

S3 Table: Mutational spectrum of five unlinked loci under two different penetrance models

Model parameters	Median number of mutations (IQR)		
	Per population	Per case	Per control
Rare disease (prevalence: 0.1-1%)			
Multiplicative			
$\gamma=0.3$	3 (3-5)	1.000 (1.000-1.000)	0.012 (0.006-0.019)
$\gamma=0.1$	4 (3-7)	1.011 (1.000-1.034)	0.055 (0.028-0.075)
Logistic			
$\alpha=-5; \beta=1$	5 (3-8)	0.384 (0.174-0.546)	0.166 (0.069-0.260)
$\alpha=-5; \beta=0.5$	9 (5-13)	0.859 (0.629-1.043)	0.627 (0.449-0.789)
Common disease (prevalence: 1-5%)			
Multiplicative			
$\gamma=0.3$	5 (3-8)	1.027 (1.007-1.055)	0.080 (0.049-0.105)
$\gamma=0.1$	8 (5-12)	1.152 (1.062-1.260)	0.361 (0.251-0.432)
Logistic			
$\alpha=-5; \beta=1$	17.50 (12-24)	2.298 (2.062-2.477)	1.435 (1.251-1.594)
$\alpha=-5; \beta=0.5$	39 (30-48)	4.389 (4.163-4.627)	3.467 (3.260-3.645)
Pandemic disease (prevalence: 10-20%)			
Multiplicative			
$\gamma=0.3$	10 (6-14.25)	1.258 (1.143-1.372)	0.453 (0.370-0.512)
$\gamma=0.1$	22 (16-30)	2.429 (2.216-2.633)	1.879 (1.696-1.991)
Logistic			
$\alpha=-5; \beta=1$	34 (26-42.25)	4.091 (3.852-4.299)	2.768 (2.578-2.942)
$\alpha=-5; \beta=0.5$	69 (57-85)	7.780 (7.550-8.010)	6.280 (6.035-6.471)

IQR: inter-quartile range