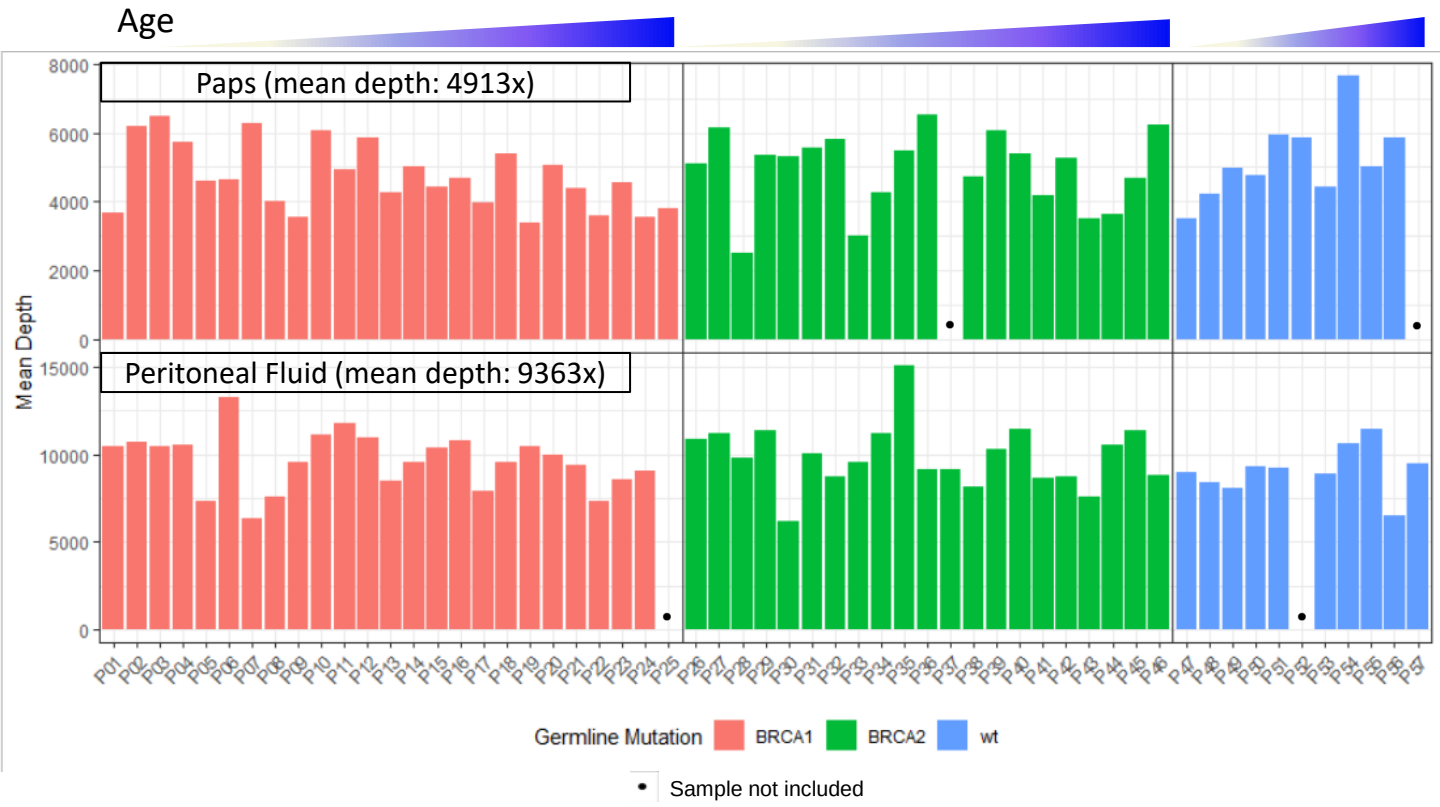
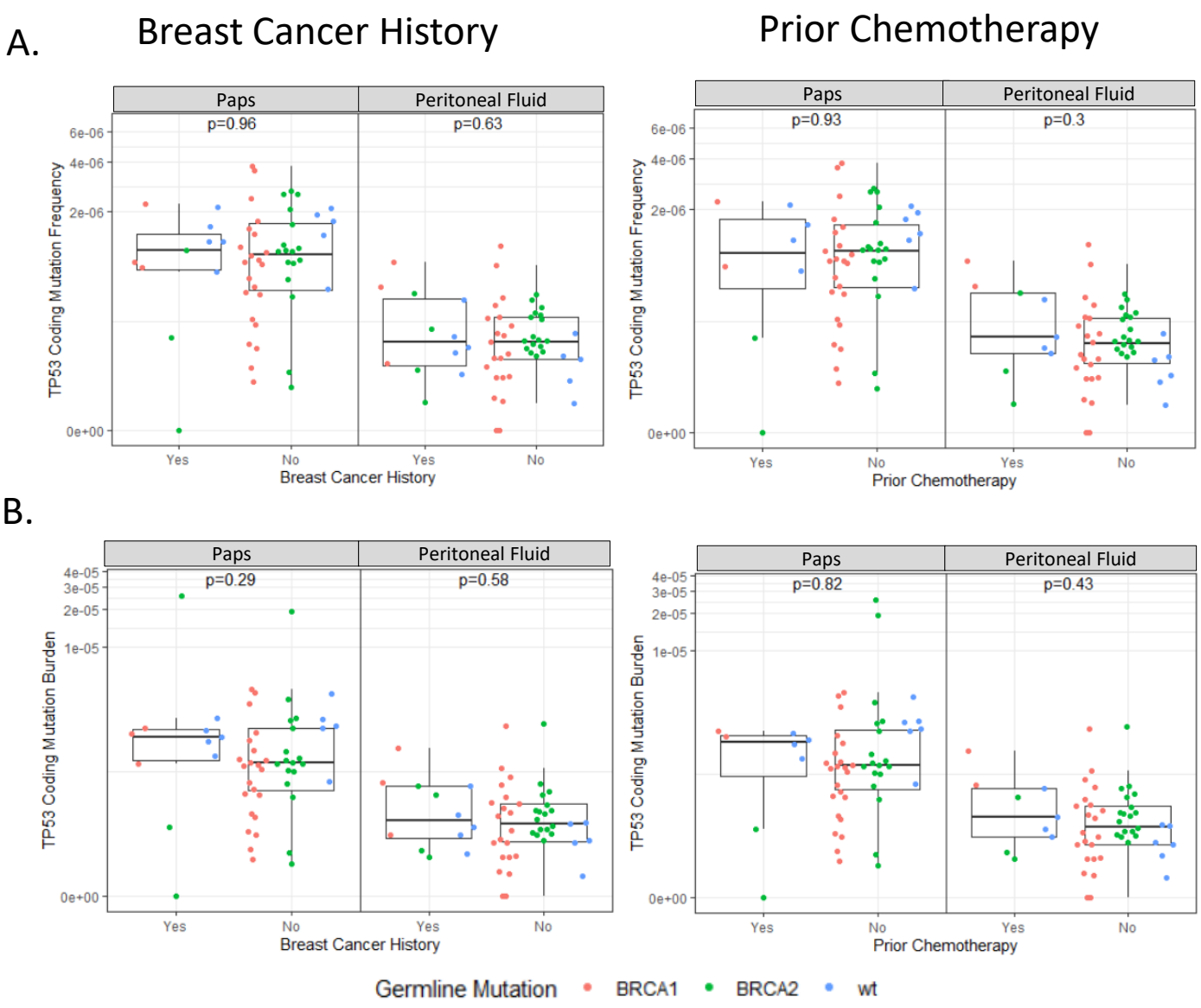
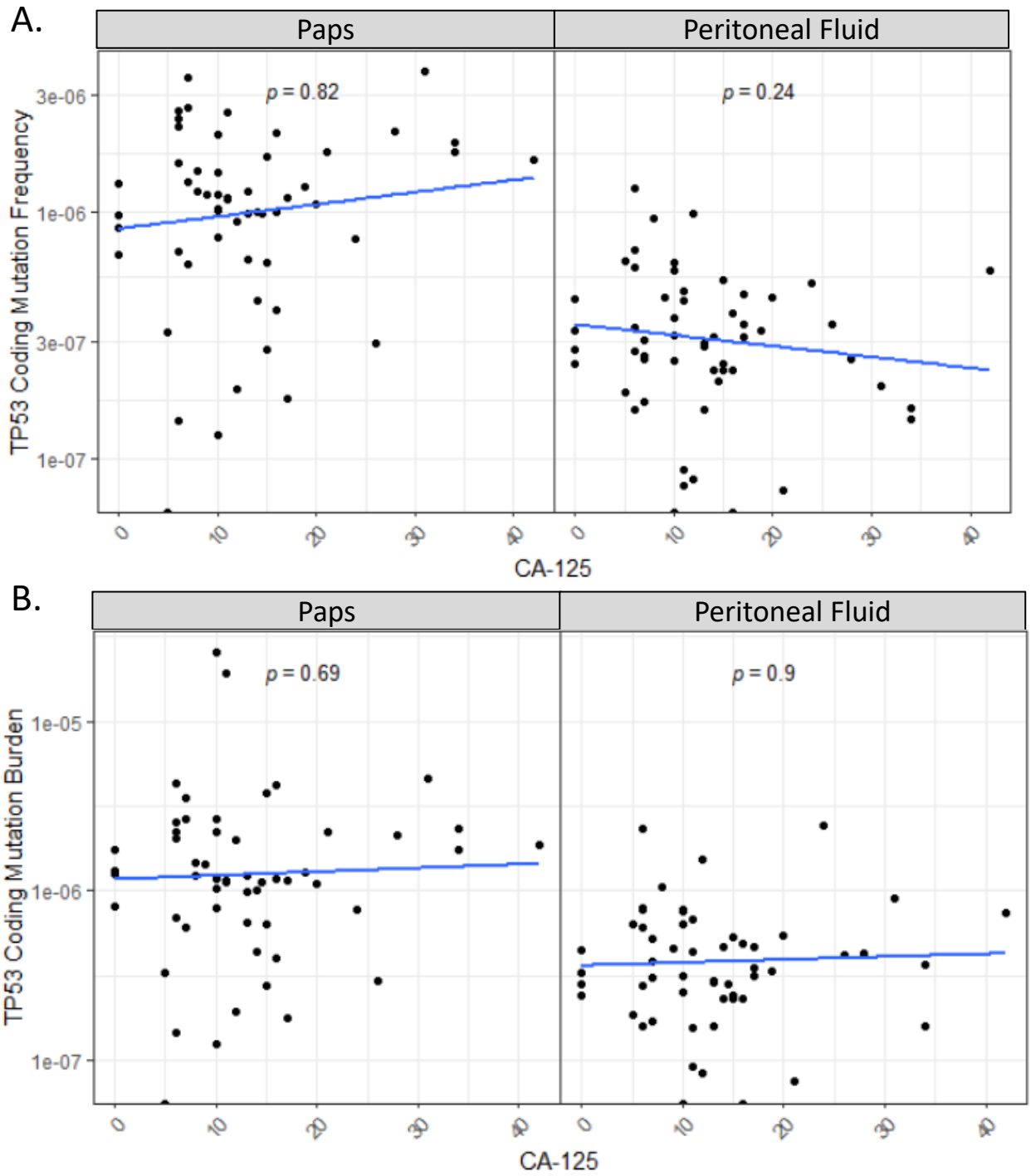


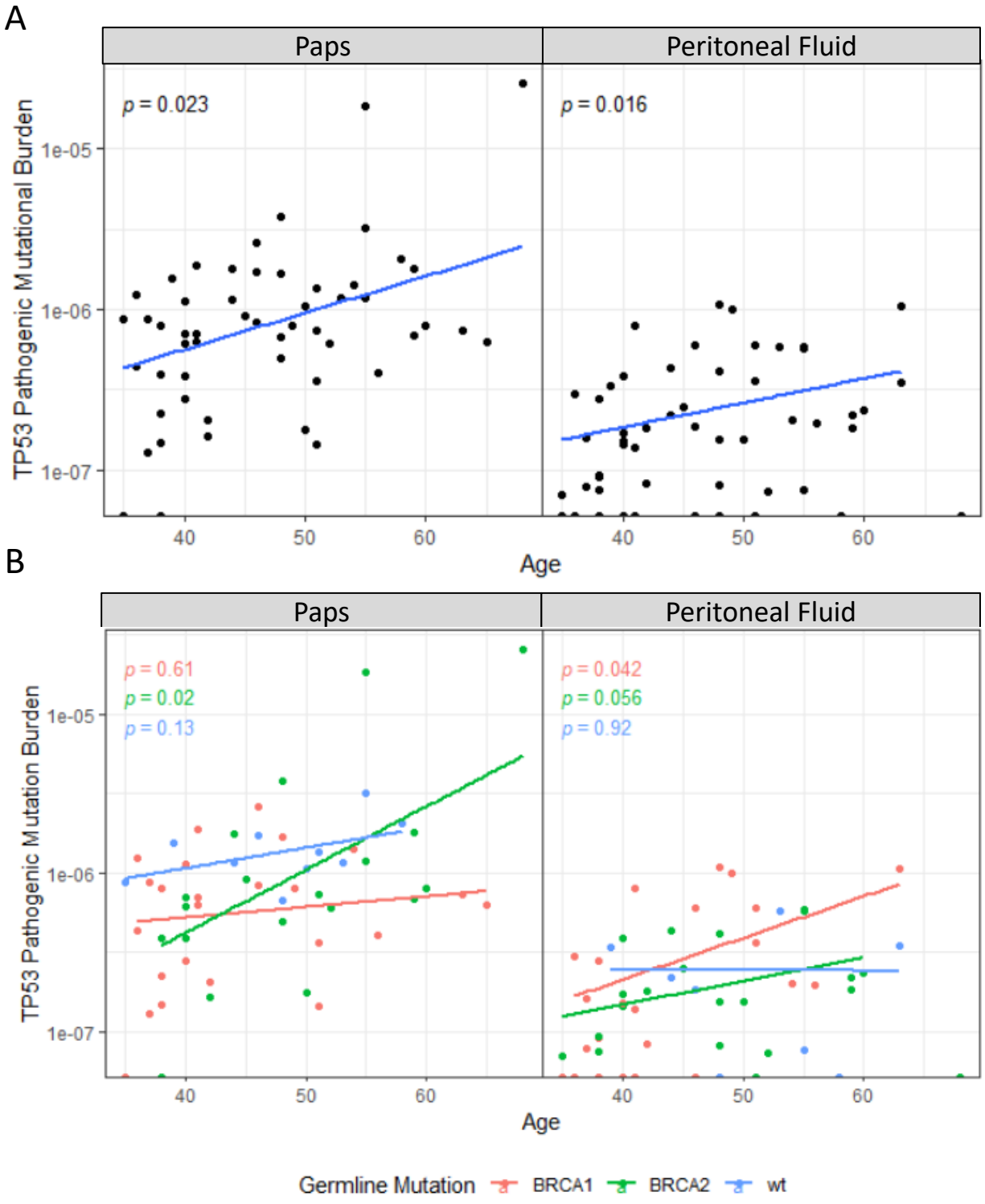
Supplementary Figure S1. Summary of average *TP53* duplex sequencing depth of each sample type. Average *TP53* duplex sequencing depth of Paps (top) and peritoneal fluid (bottom) plotted per individual. Each column corresponds to a patient. Patients are grouped by germline mutation and sorted by ascending age. Depth indicates the average duplex depth for all *TP53* positions sequenced. Missing samples are indicated with a black dot.
