

## Summary of Results

- Primary outcome - plots and ORs indicate reduced proportions and odds of grade 3 toxicity or higher for cases vs controls, particularly for the DPYD sub-group. This effect not apparent in UGT1A1 subgroup. However, tests don't indicate differences are significant.
- Secondary outcomes - plots and ORs indicate reduced odds of all three secondary outcomes for cases vs controls. Statistically significant difference in proportions for **treatment delay** and **dose change**. Drug discontinuation trending (p=0.06)

## Descriptive Data Analysis

Variable	Control	Case
n	75	16
Age (mean (SD))	57.49 (10.27)	56.25 (12.06)
Race (%)		
Asian	1 (1.3)	0 (0.0)
Black	5 (6.7)	0 (0.0)
White	67 (89.3)	16 (100.0)
Other	2 (2.7)	0 (0.0)
Gender = Male (%)	32 (42.7)	9 (56.2)
Eligible Gene = UGT1A1 (%)	19 (25.3)	4 (25.0)
DPYD AS = 1.5 (%)	47 (83.9)	9 (75.0)
Cancer Type (%)		
Colon	19 (25.7)	5 (31.2)
Rectal	8 (10.8)	5 (31.2)
Breast	12 (16.2)	3 (18.8)
Gastric	2 (2.7)	1 (6.2)

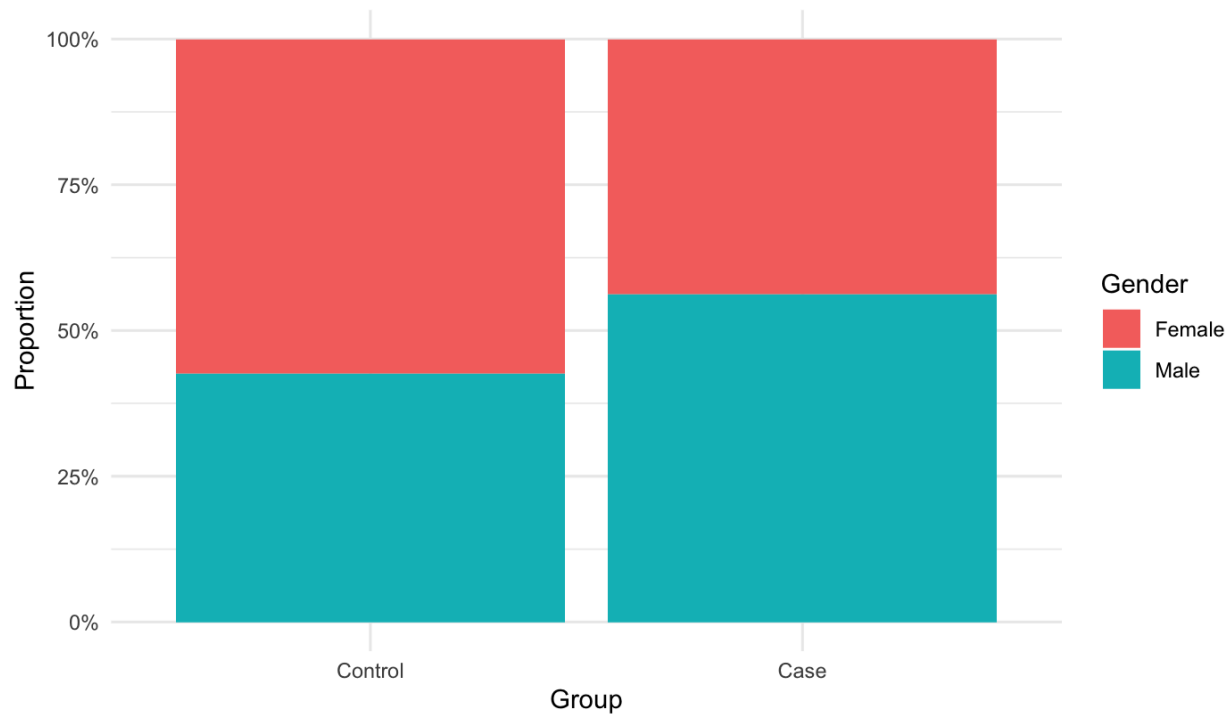
Pancreatic	19 (25.7)	2 (12.5)
Esophageal	1 (1.4)	0 (0.0)
Head and Neck	2 (2.7)	0 (0.0)
Anal	2 (2.7)	0 (0.0)
Hepatic	1 (1.4)	0 (0.0)
Other	8 (10.8)	0 (0.0)
Cancer Stage and Grade (mean (SD))	3.01 (1.01)	3.19 (0.91)
Chemo Regimen (%)		
Single Irinotecan	3 (4.1)	0 (0.0)
Single Capecitabine	19 (25.7)	4 (25.0)
Combo Capecitabine	4 (5.4)	2 (12.5)
Combo 5-FU	23 (31.1)	5 (31.2)
Folfiri	10 (13.5)	2 (12.5)
Folfirinox	15 (20.3)	3 (18.8)

