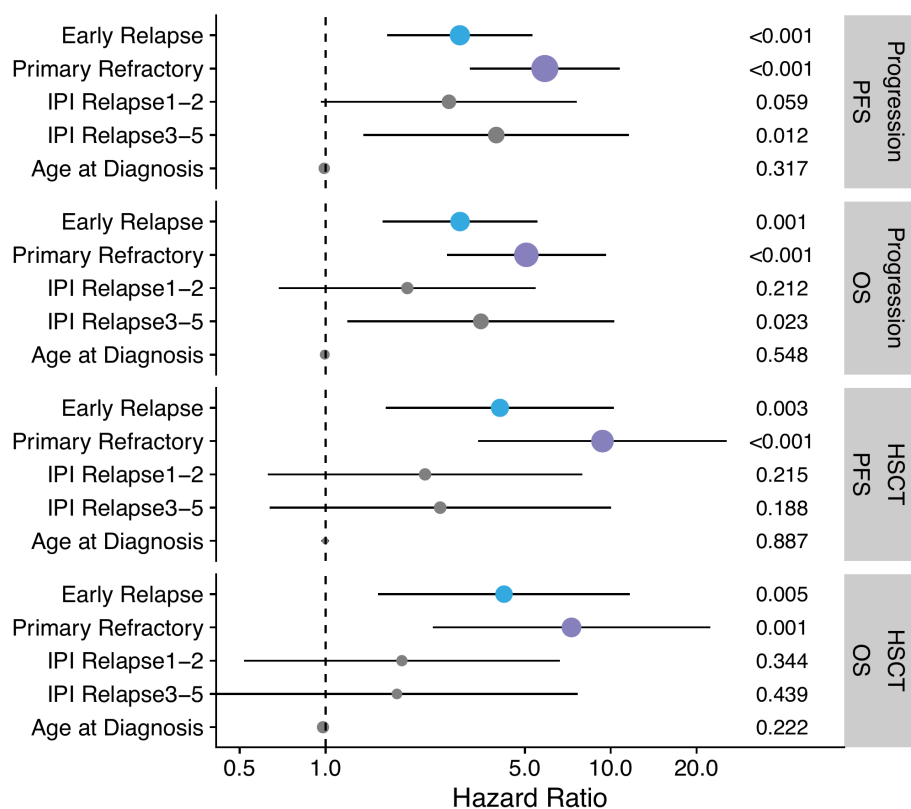
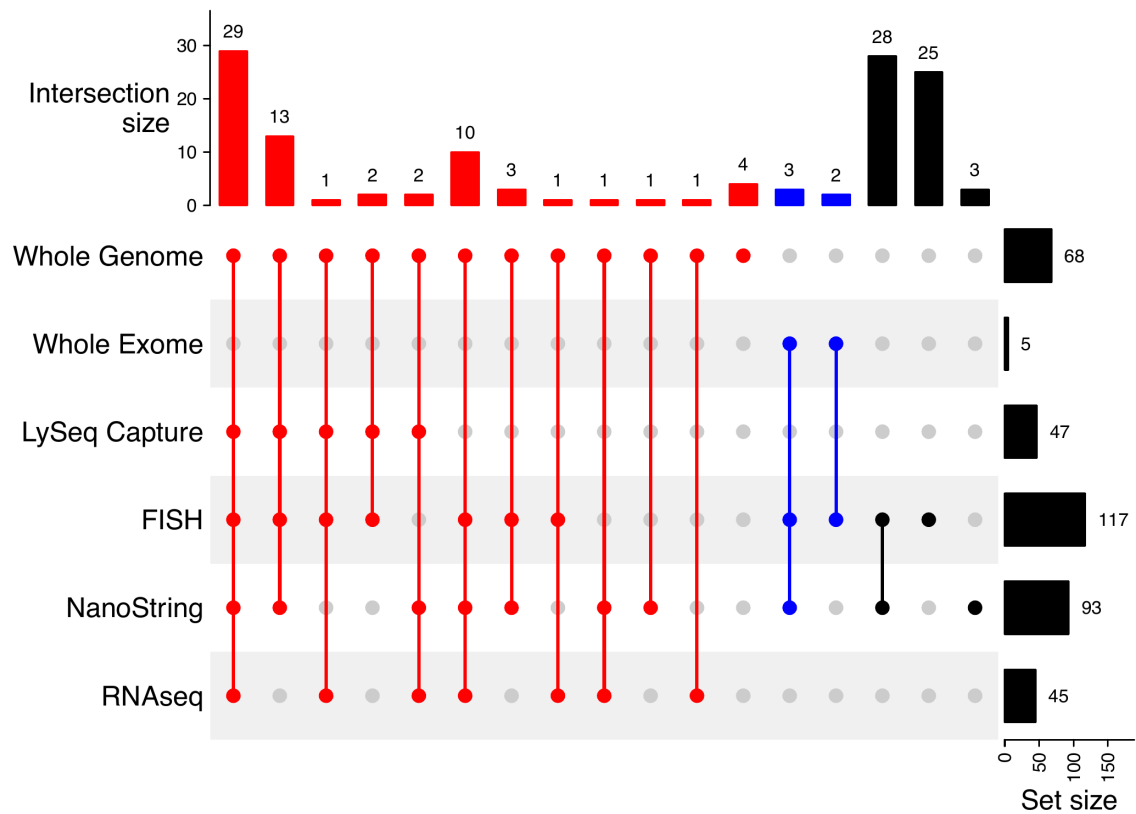


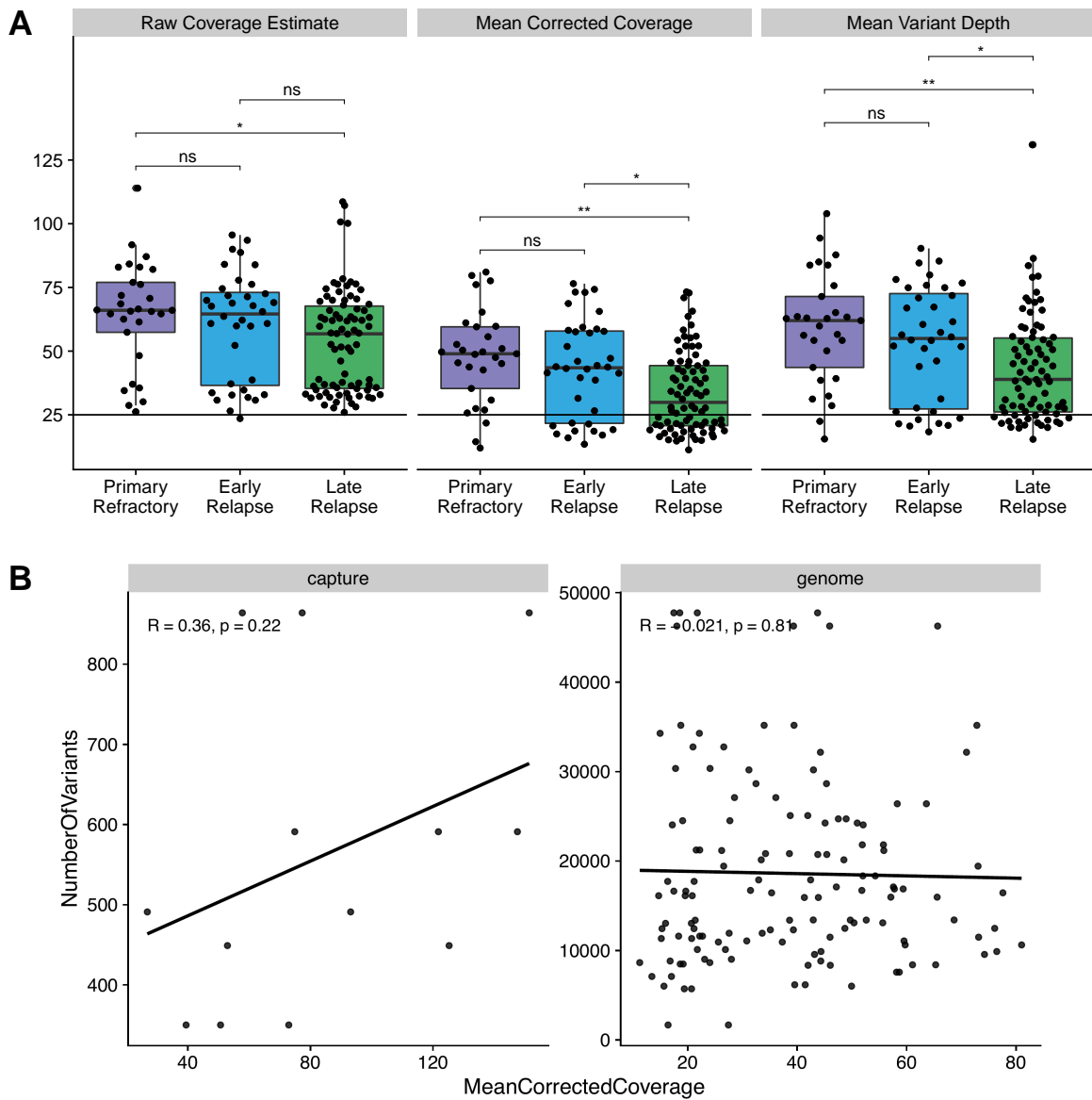
Extended Data



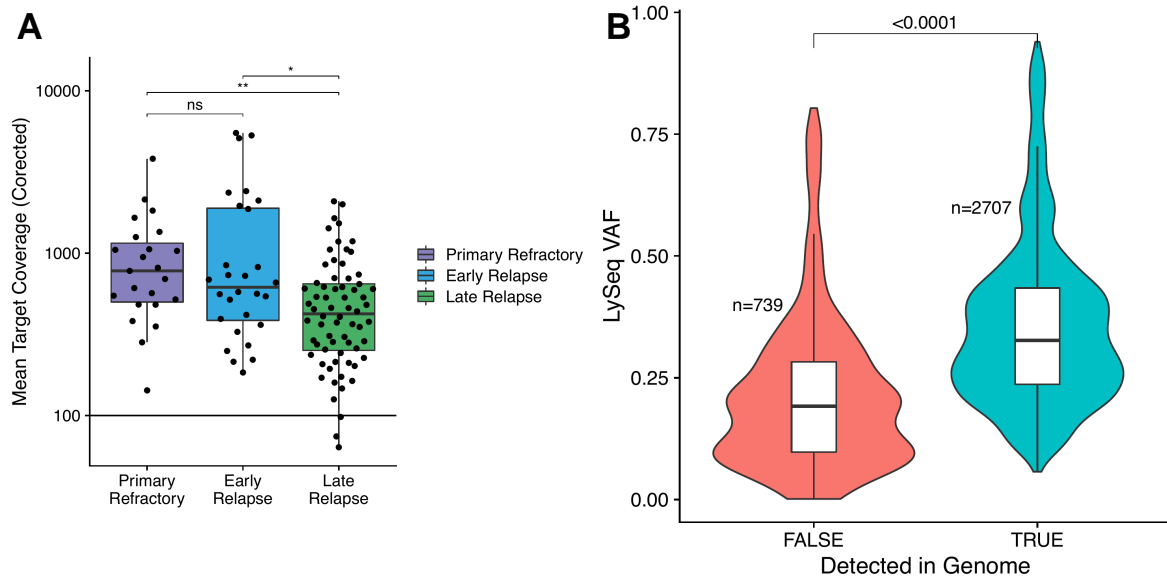
Extended Data Figure 1. Hazard ratios and P-values from Cox models of OS and PFS from time of progression