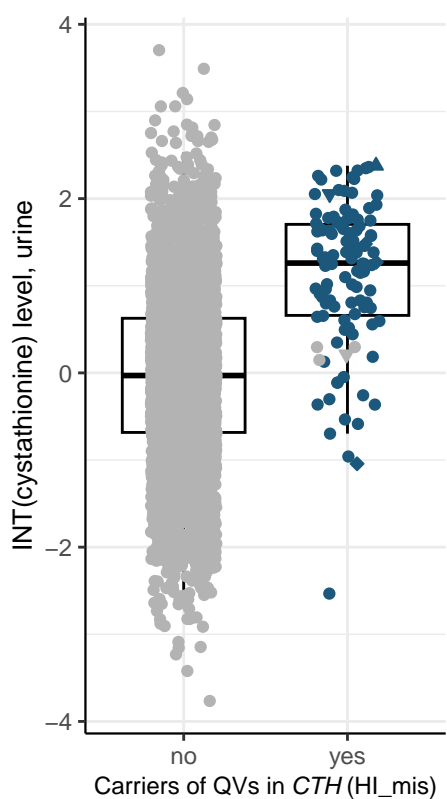


Variant status

- non-driver
- driver

Variant consequence

- missense
- frameshift
- stop gained
- splicing

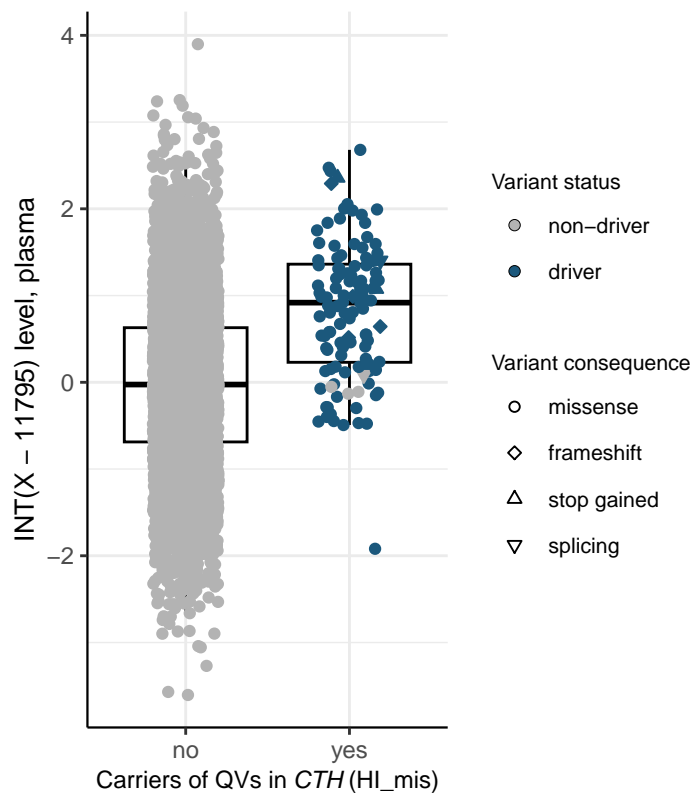
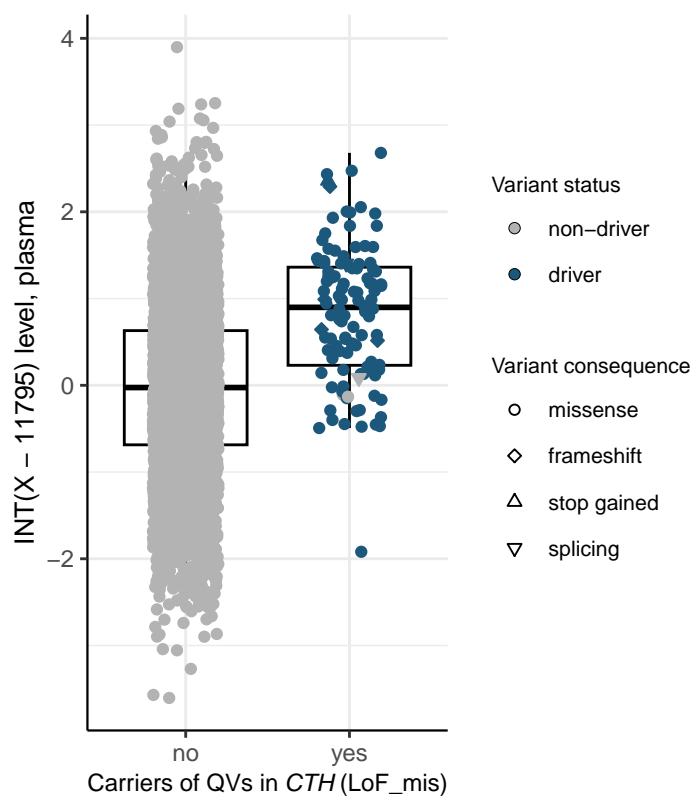


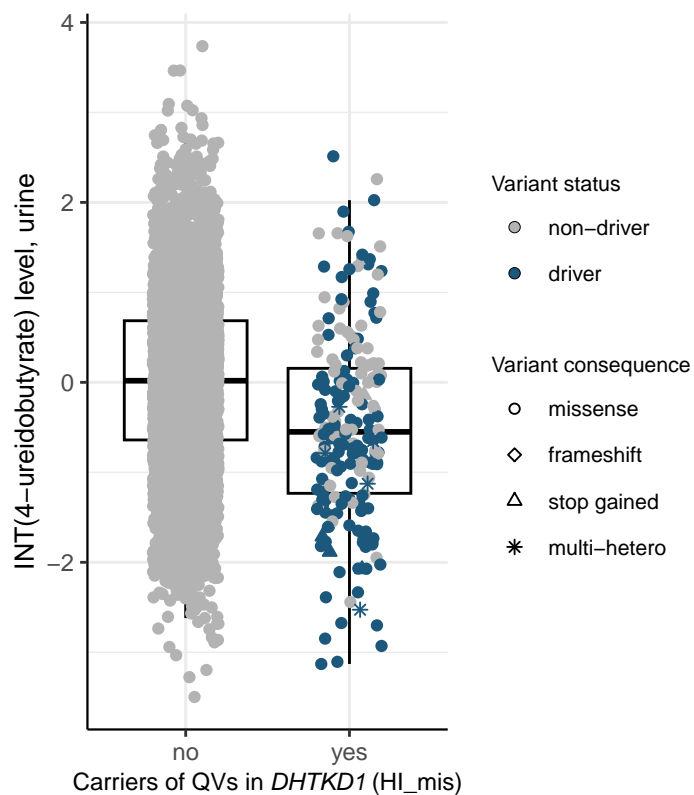
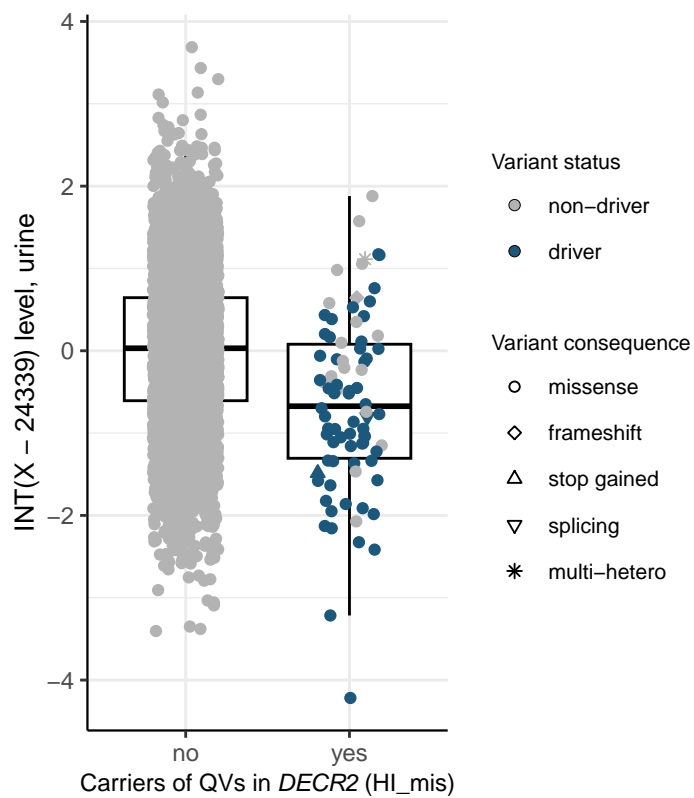
Variant status

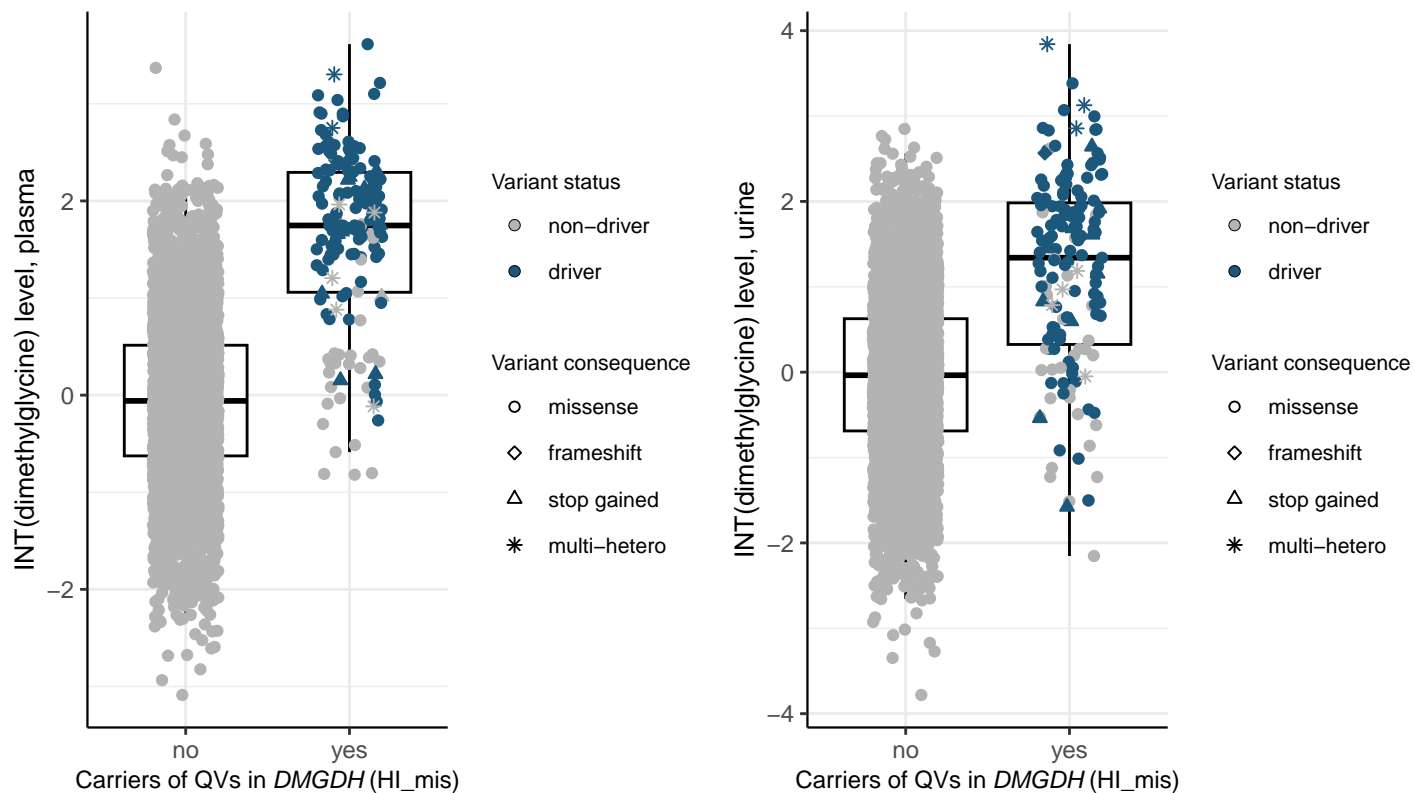
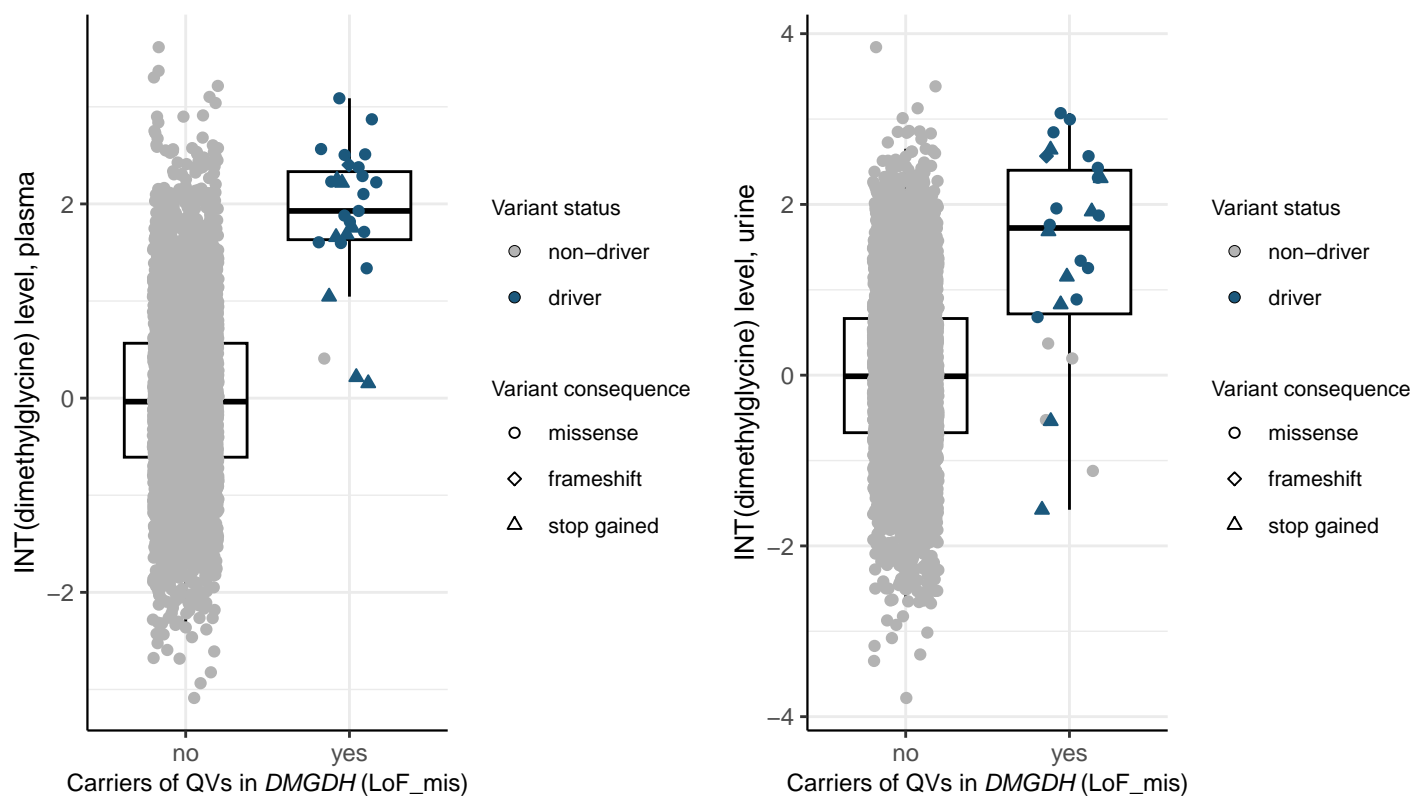
- non-driver
- driver

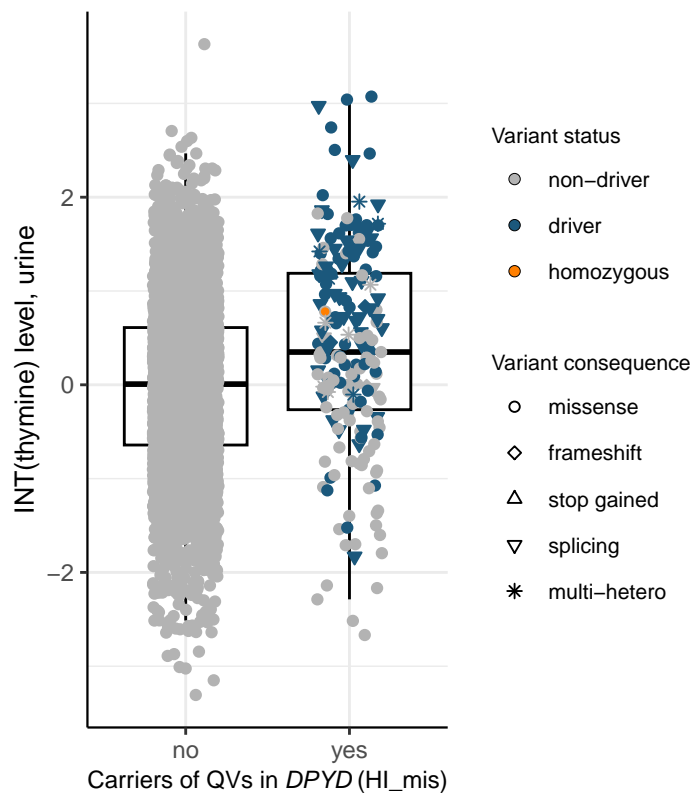
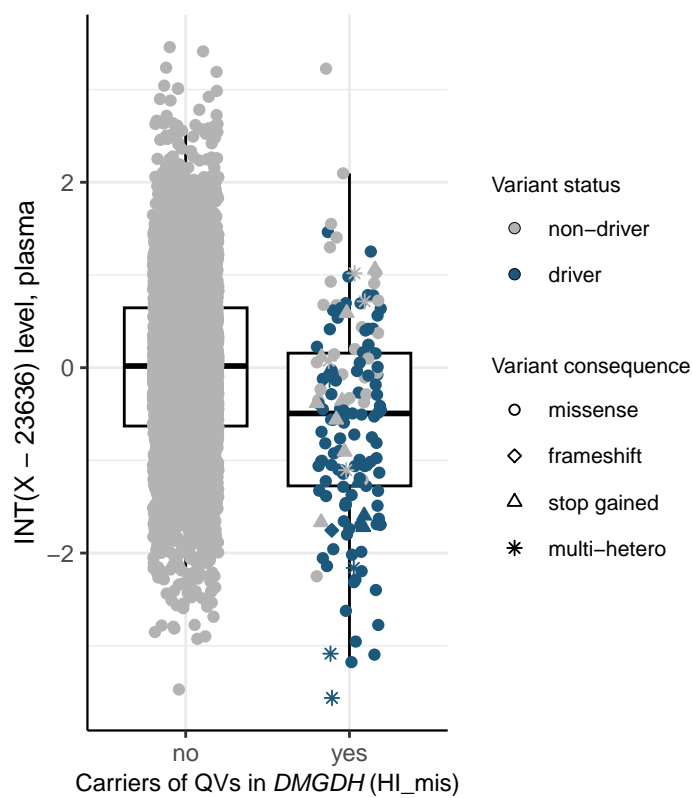
Variant consequence

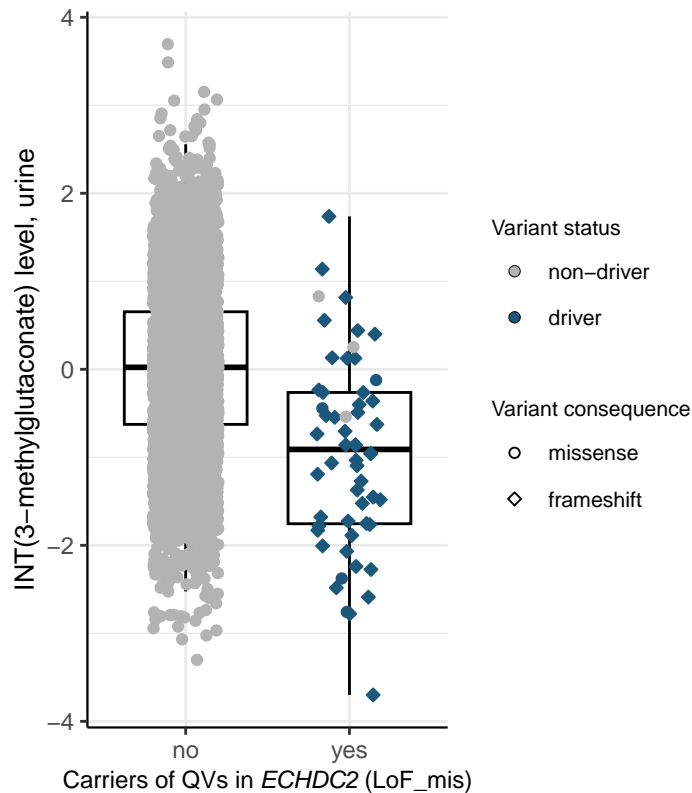
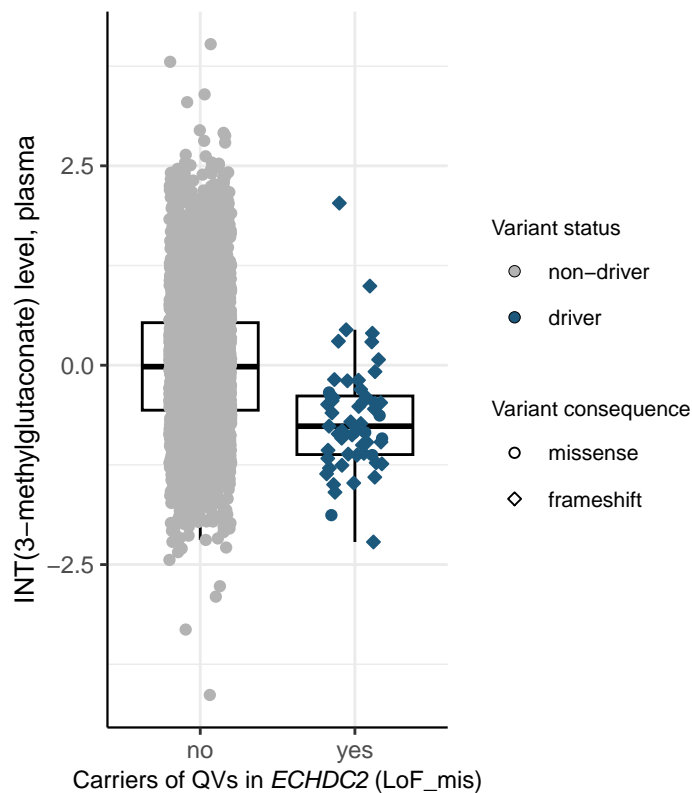
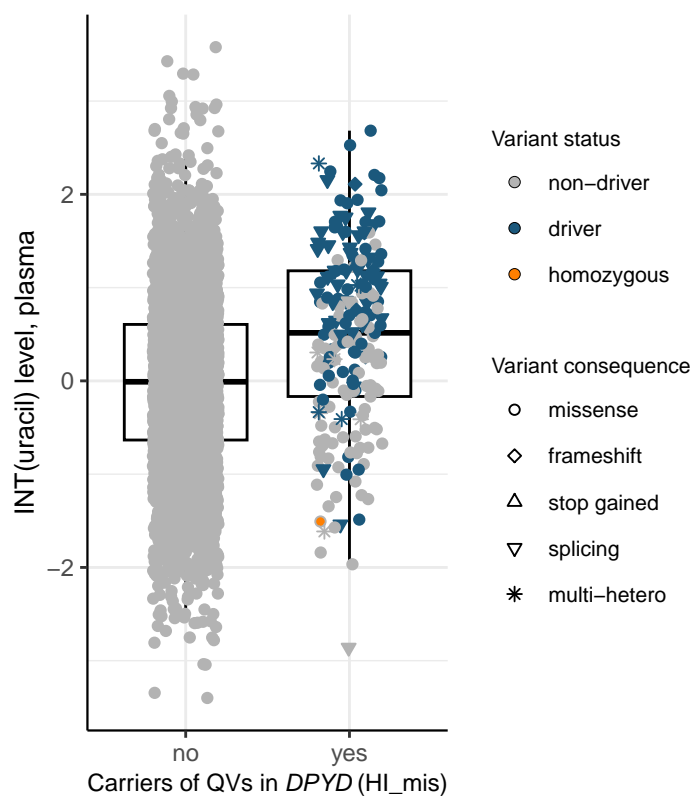
- missense
- frameshift
- stop gained
- splicing

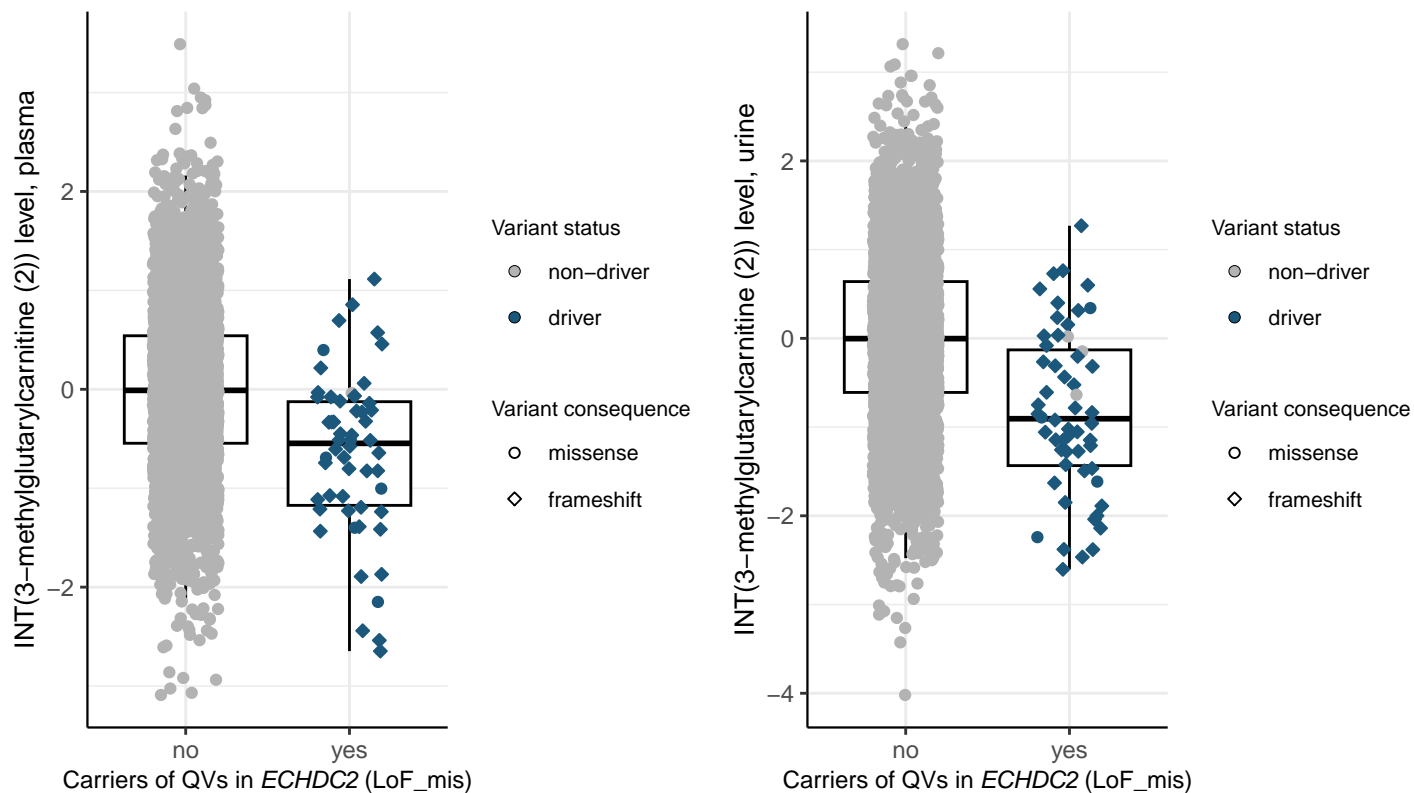
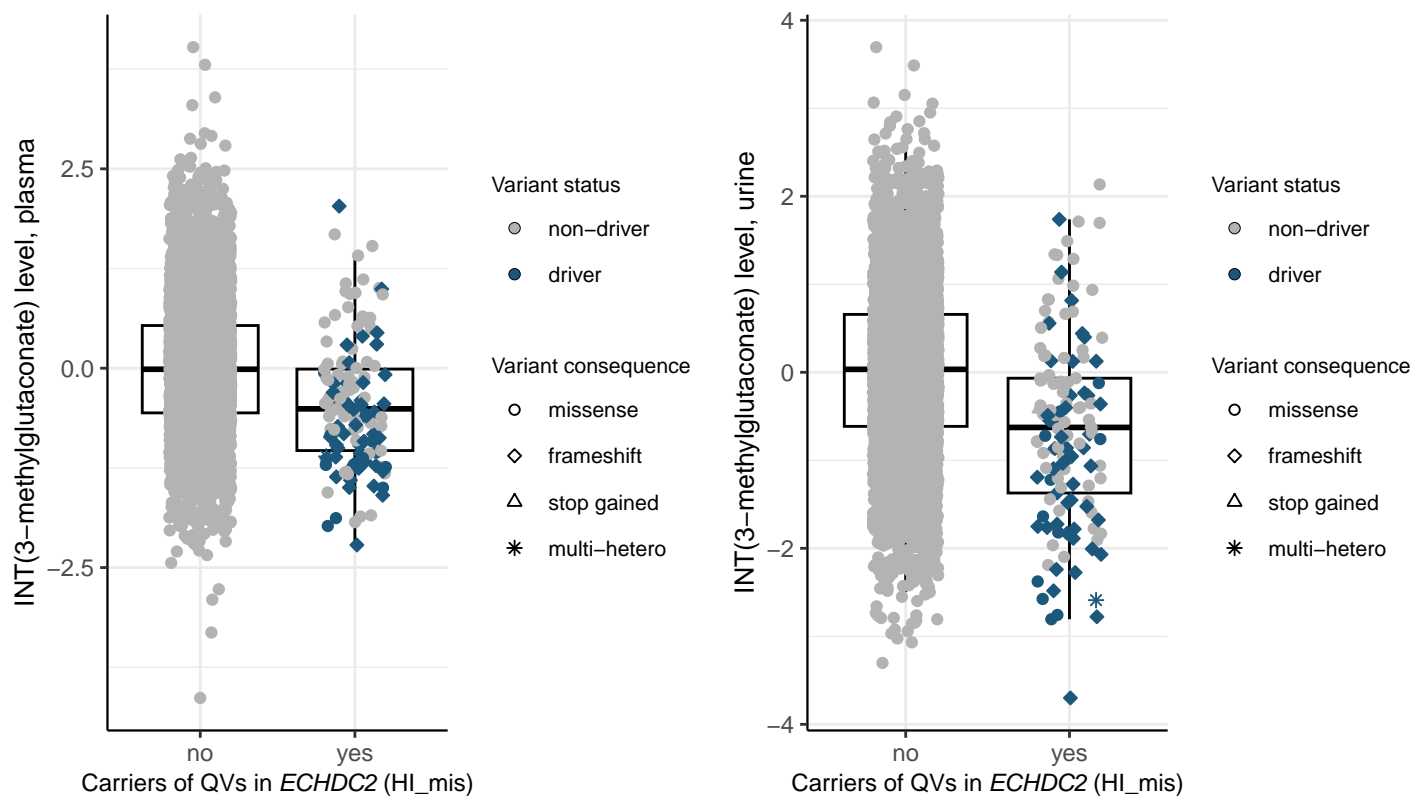


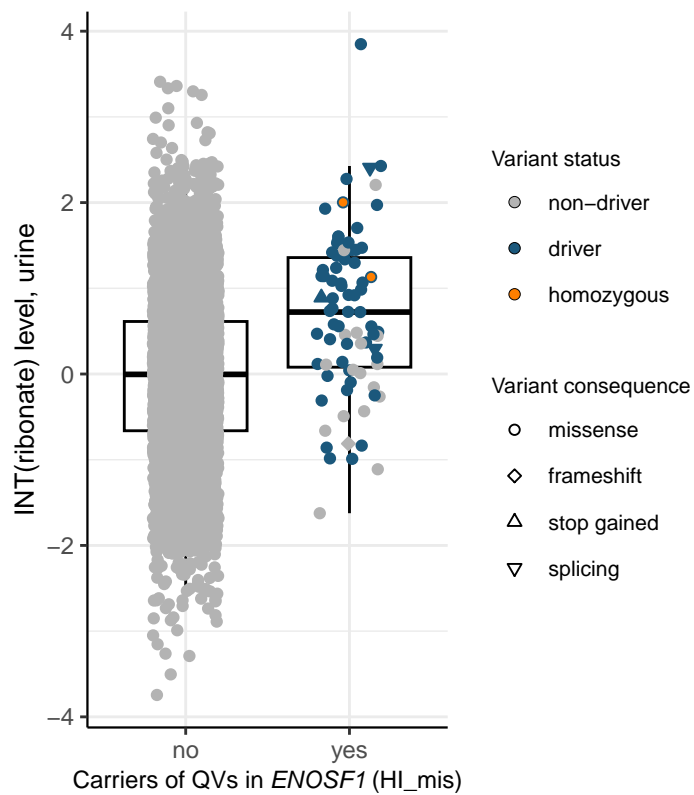
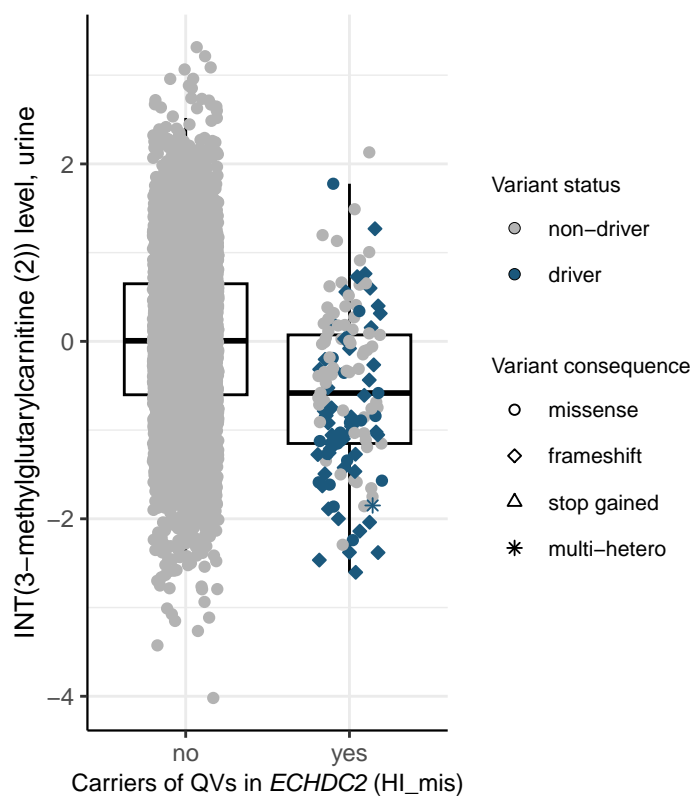


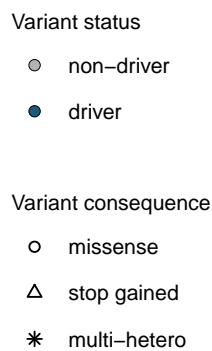
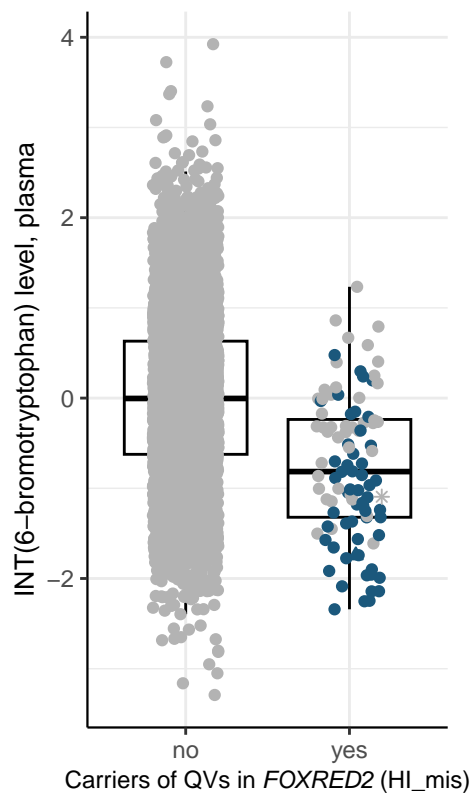
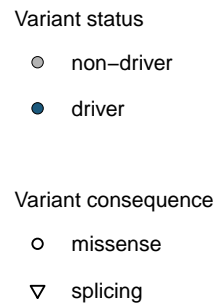
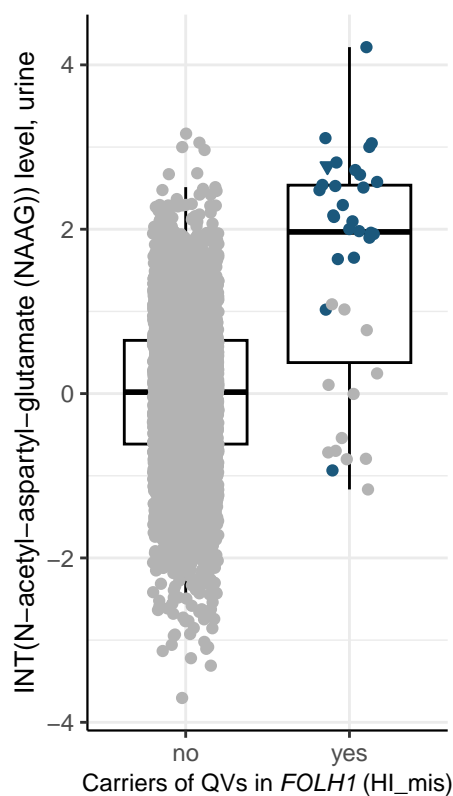
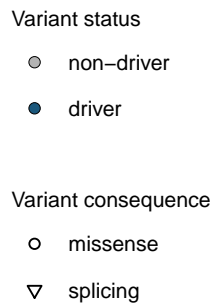
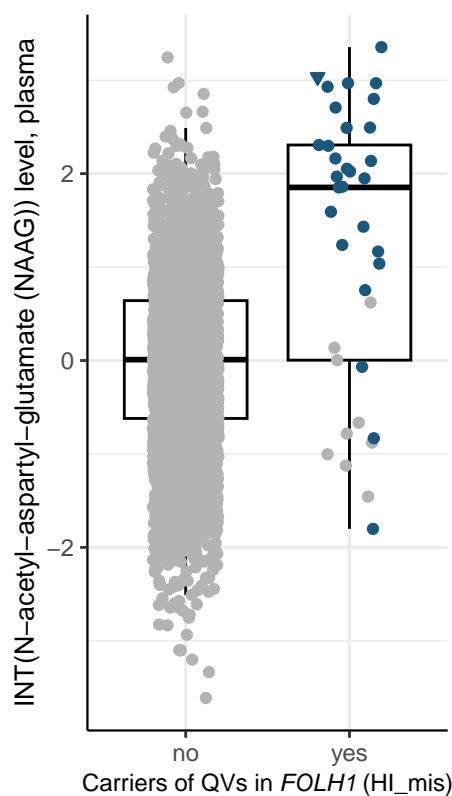


