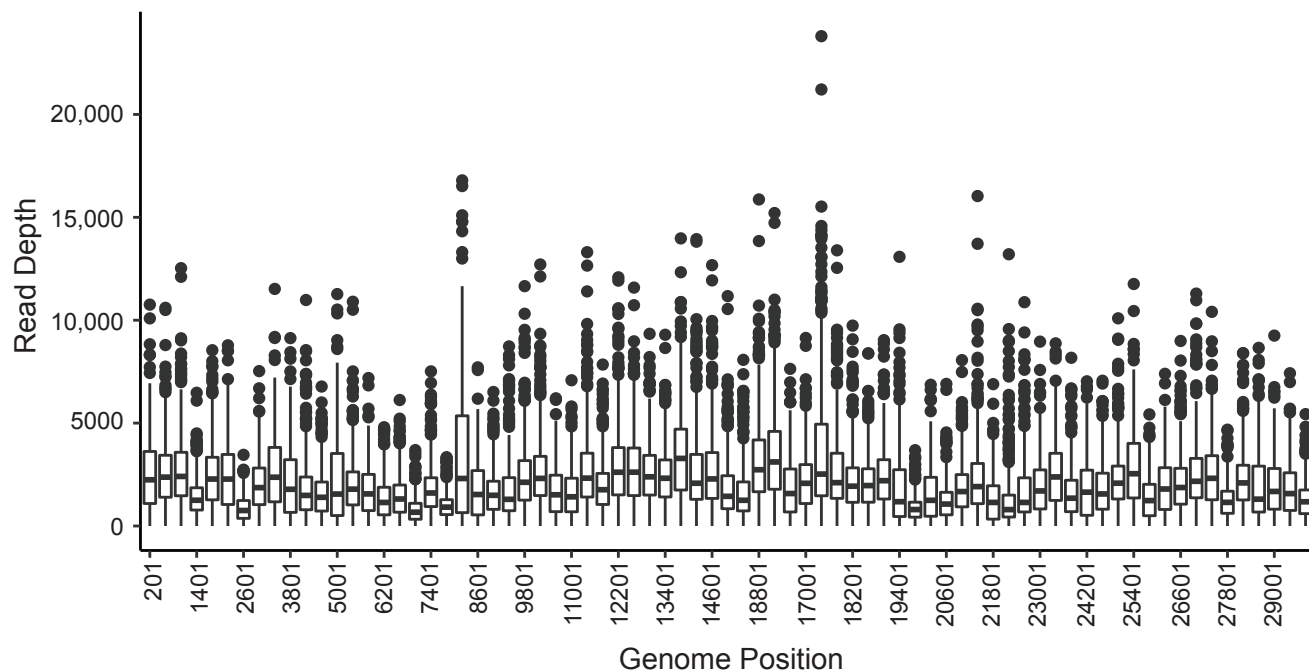
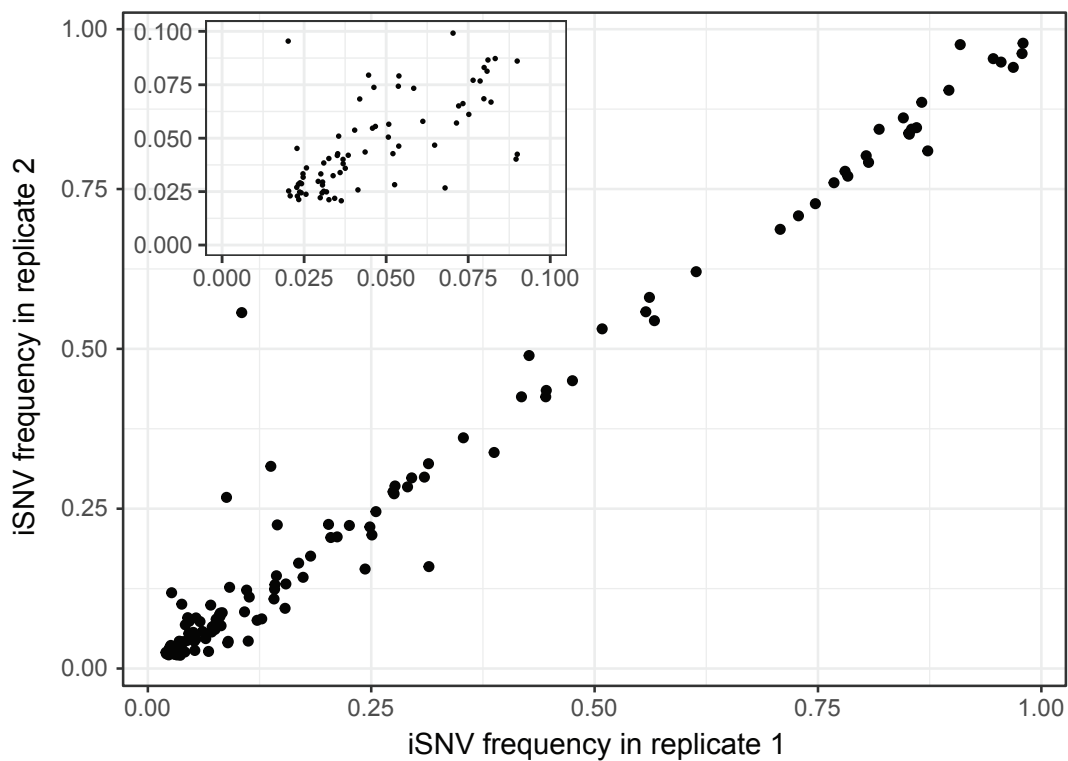
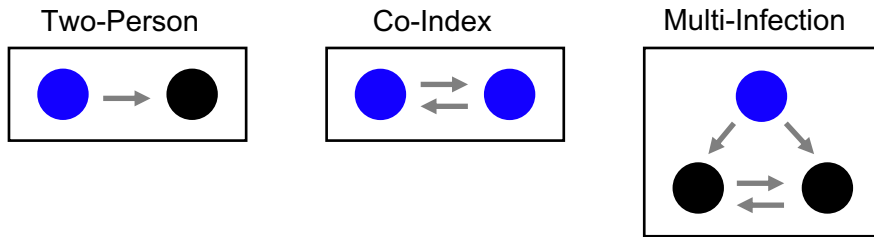