Table 1 - *Data Summary*

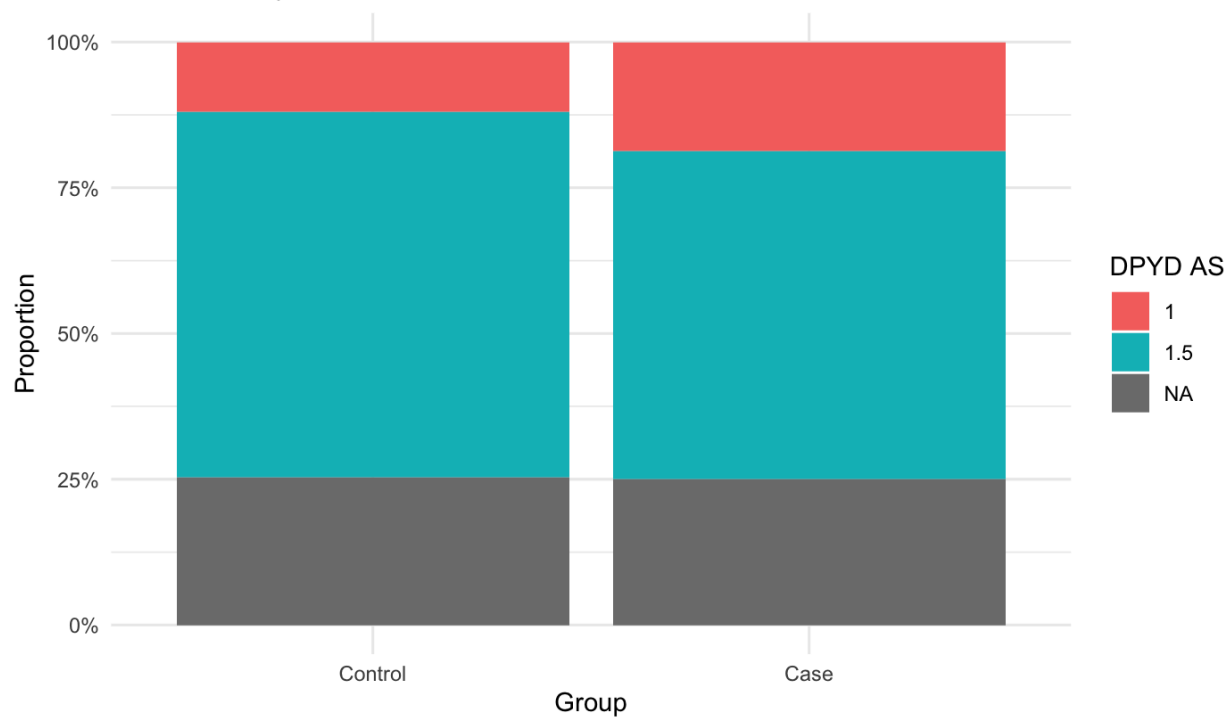
Variable	Test	Statistic	p.value
Age	t-test	0.381	0.707
Race	Chi-square	1.871	0.600
Gender	Chi-square	0.511	0.475
Eligible Gene	Chi-square	0.000	1.000
DPYD Activity Score	Chi-square	0.102	0.750
Cancer Type	Chi-square	8.511	0.484
Cancer Stage and Grade	Chi-square	2.124	0.547
Chemotherapy Regimen	Chi-square	0.006	0.941