or time of transplant, adjusted for age at diagnosis, sex, and IPI at relapse.



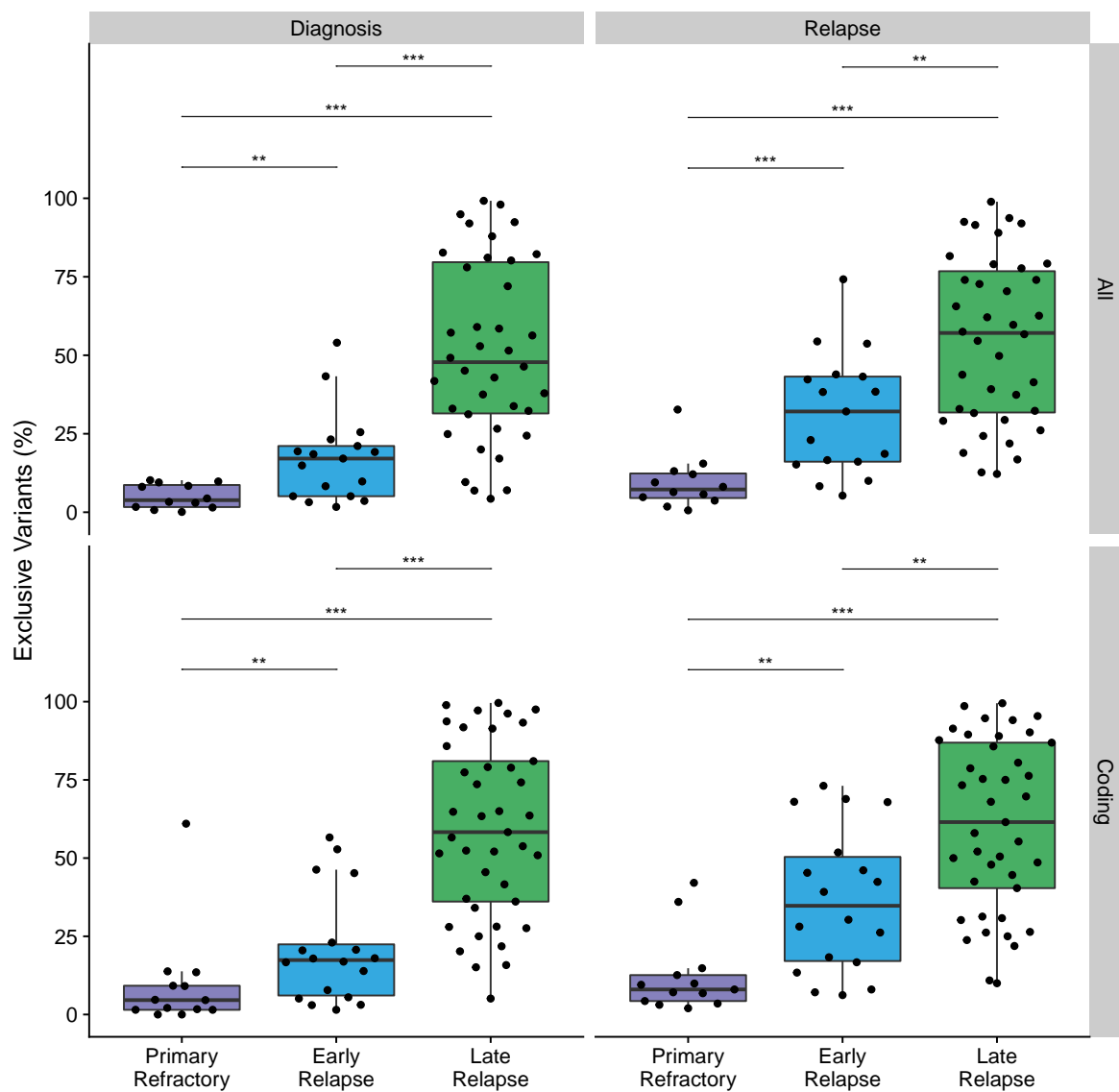
Extended Data Figure 2. UpSet plot summarizing assays completed on multiple biopsies per patient.



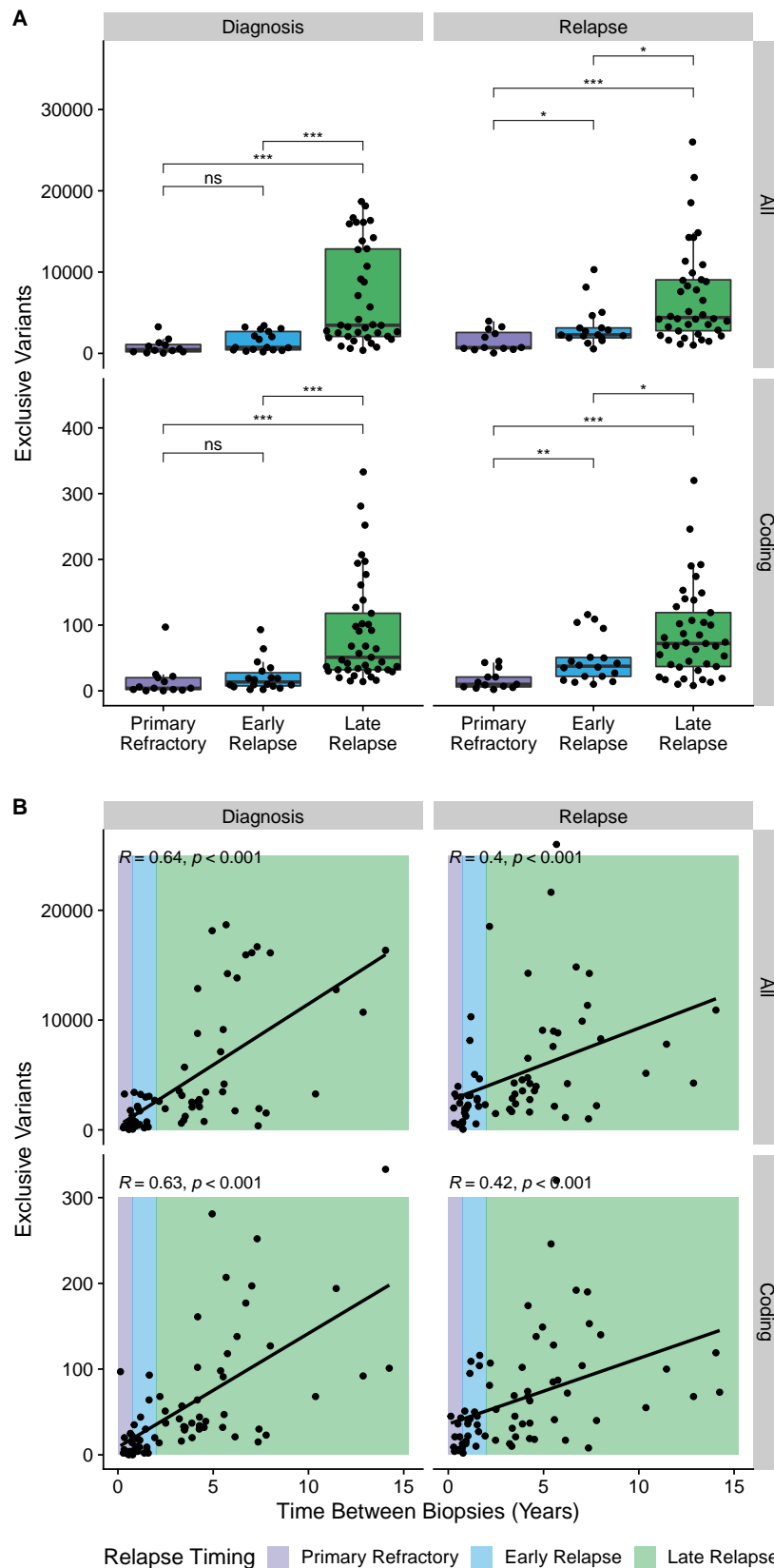