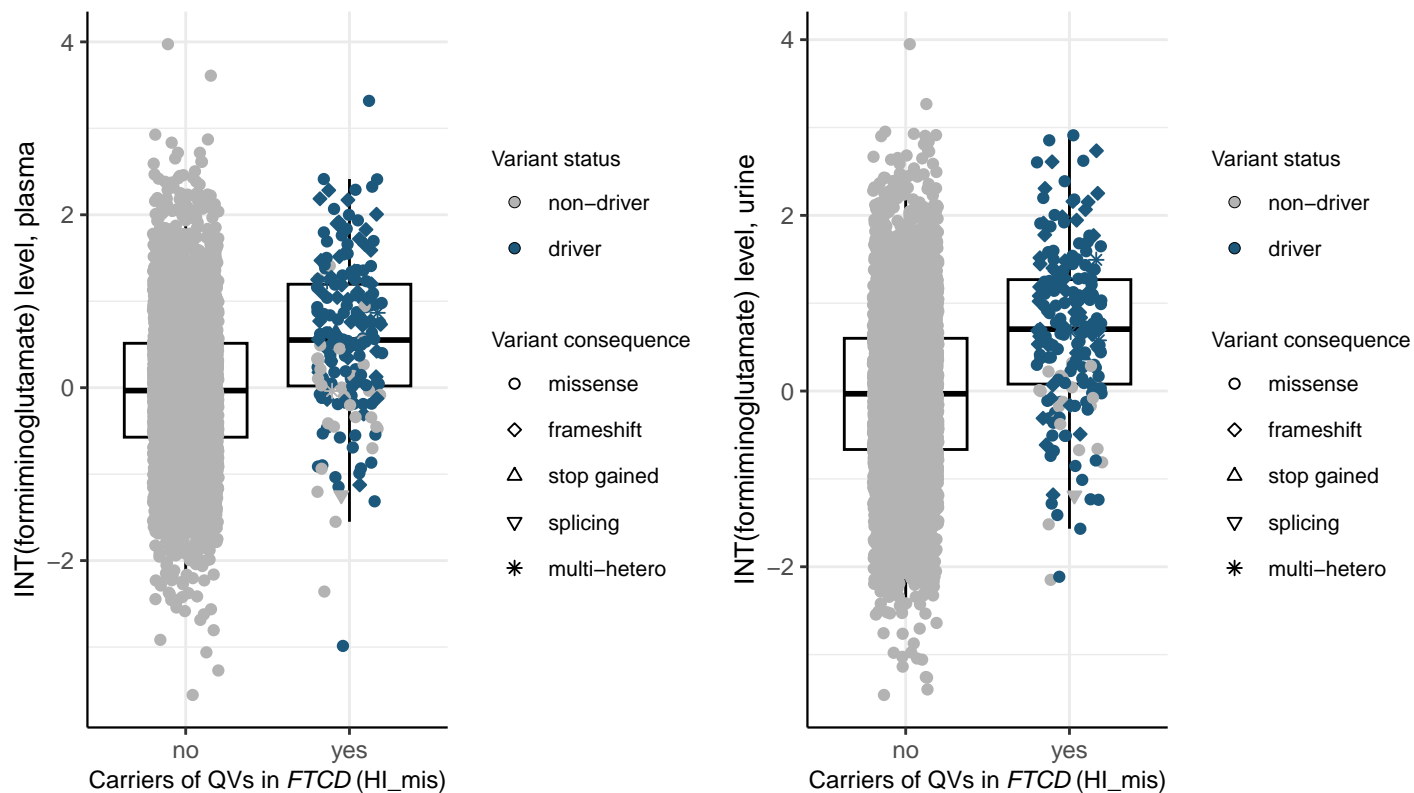
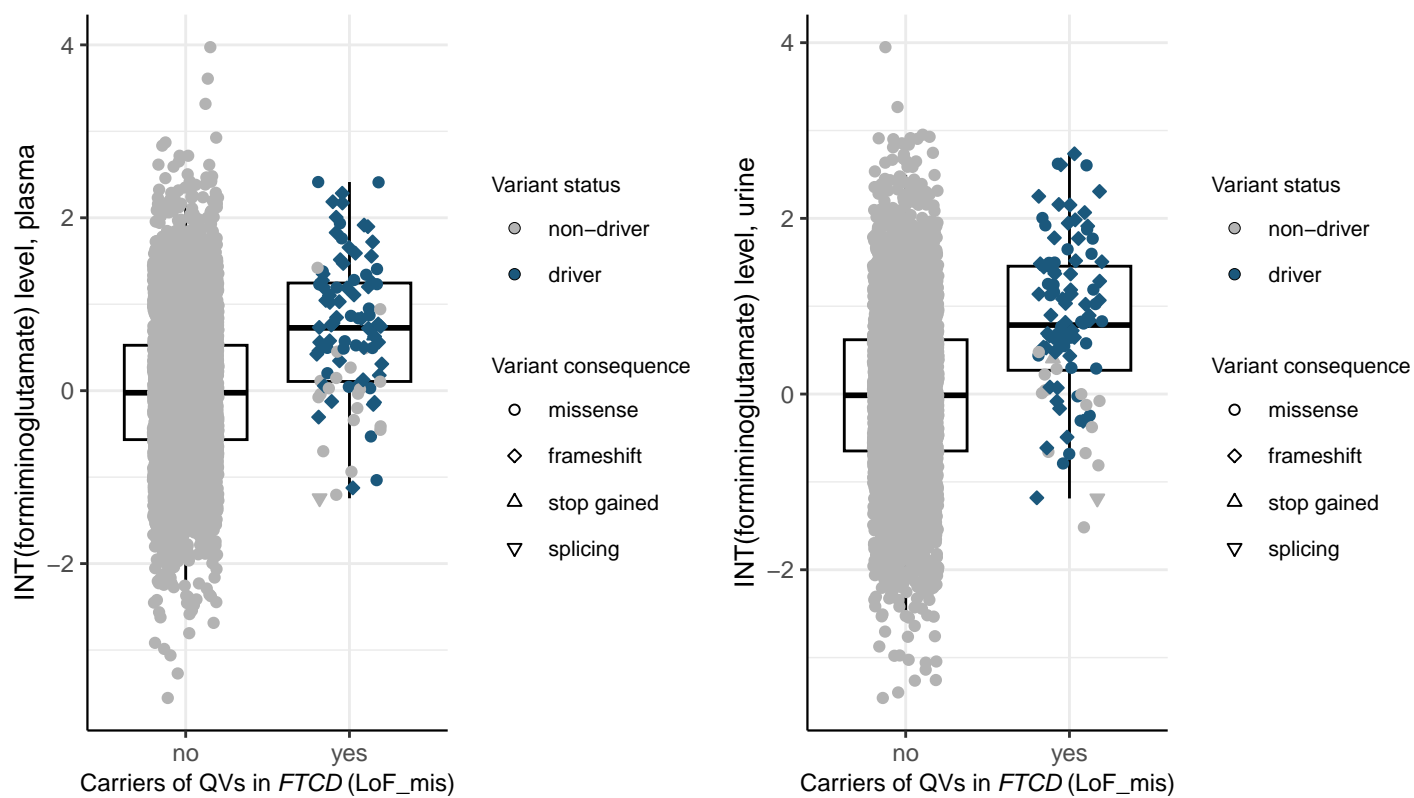


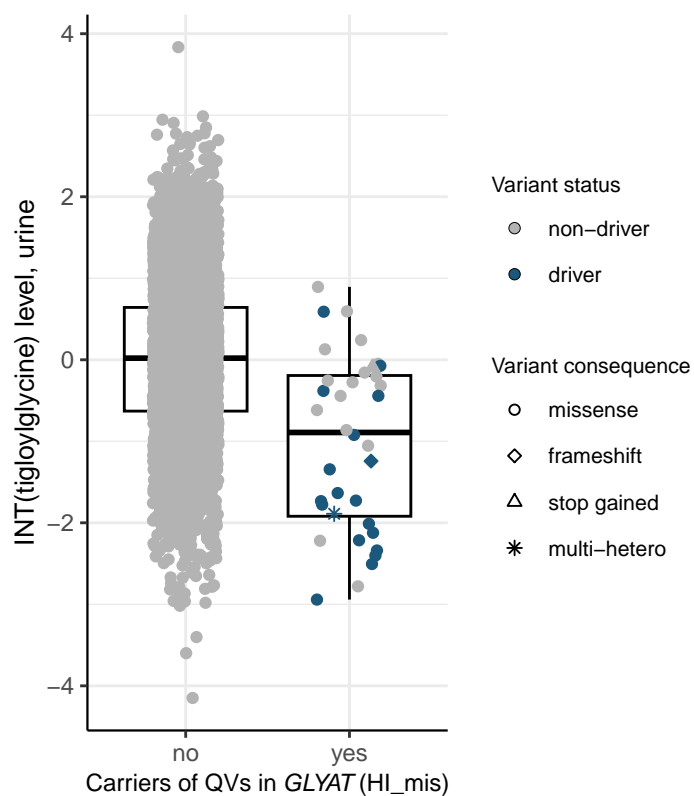
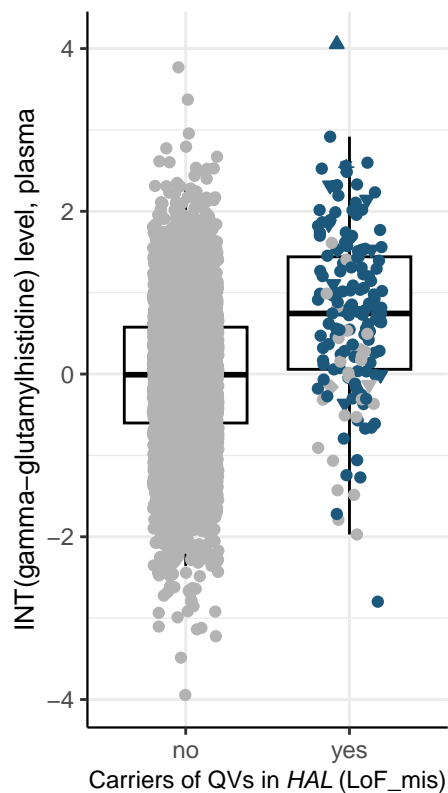


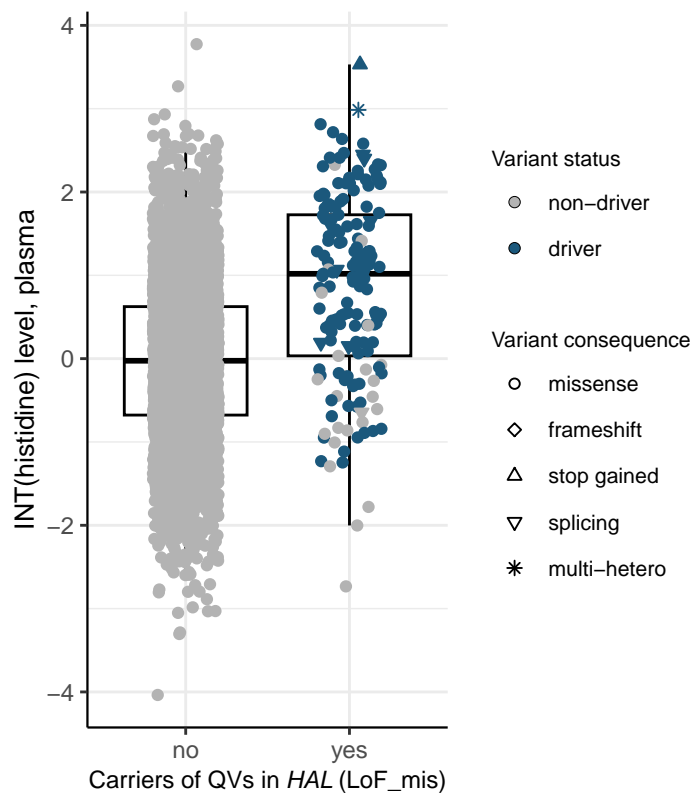
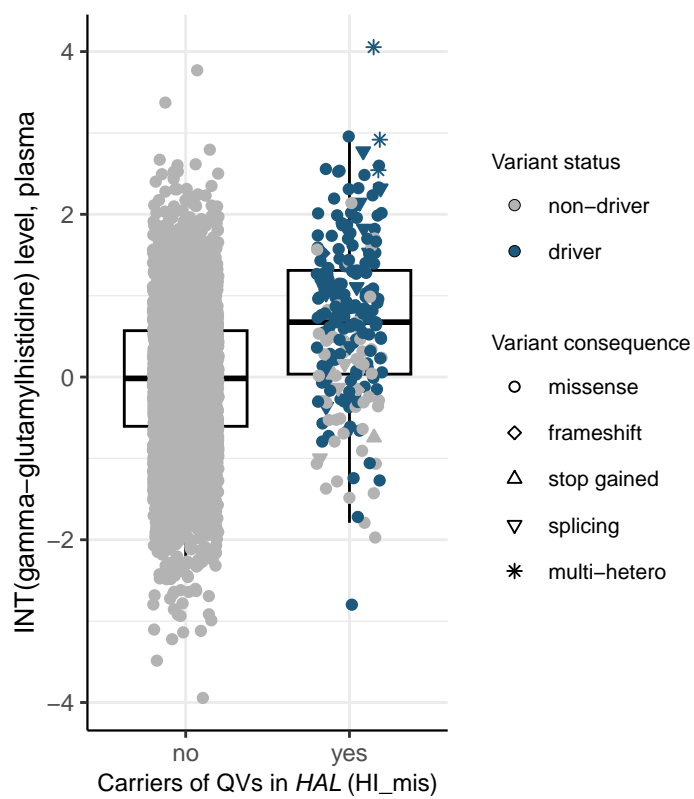


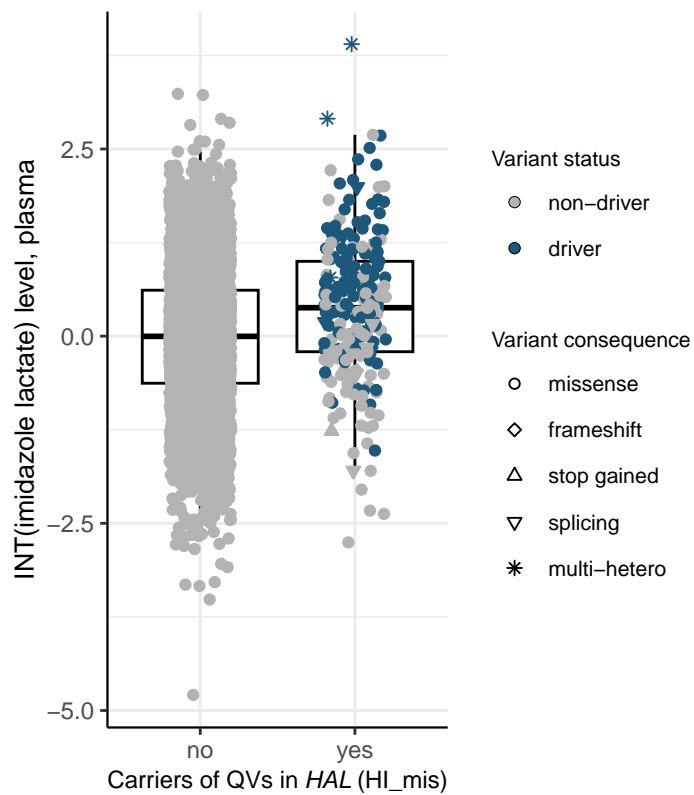
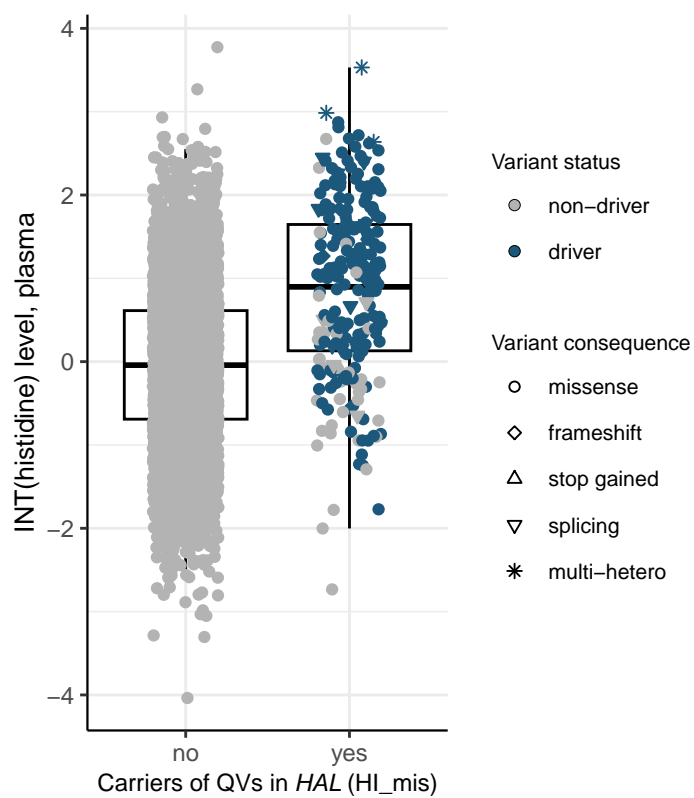


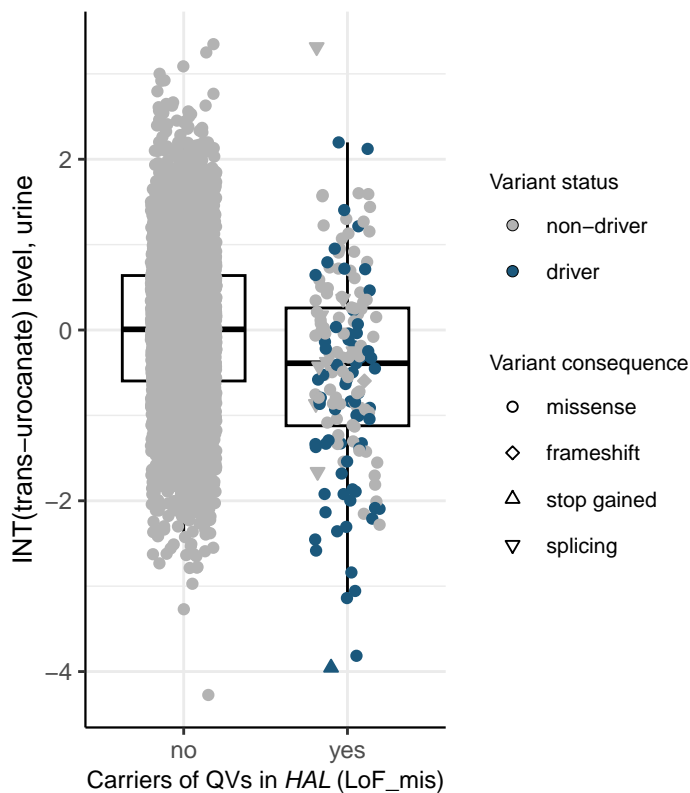
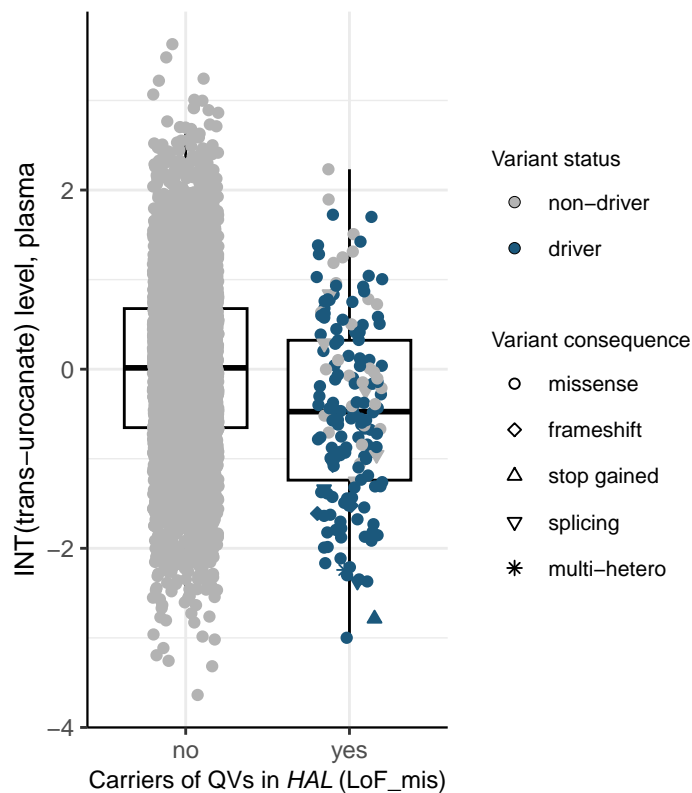
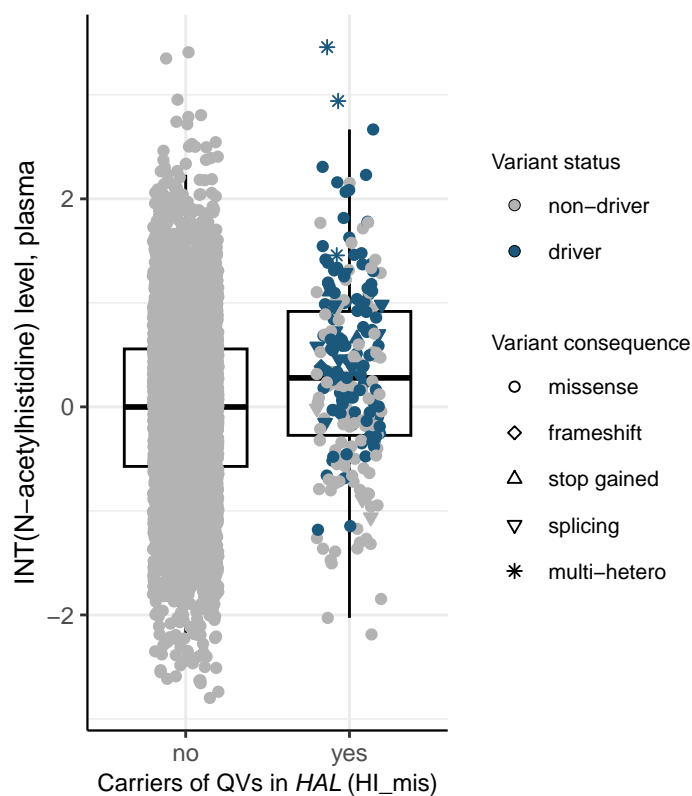


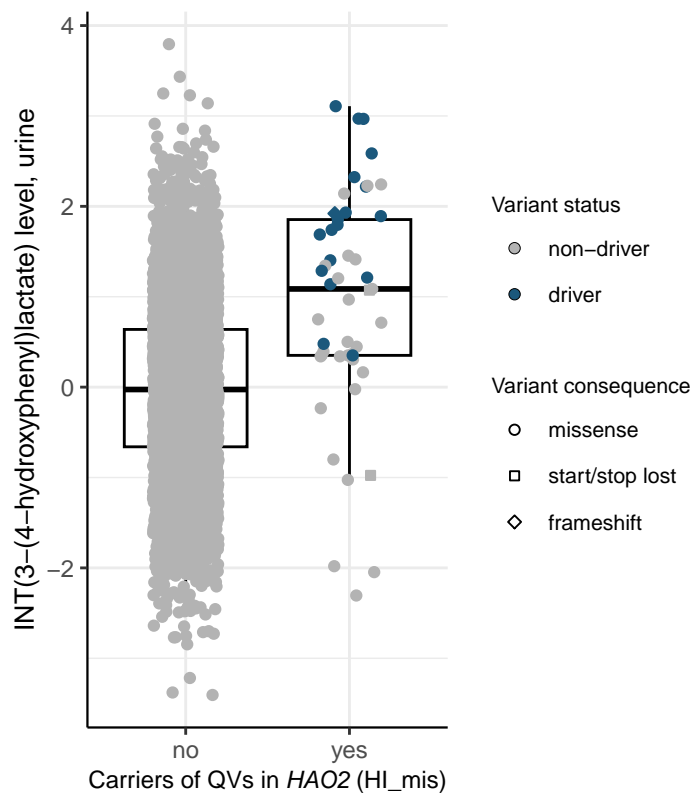
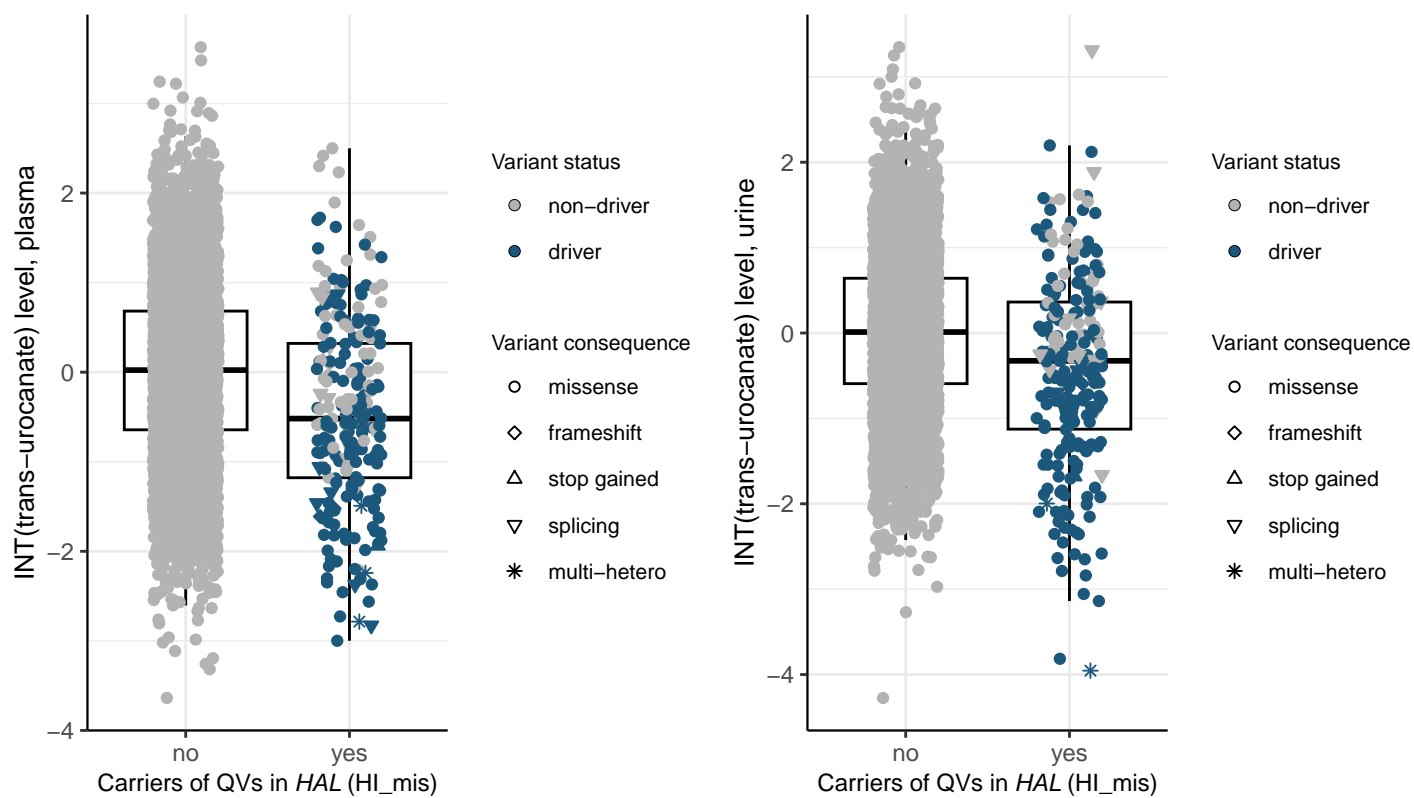


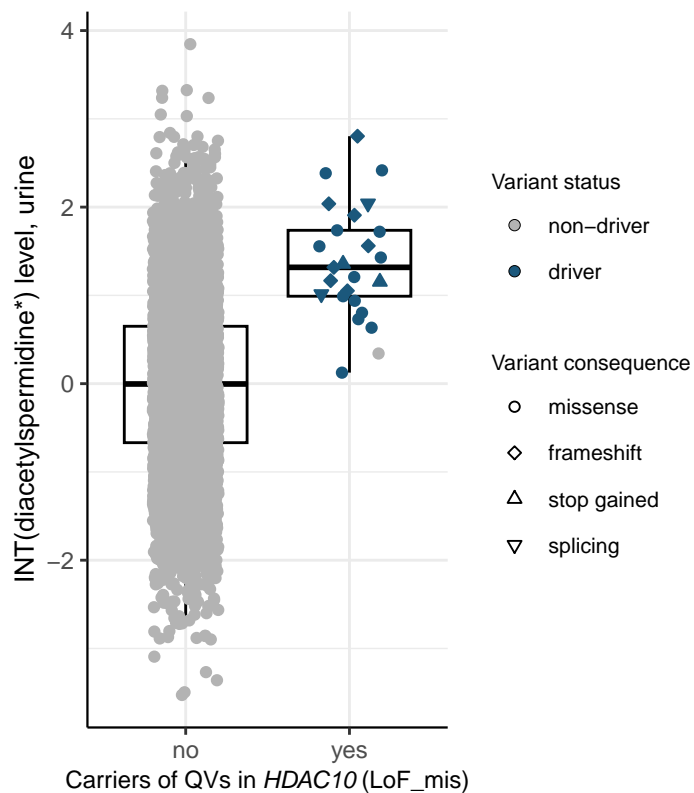
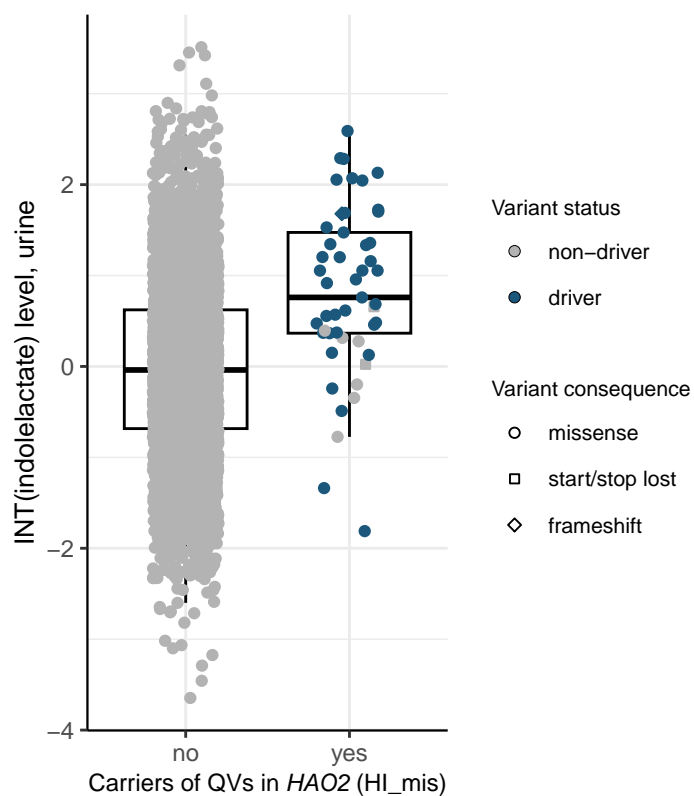


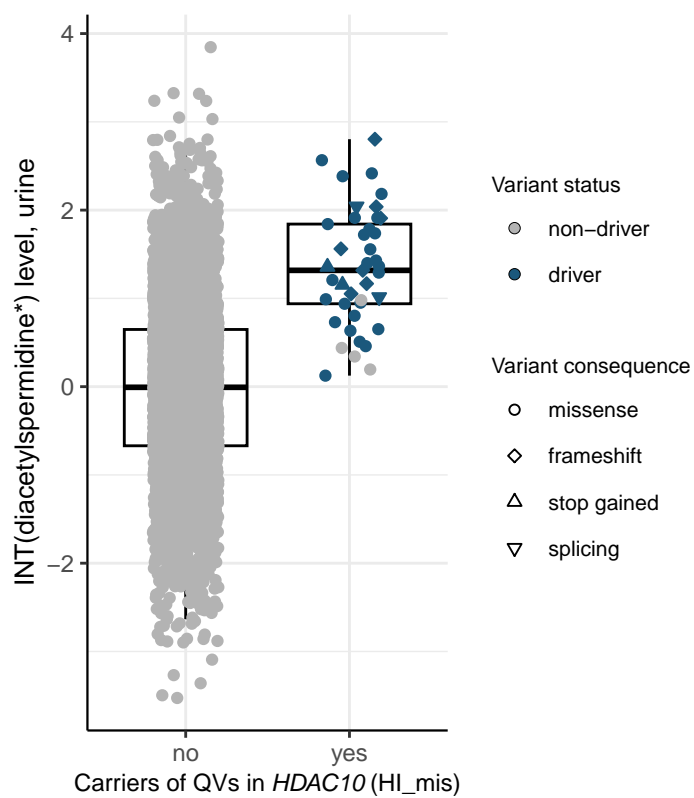
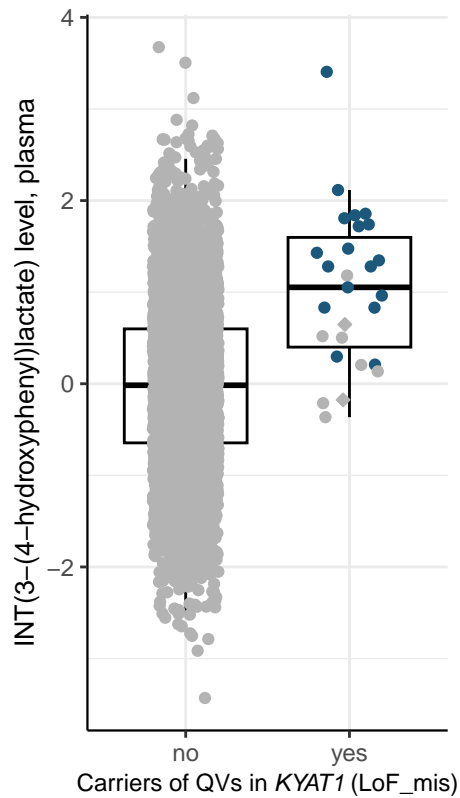


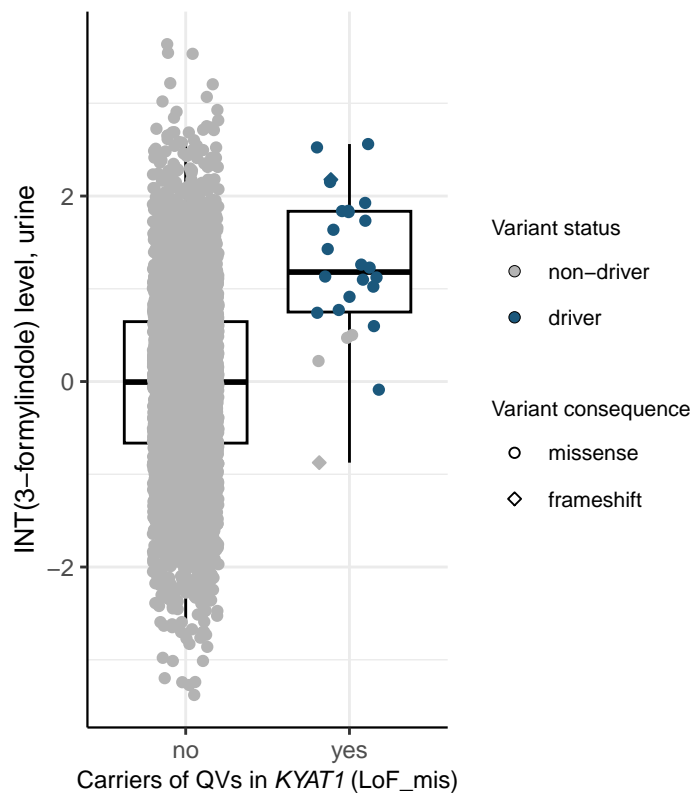
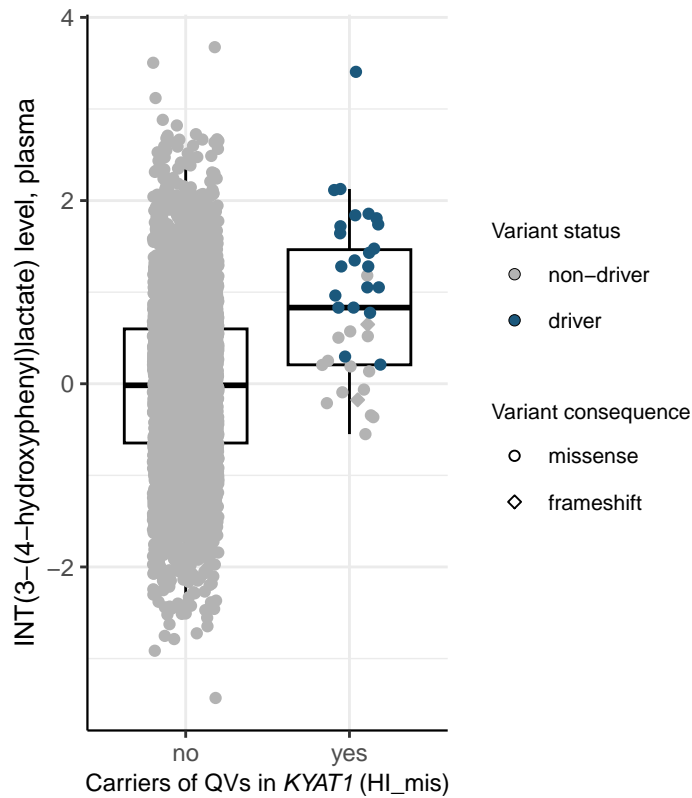


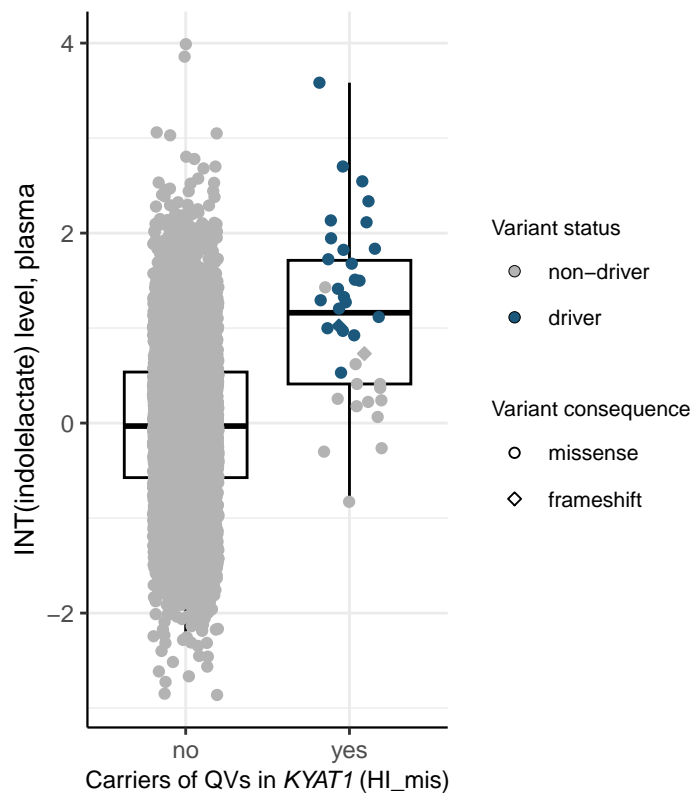
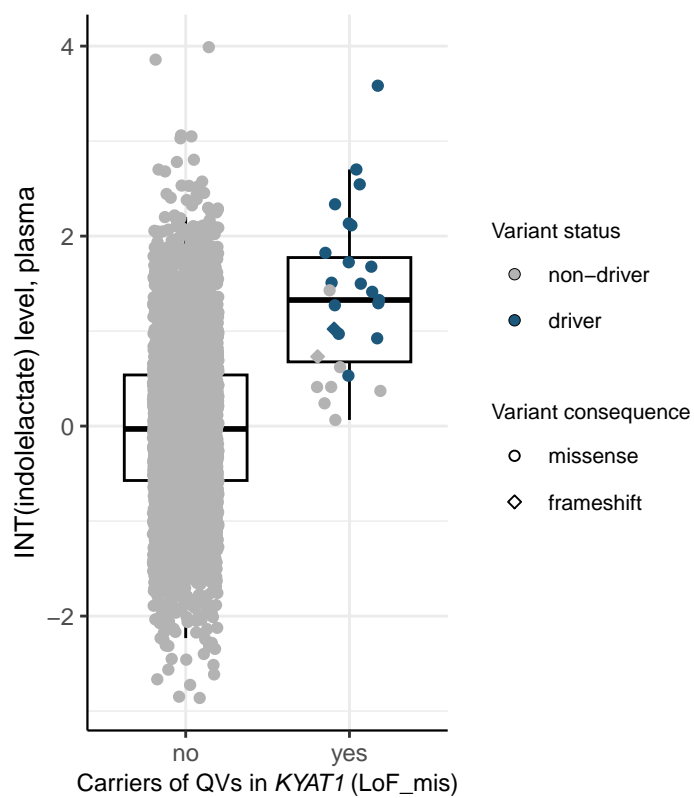


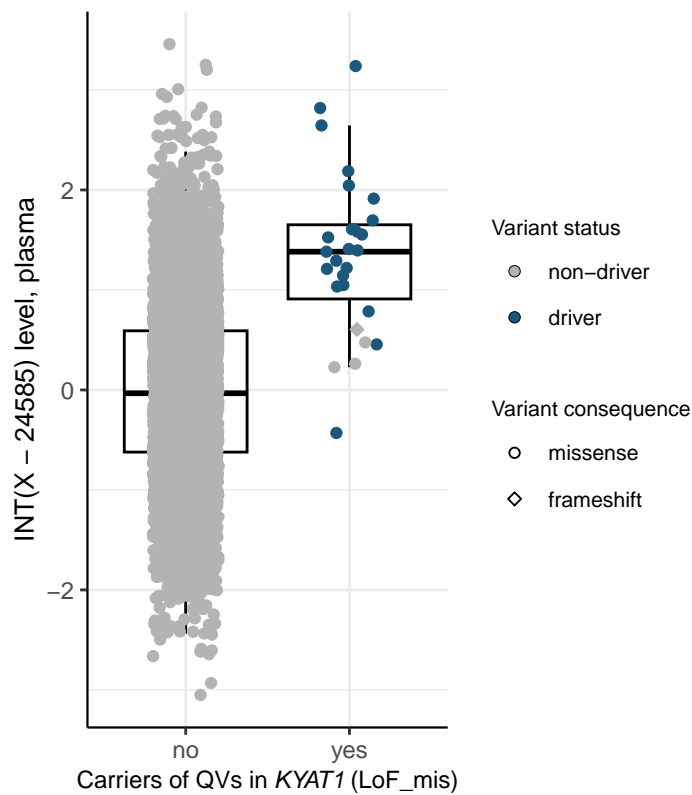
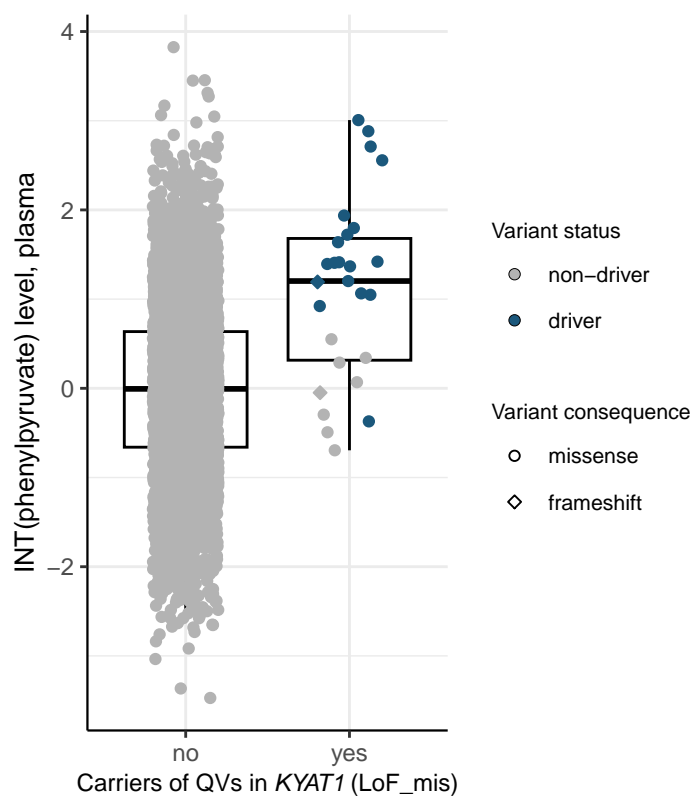