Table 2 - *Demographic Variables comparison test results*

Gender Distribution by Case vs. Control



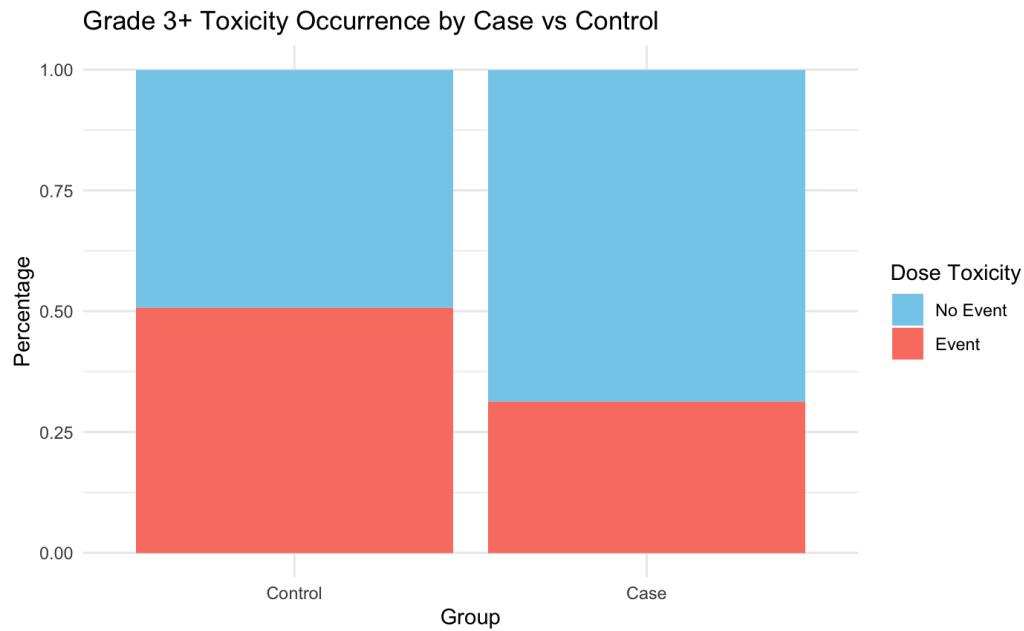
DYPD AS by Case vs. Control



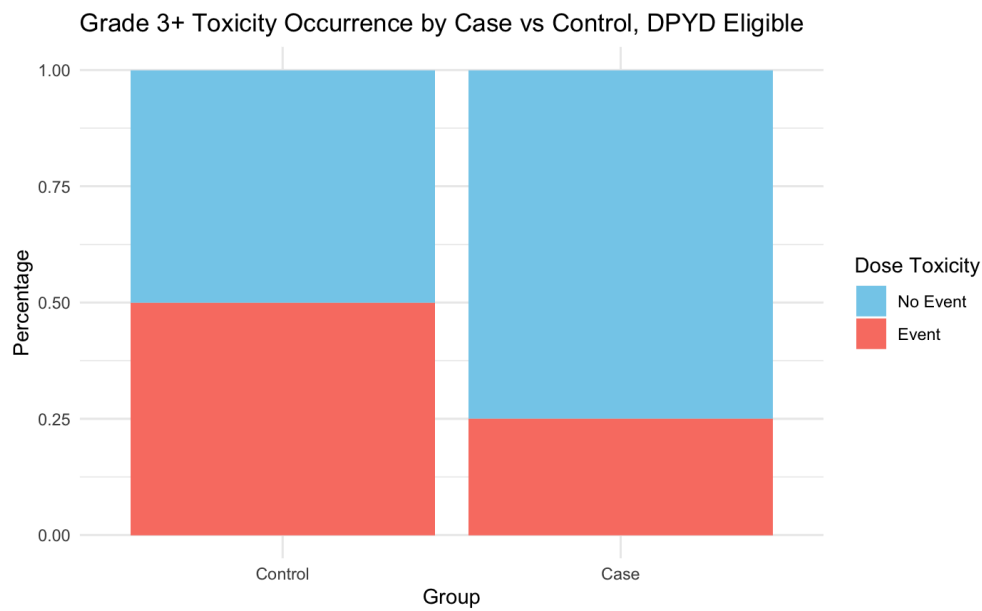
# Primary Outcome: Incidence of >Grade 3 toxicity