Technically it's the filtered MAF (so already filtered out VAF>0.4, outliers, and masking etc.)



Supplementary Figure S2. *TP53* mutation frequency and mutation burden in Paps and peritoneal fluid are not associated with breast cancer history or prior chemotherapy history. A. Comparison of *TP53* coding mutation frequency by breast cancer history and prior chemotherapy in Paps (left panels) and peritoneal fluid (right panels) of *BRCA1* carriers, *BRCA2* carriers, and *BRCA wt* individuals. *TP53* coding mutation frequency was calculated as the number of *TP53* coding mutations divided by the total number of duplex nucleotides sequenced in coding regions. **B.** Comparison of *TP53* coding mutation burden by breast cancer history and prior chemotherapy in Paps (left panels) and peritoneal fluid (right panels) of *BRCA1* carriers, *BRCA2* carriers, and *BRCA wt* individuals.*TP53* mutation burden was calculated as the total number of mutant duplex reads divided by the total number of duplex nucleotides sequenced in the *TP53* coding region. **In A and B,** each dot represents a sample, and box plots display the quartiles with whiskers extending up to 1.5x the interquartile range. p-values correspond to Mann-Whitney U tests for two-group comparisons.

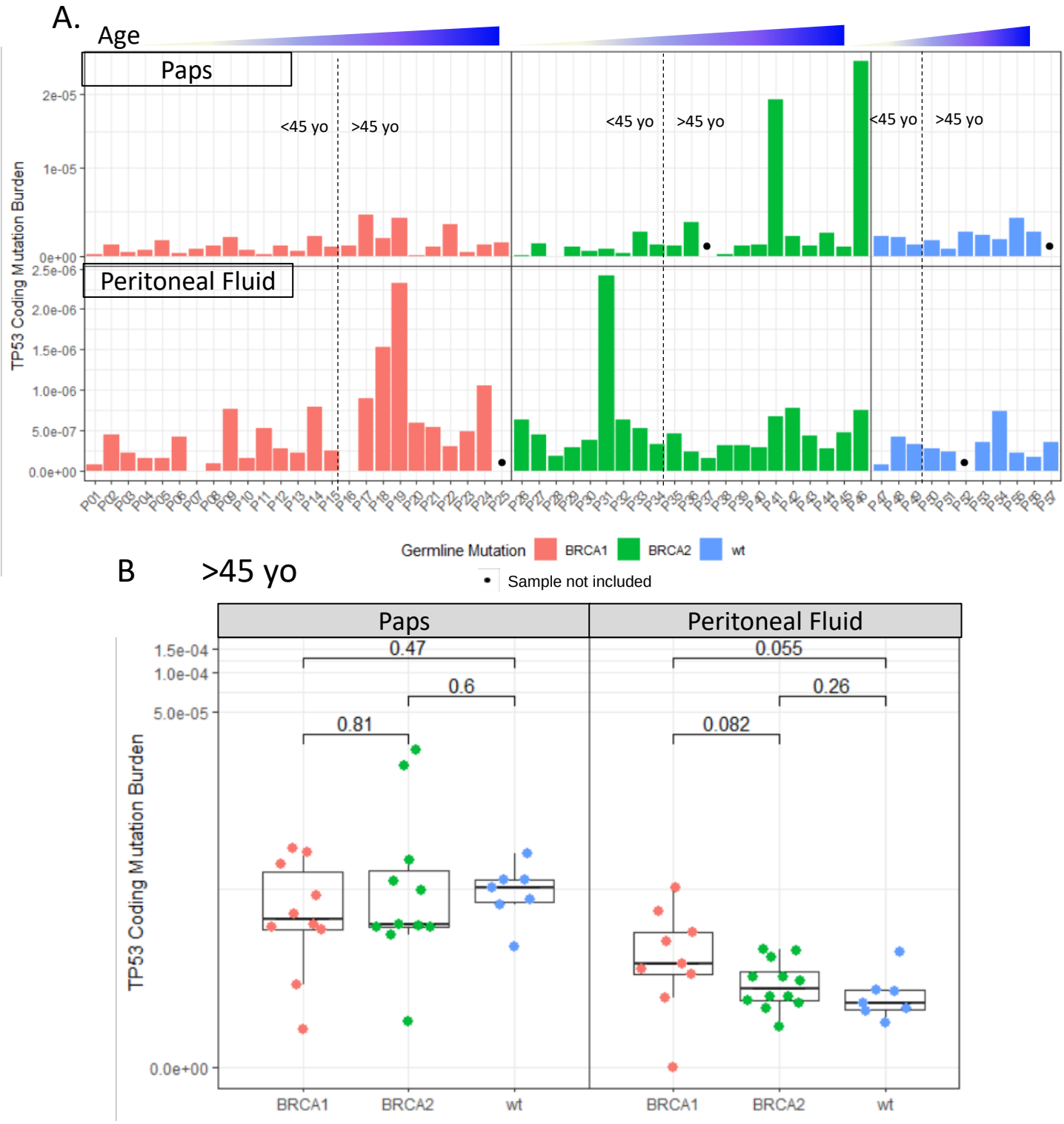