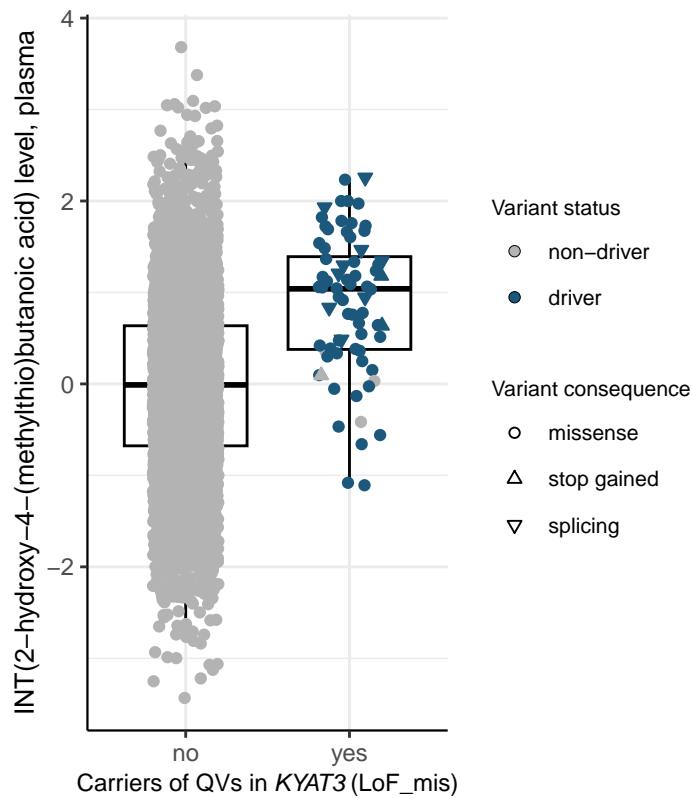
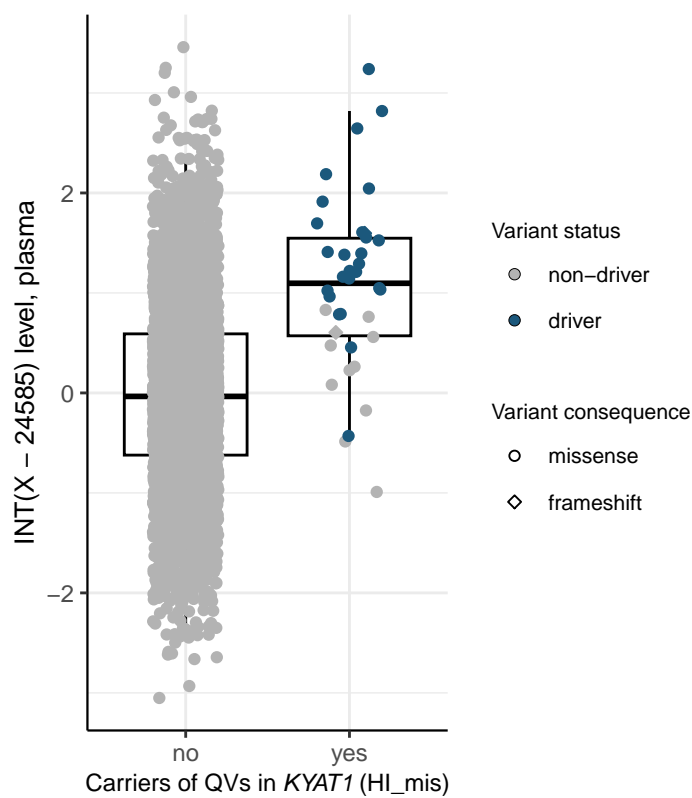


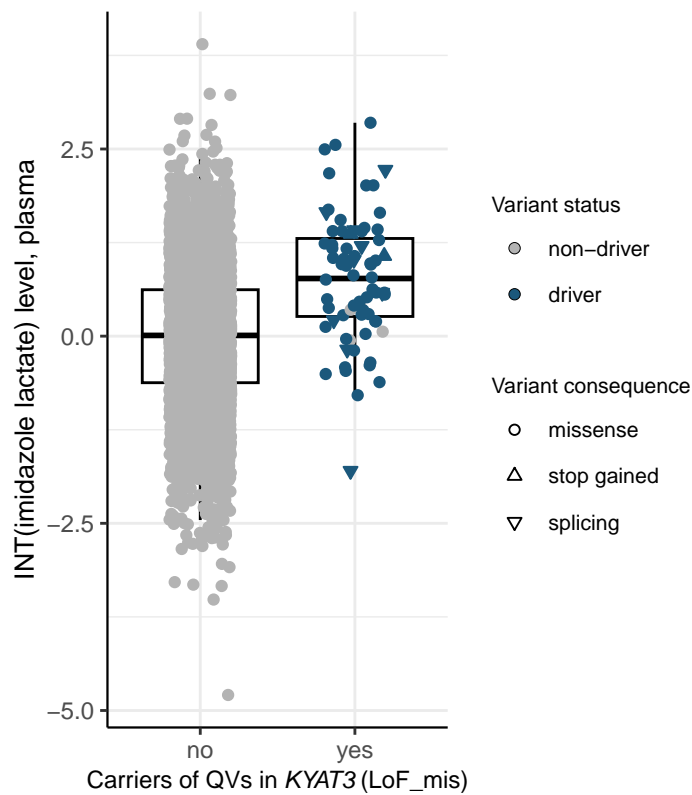
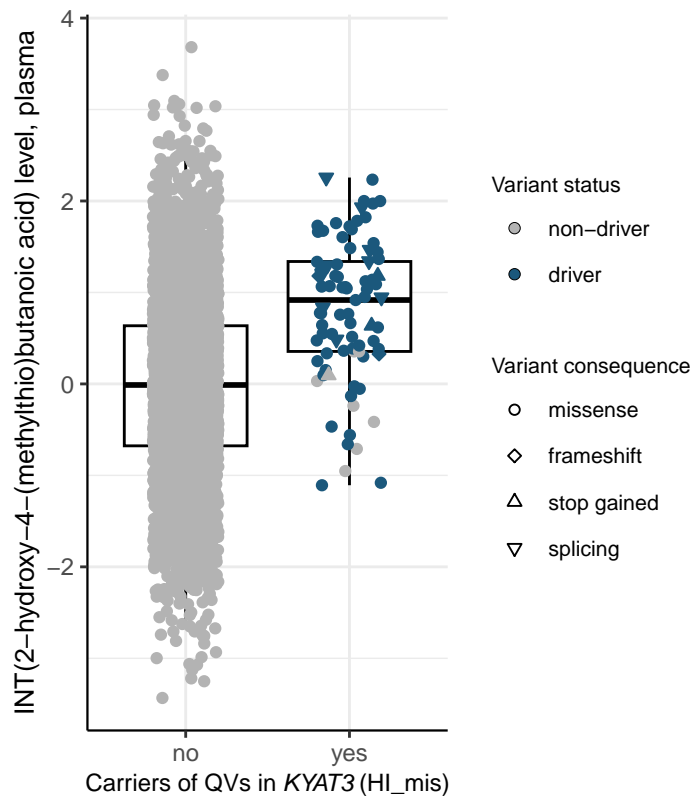


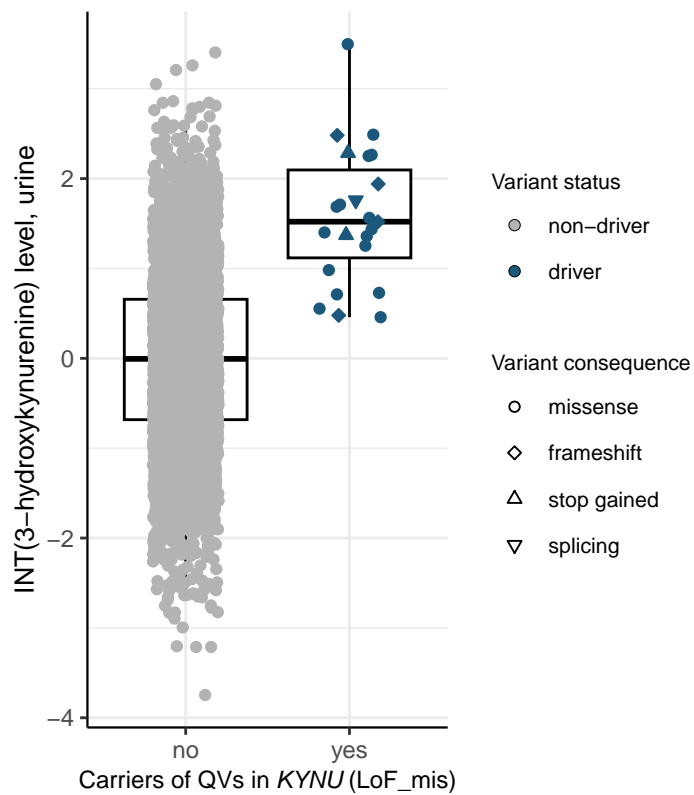
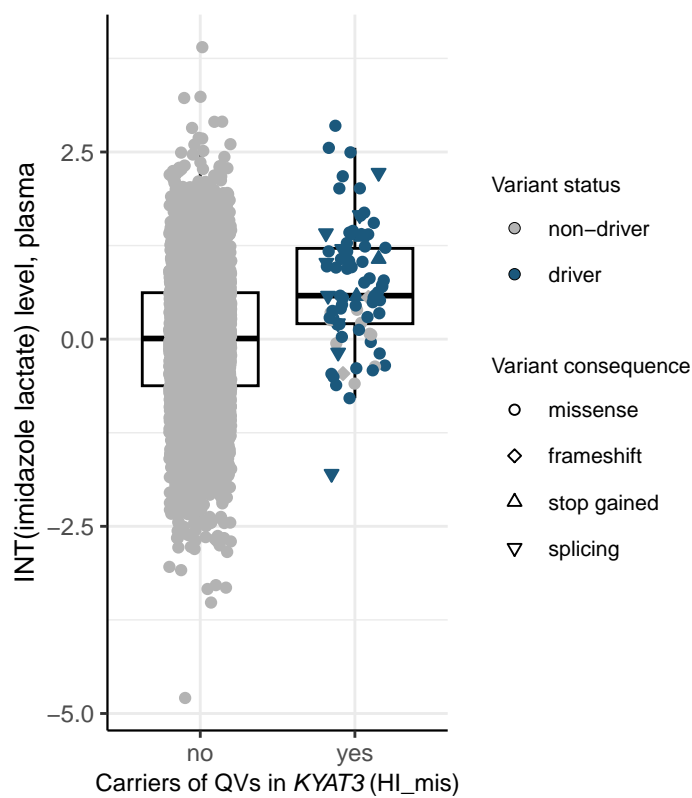


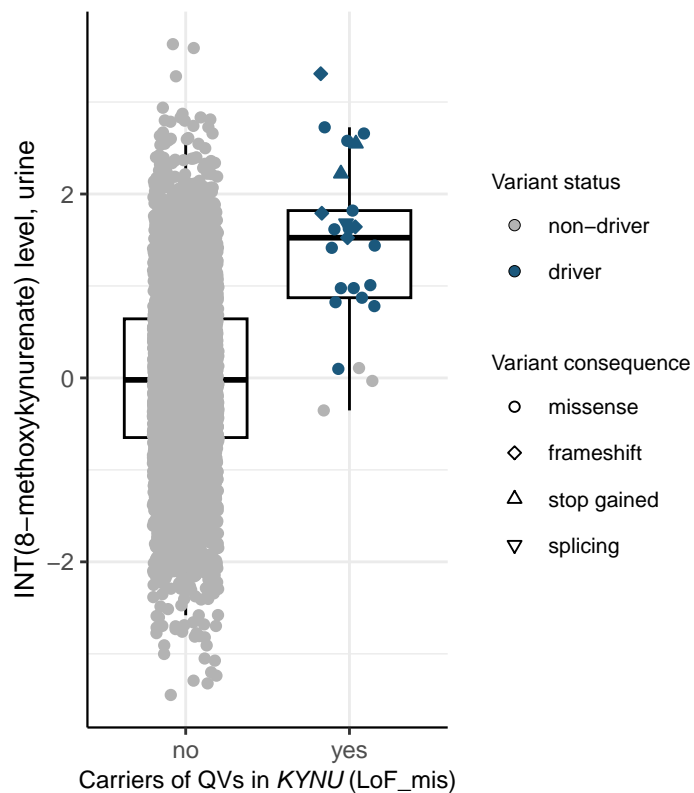
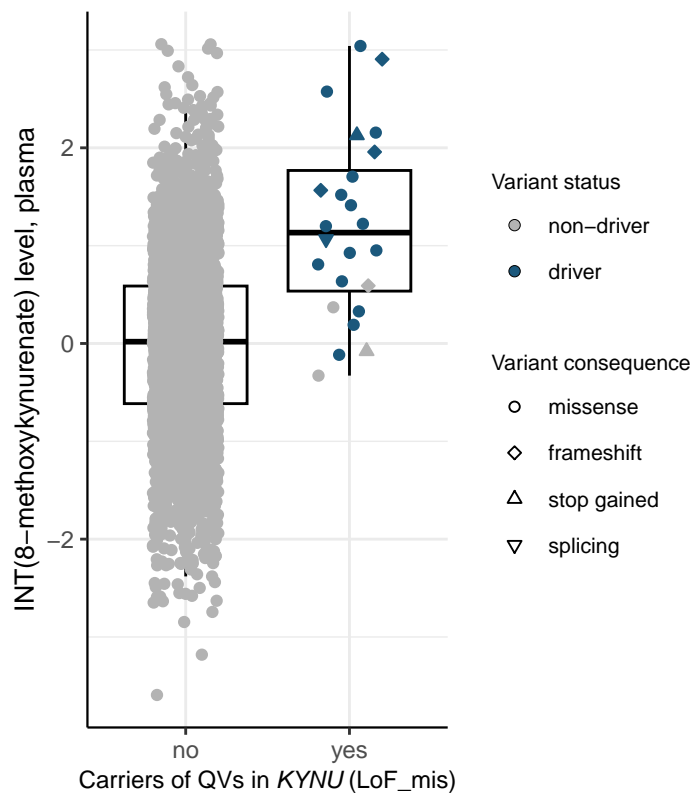
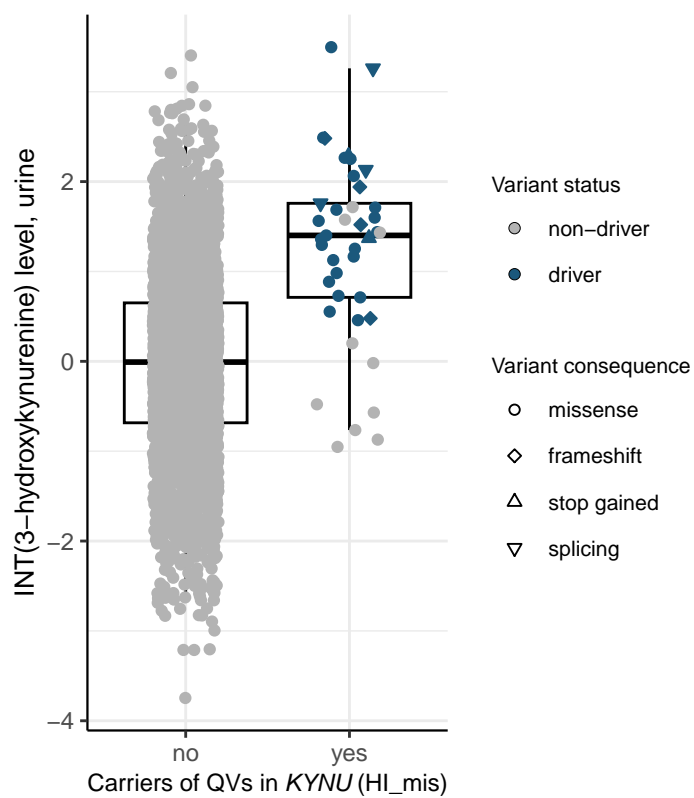


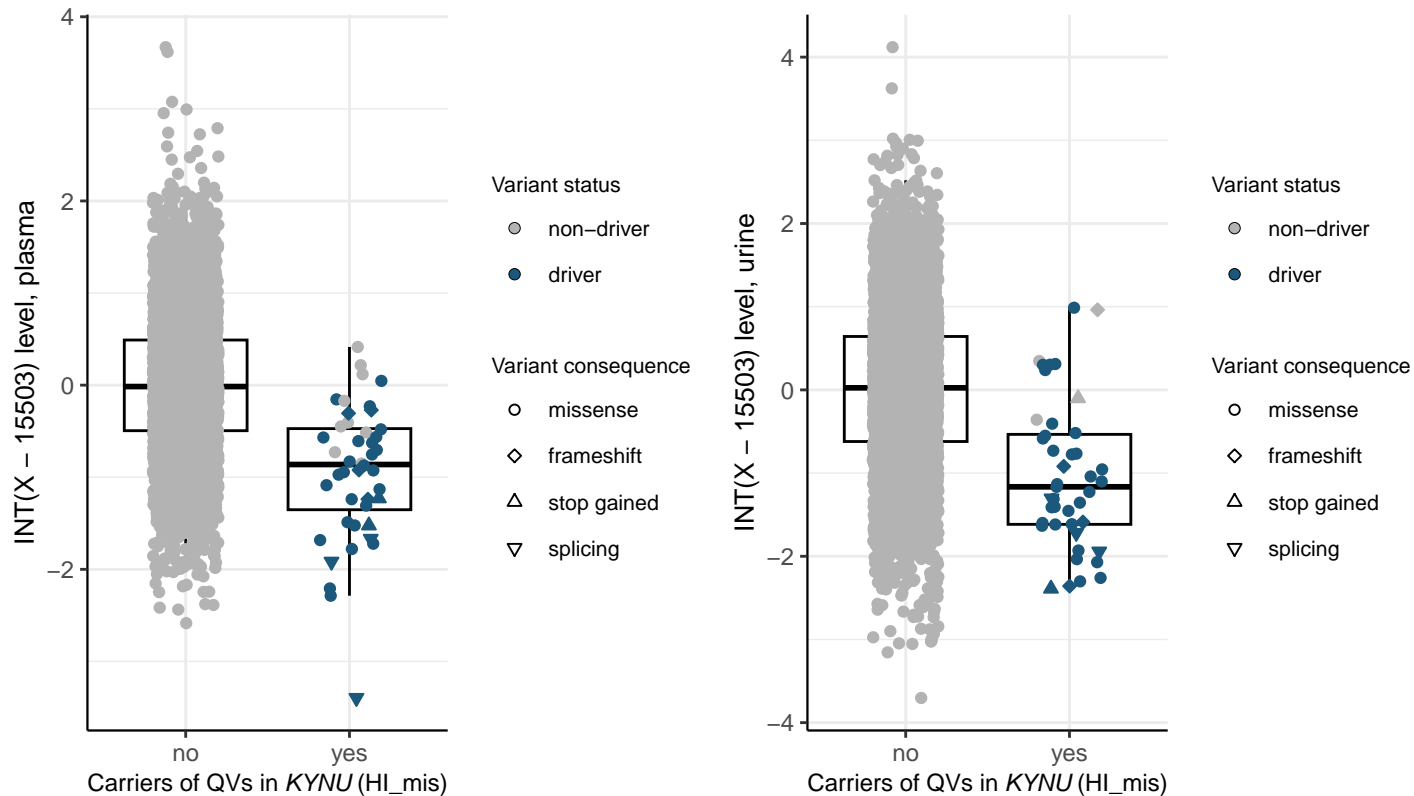
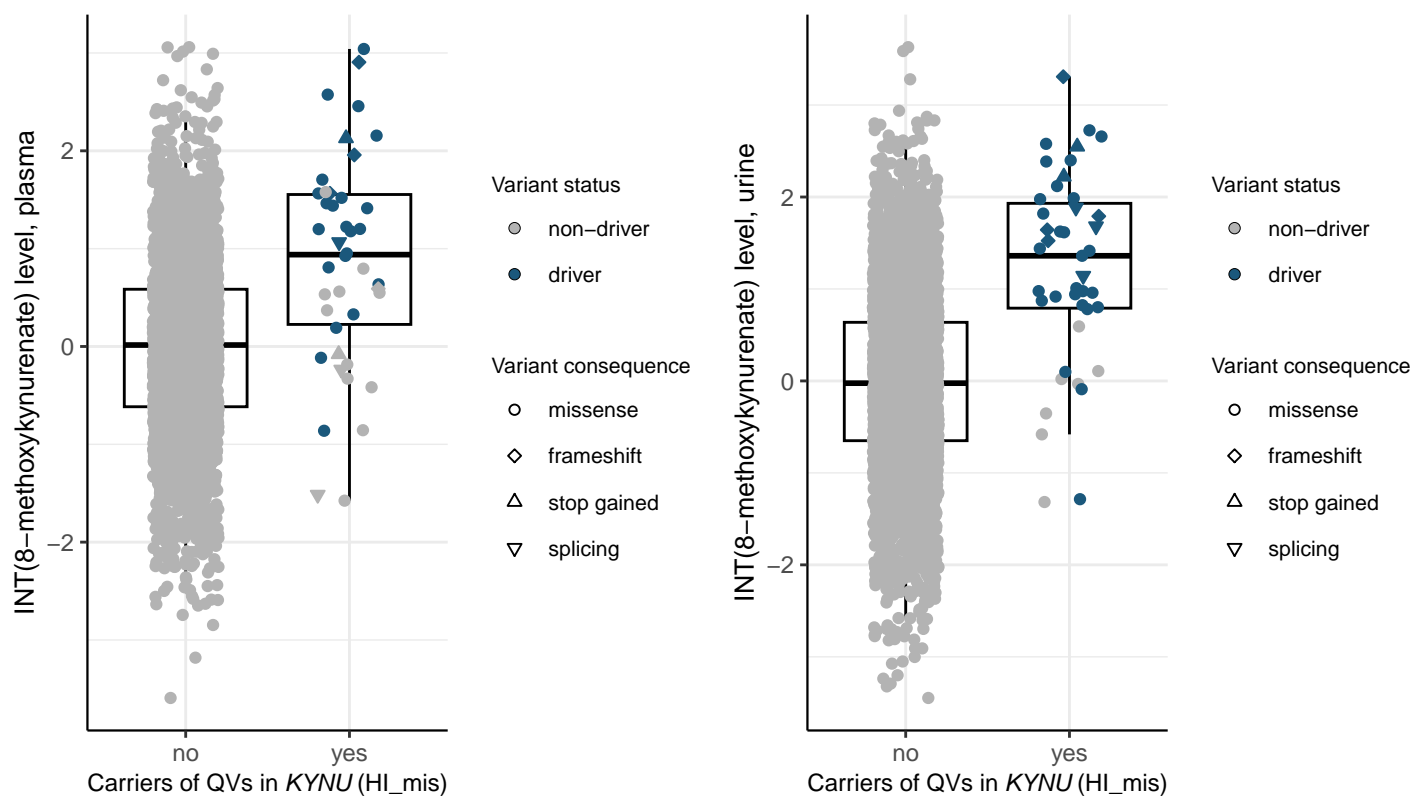


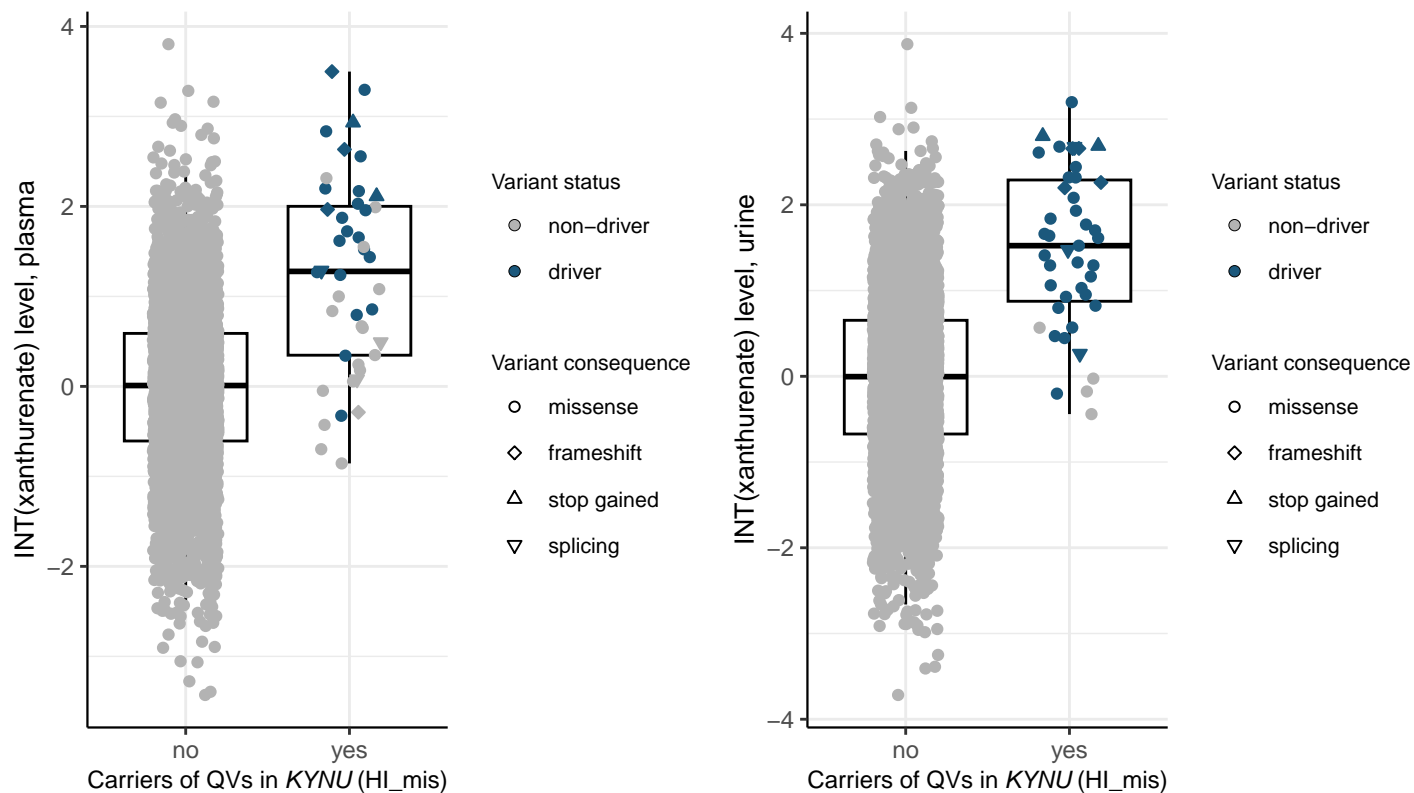
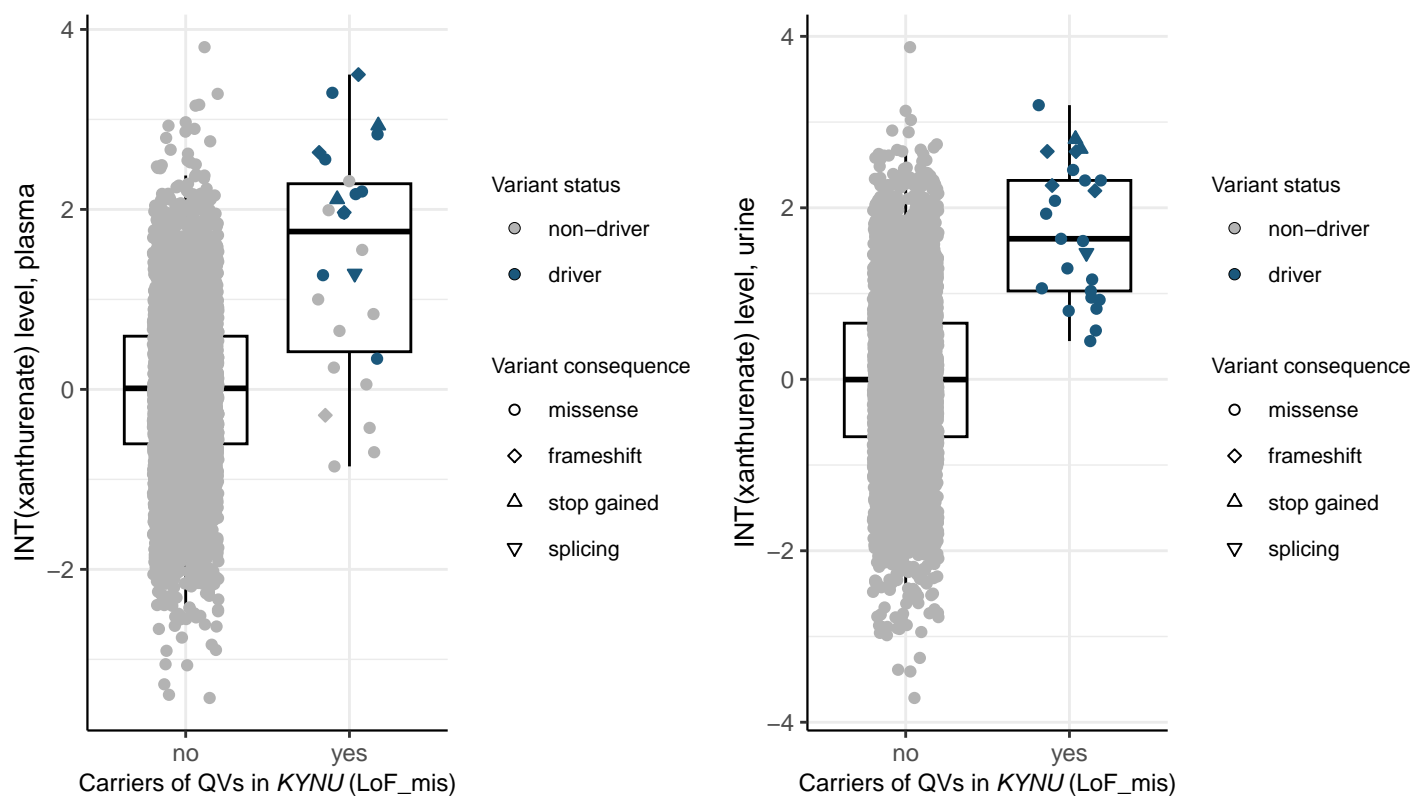


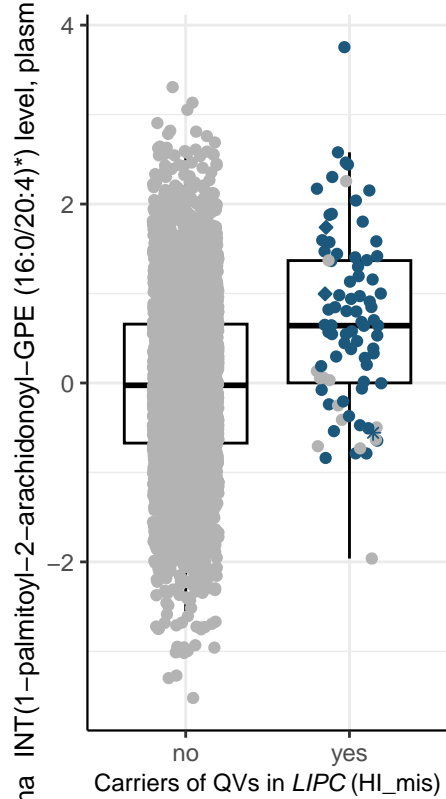










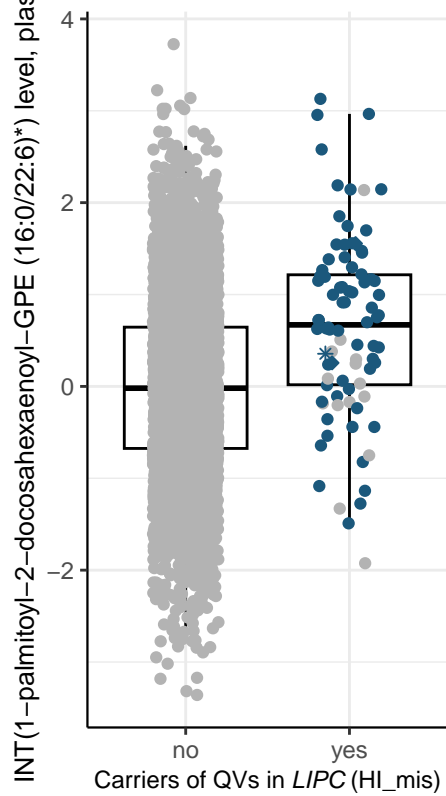


Variant status

- non-driver
- driver

Variant consequence

- missense
- frameshift
- multi-hetero

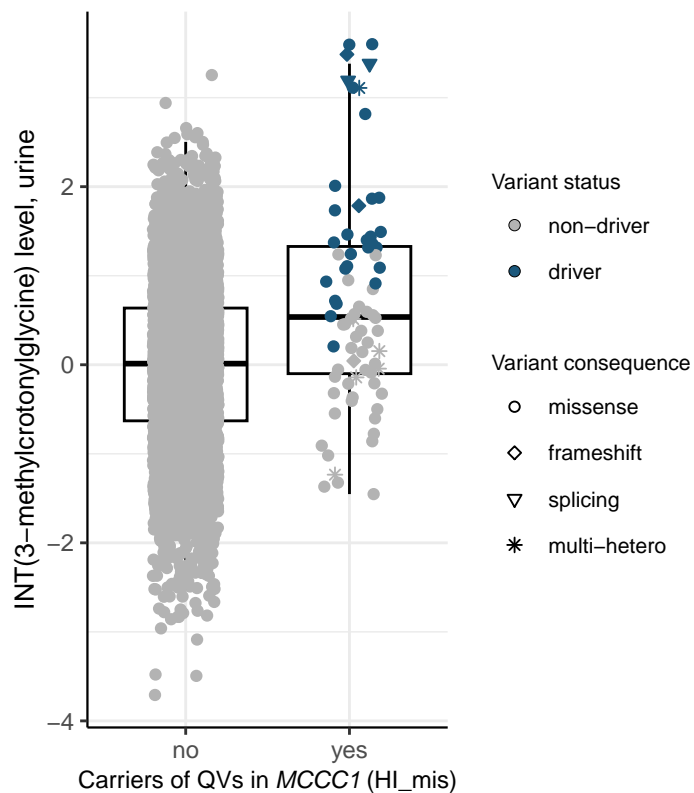
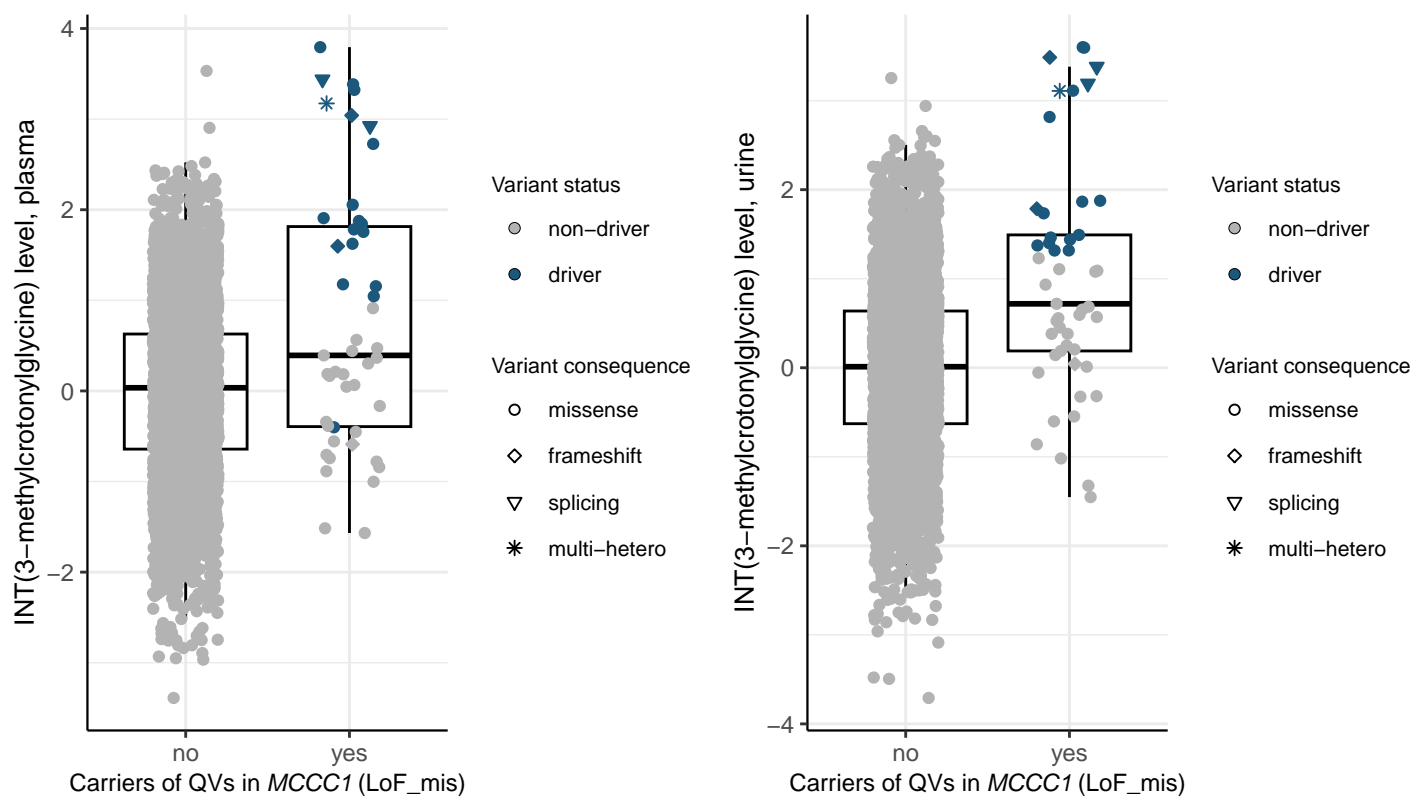