- TOX\_grade3up

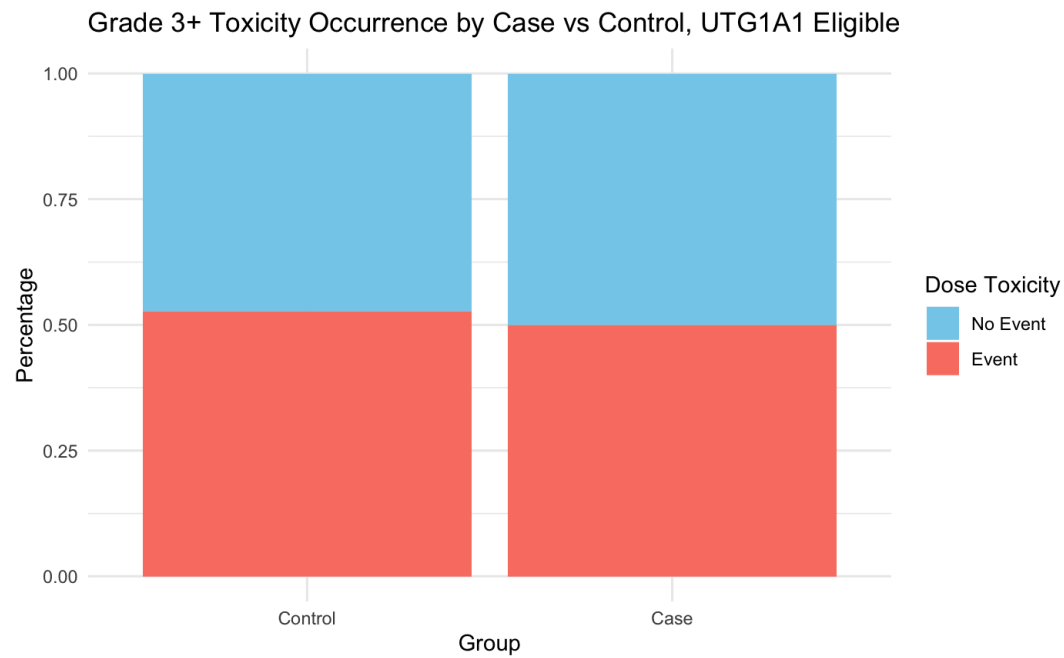
All observations



Eligible Gene = DPYD



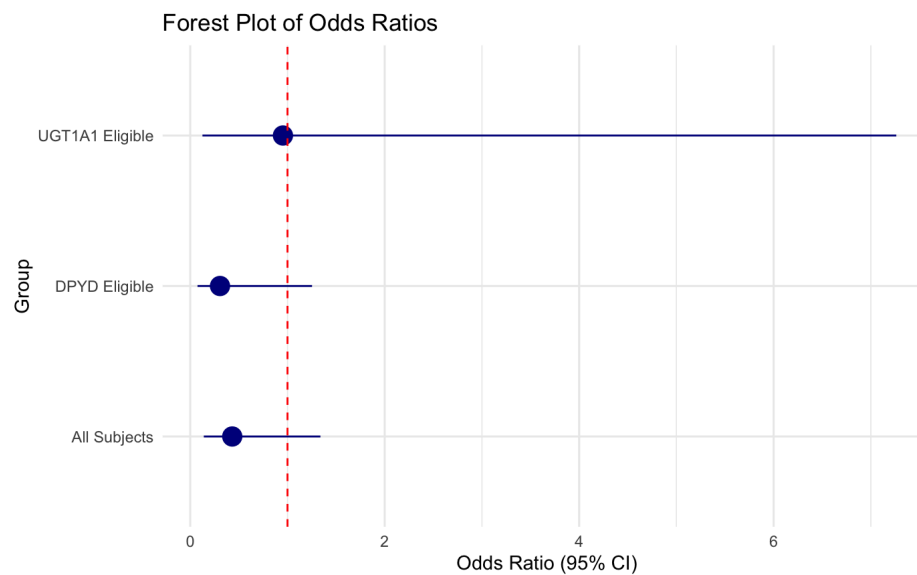
## Eligible Gene = UGT1A1



## Summary:

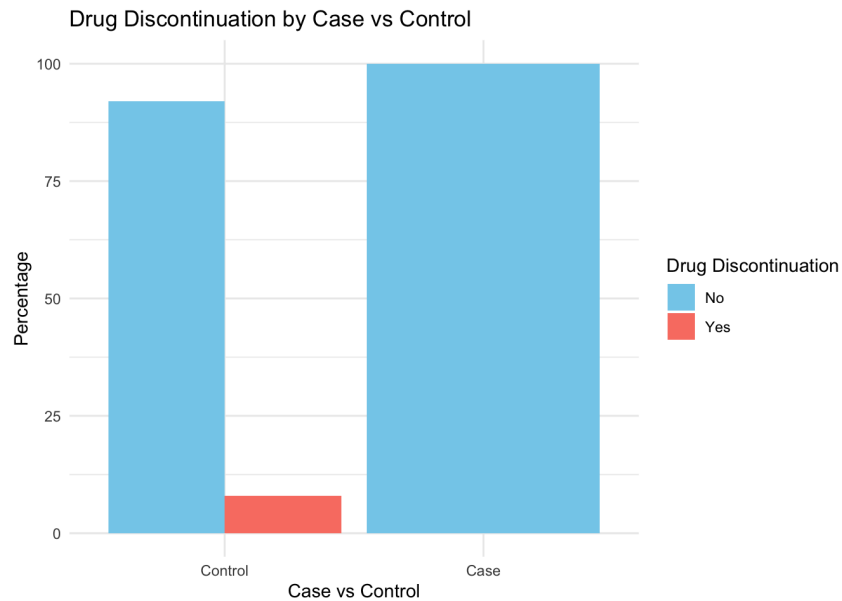
using conditional logistic regression as proportions testing, i.e.:

$$\text{logit}(P(\text{TOX\_grade3up}=1)) = \beta_0 + \beta_1 \text{case\_control} + \text{strata}(\text{Pair\_ID})$$

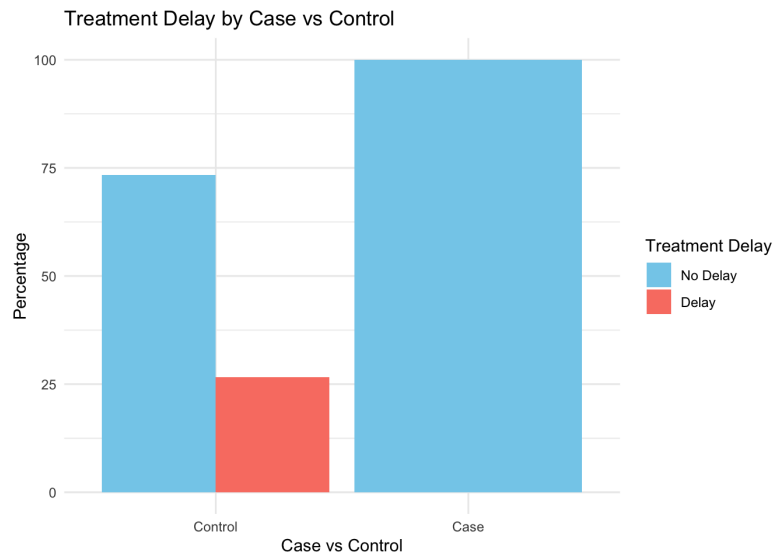