Supplementary Figure S3. *TP53* mutation frequency and mutation burden in Paps and peritoneal fluid are not associated with serum CA-125 levels. A. Correlation between serum CA-125 levels and *TP53* coding mutation frequency for Paps (left) and peritoneal fluid (right). *TP53* coding mutation frequency was calculated as the number of *TP53* coding mutations divided by the total number of duplex nucleotides sequenced in coding regions. p-values were calculated with Spearman's rank correlation test. **B.** Correlation between serum CA-125 levels and *TP53* coding mutation burden for Paps (left) or peritoneal fluid (right). *TP53* coding mutation burden was calculated as the total number of mutant duplex reads divided by the total number of duplex nucleotides sequenced in the *TP53* coding region. p-values were calculated with Spearman's rank correlation test.

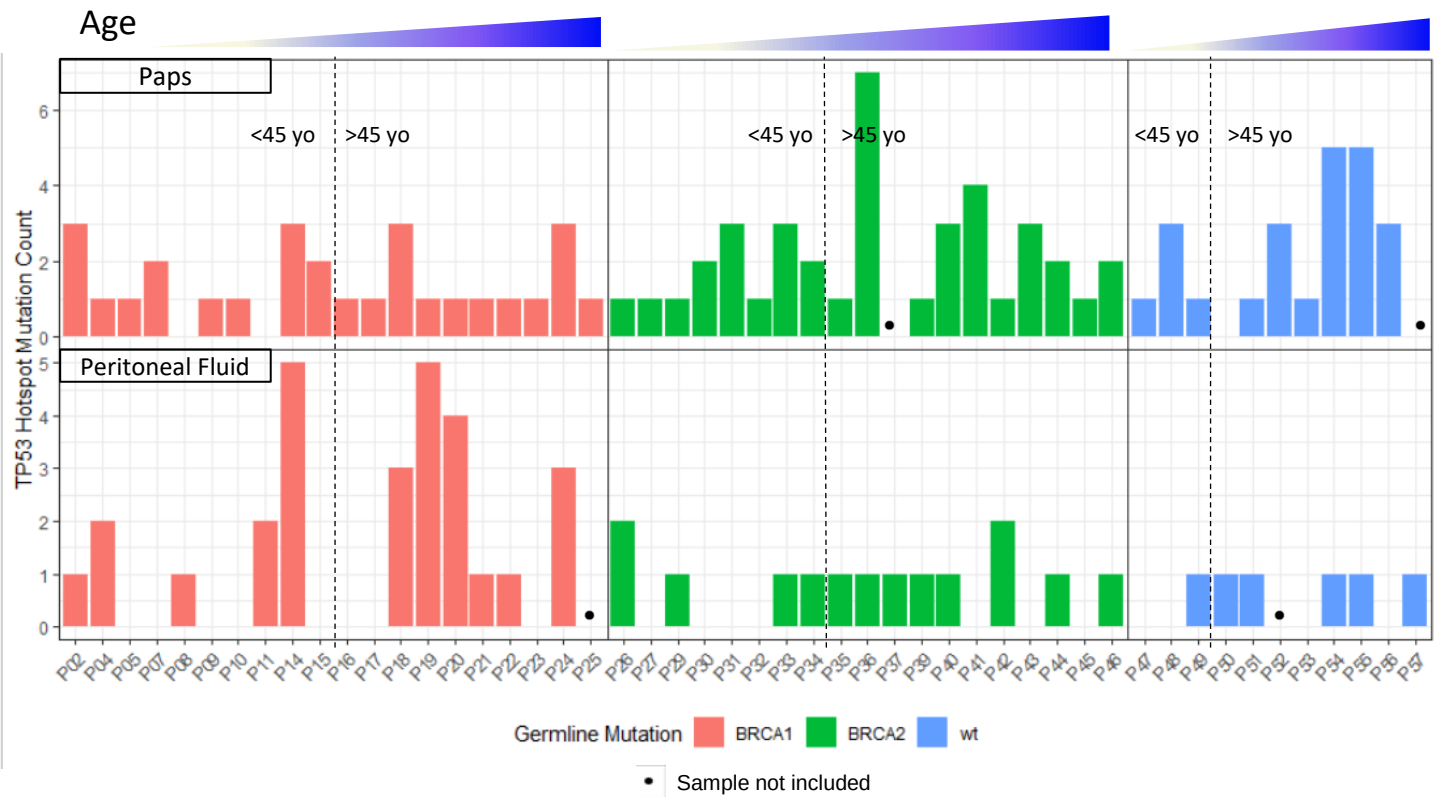


Supplementary Figure S4. *TP53* pathogenic mutation burden is associated with age in both Paps and peritoneal fluids. A. Age is correlated with *TP53* pathogenic mutation burden identified in Paps (left) and peritoneal fluids (right). *TP53* pathogenic mutation burden was calculated as the total number of pathogenic mutant duplex reads divided by the total number of duplex nucleotides sequenced in the *TP53* coding region. Pathogenicity was defined by the Seshat algorithm (Tikkanen, Leroy et al. 2018). p-values were calculated with Spearman's rank correlation test. **B.** Correlation plot of age and *TP53* pathogenic mutation burden color-coded by *BRCA1* carriers, *BRCA2* carriers, and *BRCA* non-carriers (*wt*) for Paps (left) and peritoneal fluids (right). p-values were calculated with Spearman's rank correlation test.