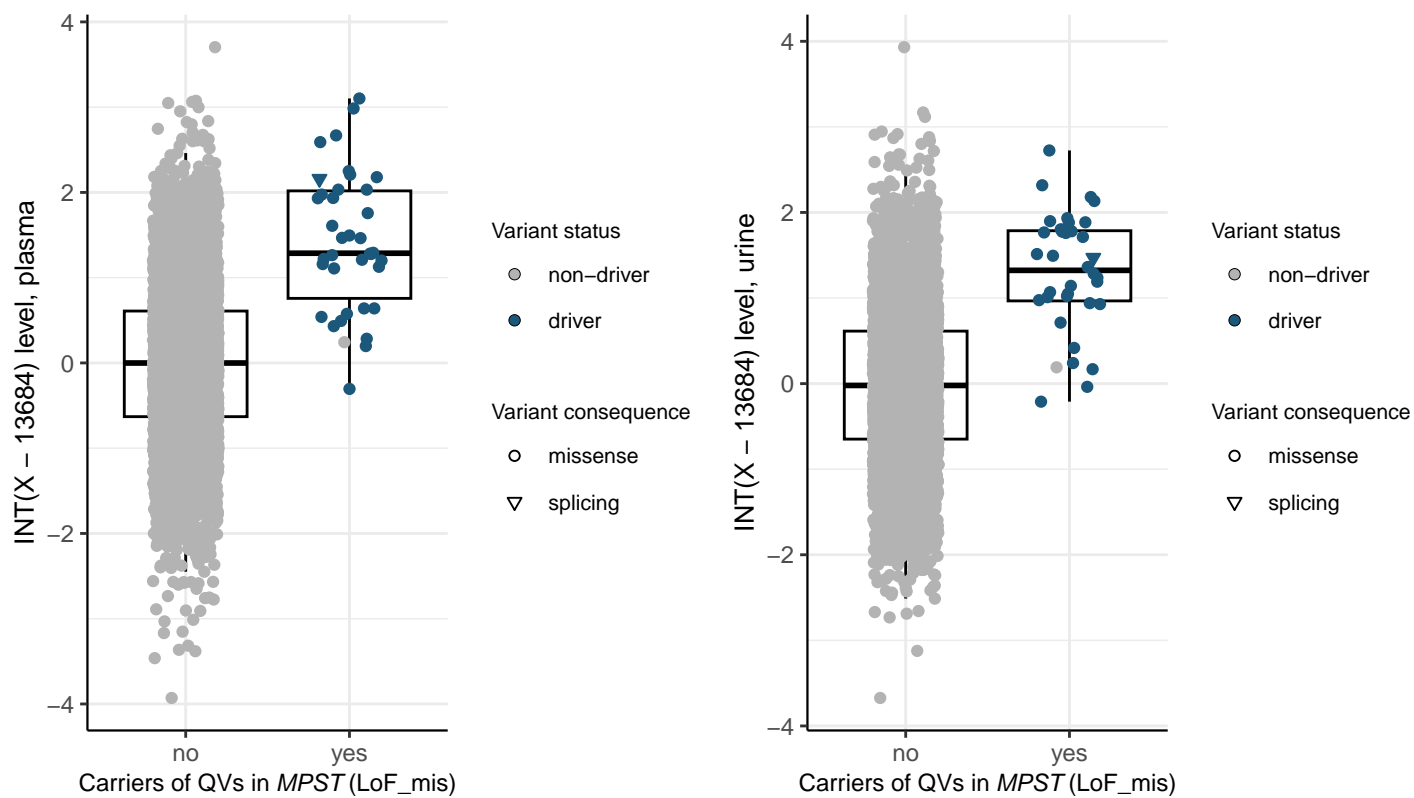
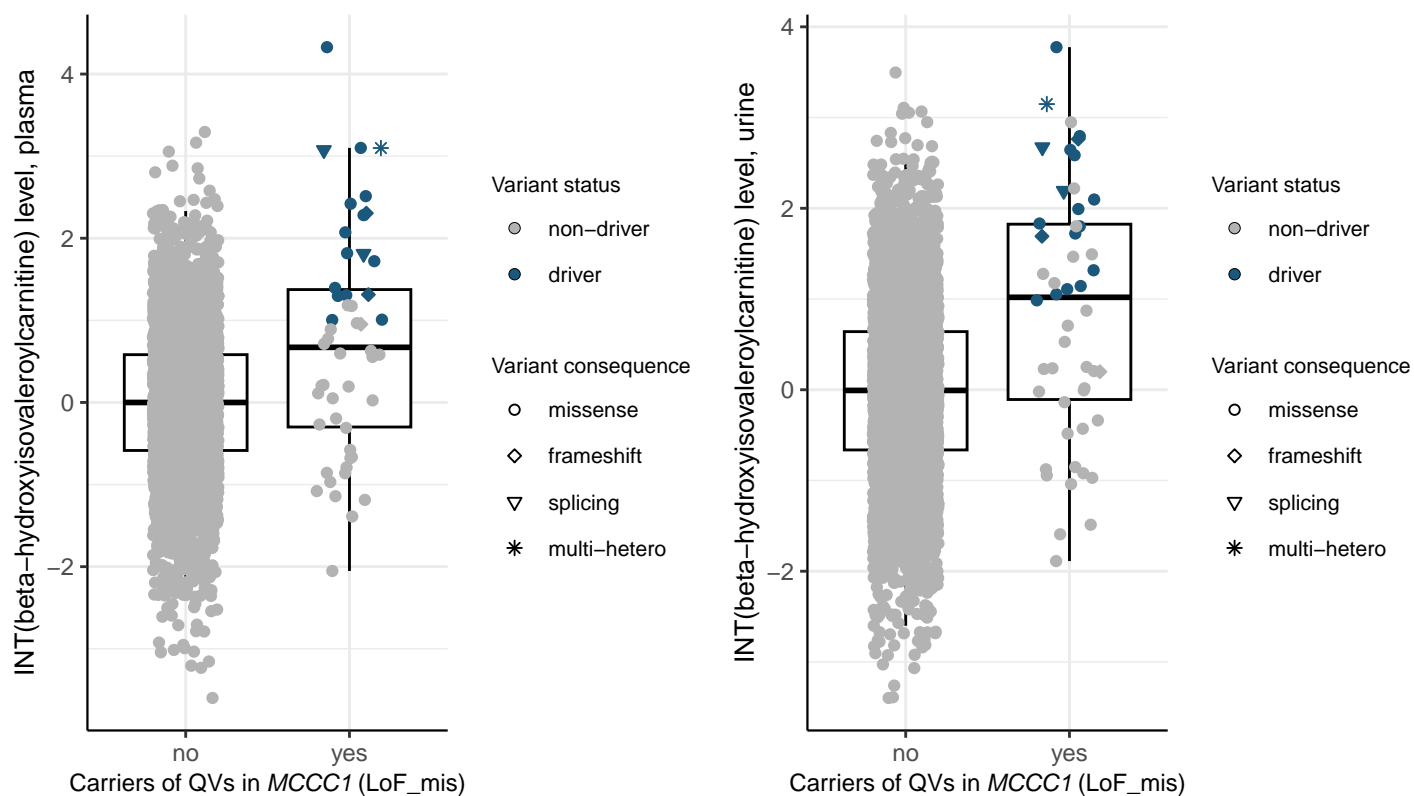
Variant status

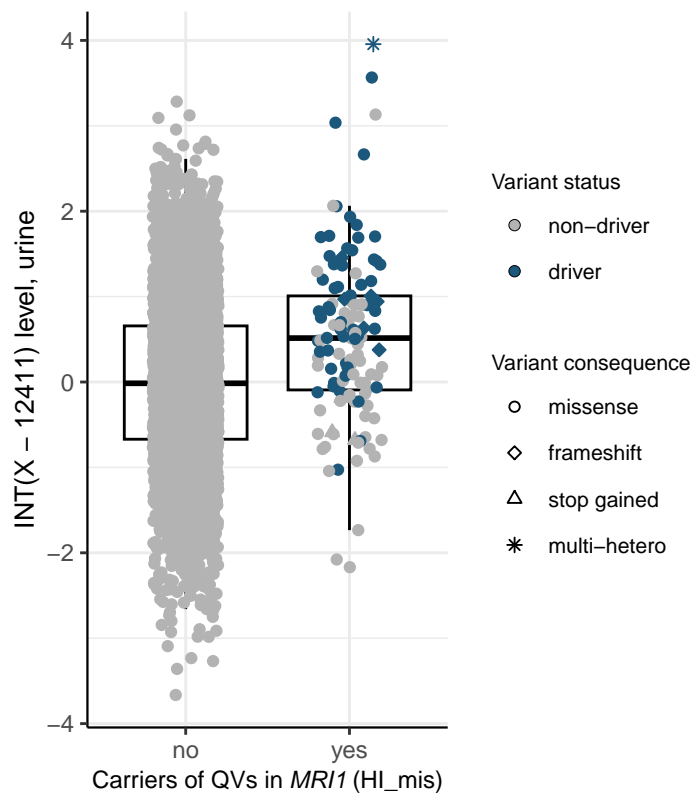
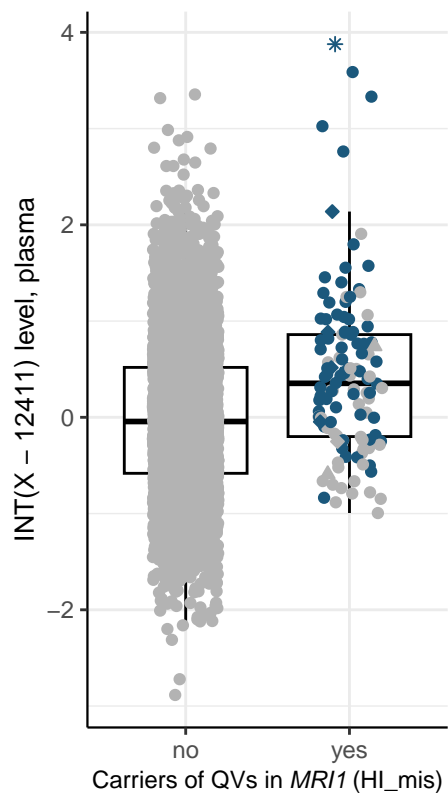
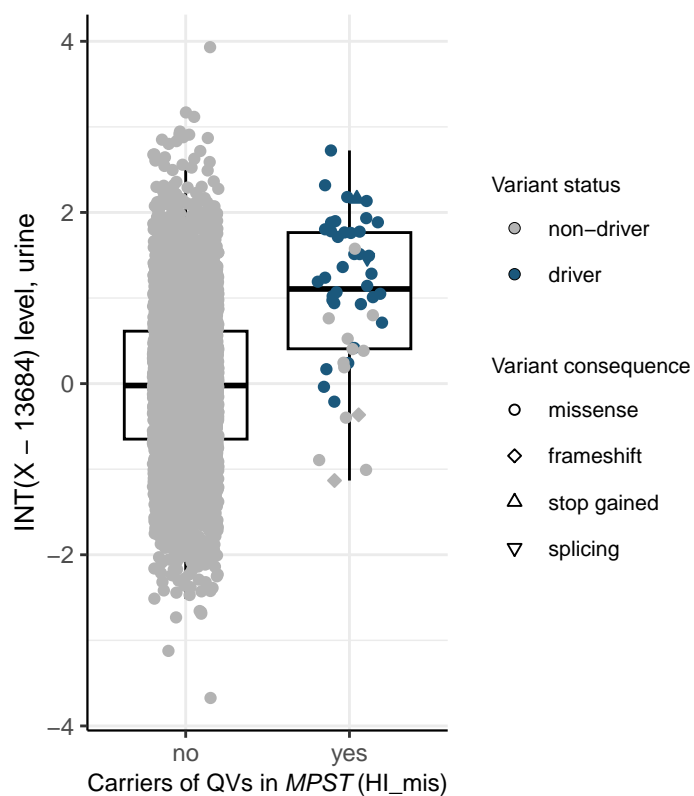
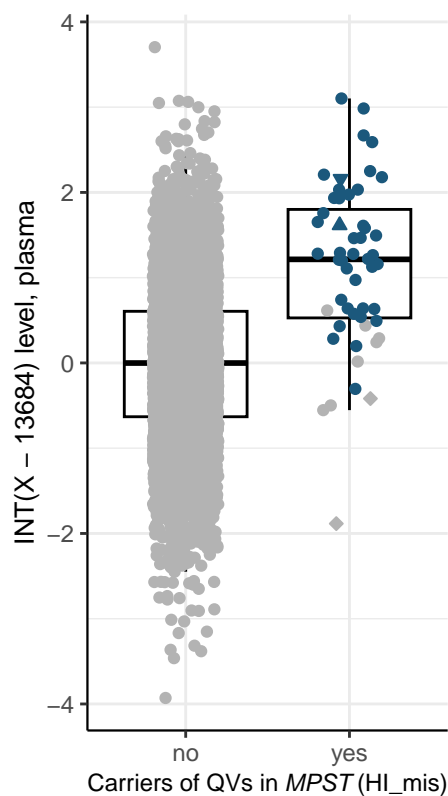
- non-driver
- driver

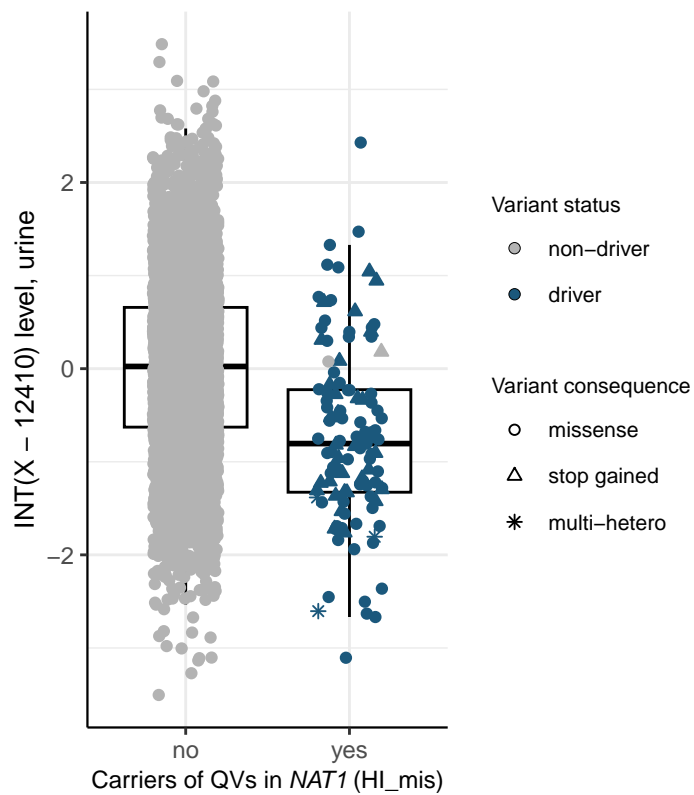
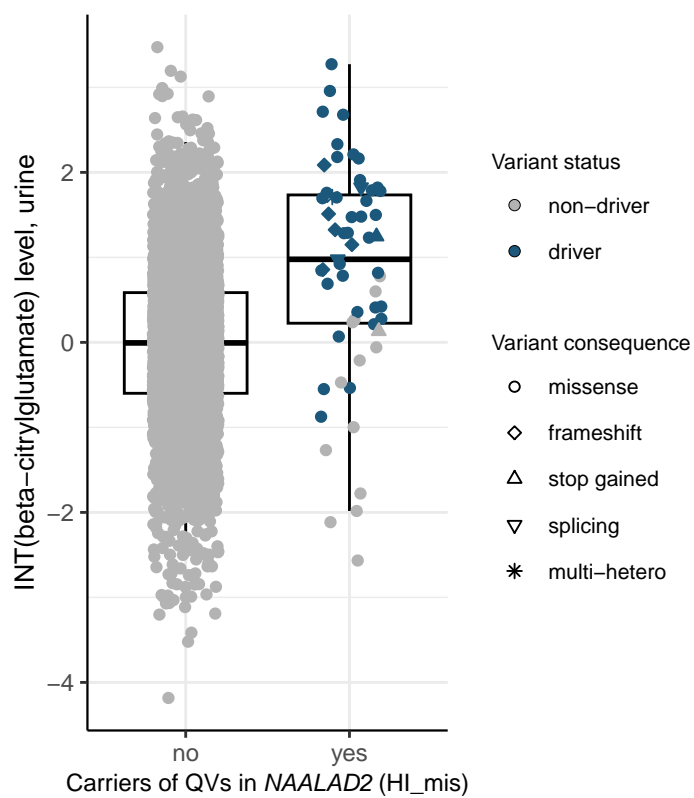
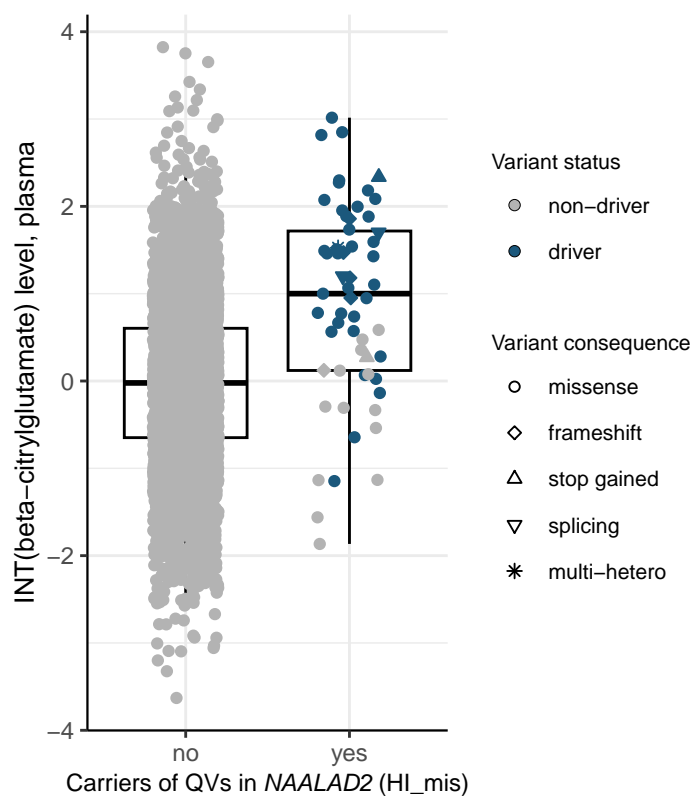
Variant consequence

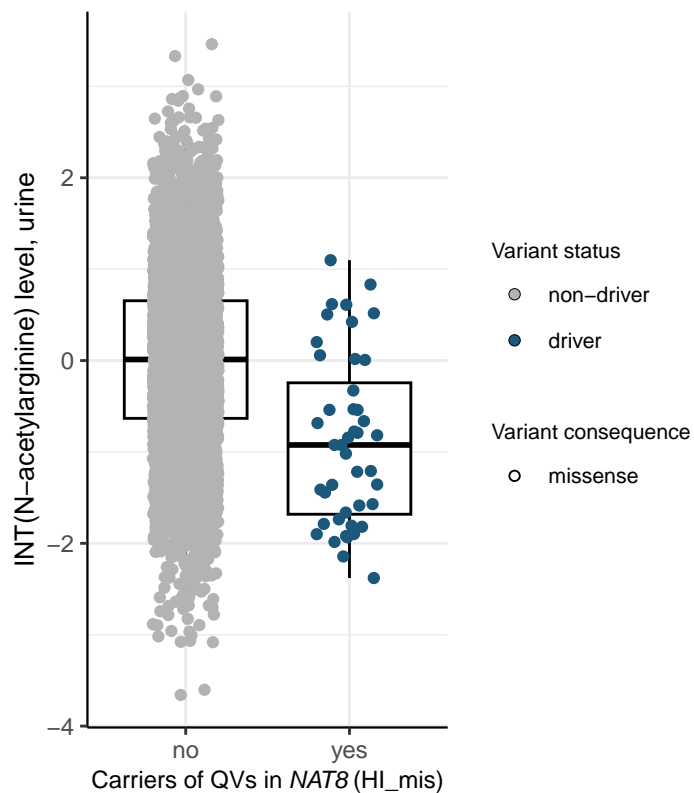
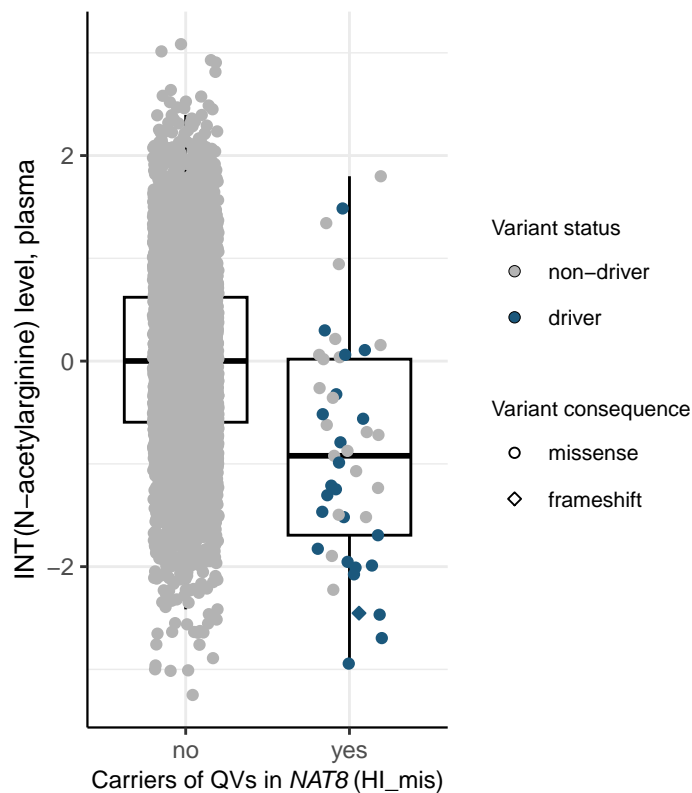
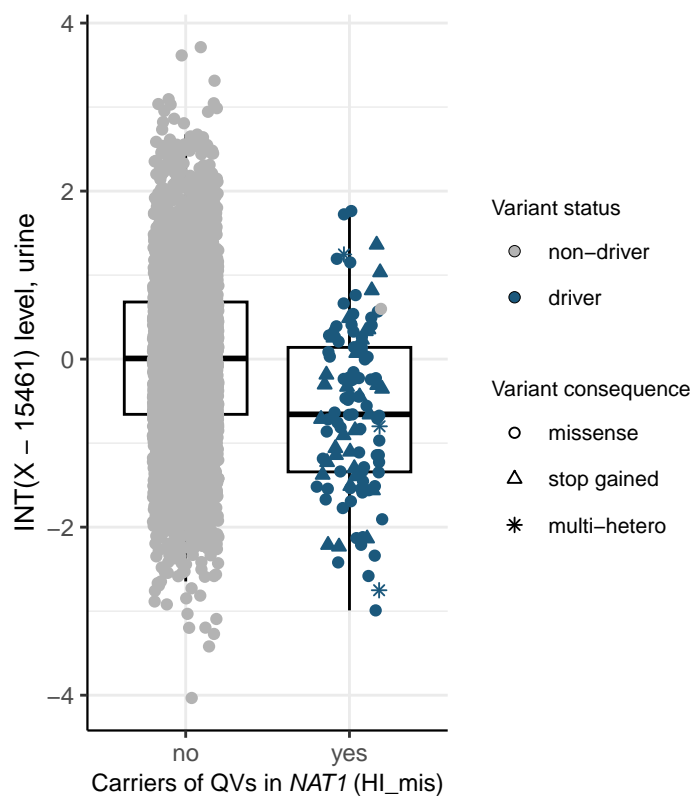
- missense
- frameshift
- multi-hetero

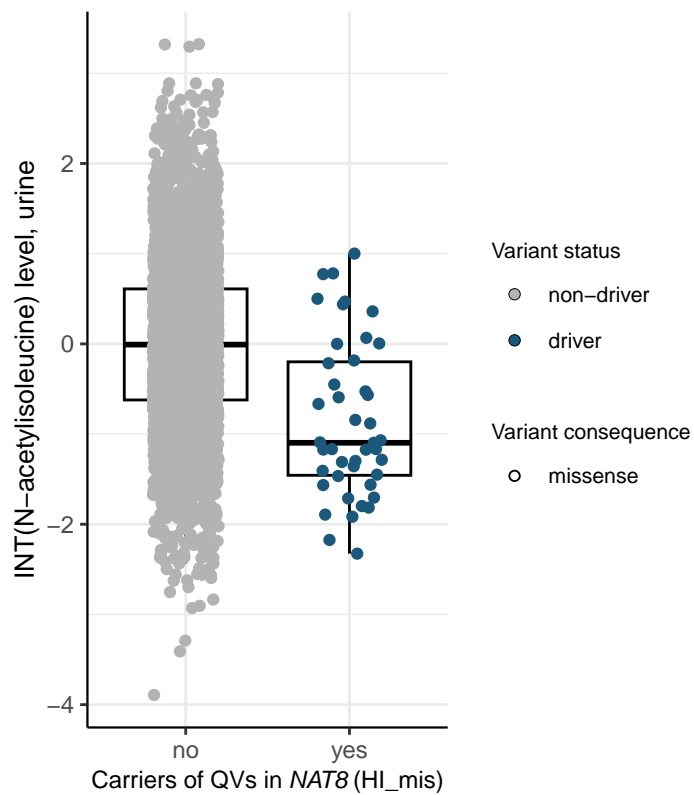
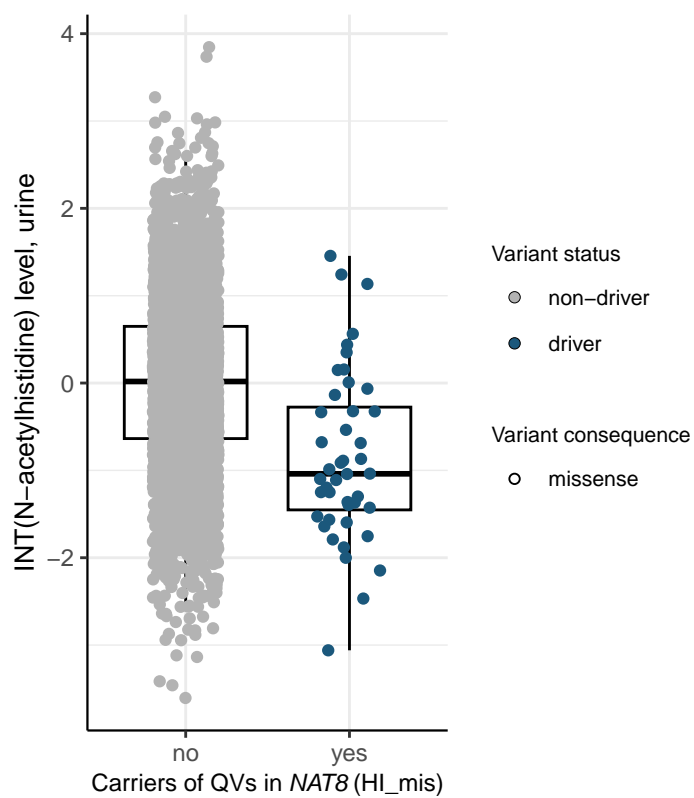


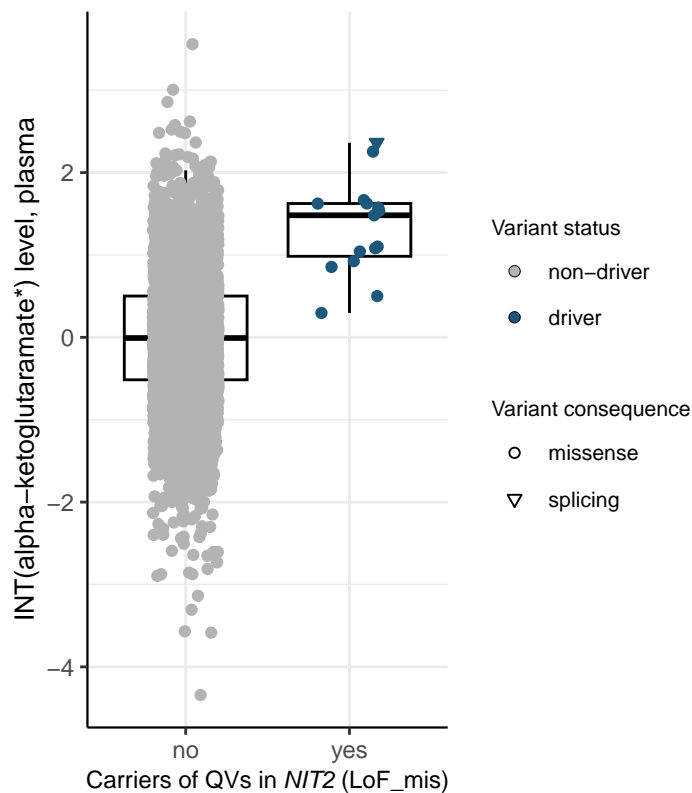
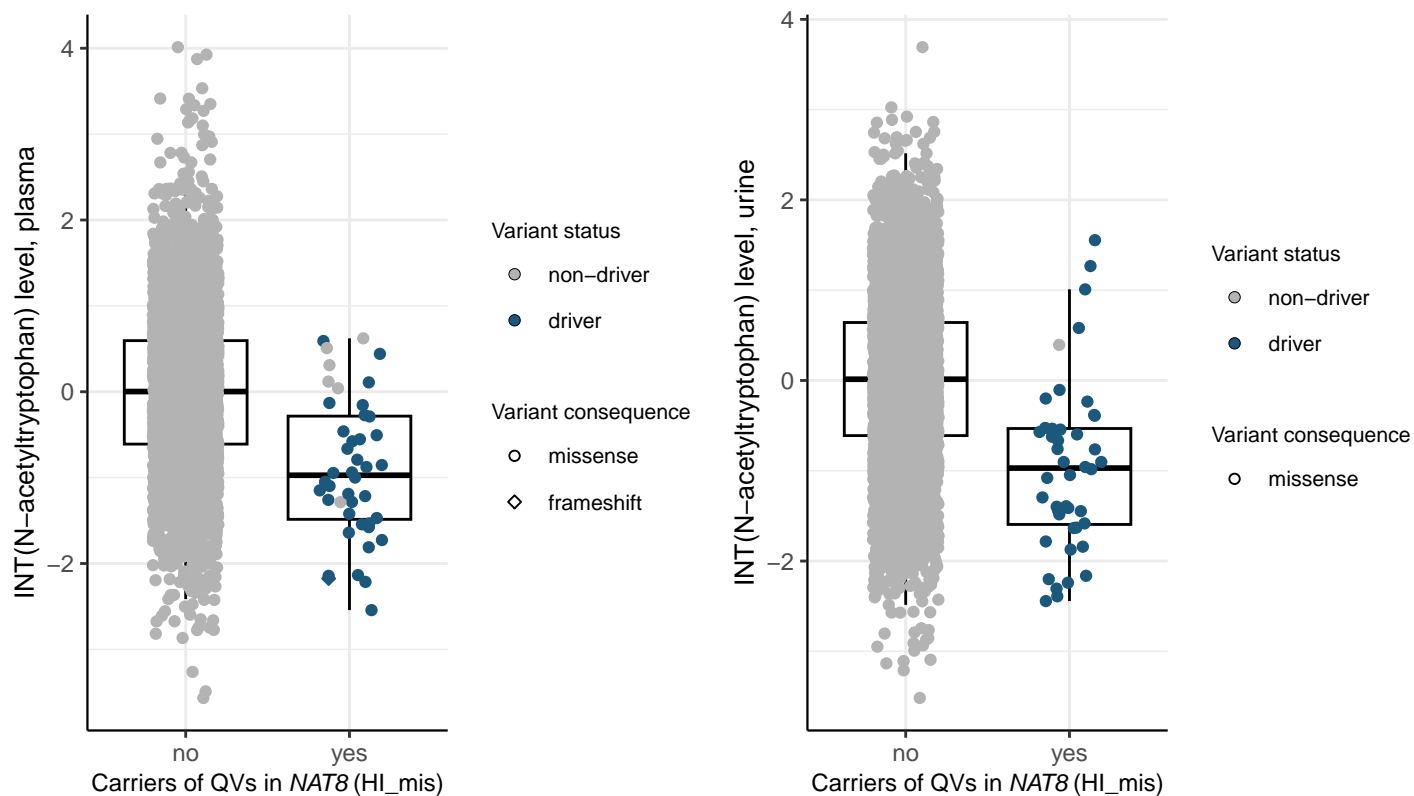


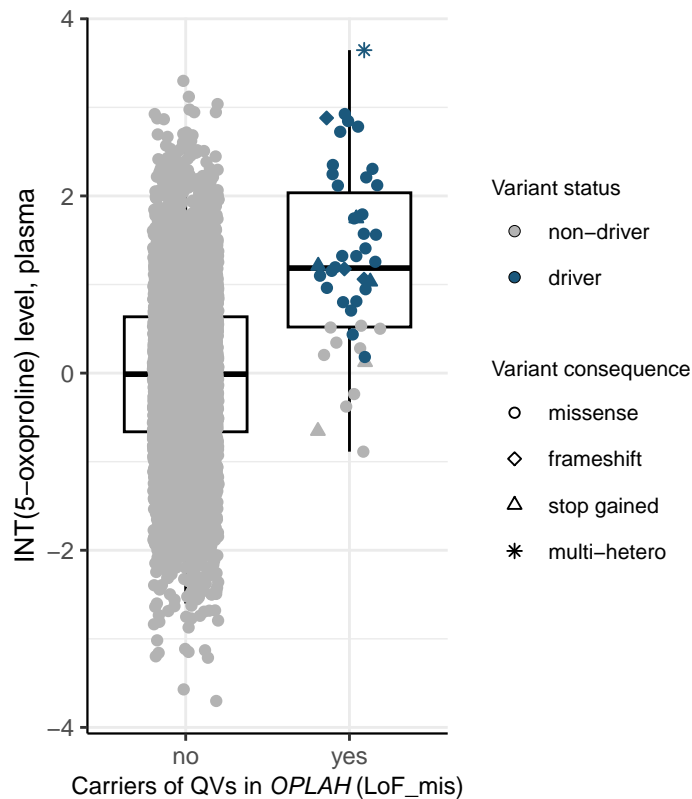
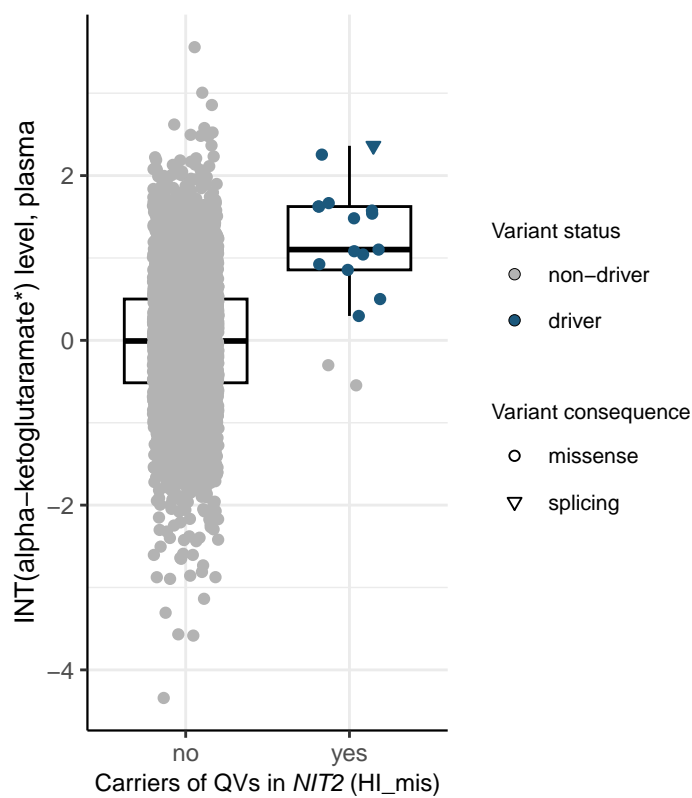


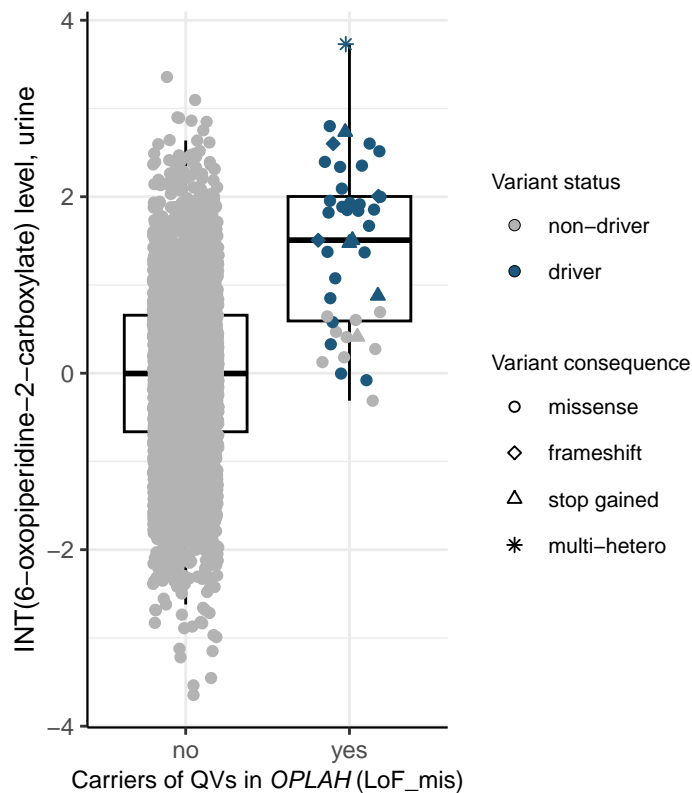
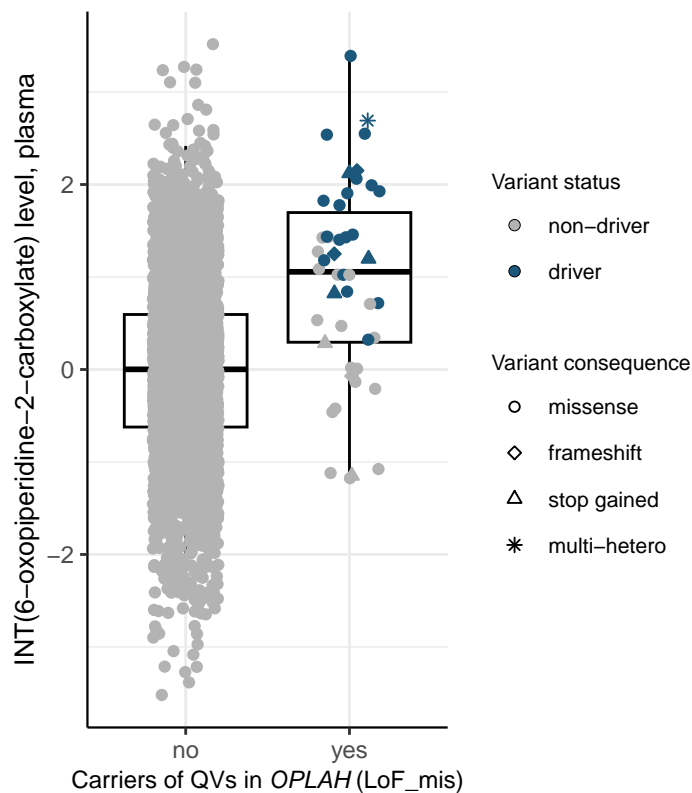
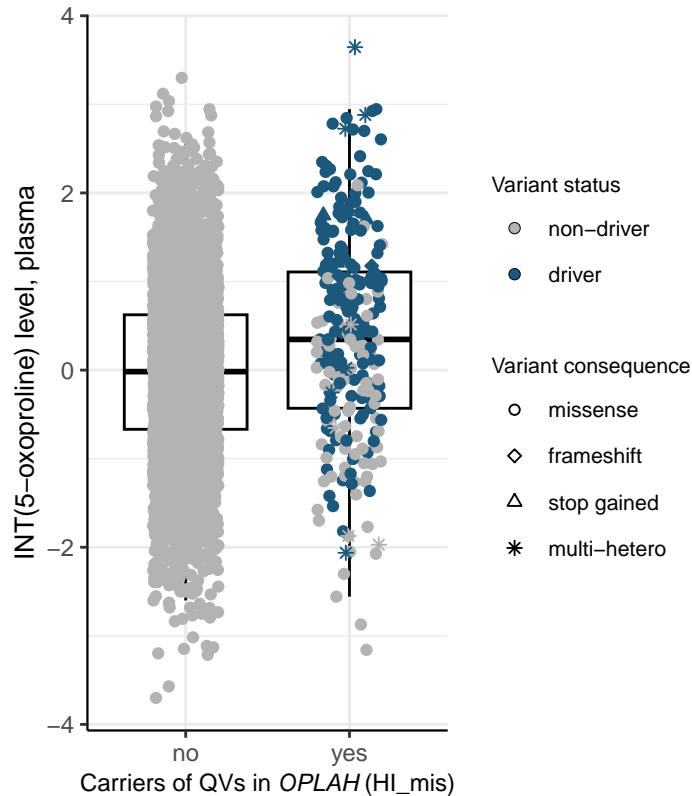


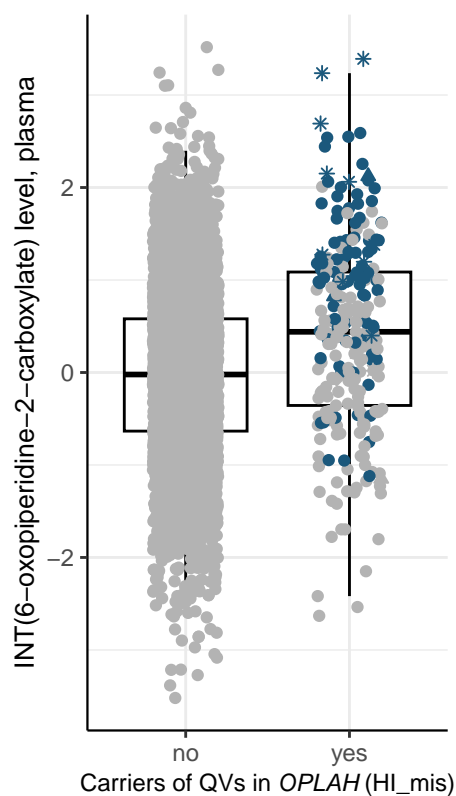










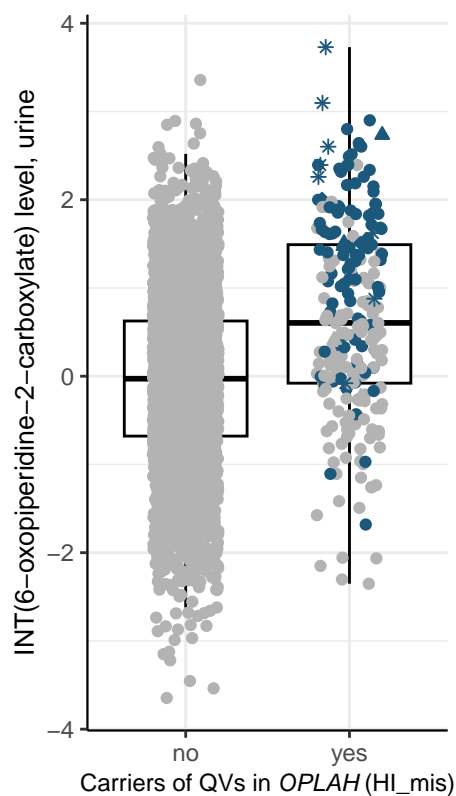


Variant status

- non-driver
- driver

Variant consequence

- missense
- frameshift
- stop gained
- multi-hetero

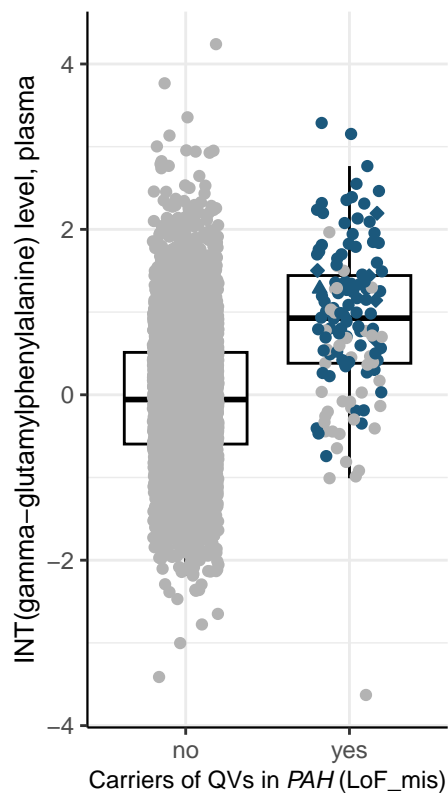


Variant status

- non-driver
- driver

Variant consequence

- missense
- frameshift
- stop gained
- multi-hetero

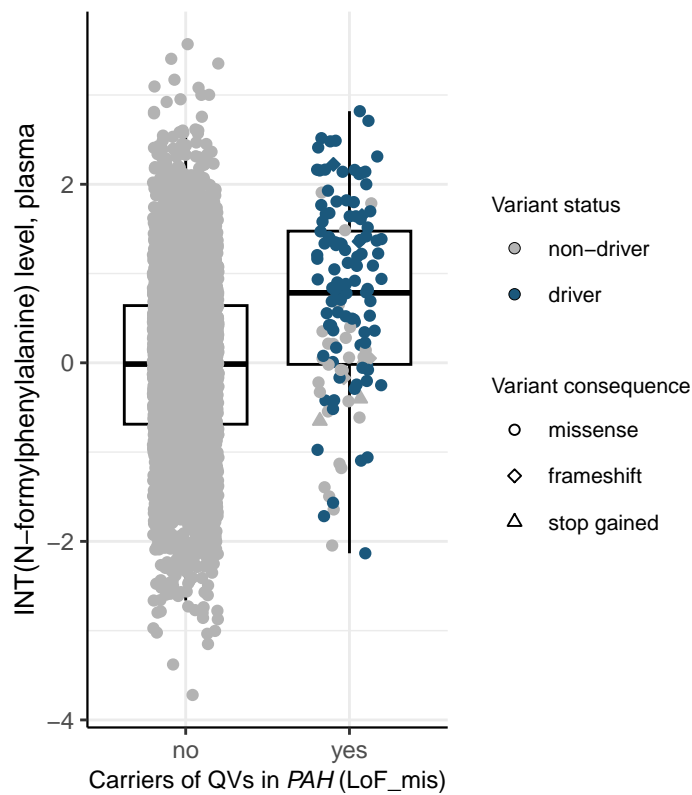
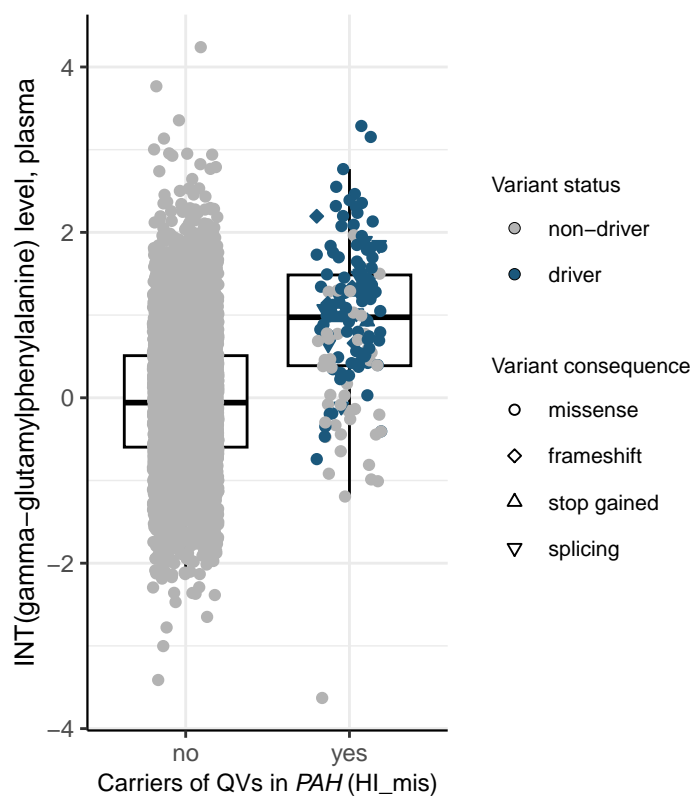