# Secondary Outcomes: drug discontinuation, treatment delay, dose change

## Drug discontinuation



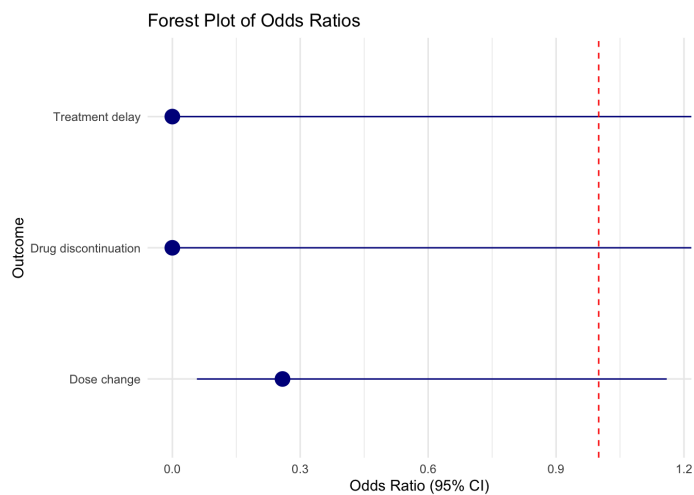
## Treatment Delay



## Dose Change



## Summary



Tx delay and drug continuation having no observations for cases → OR = 0 → 97.5% CI = Inf  
Reporting results of LRT from Clogit as well\*:

Endpoint	Test.Statistic	p.value
Drug Discontinuation	3.502	0.061
Treatment Delay	9.000	0.003 **
Dose Change	4.193	0.041 *