**A****B**

Supplementary Figure 1. Sequencing coverage and consistency. (A) Boxplot of median (+/- IQR) coverage across the genome in 400bp non-overlapping sliding windows. (B) Frequency of iSNV in each replicate for iSNV that were identified in both replicates. The inset shows replicate frequencies between 0 and 0.1.

**A****B****HH24**

HS10818	21J (Delta)	AY.3	
HS10820	21J (Delta)	AY.3	
HS10822	21J (Delta)	AY.3	
HS10803 *	21J (Delta)	AY.3	

**HH25†**

HS10875	21J (Delta)	AY.100	
HS10879	21J (Delta)	AY.100	
HS10876	21J (Delta)	AY.3	
HS10878	21J (Delta)	AY.3	

**HH32\***

HS11314	21K (Omicron)	BA.1.1	
HS11315	21K (Omicron)	BA.1.1	

**HH33**

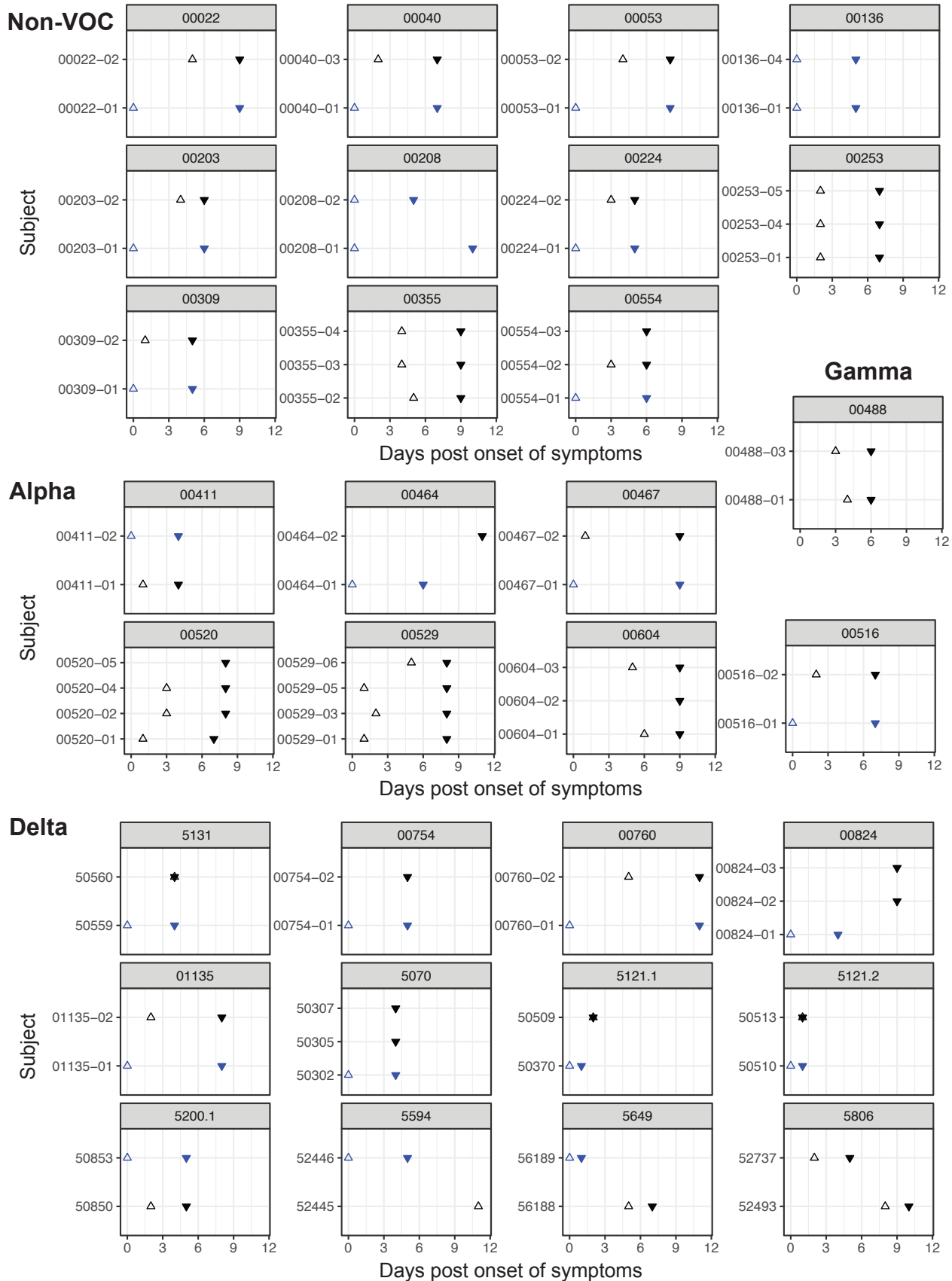
HS11484	21K (Omicron)	BA.1.1	
HS11608	21K (Omicron)	BA.1.1	
HS11438 *	21K (Omicron)	BA.1	

**HH47\***

HS11540	21K (Omicron)	BA.1.15	
HS11493	21K (Omicron)	BA.1.1	

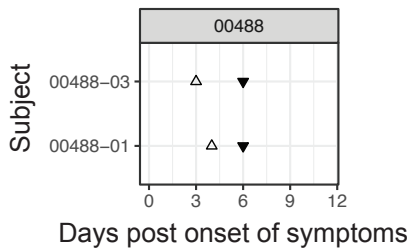
5,000 10,000 15,000 20,000 25,000 30,000