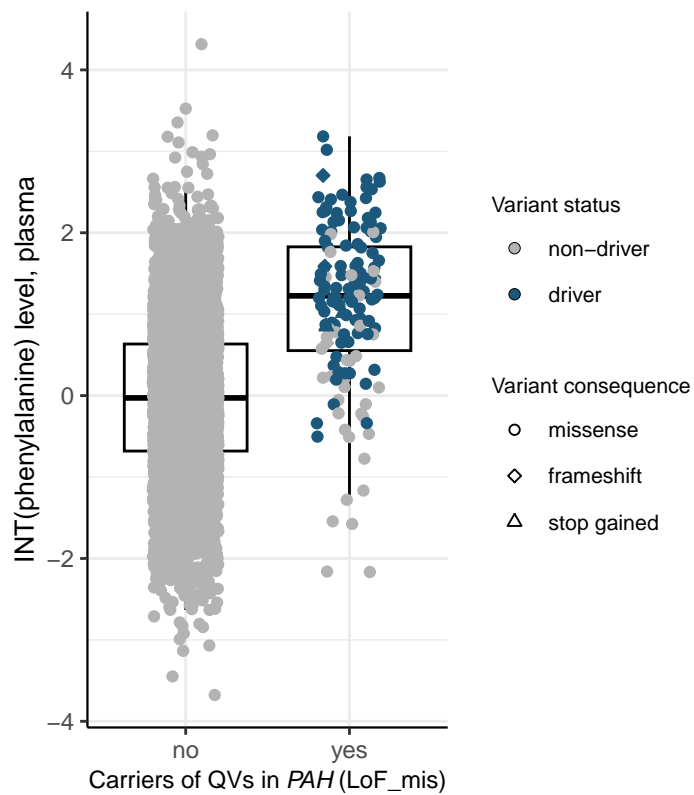
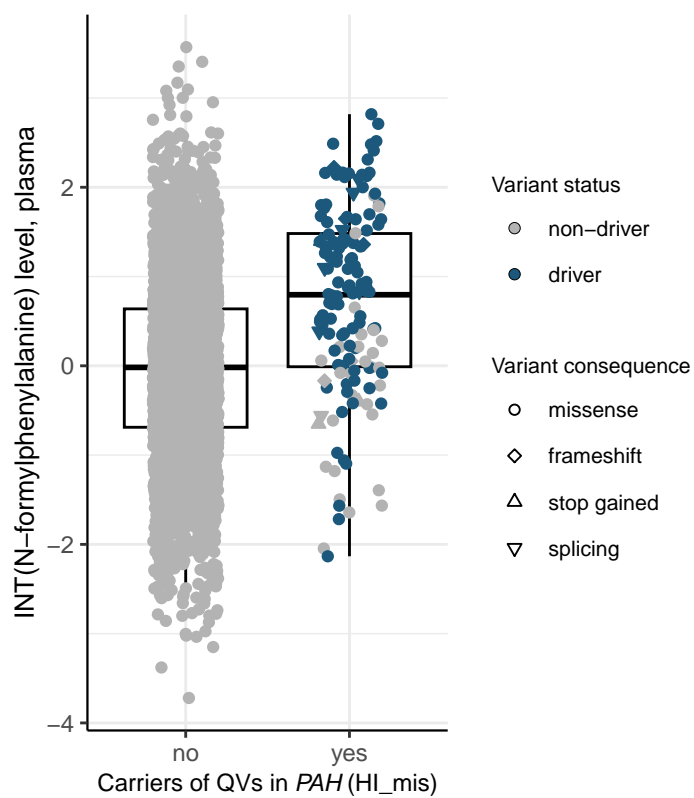
Variant status

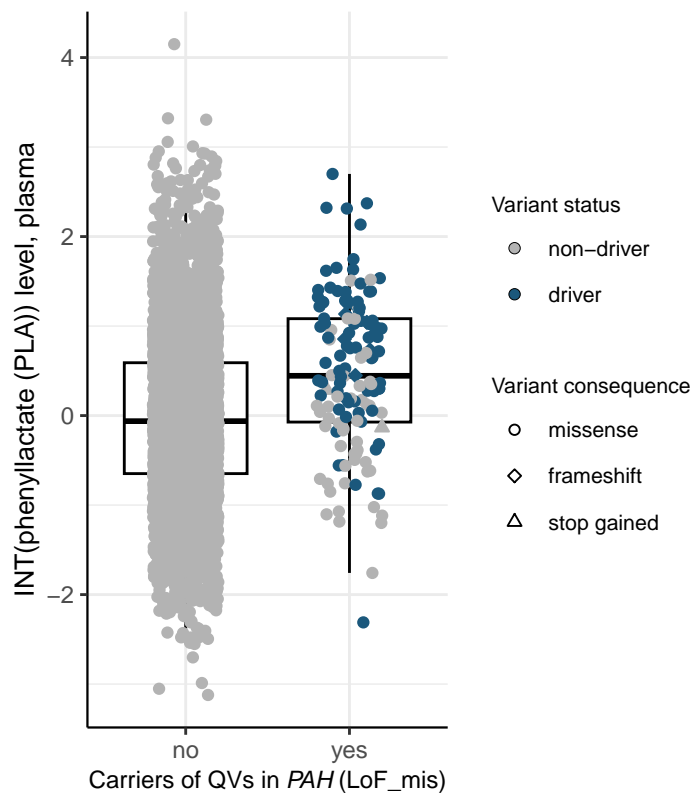
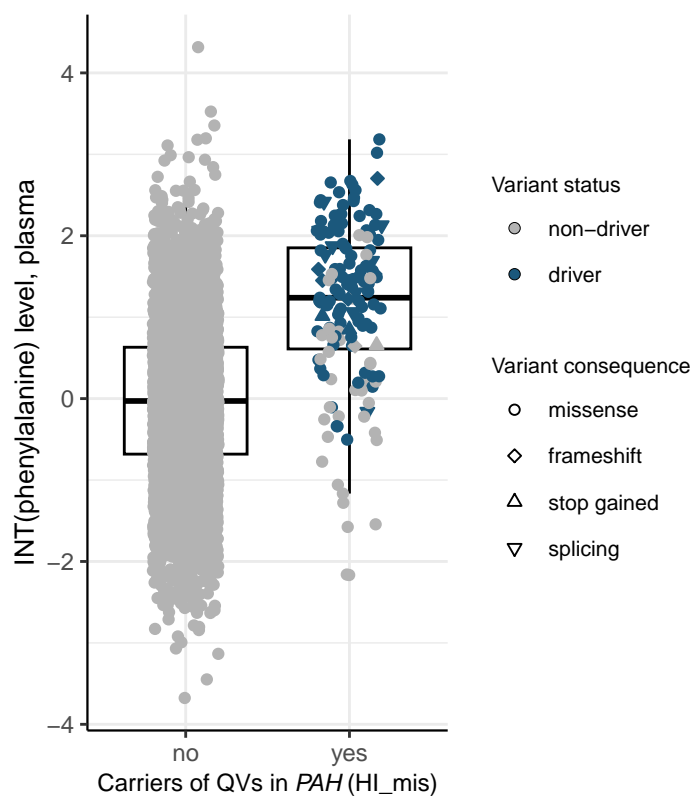
- non-driver
- driver

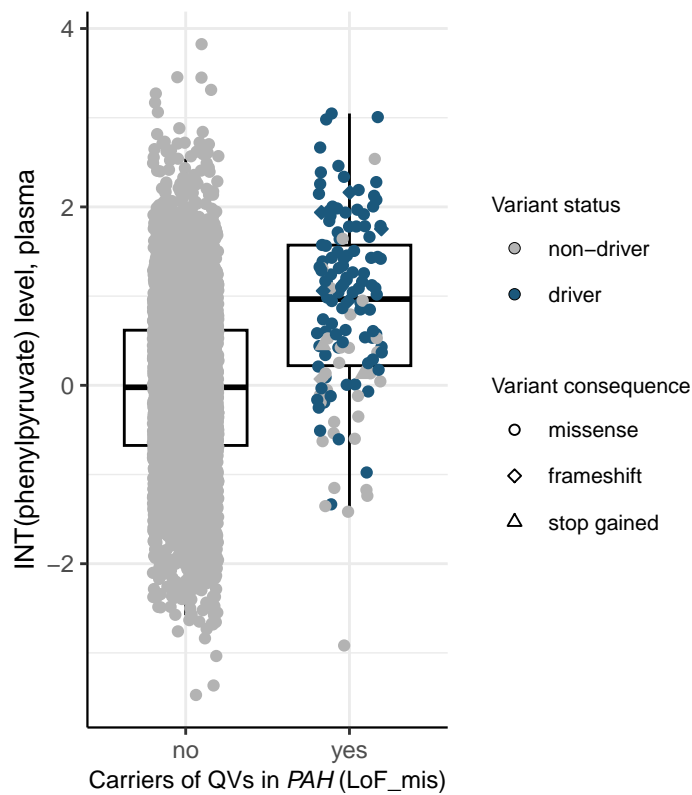
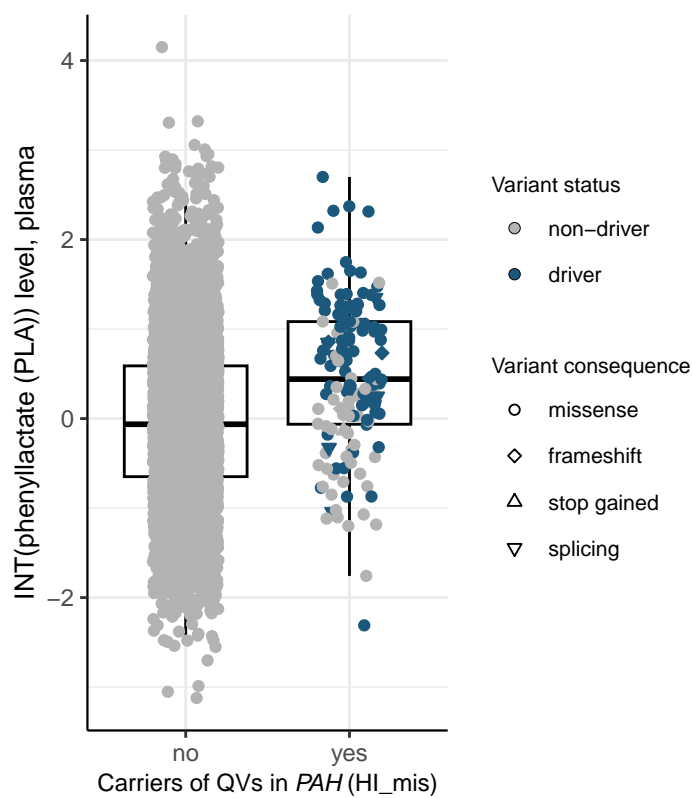
Variant consequence

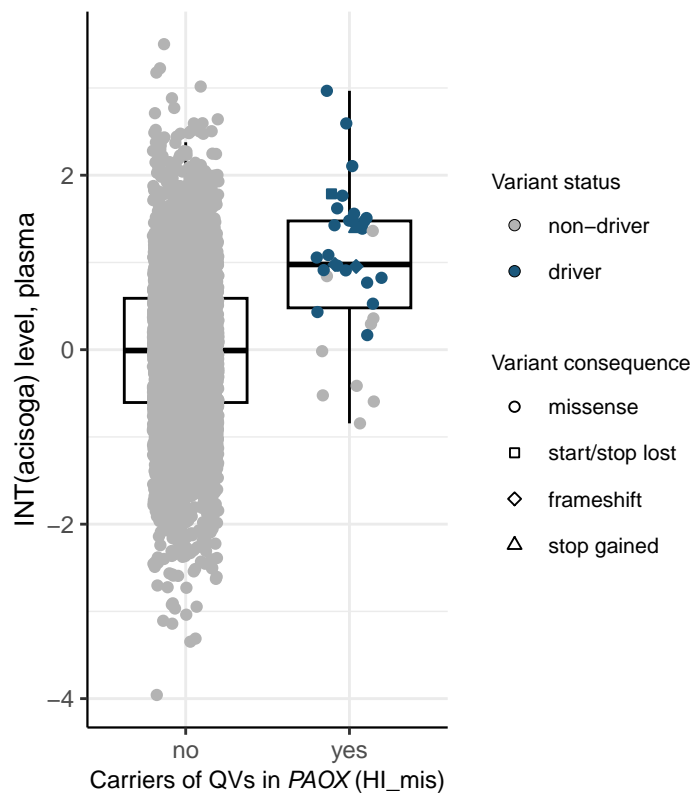
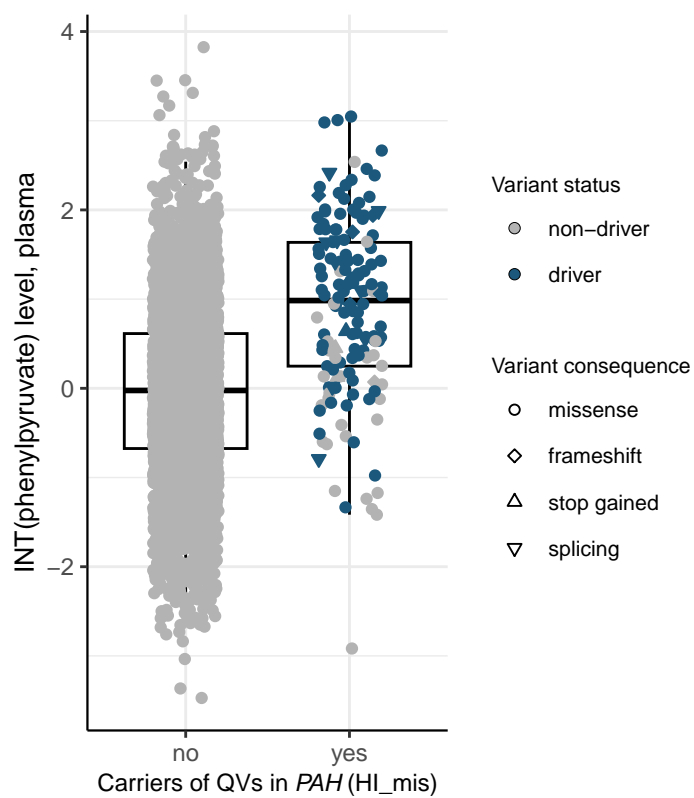
- missense
- frameshift
- stop gained

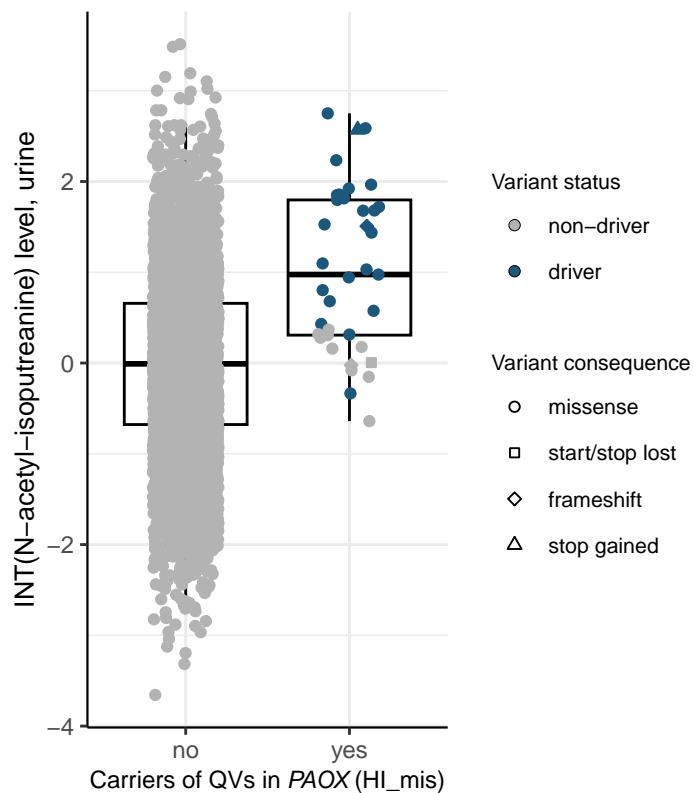
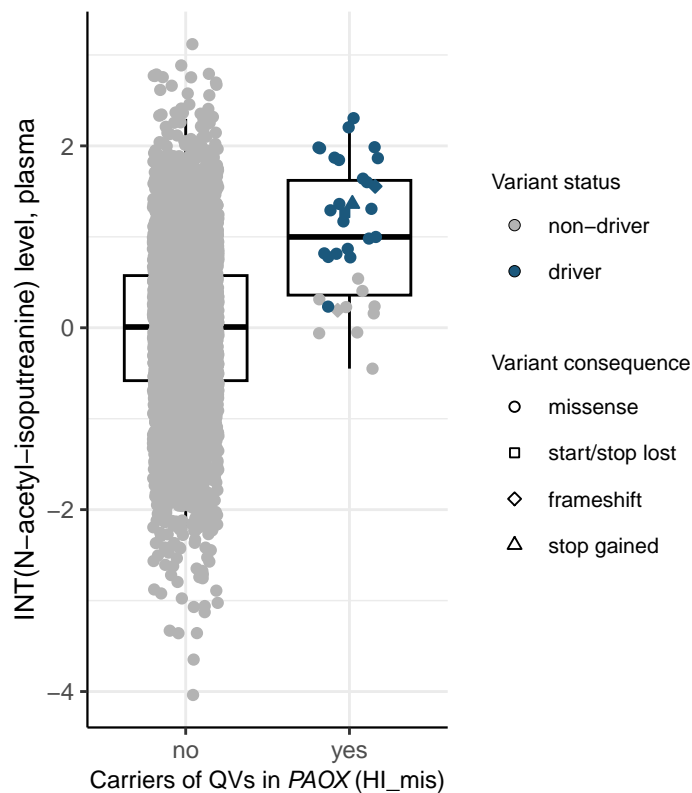
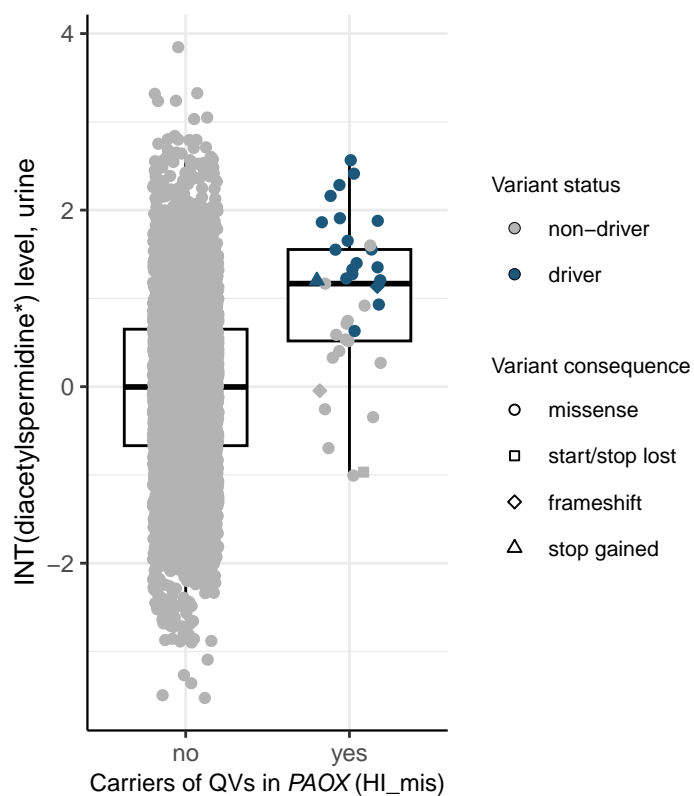


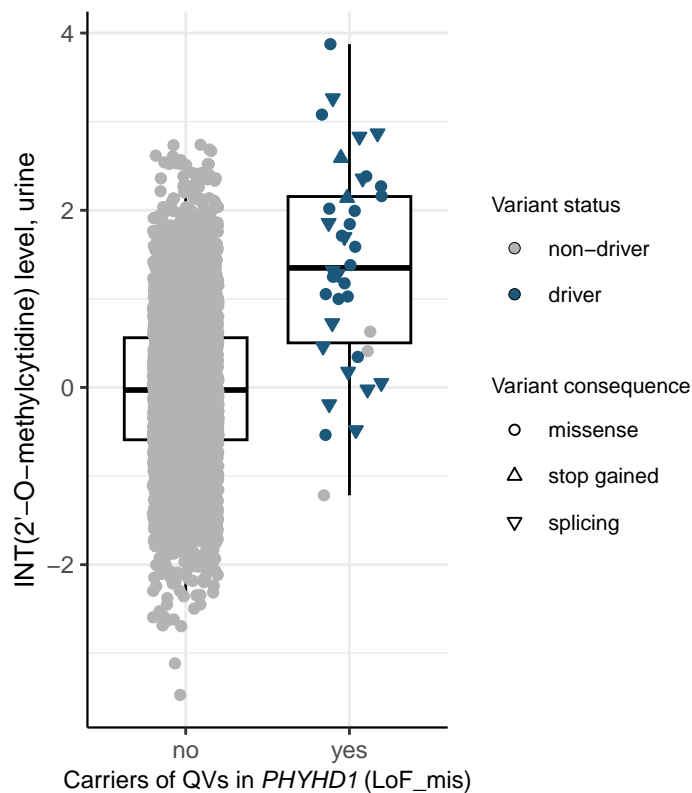
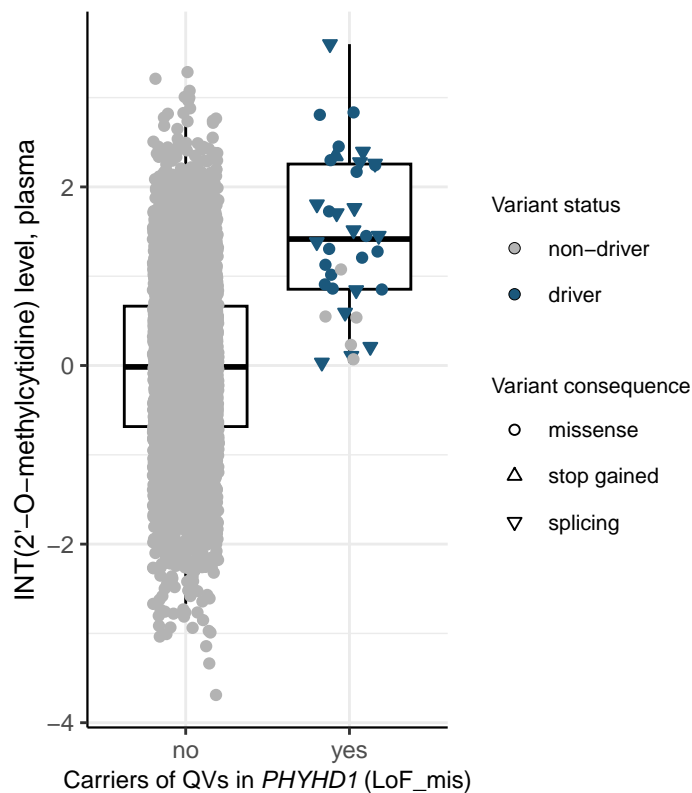
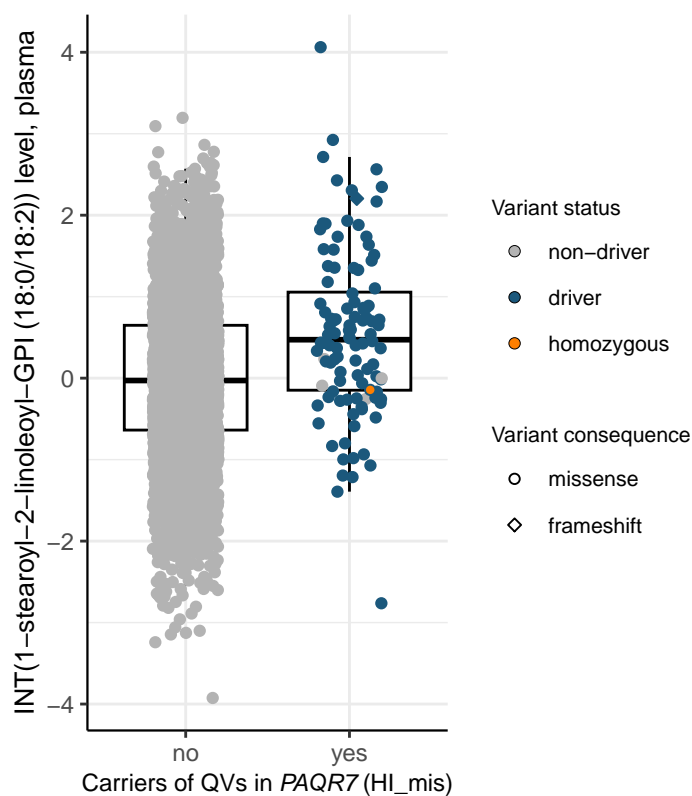


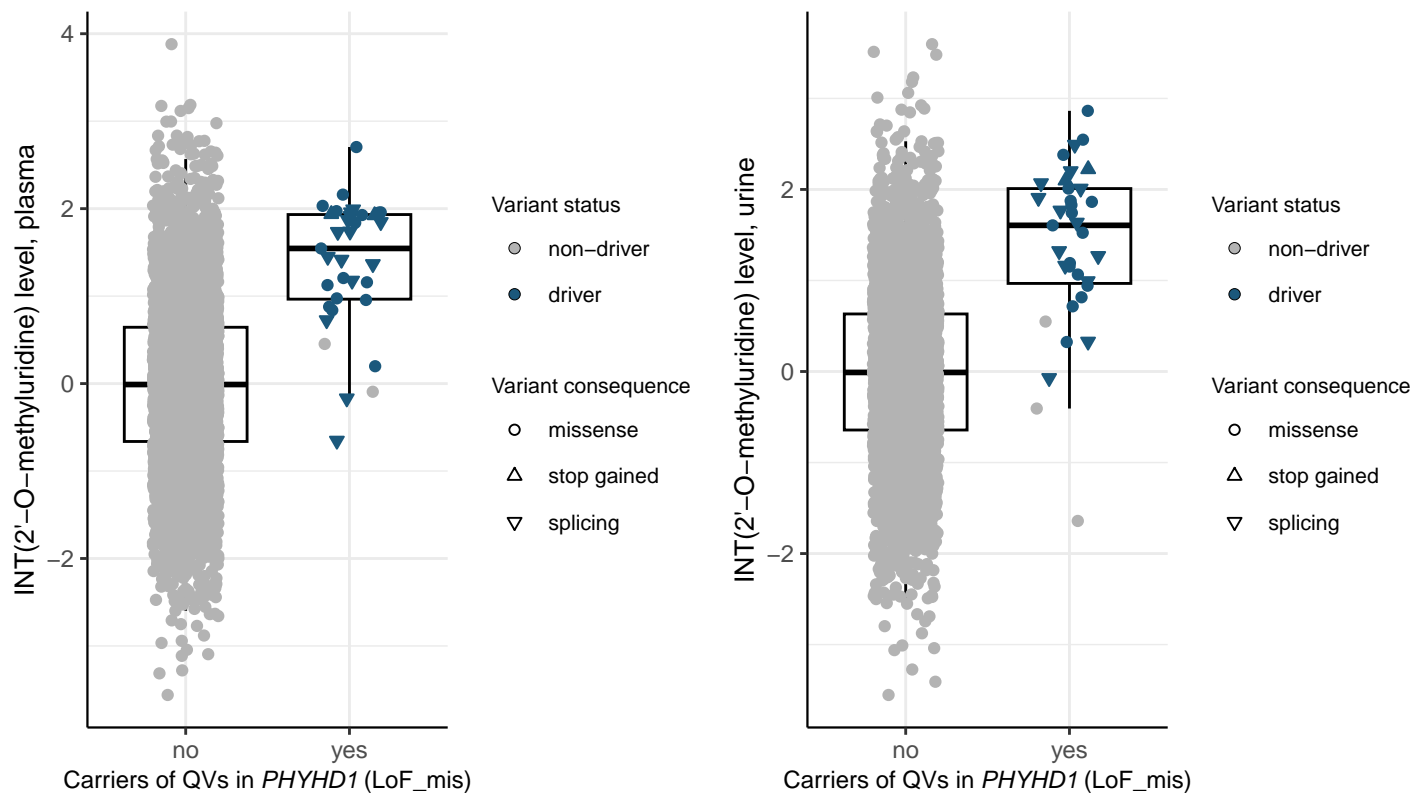
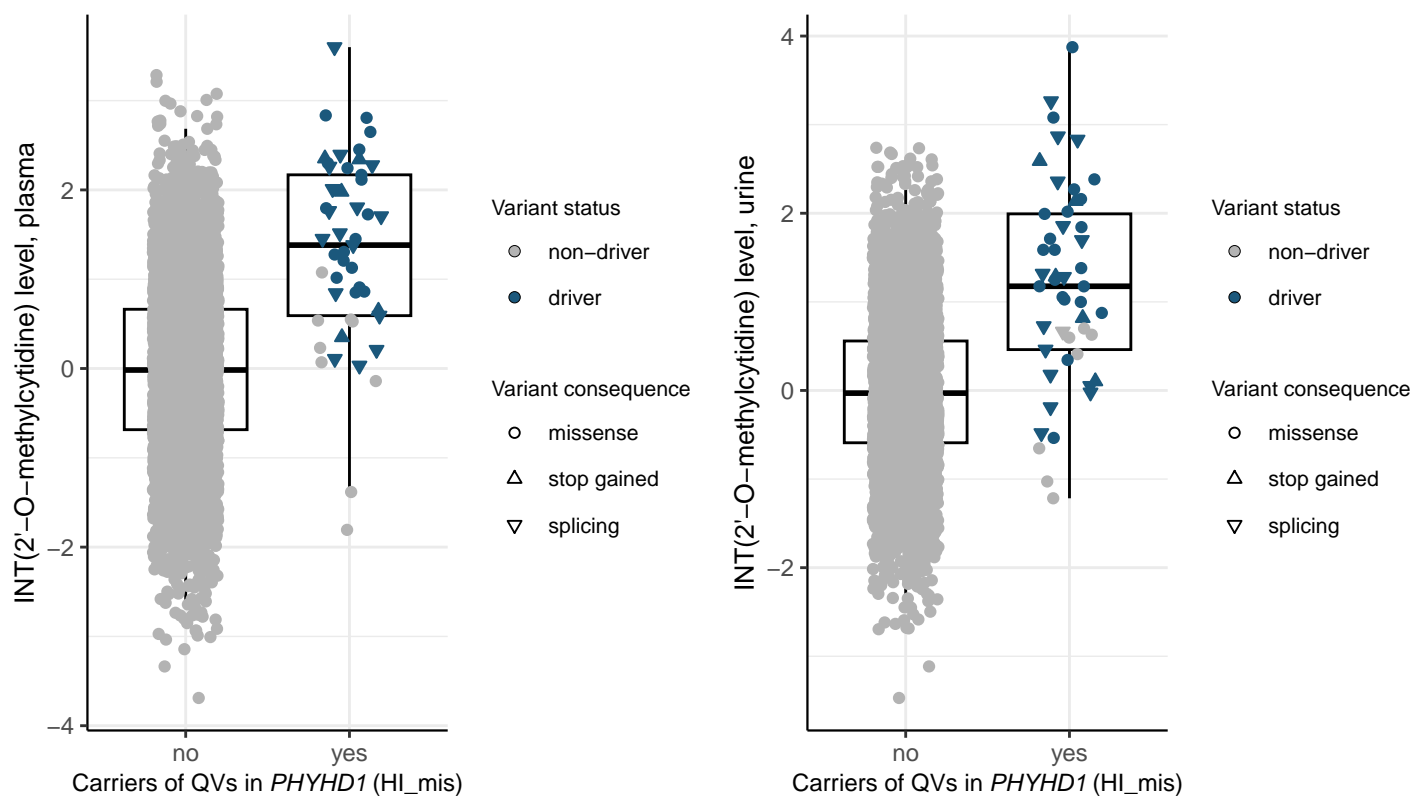


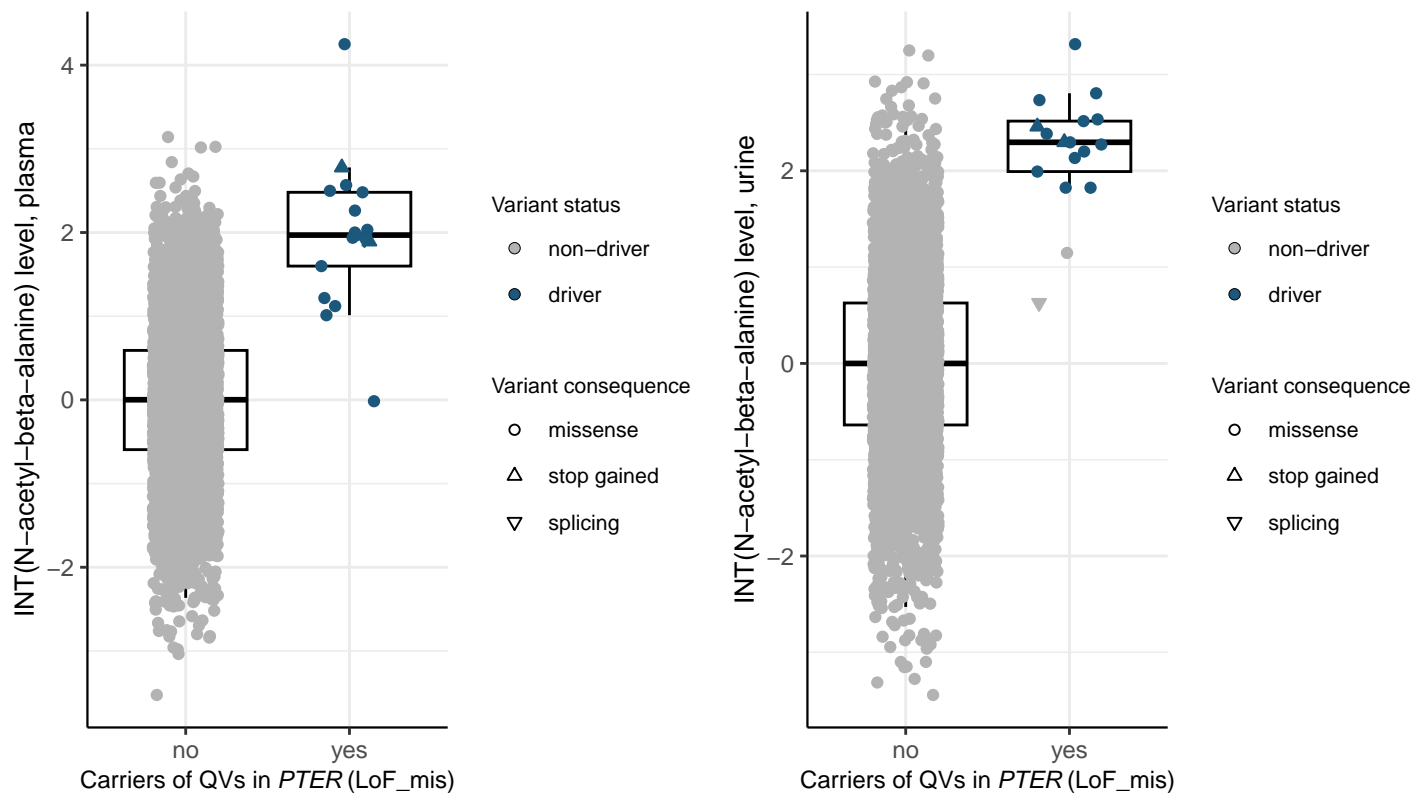
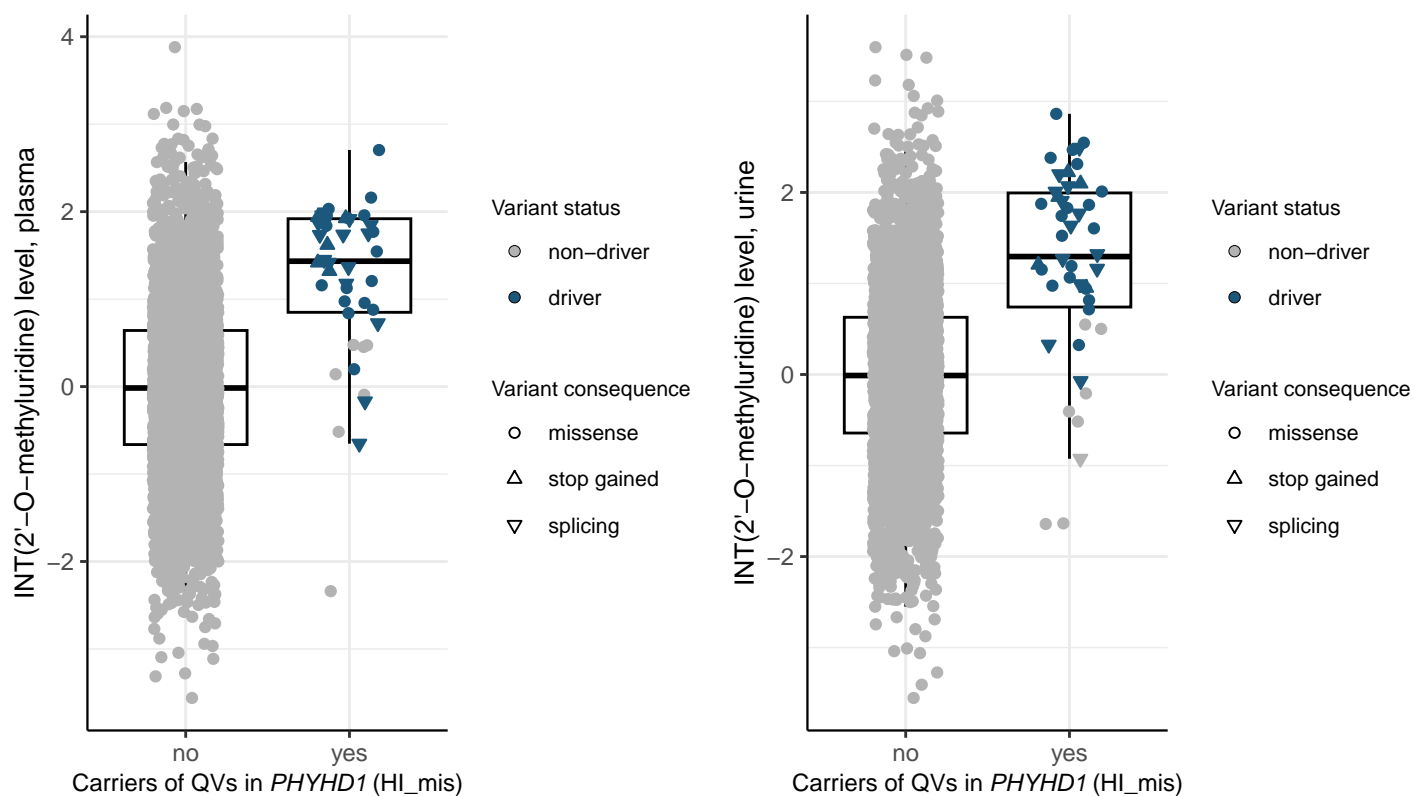