\*I.e.

```
coxph(formula = Surv(rep(1, 91L), Dose_change_fixed) ~ case_control + strata(Pair_ID), data = data)
n= 91, number of events= 30
```

	coef	exp(coef)	se(coef)	z	Pr(> z )
case_controlCase	-1.353	0.258	0.766	-1.77	0.077

Concordance= 0.578 (se = 0.049 )

**Likelihood ratio test = 4.19 on 1 df, p=0.04**

Wald test = 3.12 on 1 df, p=0.08

Score (logrank) test = 3.59 on 1 df, p=0.06

## Modeling

### Model 1

$$\text{logit}(P(\text{T0X\_grade3up} = 1)) = \beta_0 + \beta_1(\text{case\_control}) + \beta_2(\text{gender}) + \beta_3(\text{dpyd\_as}) + \text{strata}(\text{Pair\_ID})$$

Table 5a: Conditional Logistic Regression Results  
(Model 1)

	Odds Ratio	2.5% CI	97.5% CI
case_controlCase	0.322	0.078	1.323
genderMale	0.943	0.263	3.376
dpyd_as1.5	0.459	0.080	2.622

### Model 2

$$\text{logit}(P(\text{T0X\_grade3up} = 1)) = \beta_0 + \beta_1(\text{case\_control}) + \beta_2(\text{gender}) + \beta_3(\text{dpyd\_as}) + \beta_4(\text{chemo\_reg\_condensed}) + \text{strata}(\text{Pair\_ID})$$



Table 5b: Conditional Logistic Regression Results (Model 2)

	<b>Odds Ratio</b>	<b>2.5% CI</b>	<b>97.5% CI</b>
case_controlCase	0.328	0.081	1.336
genderMale	0.897	0.244	3.303
dpyd_as1.5	0.460	0.080	2.635
chemo_reg_condensed2	NA	NA	NA

## Model 3

$\text{logit}(P(\text{TOX\_grade3up} = 1)) = \beta_0 + \beta_1(\text{case\_control}) + \beta_2(\text{gender}) + \beta_3(\text{dpyd\_as}) + \beta_4(\text{chemo\_reg\_condensed}) + \beta_5(\text{cancer\_stage\_and\_grade}) + \text{strata}(\text{Pair\_ID})$

Table 5c: Conditional Logistic Regression Results (Model 3)

	<b>Odds Ratio</b>	<b>2.5% CI</b>	<b>97.5% CI</b>
case_controlCase	0.318	0.076	1.336
genderMale	0.782	0.192	3.193
dpyd_as1.5	0.396	0.060	2.599
chemo_reg_condensed2	NA	NA	NA
cancer_stage_and_grade	1.712	0.926	3.166

## LRT of Models 2 and 3:

Analysis of Deviance Table

Cox model: response is Surv(rep(1, 68L), TOX\_grade3up)

Model 1: ~ case\_control + gender + dpyd\_as + chemo\_reg\_condensed + strata(Pair\_ID)

Model 2: ~ case\_control + gender + dpyd\_as + chemo\_reg\_condensed + cancer\_stage\_and\_grade + strata(Pair\_ID)

loglik Chisq Df Pr(>|Chi|)

1 -26.8

2 -25.1 3.19 1 0.074 .

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Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

Correlation Matrix of Predictors in Model 2

	<b>genderMale</b>	<b>dpyd_as1.5</b>	<b>chemo_reg_condensed2</b>
genderMale	1.00	-0.08	0.23
dpyd_as1.5	-0.08	1.00	0.07
chemo_reg_condensed2	0.23	0.07	1.00

Correlation Matrix of Predictors in Model 3

	<b>genderMale</b>	<b>dpyd_as1.5</b>	<b>chemo_reg_condensed2</b>	<b>cancer_stage_and_grade</b>
genderMale	1.00	-0.08	0.23	0.11
dpyd_as1.5	-0.08	1.00	0.07	0.03
chemo_reg_condensed2	0.23	0.07	1.00	0.15
cancer_stage_and_grade	0.11	0.03	0.15	1.00

## Major Changes 12/10/24

- Use of clogit instead of McNemar's test for testing diff proportions
- Updated dataset (uploaded to Dropbox 11/21)
  - Fixed secondary outcome columns
  - Fixed case vs control misclassification (n=2)
- Further condensed cancer stage variable to two groups
- Looking for multicollinearity issues in model(s) with corr matrices
- Updated tables and plots

Still running into NA issue from Chemo\_reg\_condensed