Supplementary Figure 2. Inclusion and exclusion of transmission pairs. (A) Examples of possible transmission pairs in households. In each panel, the index cases are in blue, and the household contacts are in black. The grey arrows indicate transmission pairs, and they point from the donor to the recipient. (B) Consensus genome alignments inconsistent with household transmission. The genomes were visualized using Nextclade. Both Nextclade and Pango lineages are reported. Colored bars are mutations with reference to the Wuhan-Hu-1/2019 (MN908947) strain. Approximate genome positions are indicated below figure. Gray partial bars indicate missing data. Asterisks next to household names indicate households that were removed from further analyses. Asterisks next to sample names indicate samples that were removed from further analyses, while the rest of the household was retained. The black cross (†) indicates a household with two separate transmission pairs.

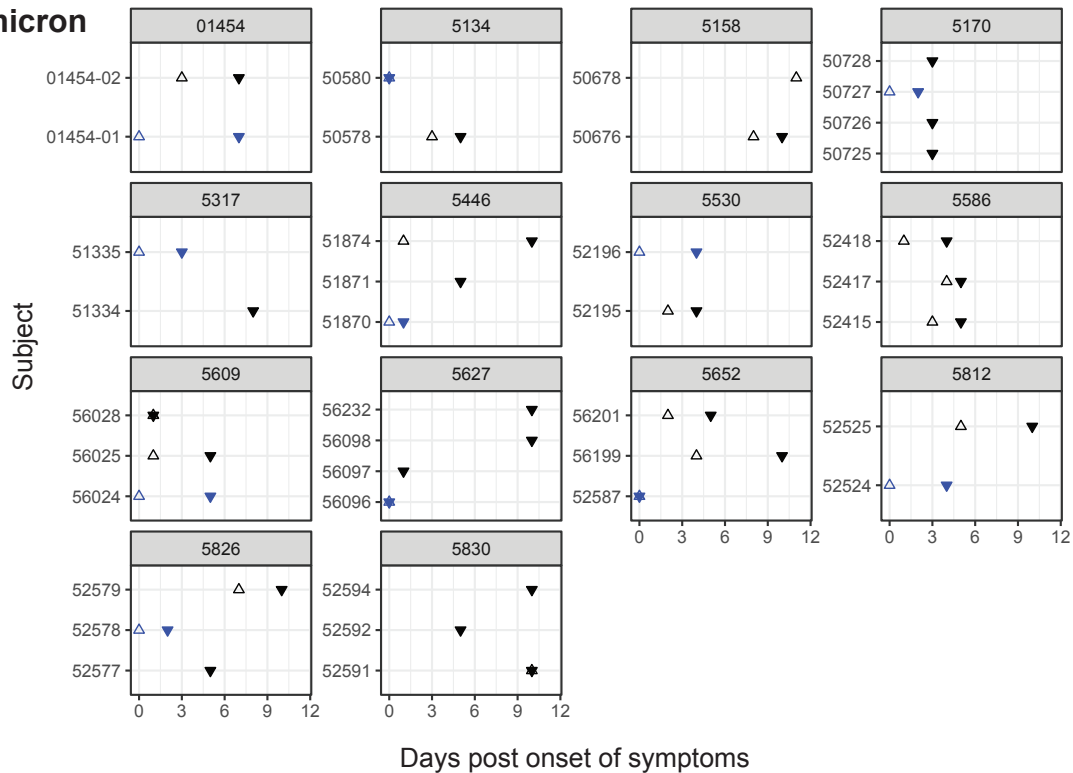


Supplementary Figure 3. Timing of symptom onset and specimen collection by household. Each panel shows a household, grouped by the indicated clades. Within each household, blue symbols indicate index case(s) and black symbols indicate household contact(s). Open triangles indicate time of symptom onset and filled triangles indicate specimens that were sequenced. When symptom onset and sample collection occur on the same day, overlapping triangles form a star. If there is no symptom onset, the case was considered to be asymptomatic.