Extended Data Figure 3. A. Raw coverage estimate, mean corrected coverage (not double-counting overlapping reads), and mean depth across each variant position across relapse timing categories. * $P < 0.05$; ** $P < 0.01$; ns not significant. B. Coverage vs. total mutation burden for exomes (“capture”) and genomes. R represents Pearson correlation coefficient.



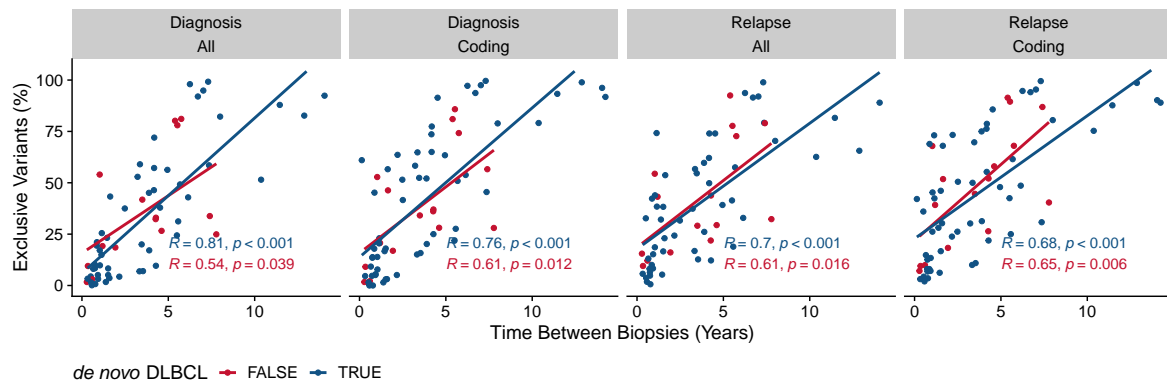
Extended Data Figure 4. A. Mean corrected coverage across capture space for the LySeqST assay stratified by relapse timing category. * $P < 0.05$; ** $P < 0.01$; ns not significant. B. VAFs of variants identified with the LySeqST assay, stratified by whether or not a variant was called in the matching WGS data. Lower VAFs of variants not detected by WGS supports that LySeqST has enhanced sensitivity for sub-clonal variants that fall below the limit of detection of WGS.