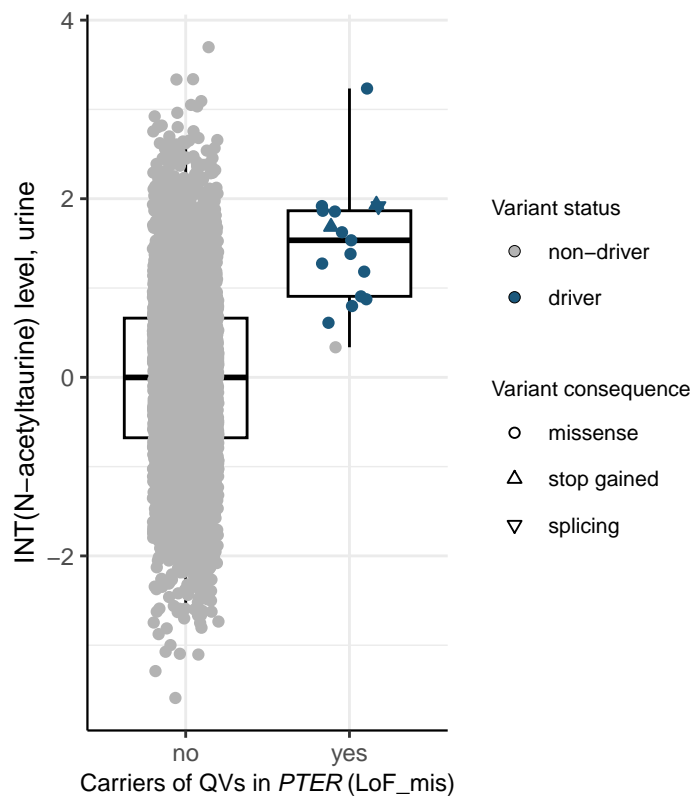
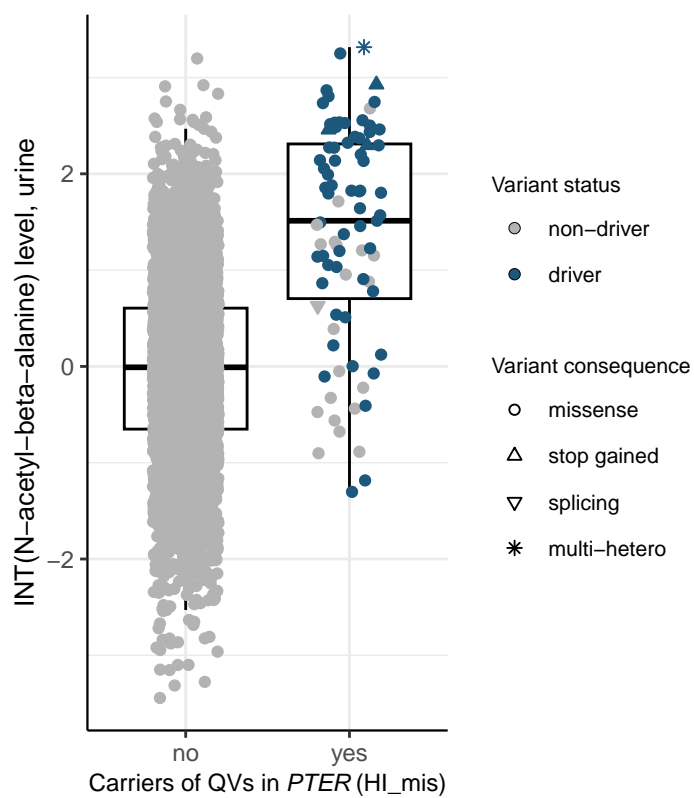
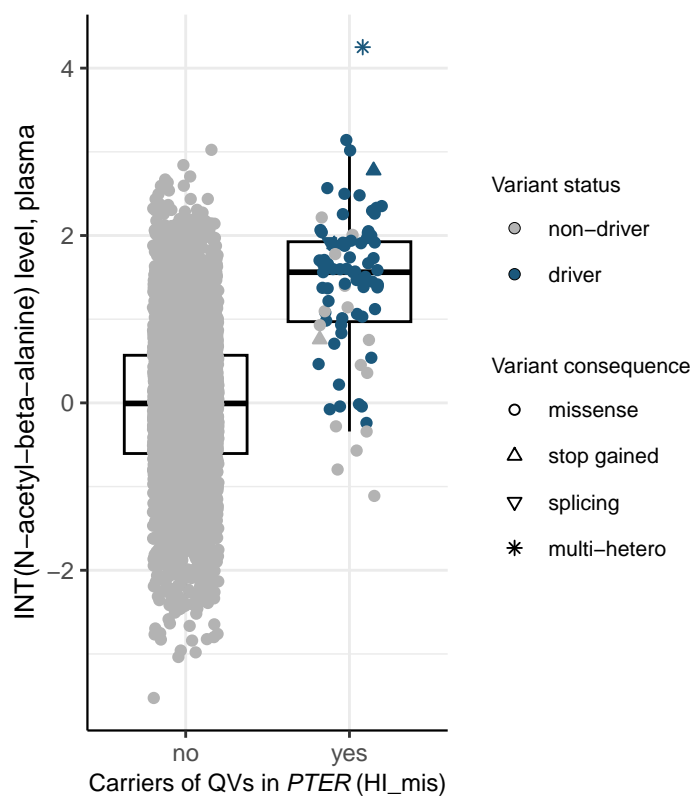


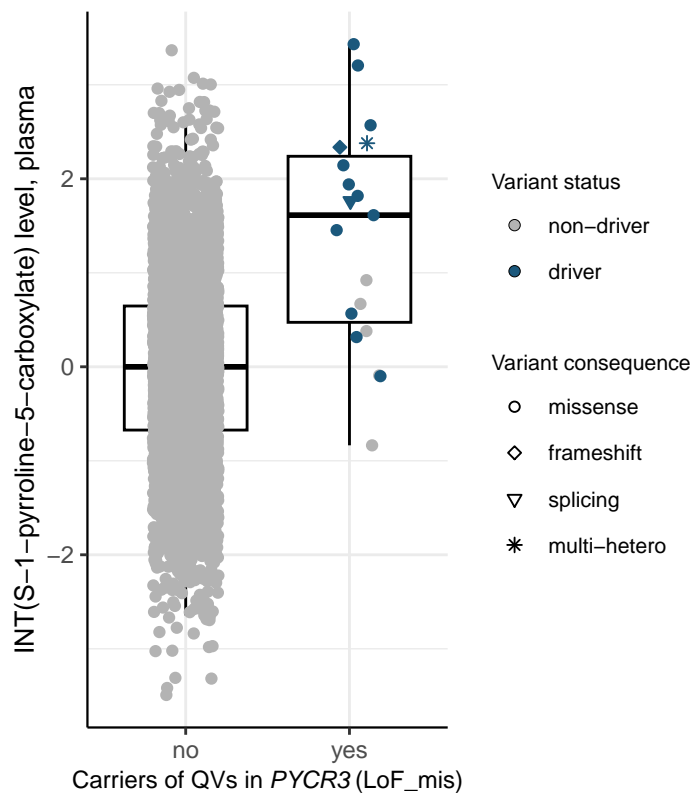
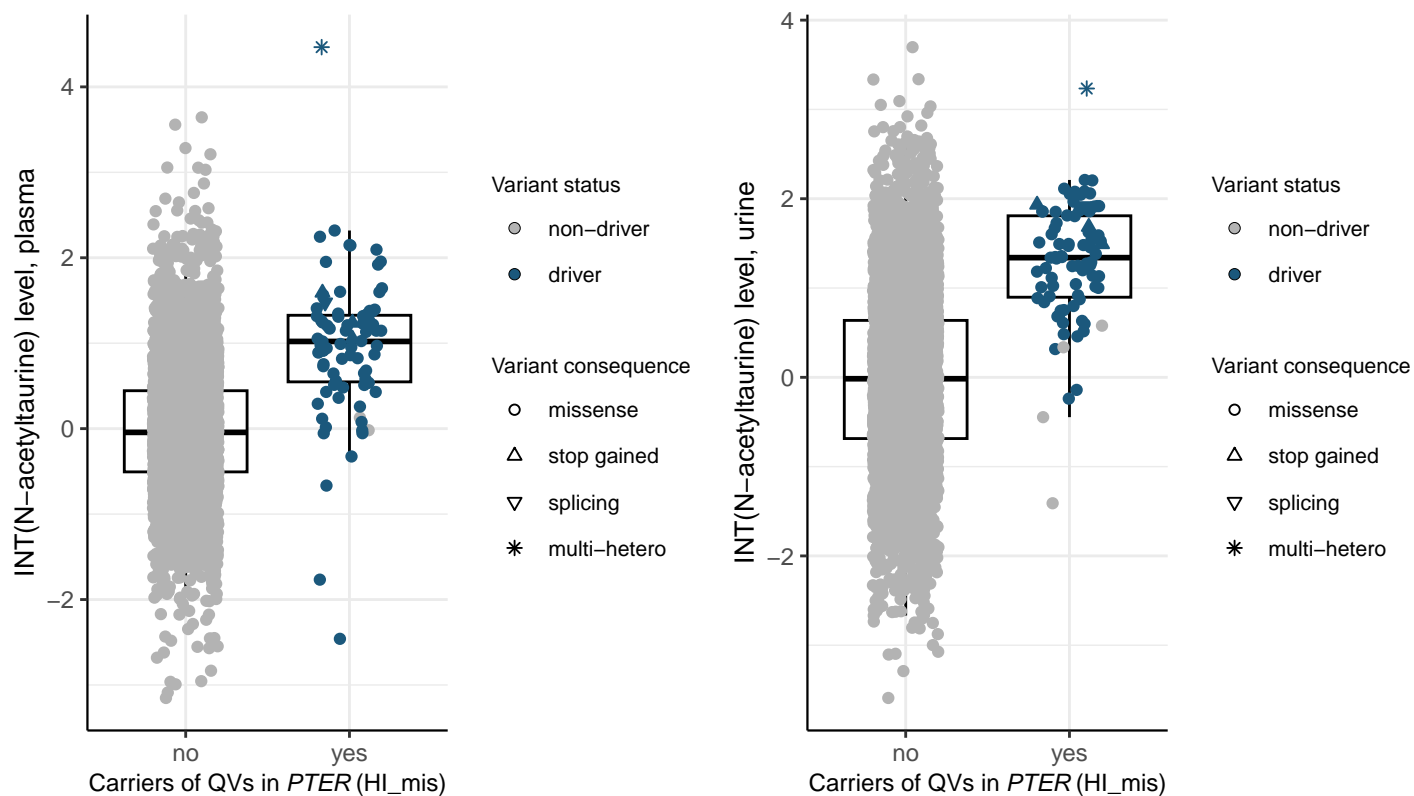


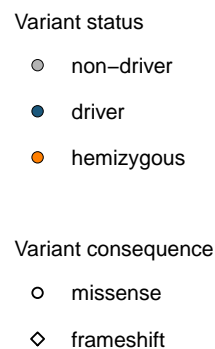
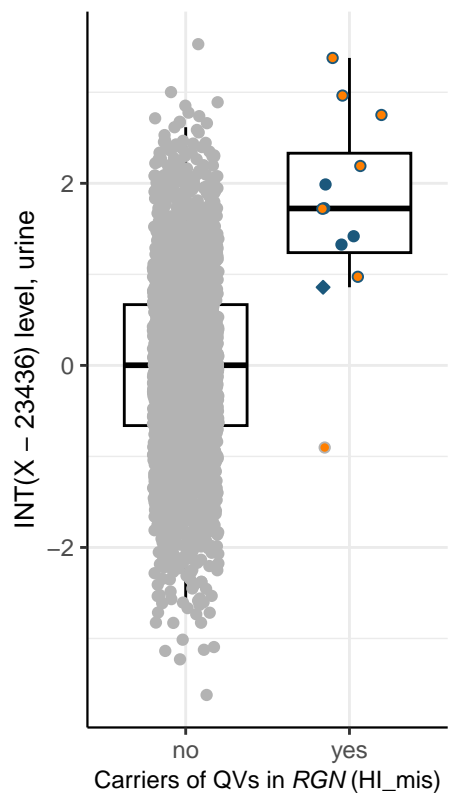
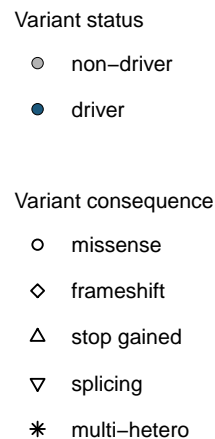
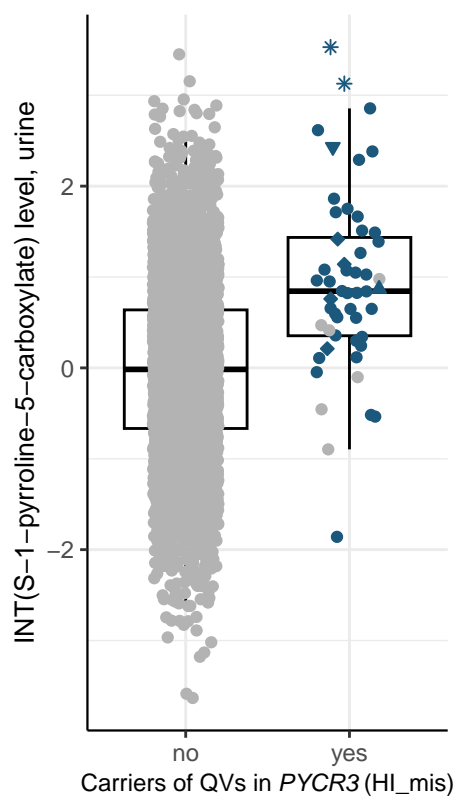
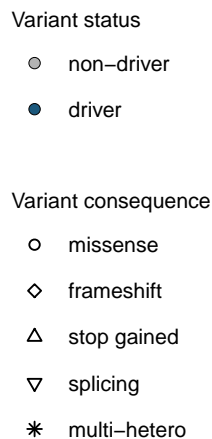
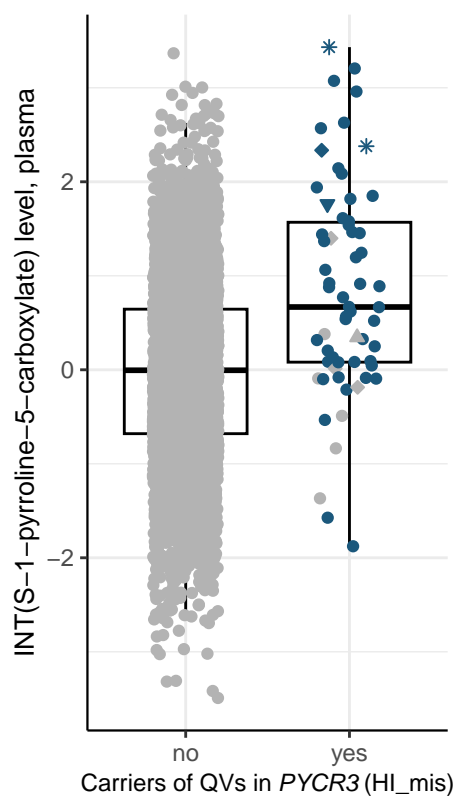


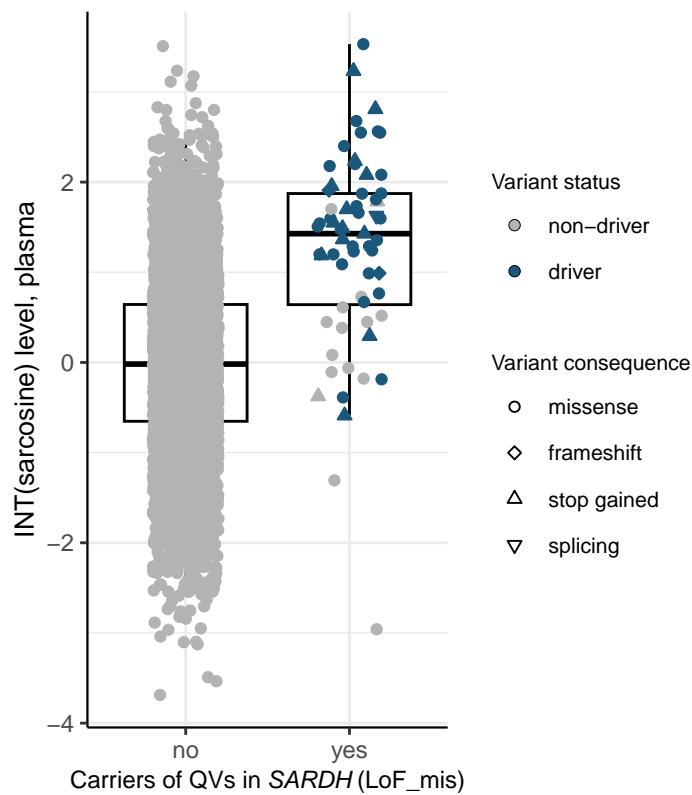
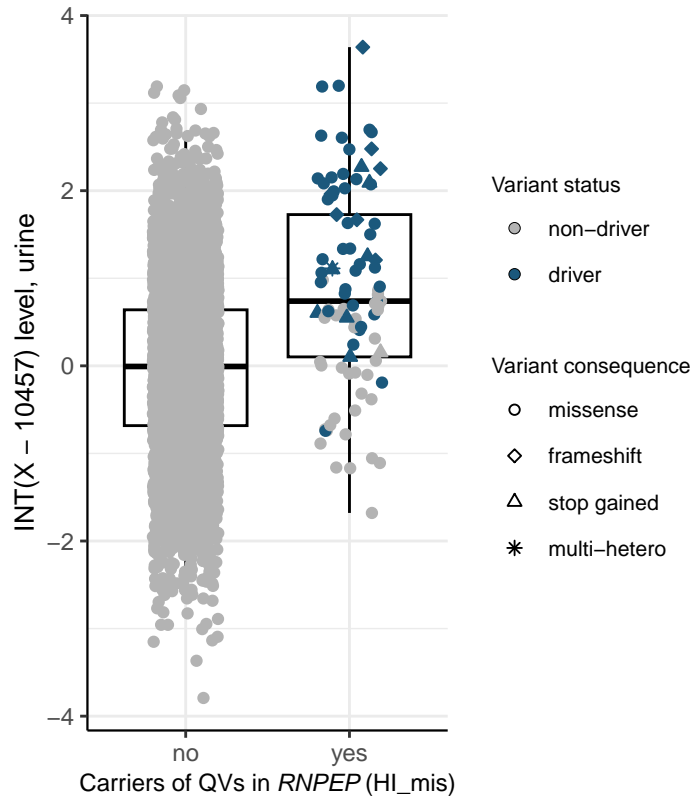


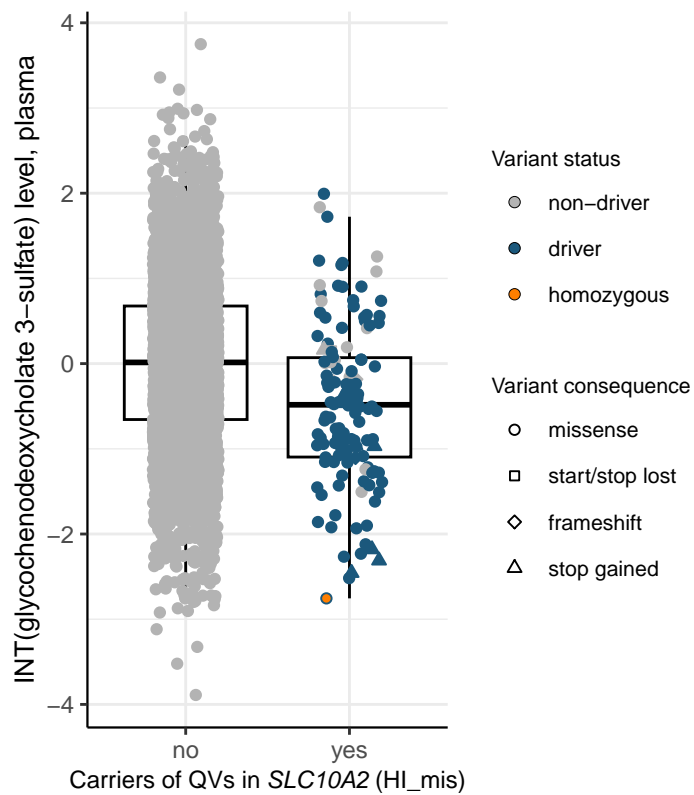
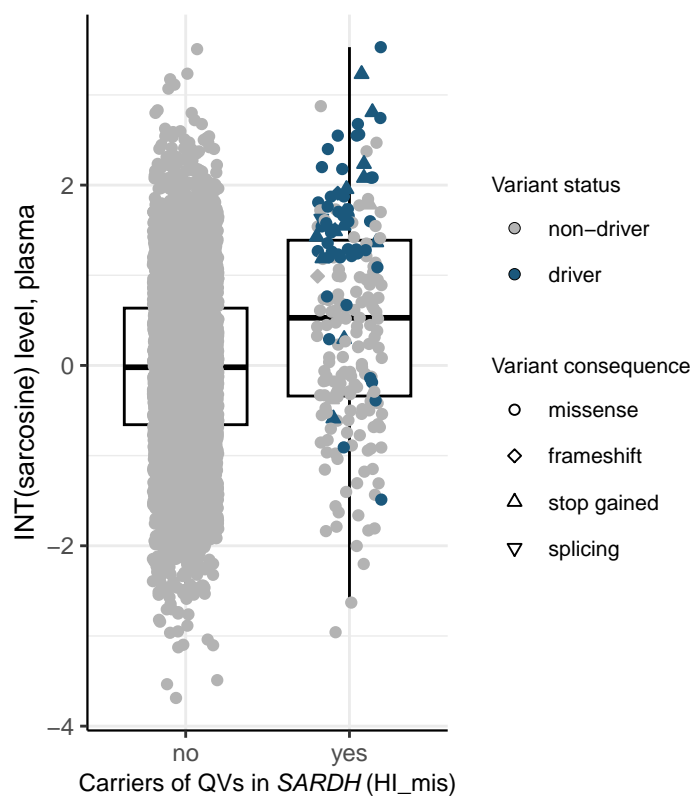


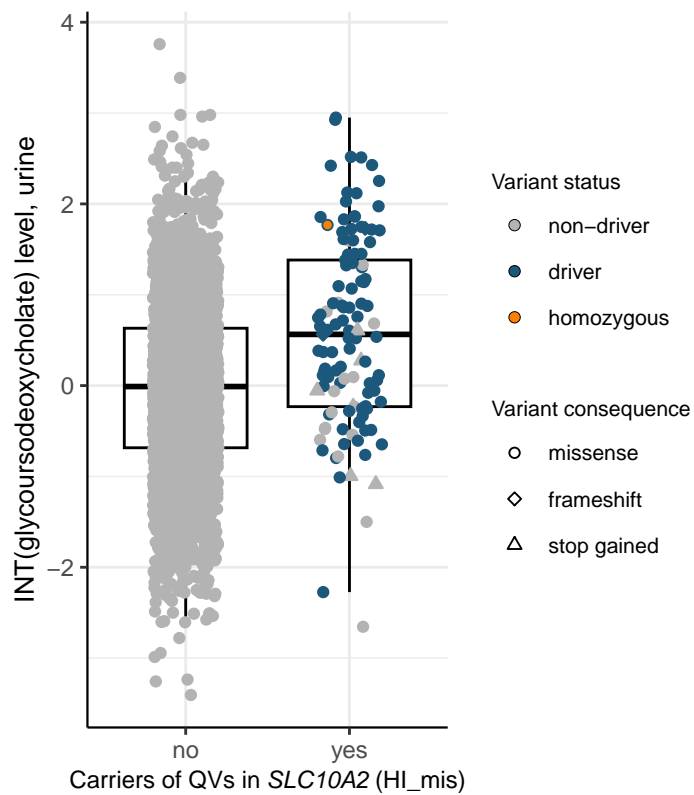
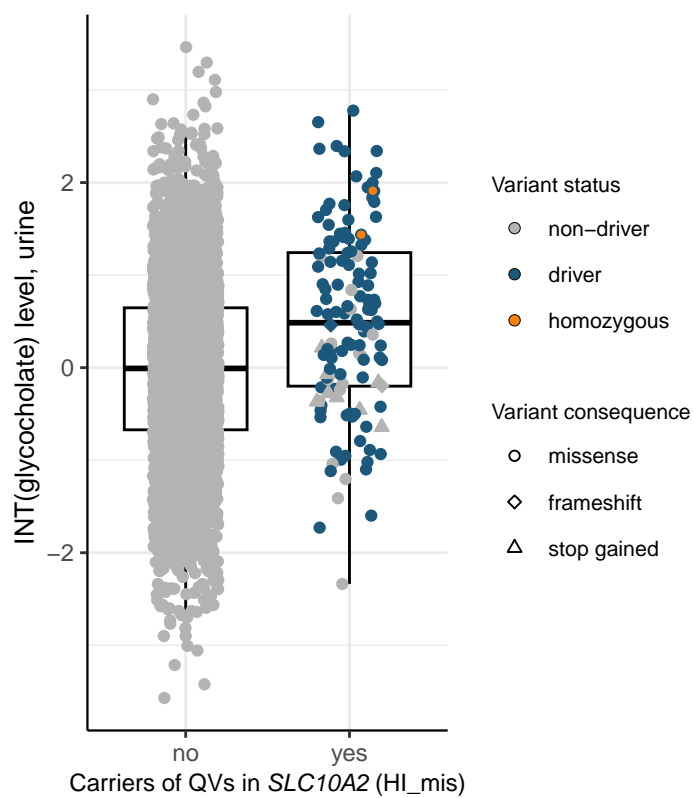


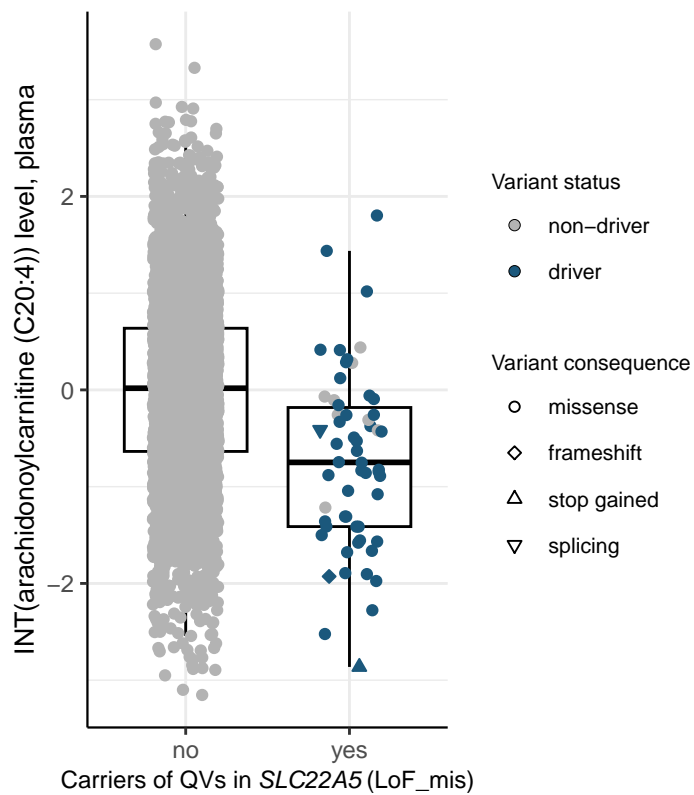
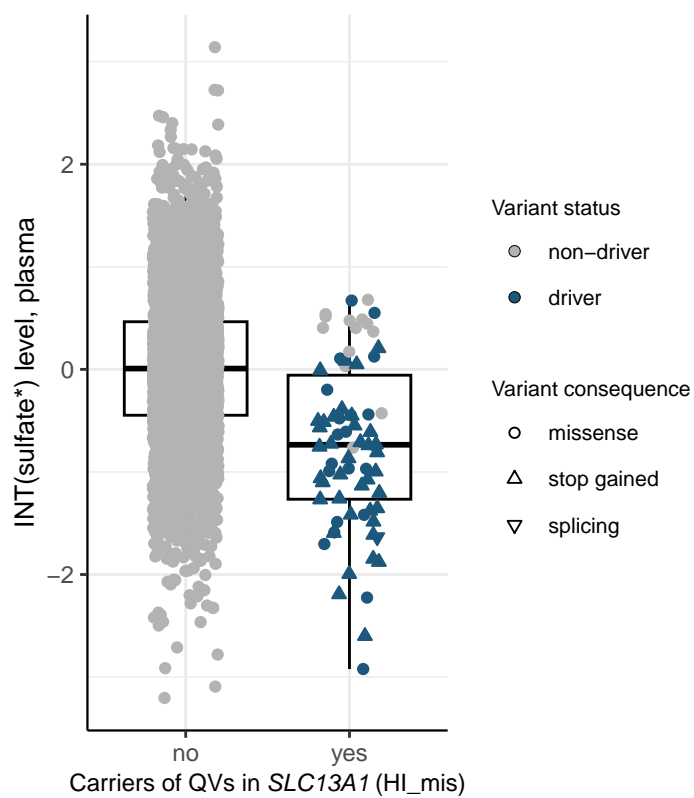


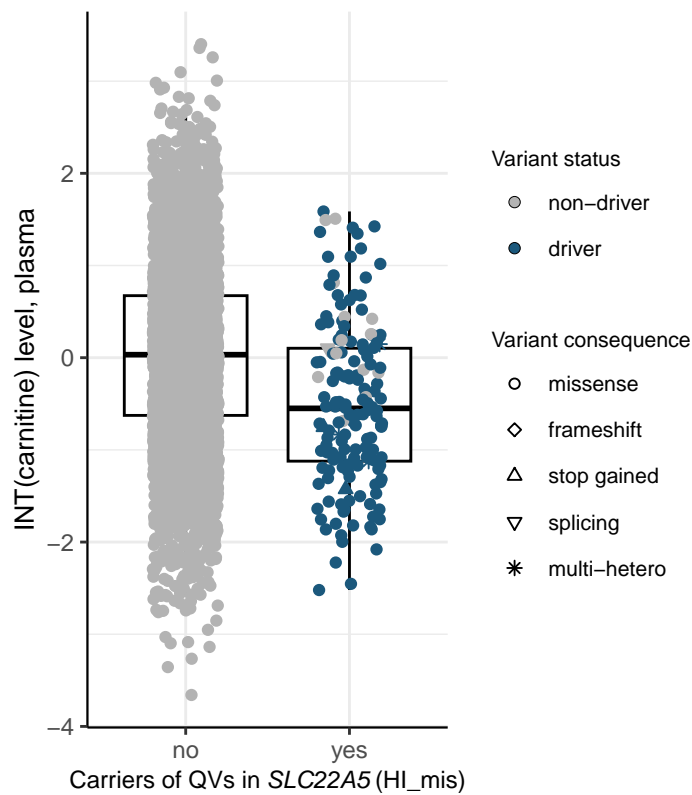
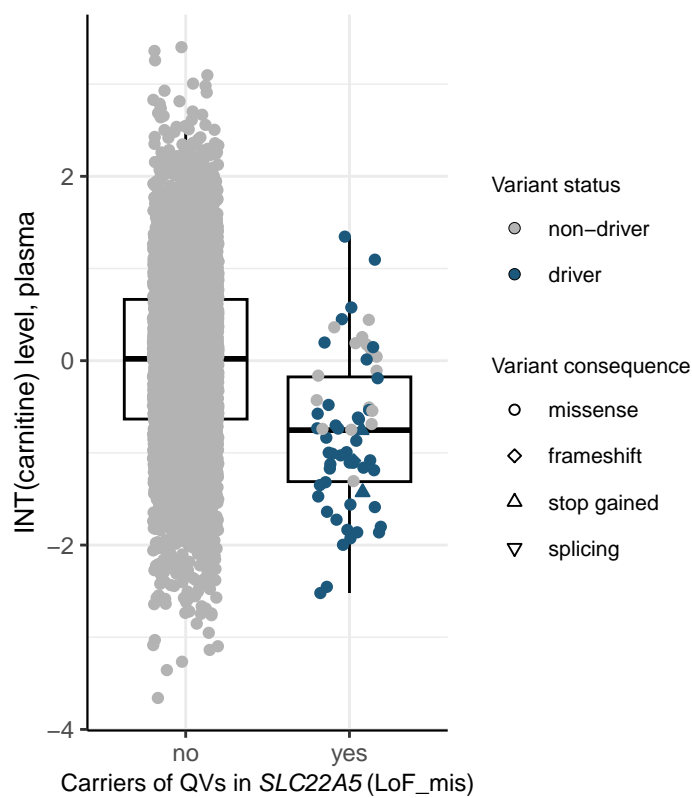


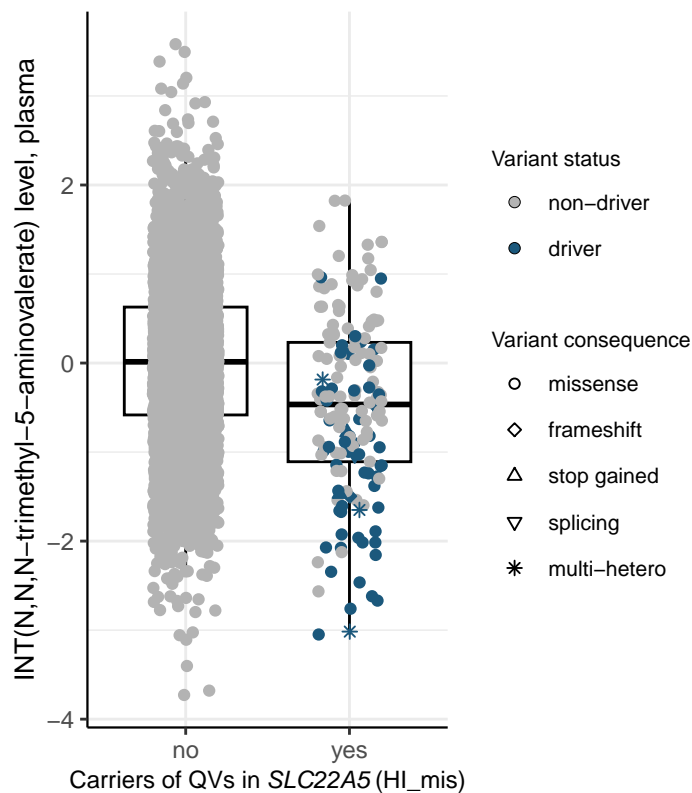
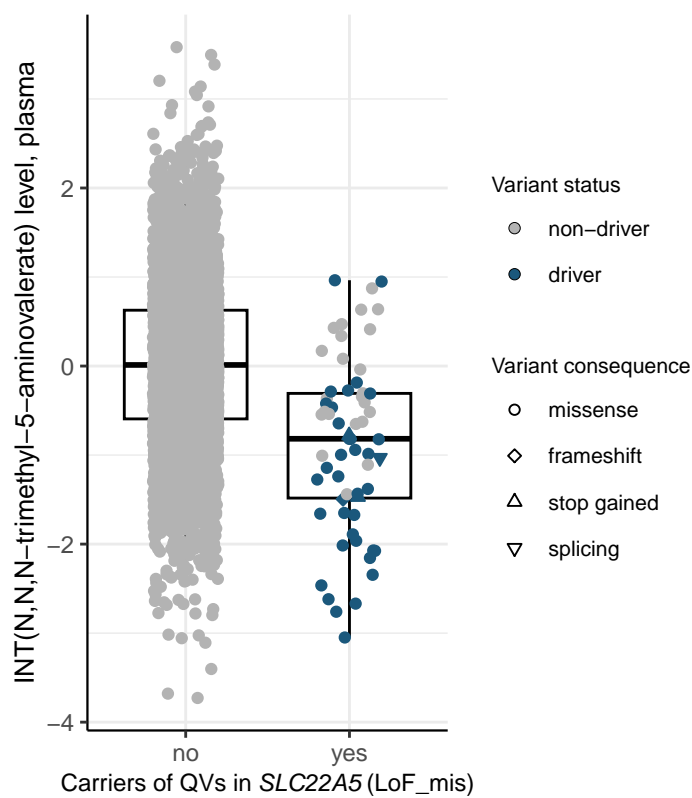


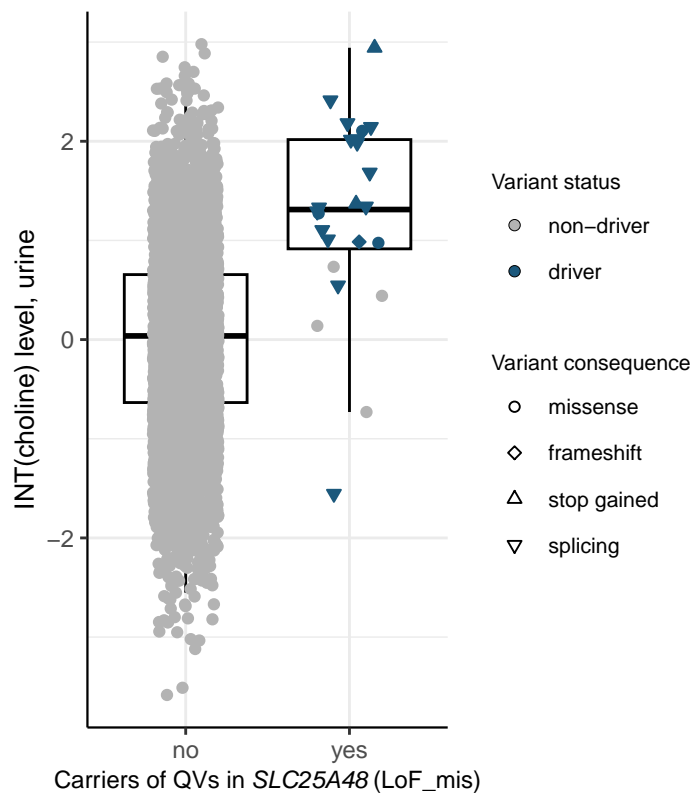
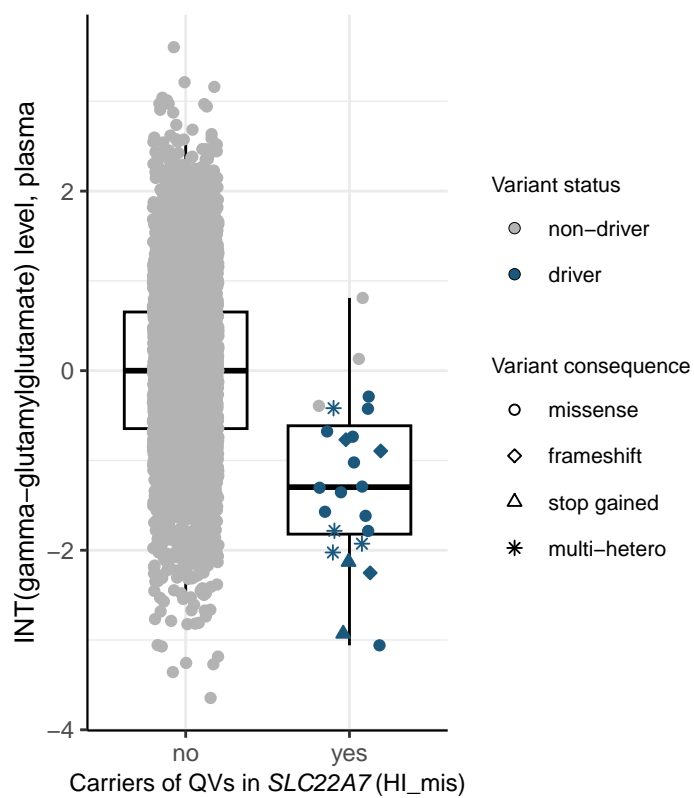