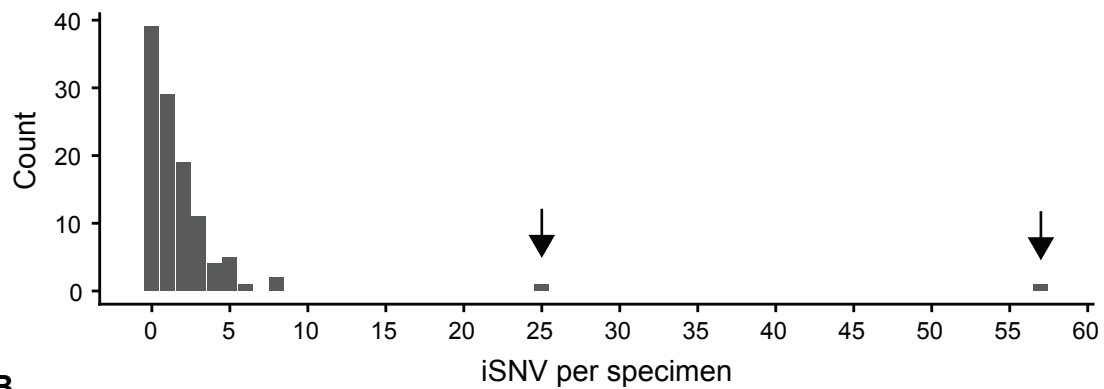
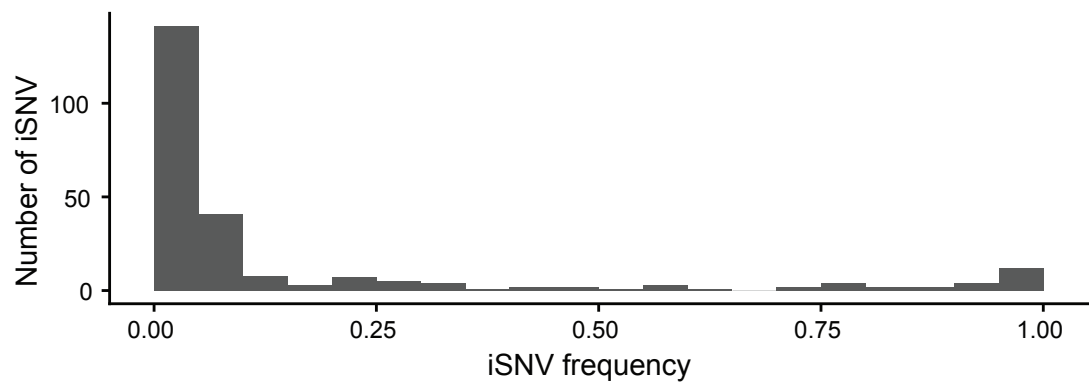
## Gamma



## Omicron



Supplementary Figure 4. Timing of symptom onset and specimen collection by household. Each panel shows a household, grouped by the indicated clades. Within each household, blue symbols indicate index case(s) and black symbols indicate household contact(s). Open triangles indicate time of symptom onset and filled triangles indicate specimens that were sequenced. When symptom onset and sample collection occur on the same day, overlapping triangles form a star. If there is no symptom onset, the case was considered to be asymptomatic.

**A****B**

Supplementary Figure 5. iSNV detected when sequencing replicates are merged. (A) The number of iSNV per specimen. Nearly all still had a low number of iSNV. However, merging the reads greatly increased the number of iSNV in two individuals. These iSNV were near the 2% threshold. (B) Most iSNV were found at low frequencies. The frequency distribution shifted toward lower frequencies compared to when iSNV had to be detected in both replicates.