Don't forget to update later



Supplementary Figure S5. *TP53* coding mutation burden is increased in *BRCA1* carriers older than 45 years of age. A. *TP53* coding mutation burden of Paps (top) and peritoneal fluid (bottom) plotted per individual. Each column corresponds to a patient. Patients are grouped by germline mutation and sorted by ascending age. *TP53* coding mutation burden was calculated as the total number of mutant duplex reads divided by the total number of duplex nucleotides sequenced in coding regions. Dashed lines indicate age 45 cutoffs. Missing samples are indicated with a black dot. **B.** Comparison of *TP53* coding mutation burden between *BRCA1* carriers, *BRCA2* carriers, and *BRCA* non-carriers (*wt*) older than 45 years in Paps (left) and peritoneal fluid (right). Overlying box plots display the quartiles with whiskers extending up to 1.5x the interquartile range. p-values correspond to Mann-Whitney U tests.



Supplementary Figure S6. Mutations in *TP53* hotspot codons. *TP53* substitution mutation count of Paps (top) and peritoneal fluid (bottom) plotted per individual. Each column corresponds to a patient. Patients are grouped by germline mutation and sorted by ascending age. Hotspots were defined as codons accounting for at least 1% of reported substitutions in HGSOC (UMD database, n=5948, see Methods). Dashed lines indicate age 45 cutoffs. Missing samples are indicated with a black dot.