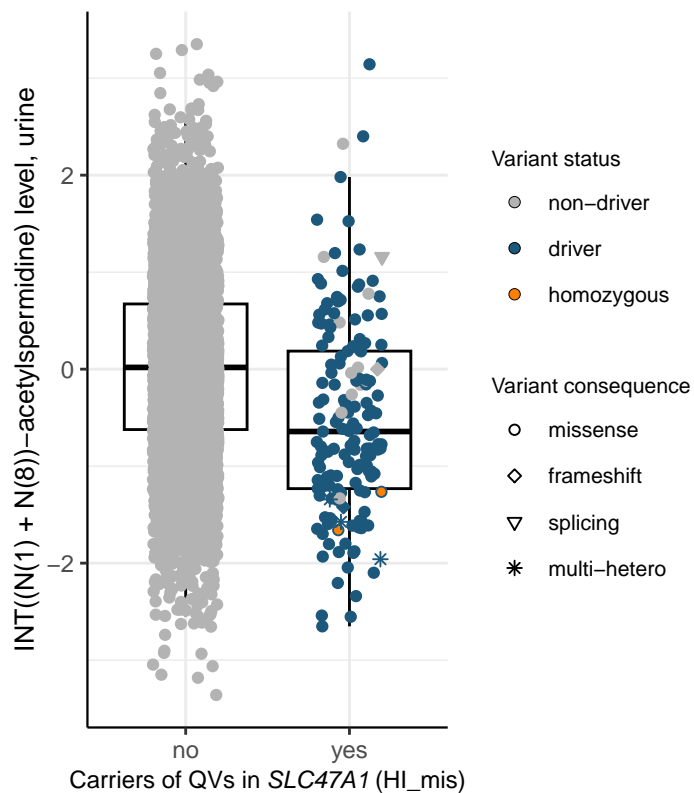
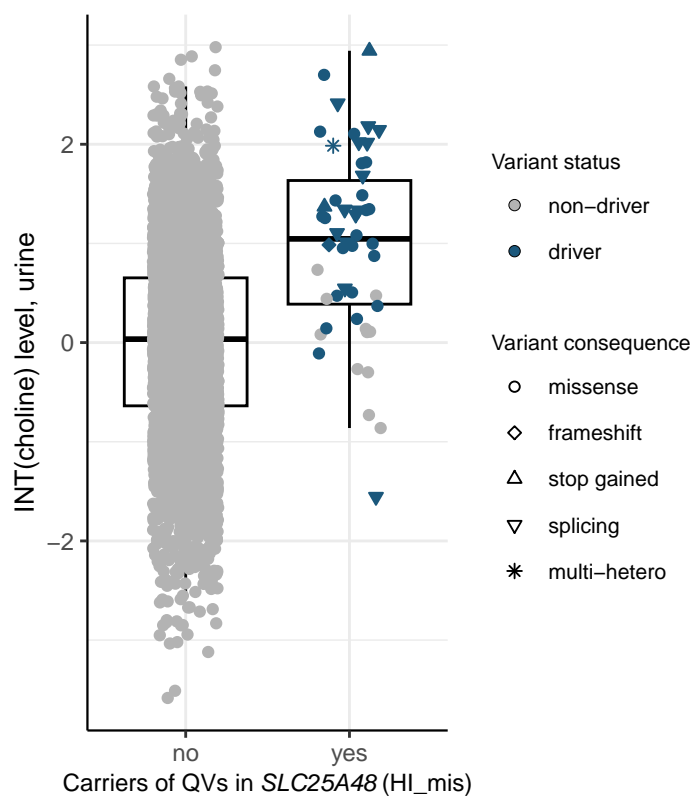


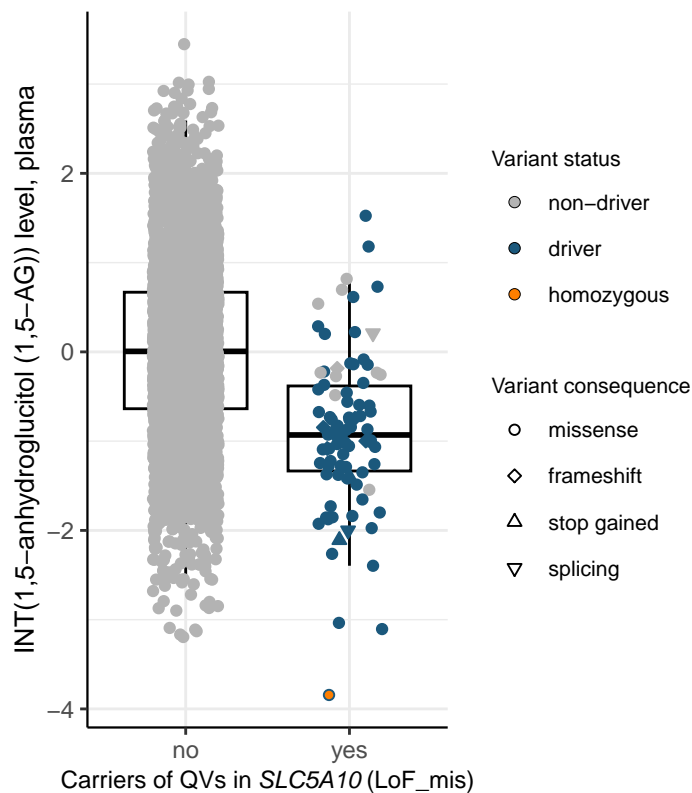
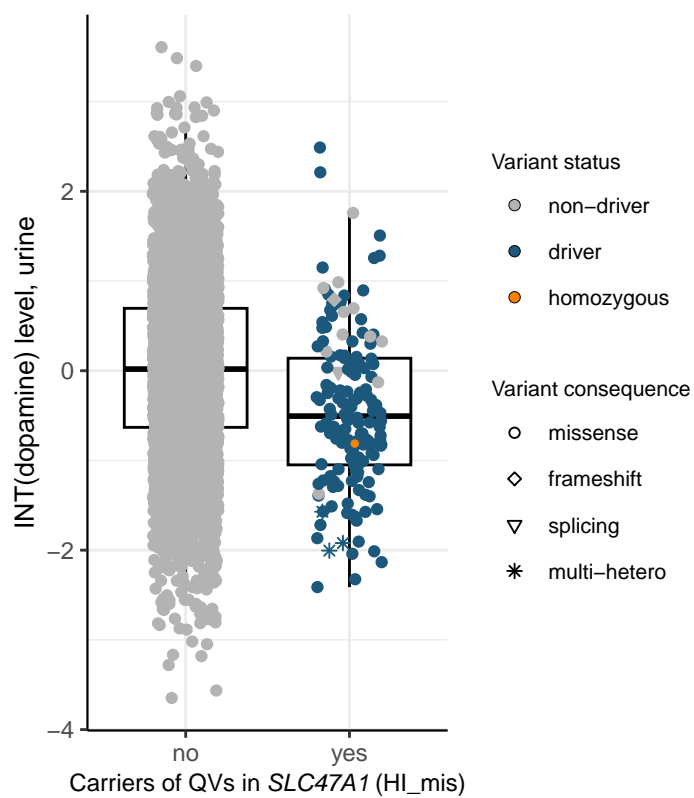


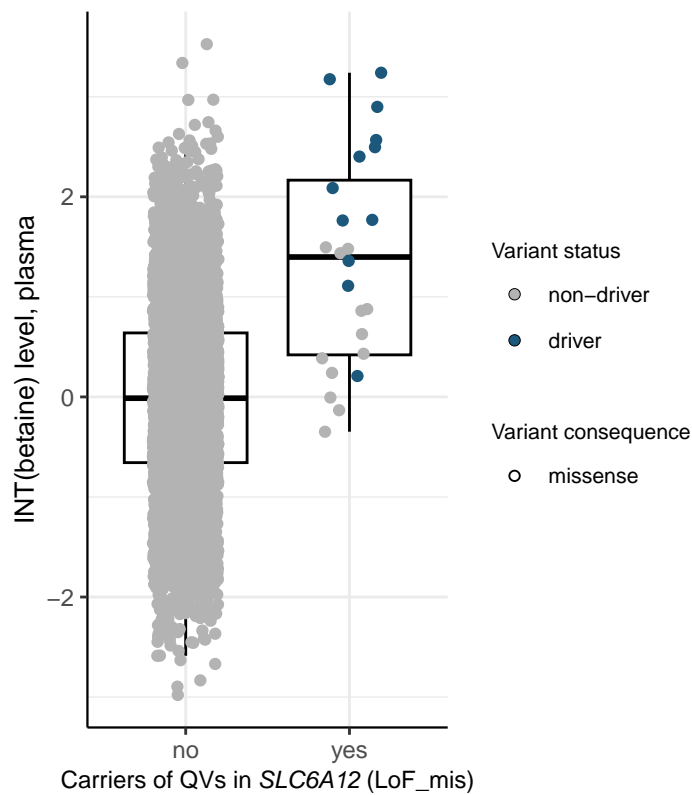
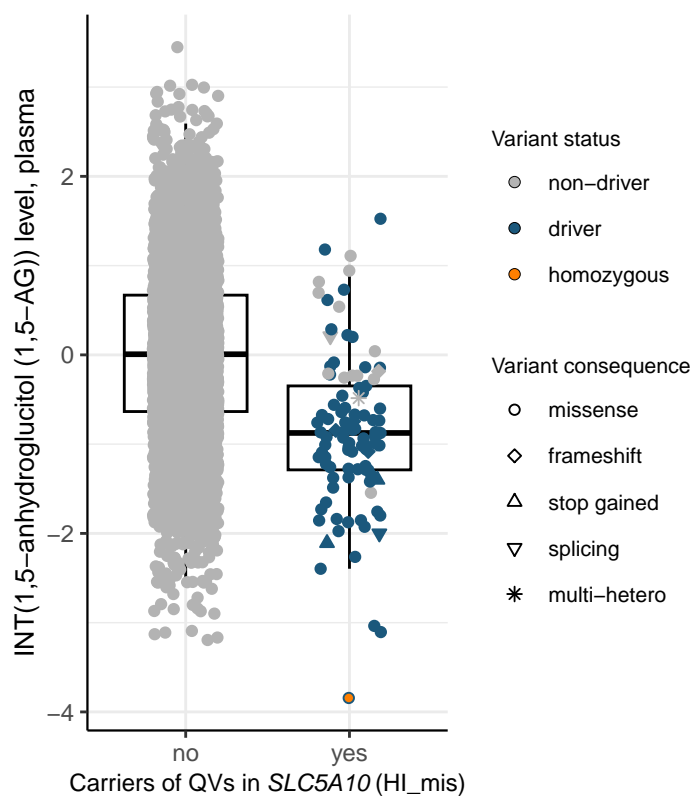


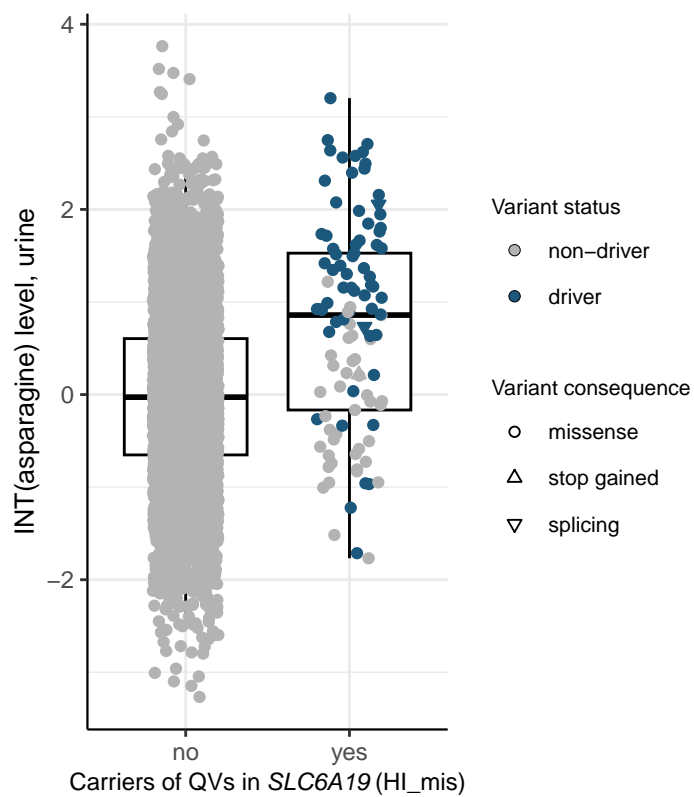
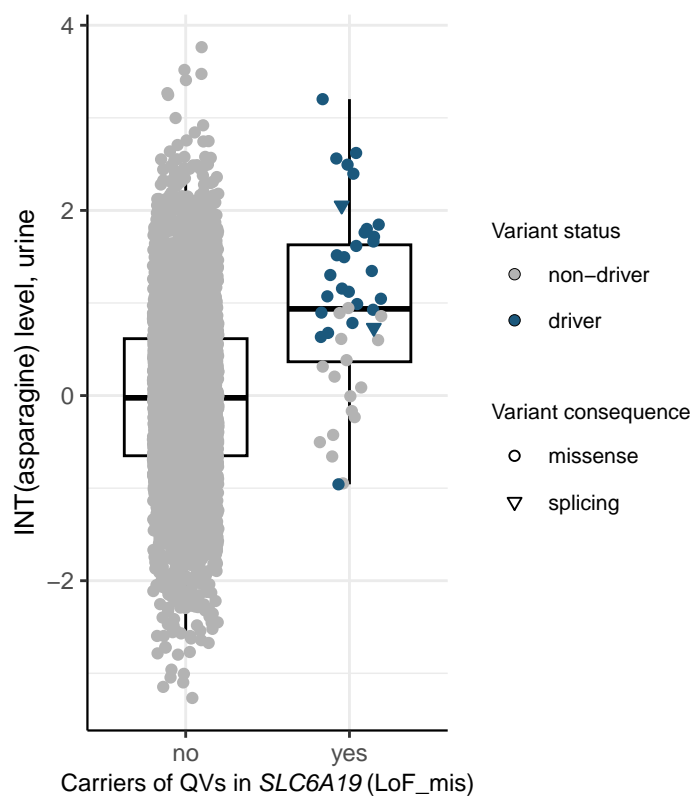


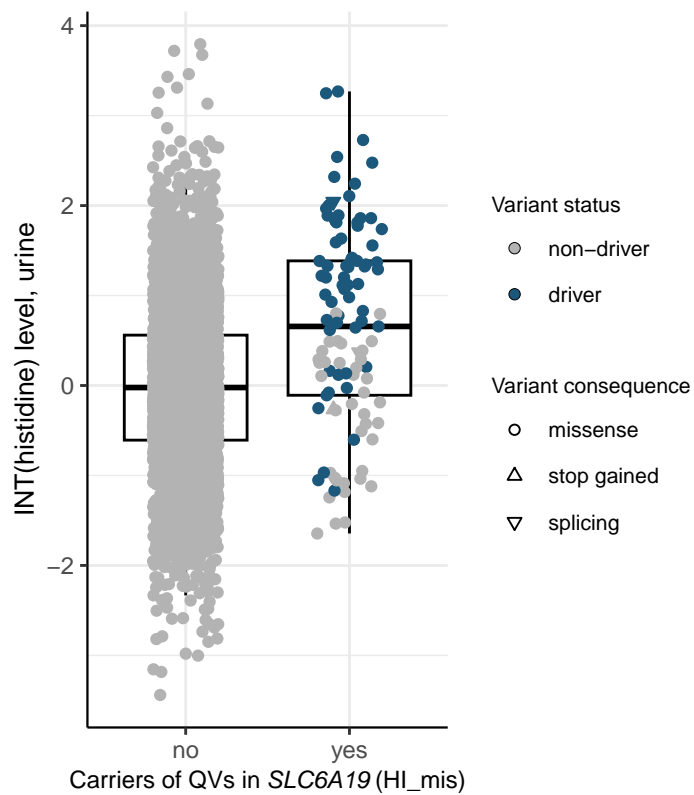
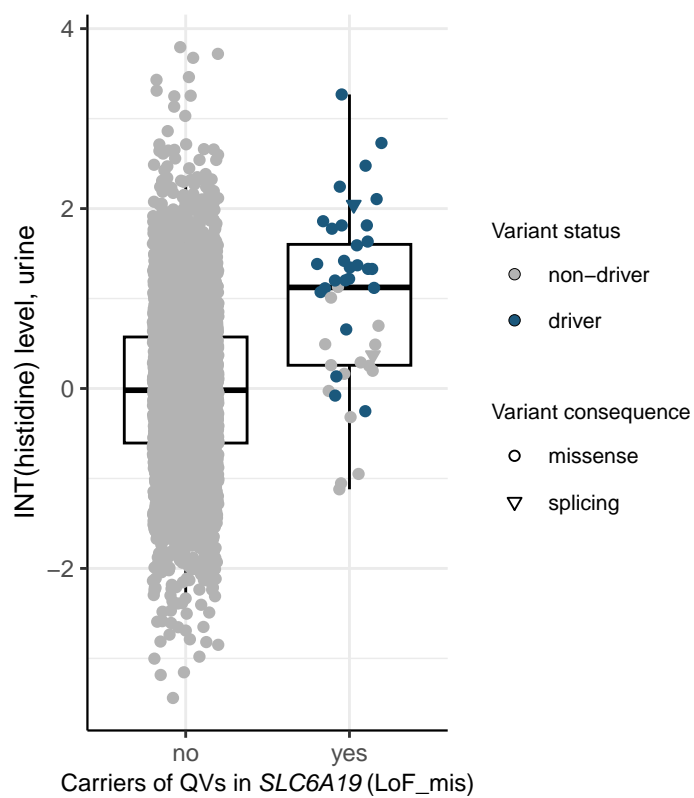


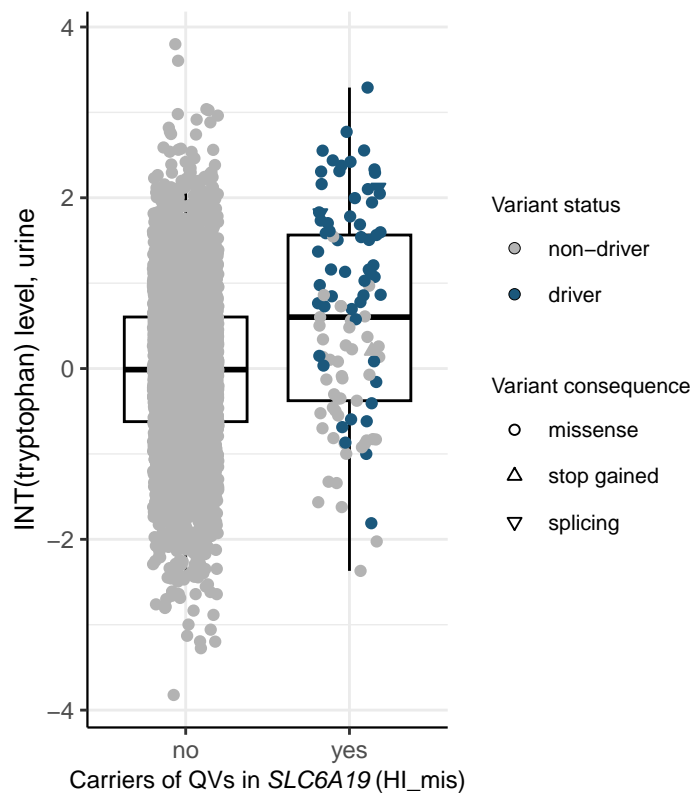
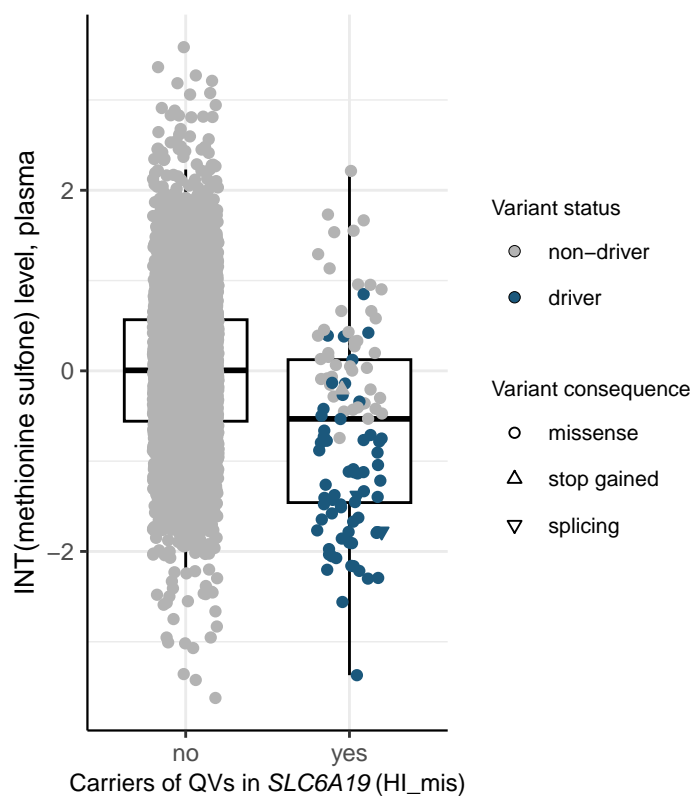


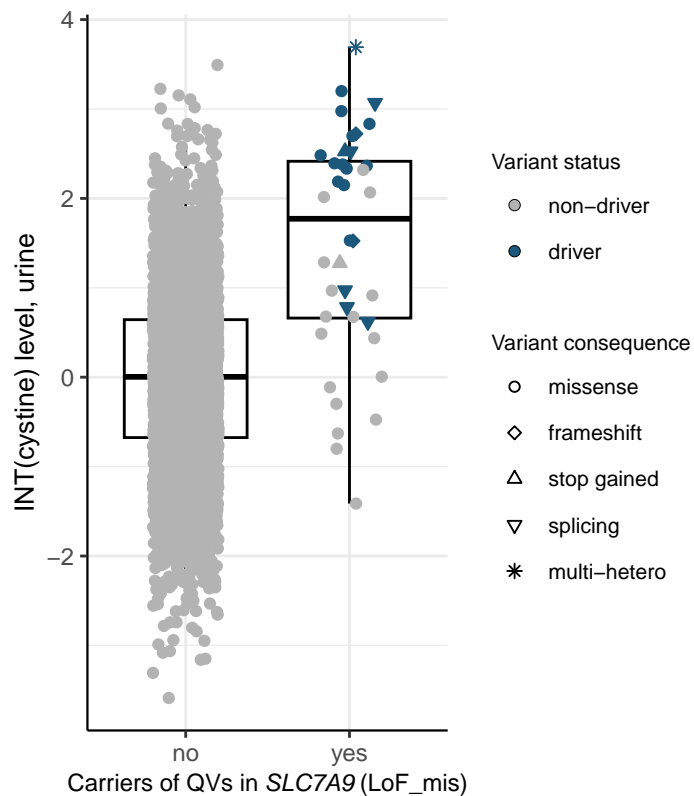
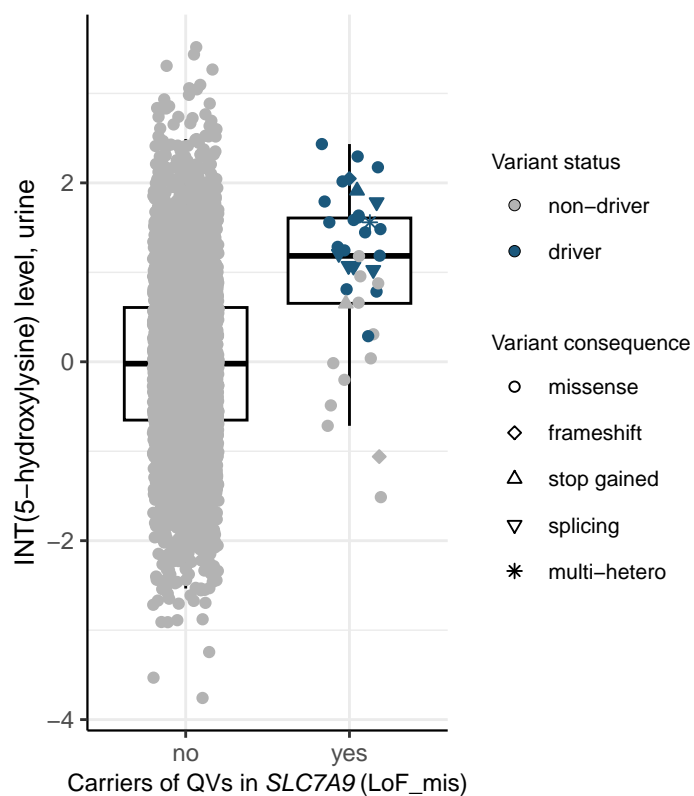


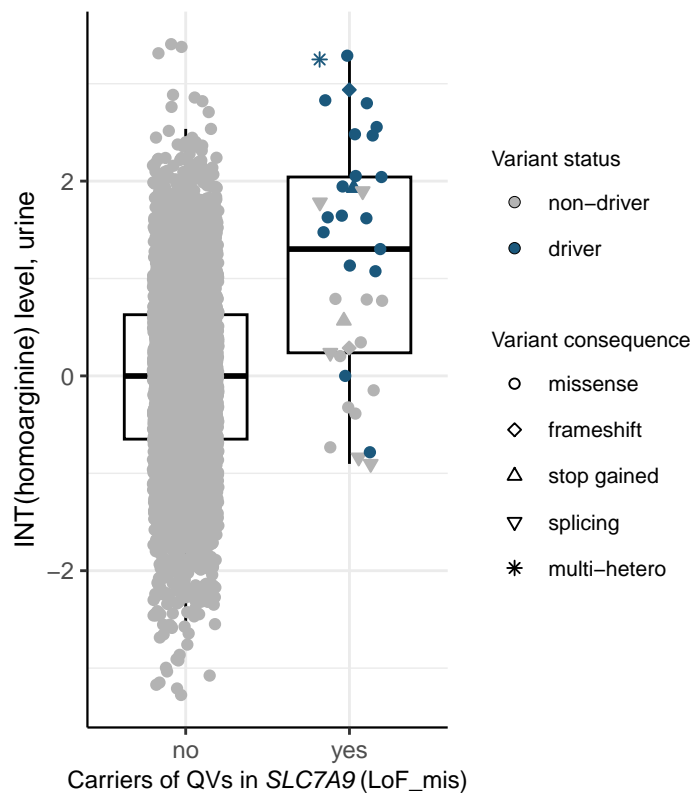
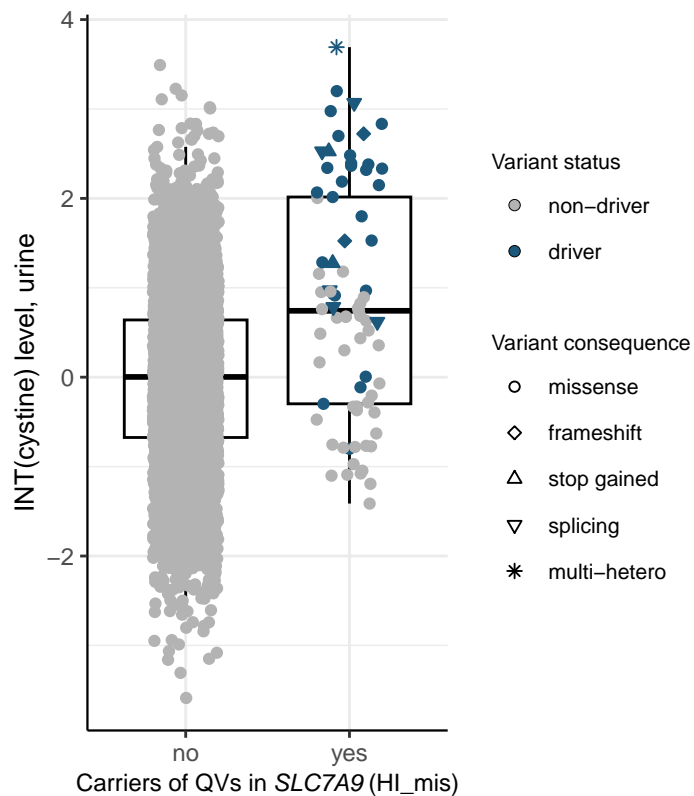


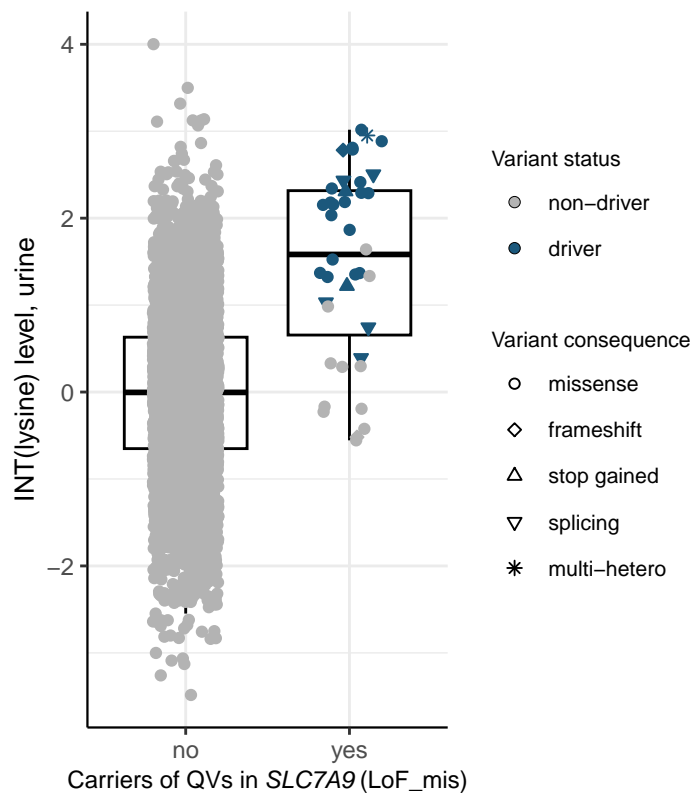
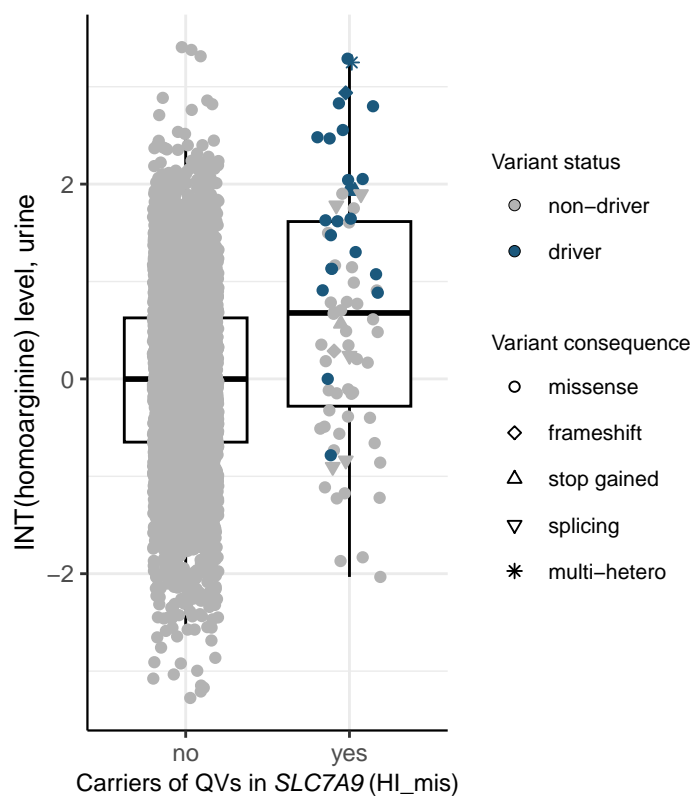


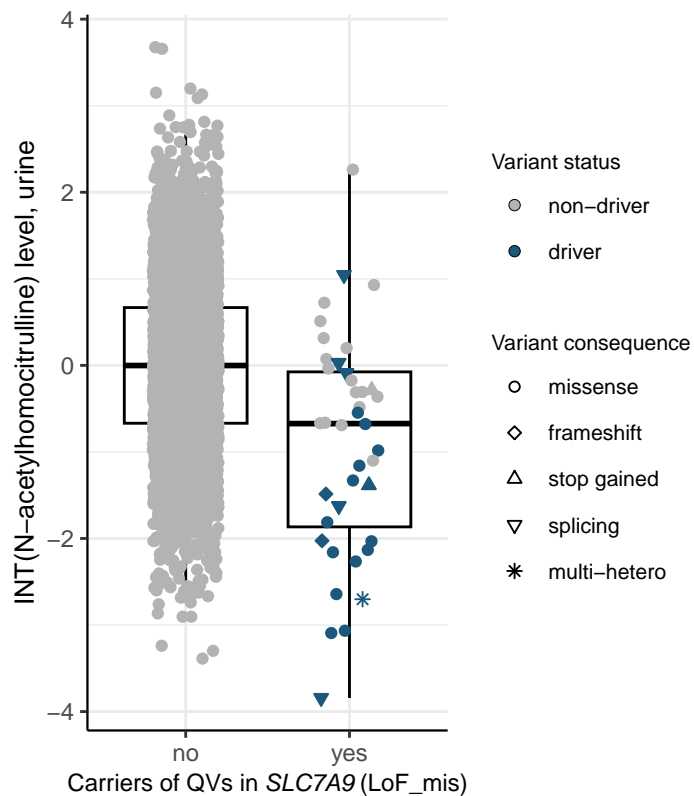
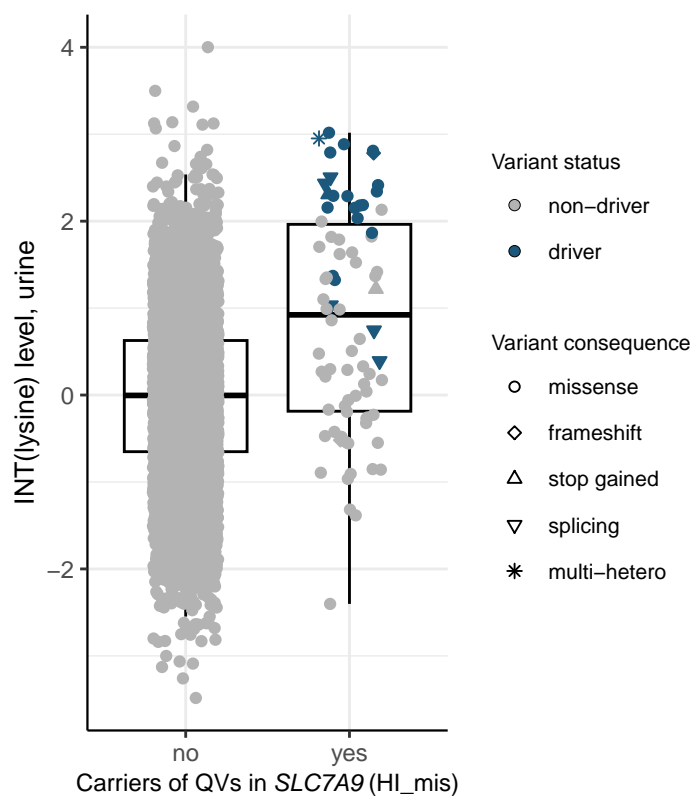


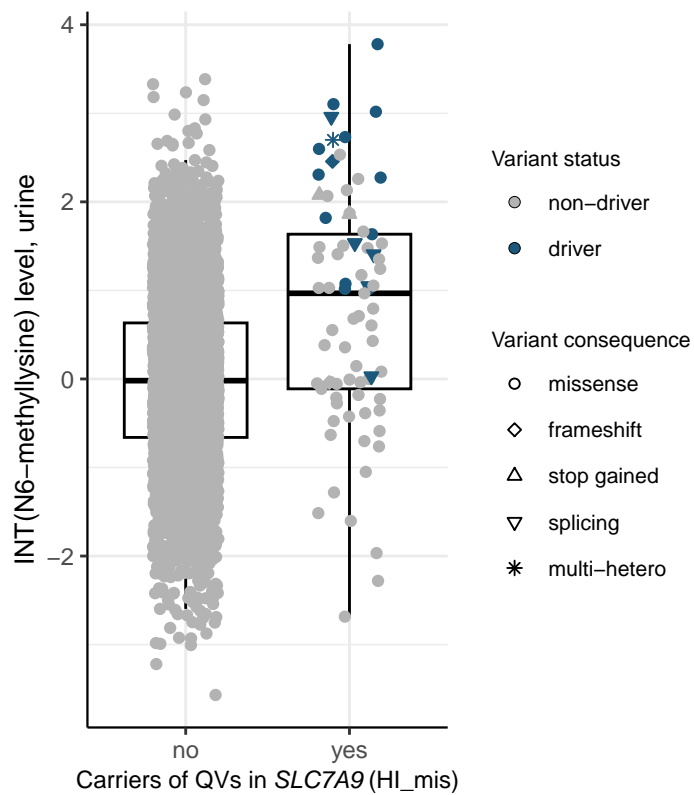
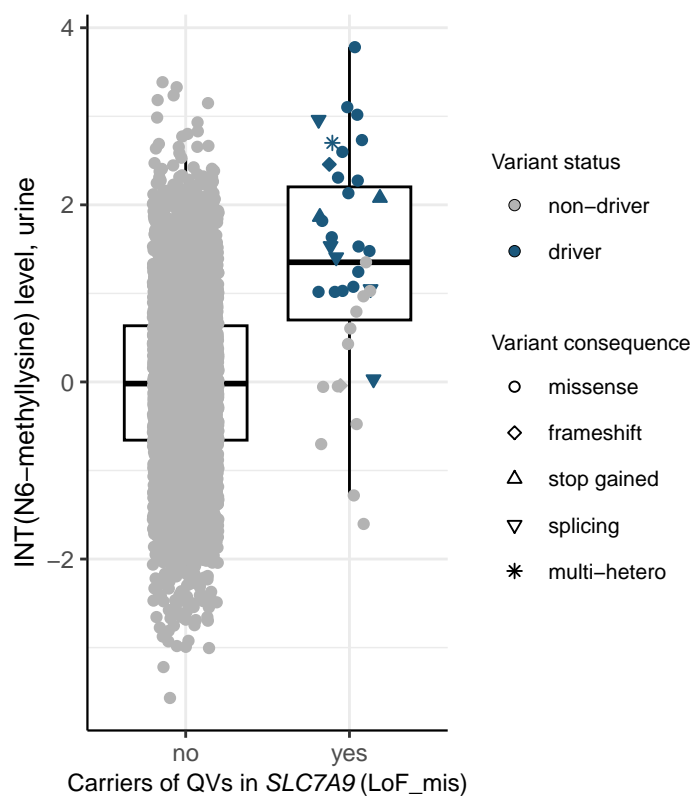


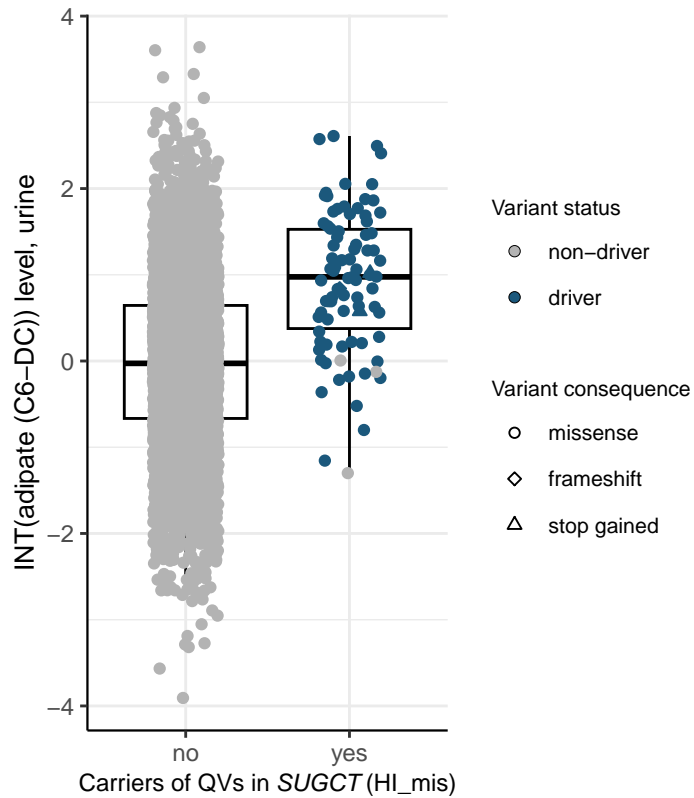
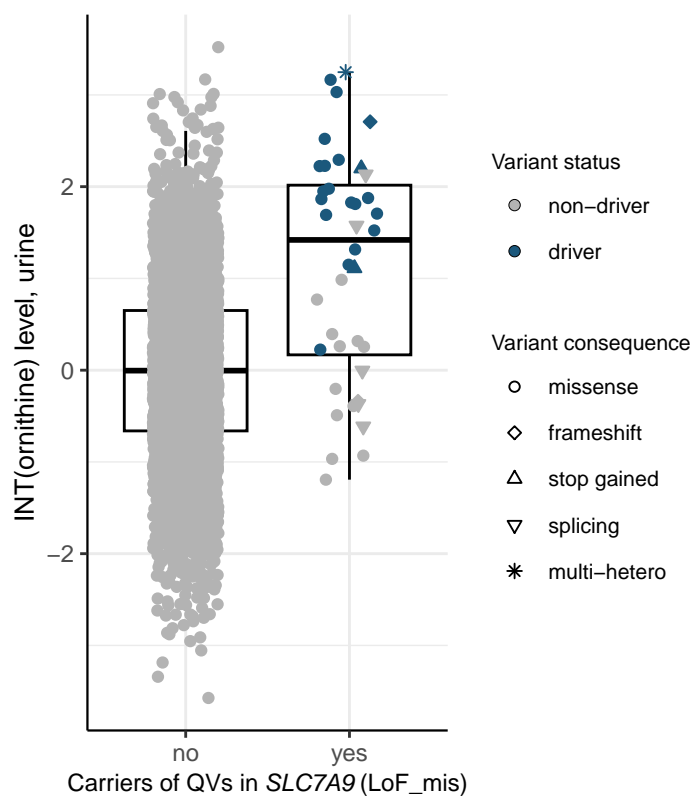