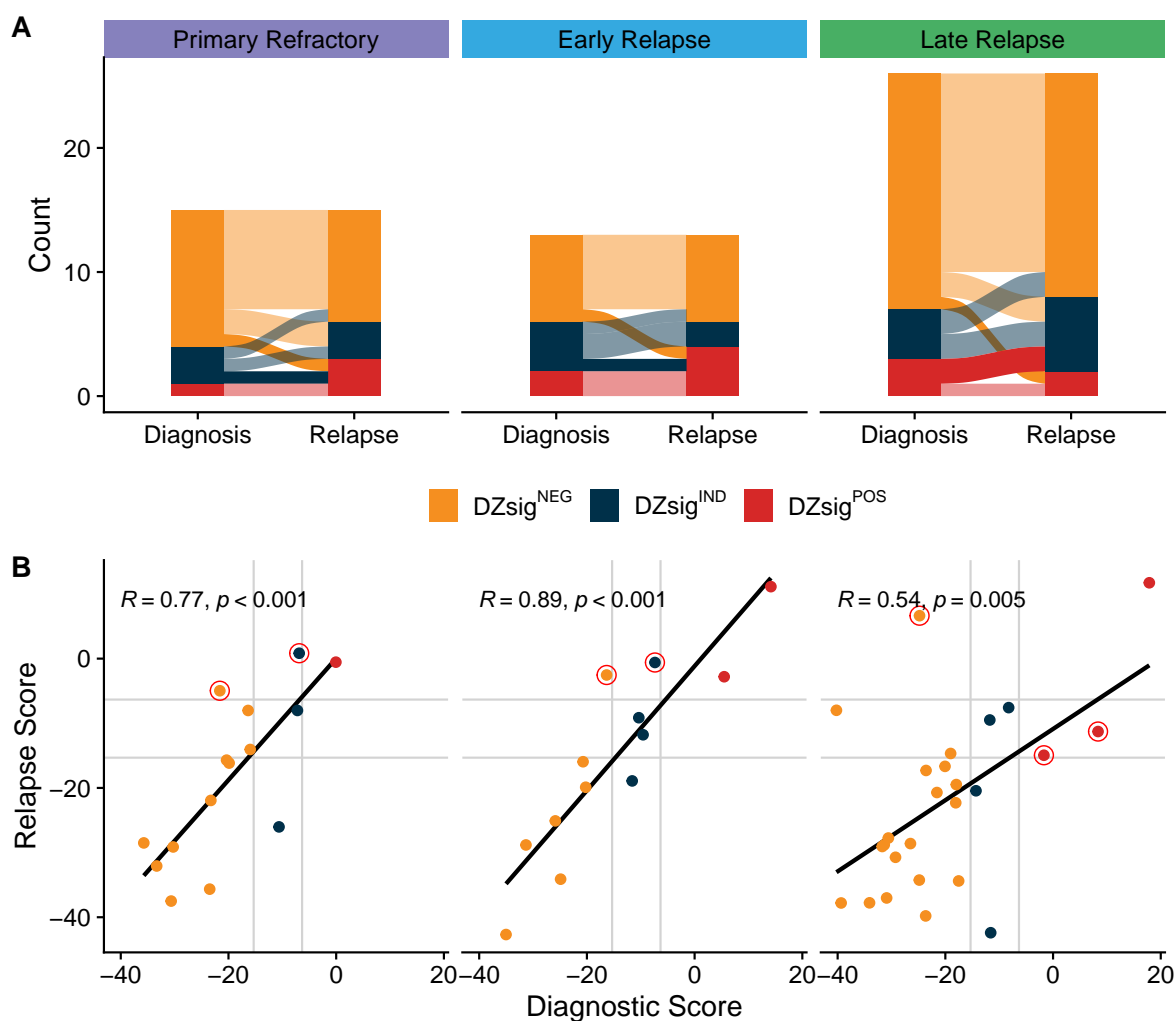
Extended Data Figure 5. A. Percent exclusive variants per biopsy vs. relapse timing as a categorical variable. *** $P < 0.001$, ** $P < 0.01$, * $P < 0.05$. B. Correlation of percent exclusive variants with relapse timing, stratified by whether or not a patient ever had indolent disease. R represents Pearson correlation coefficient.



Extended Data Figure 6. Relationship between absolute number of exclusive mutations per biopsy vs. relapse timing as a categorical (A) or continuous (B) variable.



Extended Data Figure 7. Correlation of percent exclusive variants with relapse timing, stratified by whether or not a patient had transformed disease. R represents Pearson correlation coefficient.



Extended Data Figure 8. Comparison of DZsig classifications and scores. A. Alluvial plot highlighting switches from DZsigPOS to NEG or IND with opaque alluvia. B. Comparison of DLBCL90 DZsig scores between biopsies. R represents Pearson correlation. Only tumors classified as GCB or unclassified for COO were included in this analysis.