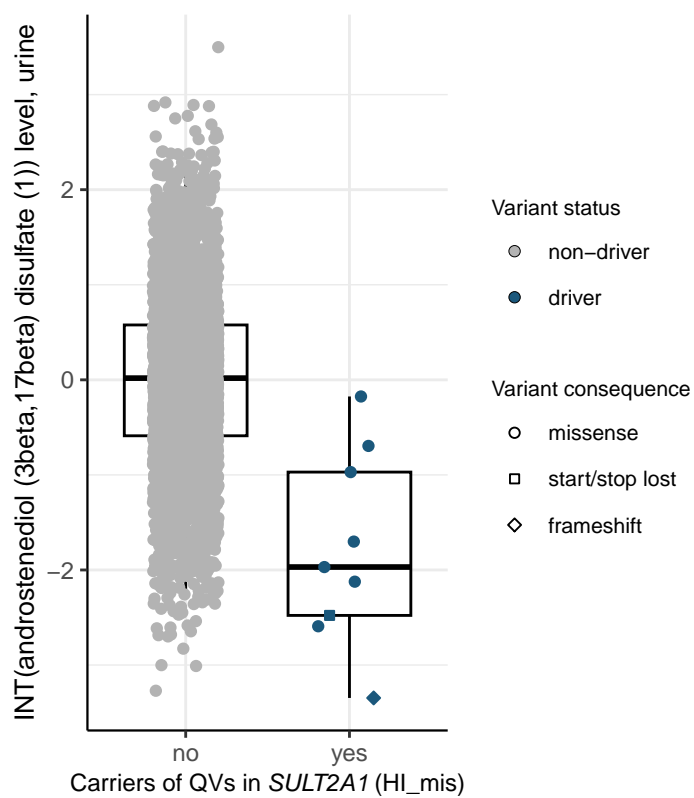
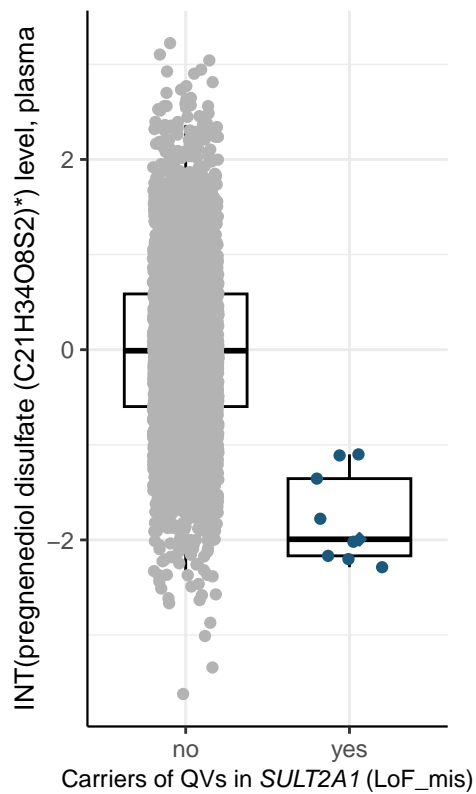


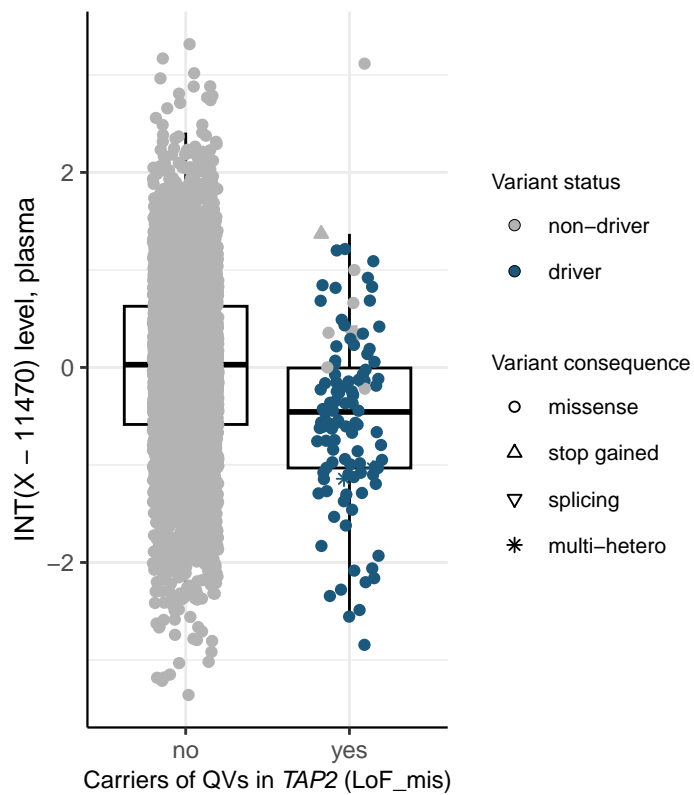
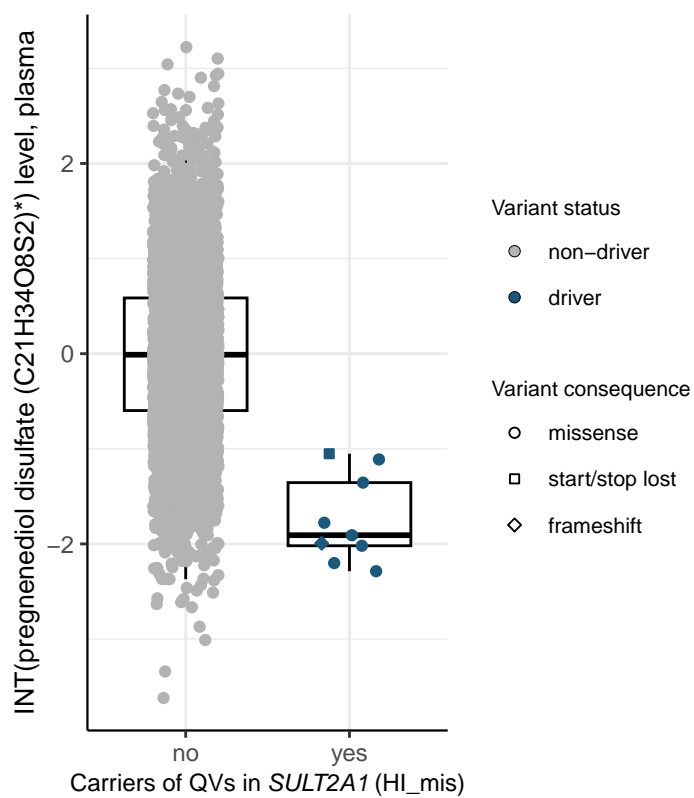


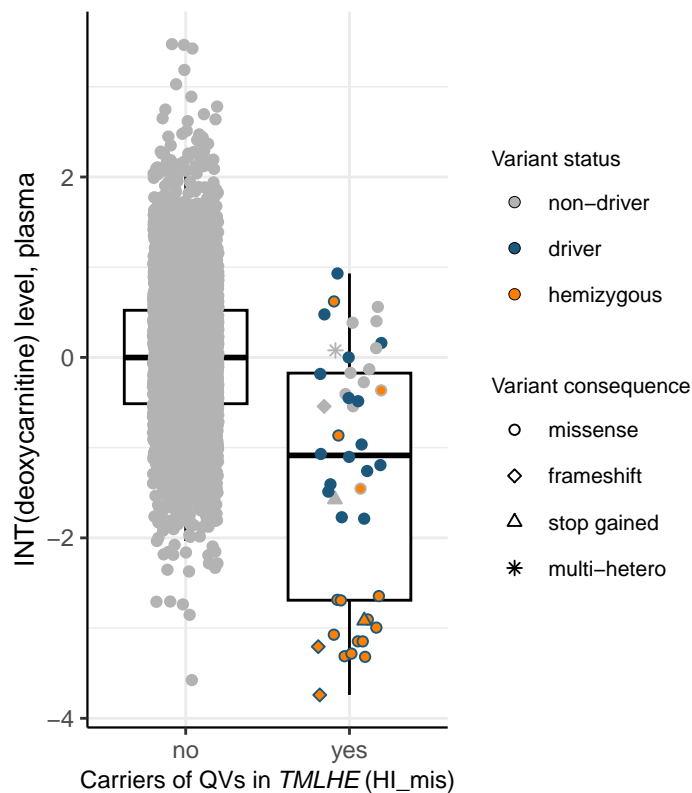
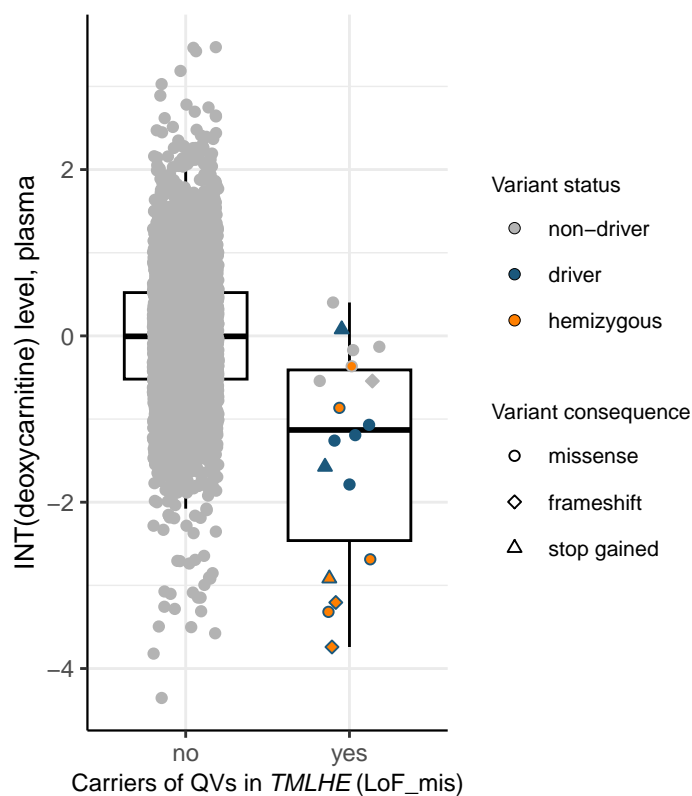


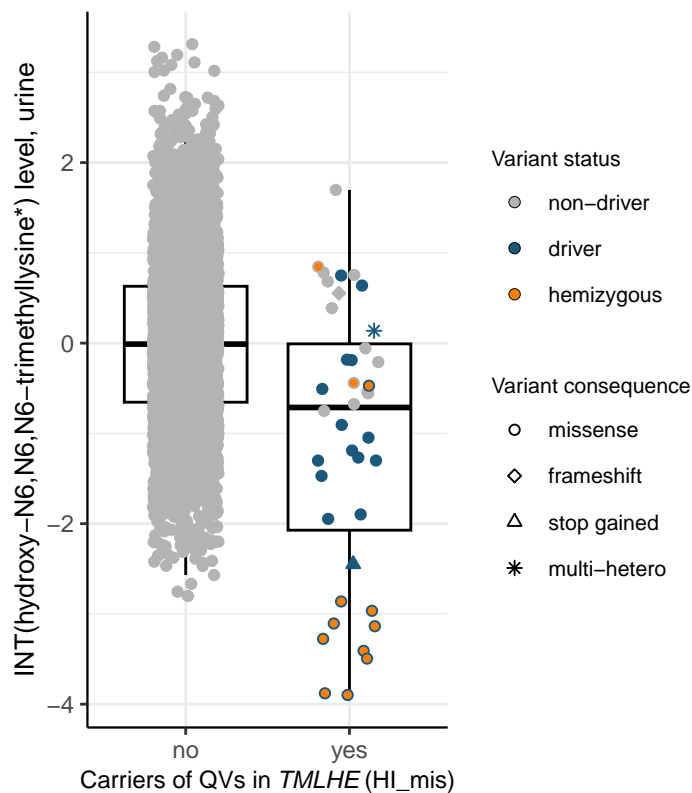
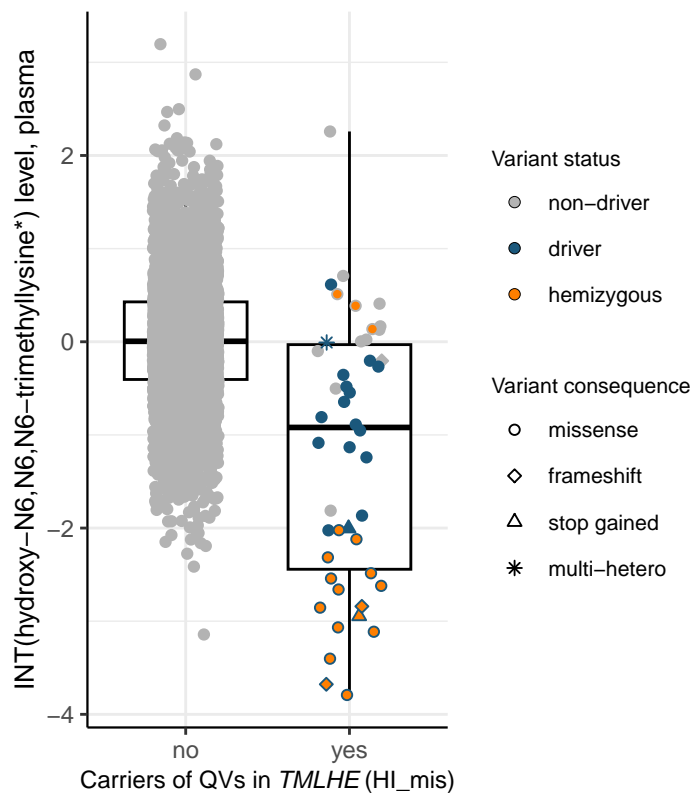
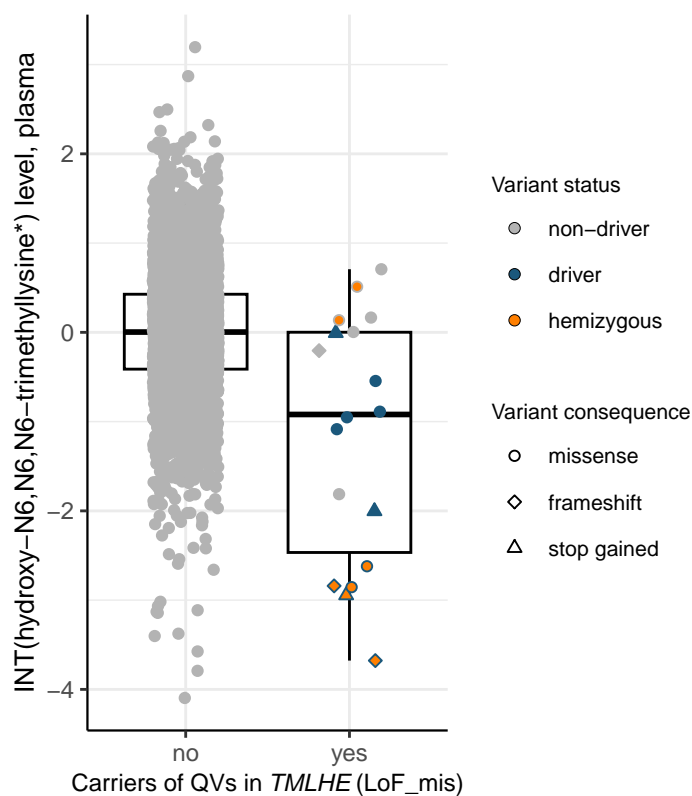


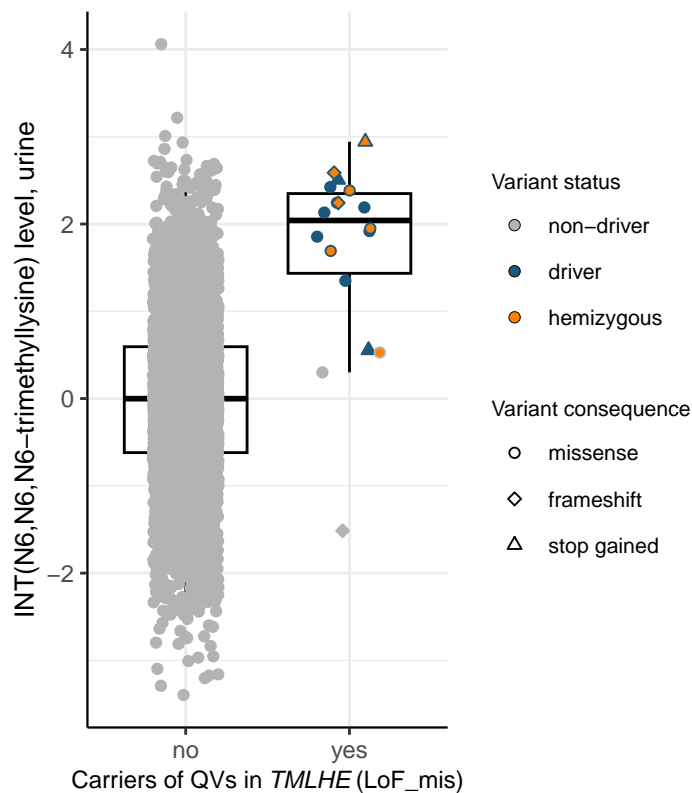
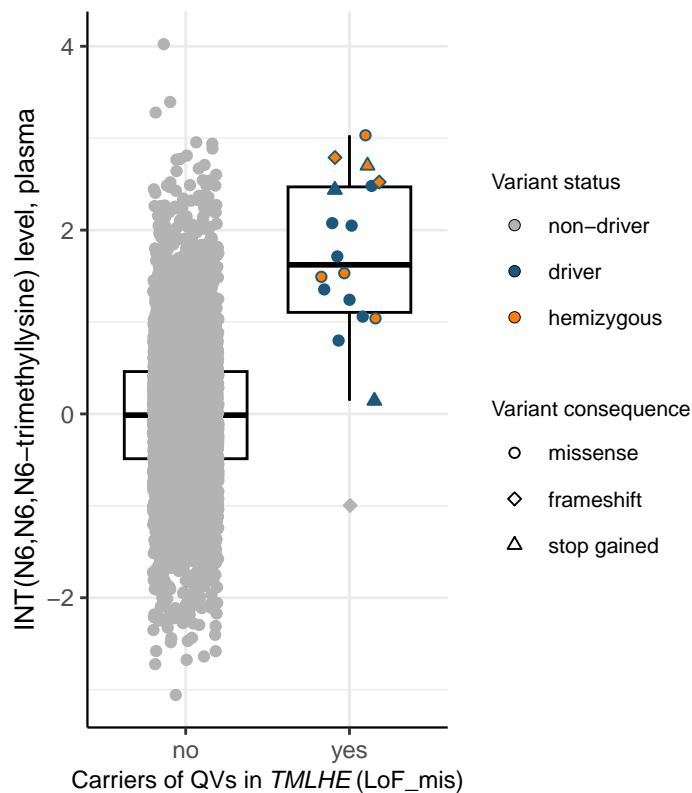
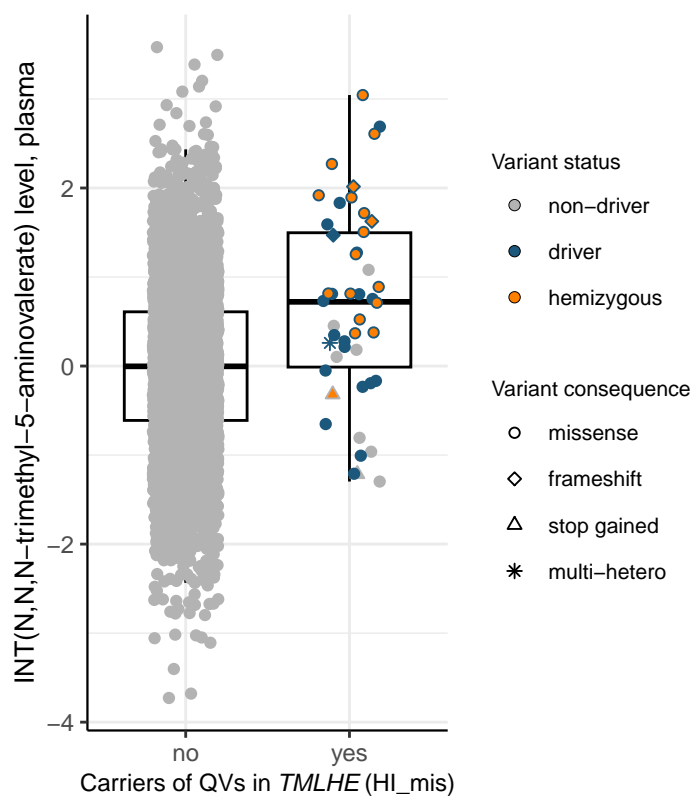


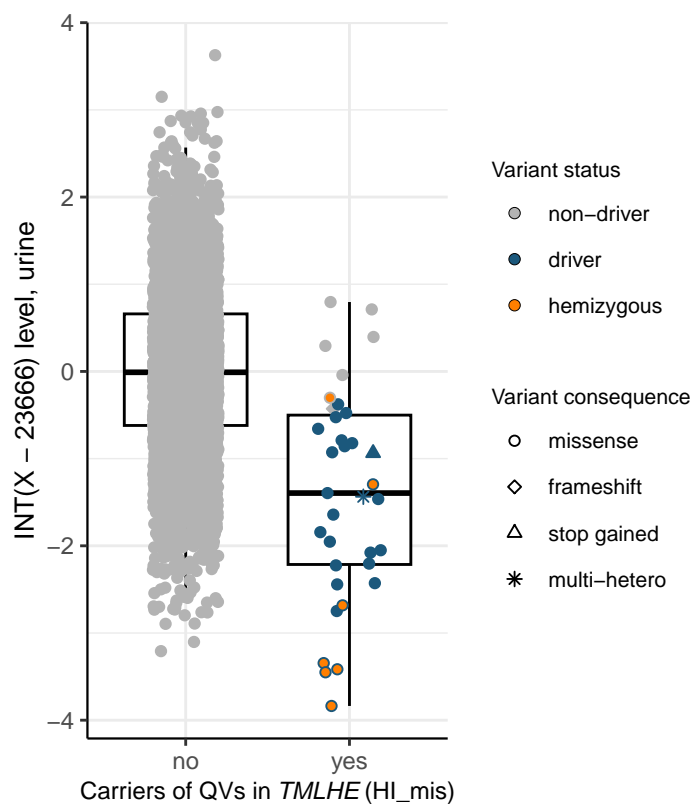
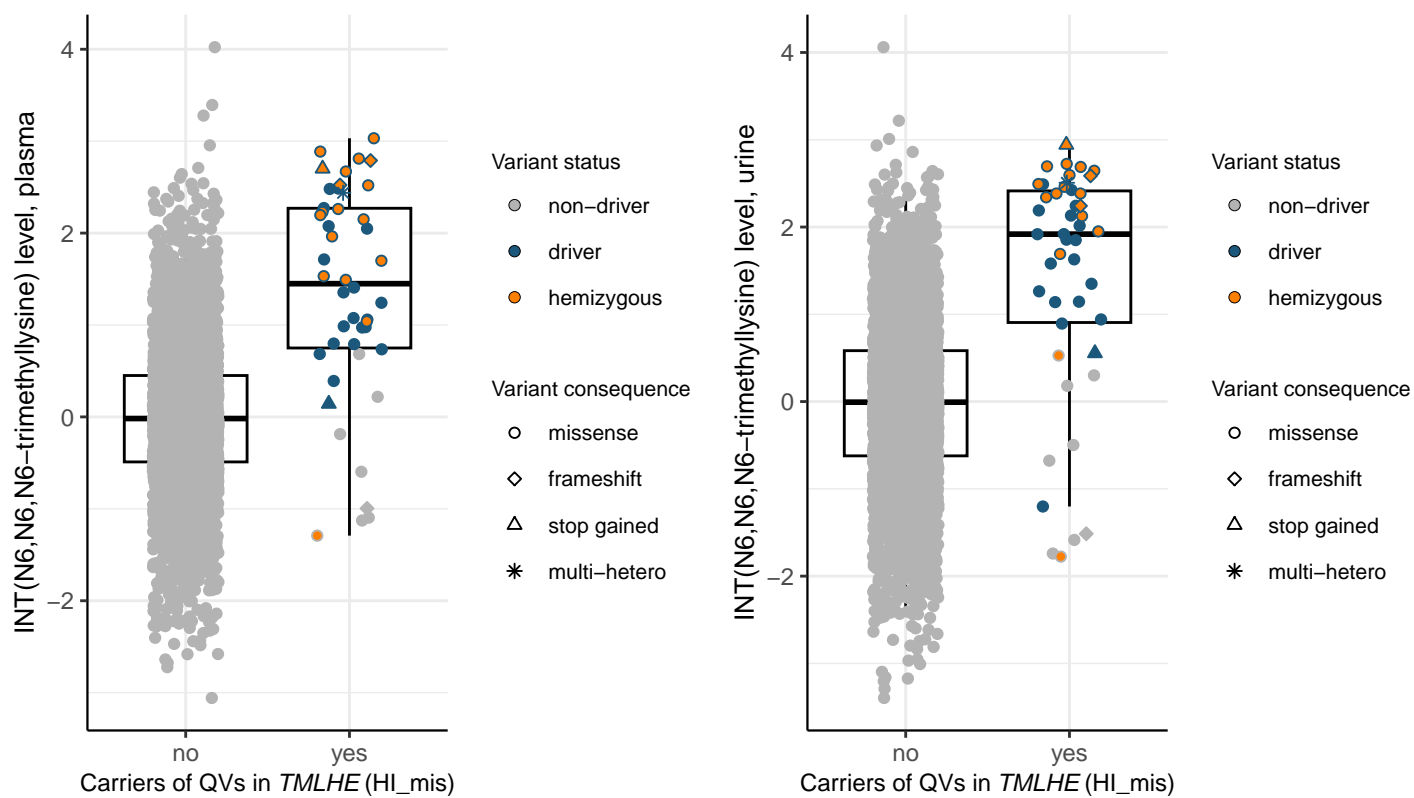


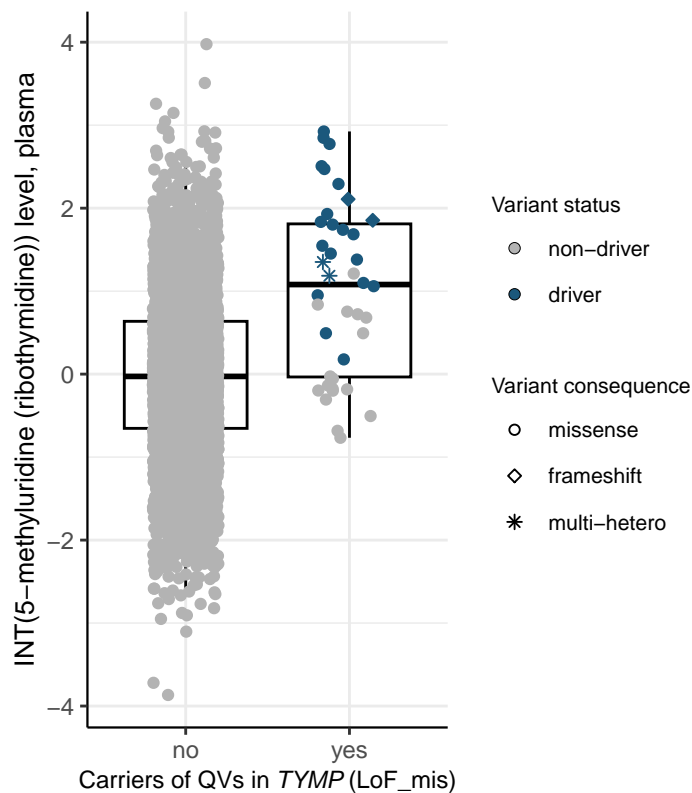
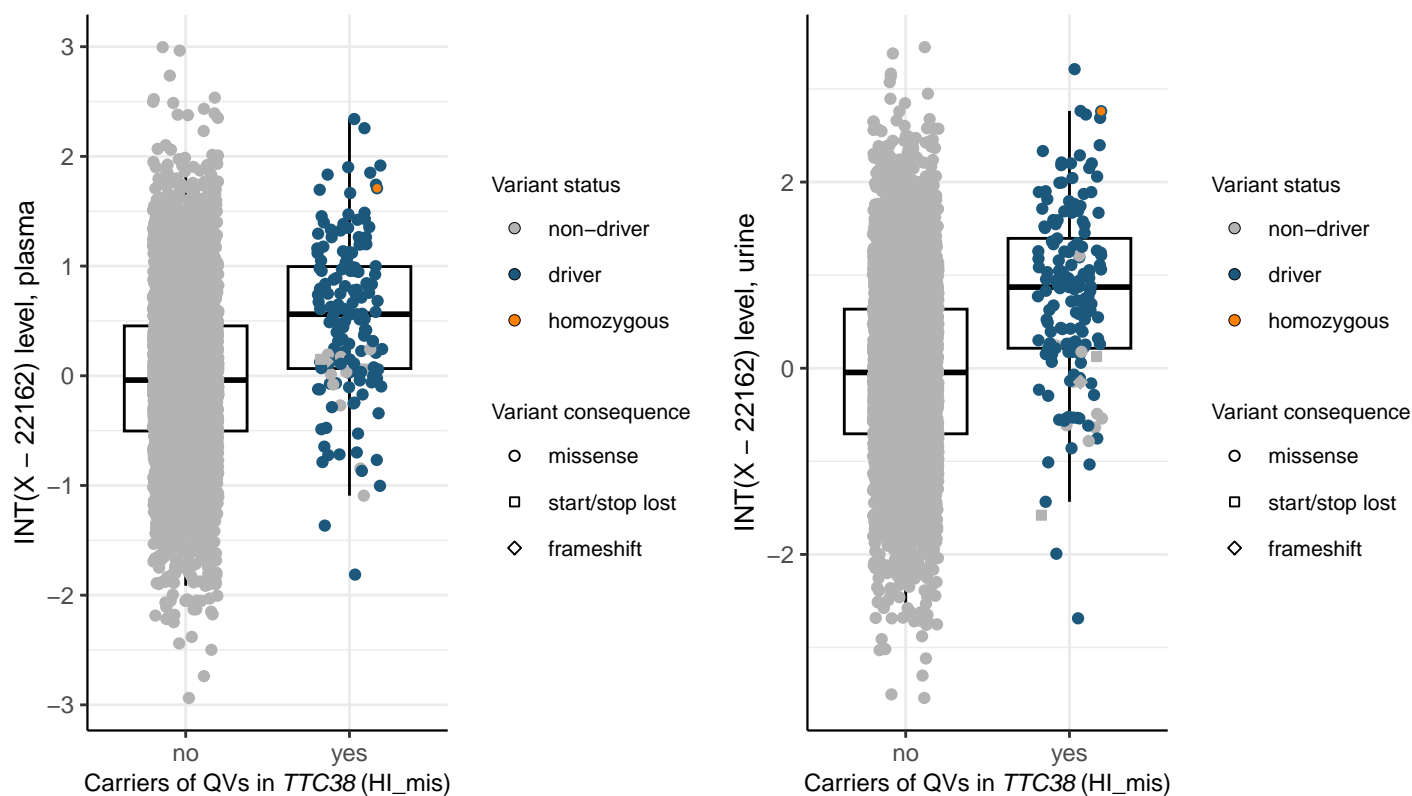


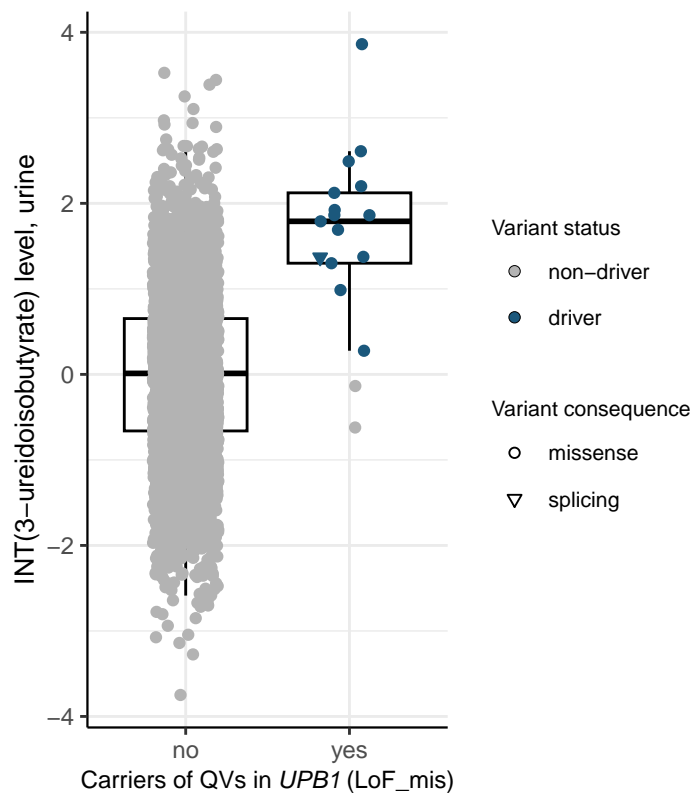
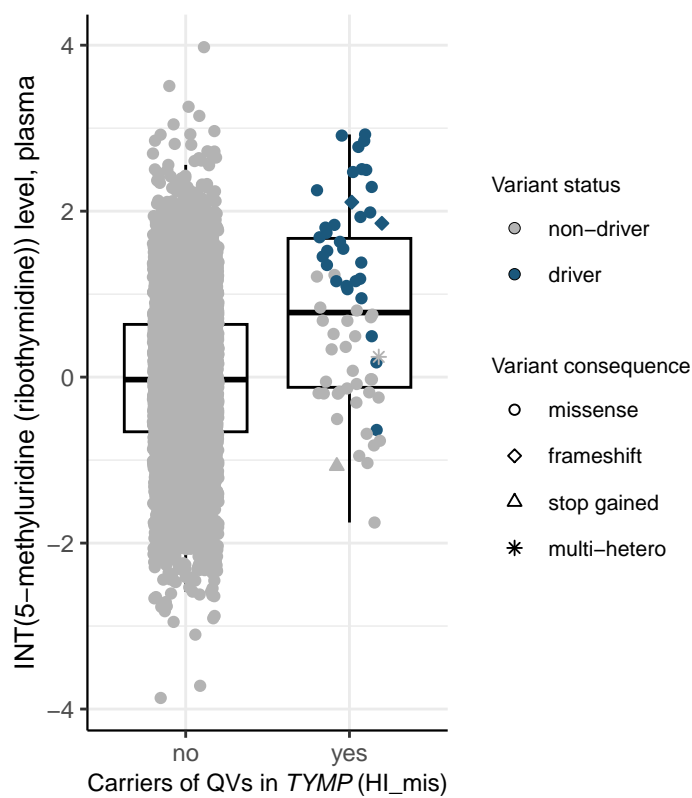


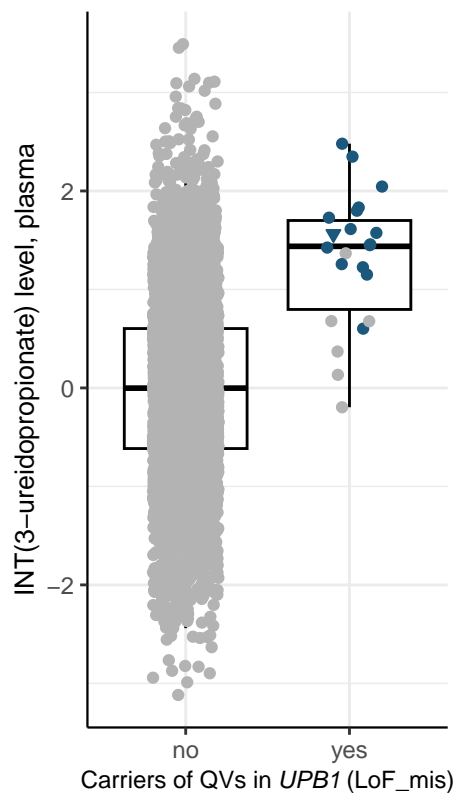










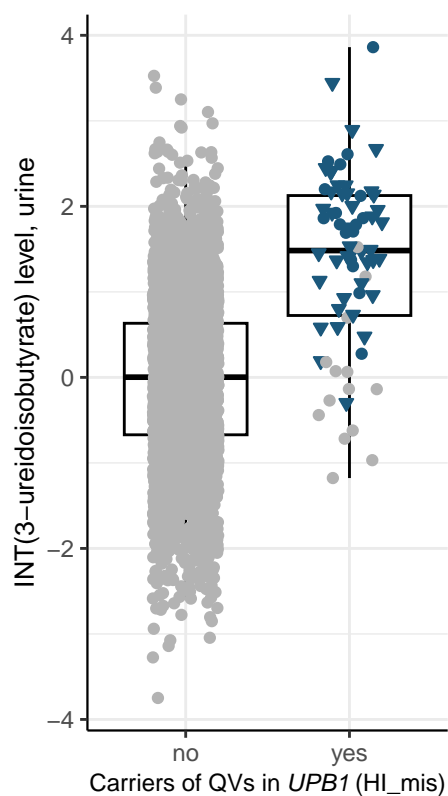


Variant status

- non-driver
- driver

Variant consequence

- missense
- splicing

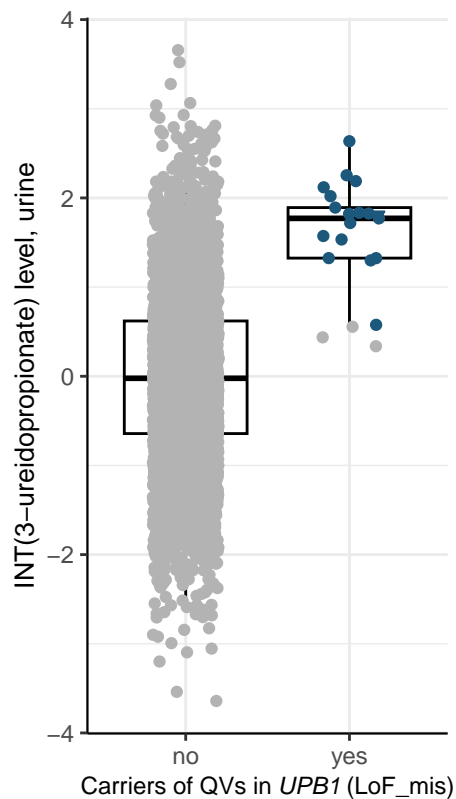


Variant status

- non-driver
- driver

Variant consequence

- missense
- splicing

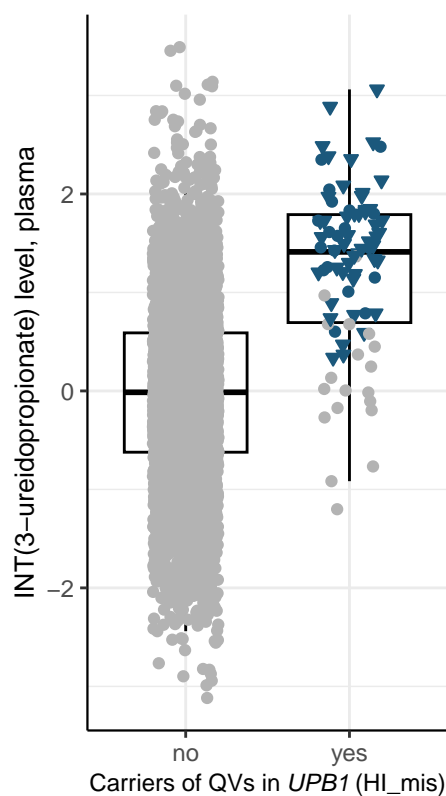


Variant status

- non-driver
- driver

Variant consequence

- missense
- splicing

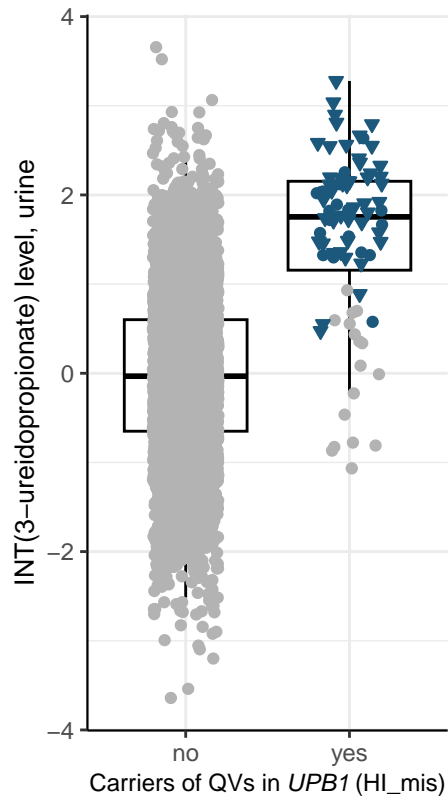


Variant status

- non-driver
- driver

Variant consequence

- missense
- splicing

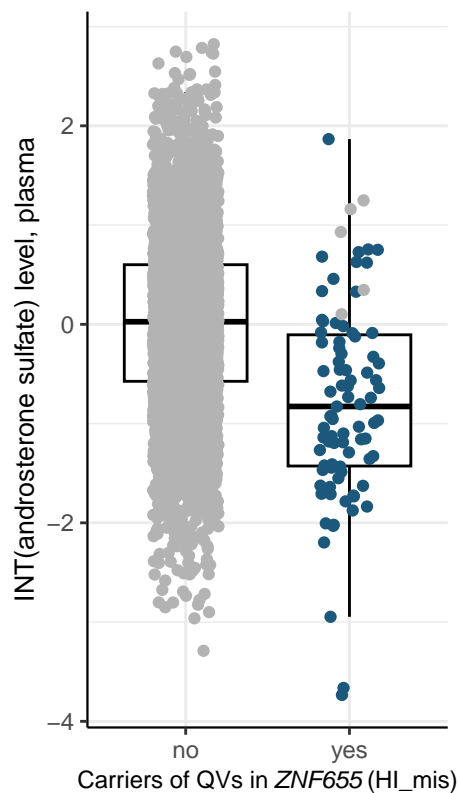


Variant status

- non-driver
- driver

Variant consequence

- missense
- splicing



Variant status

- non-driver
- driver

Variant consequence

- missense

