

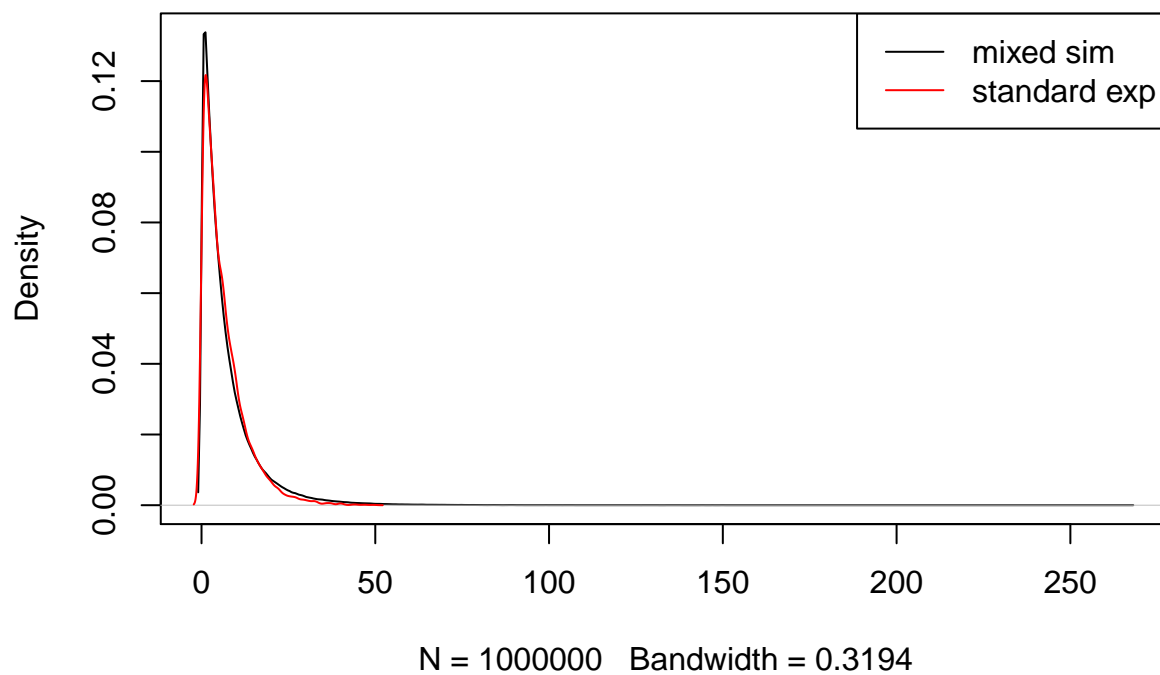
# simulation to study strategies to handle small strata

Wei Zou

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this program compare stratified vs unstratified analyses

**overall distribution from simulation, with median= 4.41**



```
## [1] "M1"
## [1] "conditional on M2+,M3+,M4+"
## [1] 0.7408182
## [1] "conditional on M2-,M3+,M4+"
## [1] 0.7408182
## [1] "conditional on M2+,M3-,M4+"
## [1] 0.7408182
## [1] "conditional on M2-,M3-,M4+"
## [1] 0.7408182
## [1] "conditional on M2+,M3+,M4-"
## [1] 0.7408182
## [1] "conditional on M2-,M3+,M4-"
## [1] 0.7408182
## [1] "conditional on M2+,M3-,M4-"
## [1] 0.7408182
## [1] "conditional on M2-,M3-,M4-"
```

```

## [1] 0.7408182
## [1] "marginal hr 0.736383665921854"
## [1] "M2"
## [1] "conditional on M1+,M3+,M4+"
## [1] 0.449329
## [1] "conditional on M1-,M3+,M4+"
## [1] 0.449329
## [1] "conditional on M1+,M3-,M4+"
## [1] 0.449329
## [1] "conditional on M1-,M3-,M4+"
## [1] 0.449329
## [1] "conditional on M1+,M3+,M4-"
## [1] 0.449329
## [1] "conditional on M1-,M3+,M4-"
## [1] 0.449329
## [1] "conditional on M1+,M3-,M4-"
## [1] 0.449329
## [1] "conditional on M1-,M3-,M4-"
## [1] 0.449329
## [1] "marginal hr 0.448546340588945"
## [1] "M3"
## [1] "conditional on M1+,M2+,M4+"
## [1] 0.8187308
## [1] "conditional on M1-,M2+,M4+"
## [1] 0.8187308
## [1] "conditional on M1+,M2-,M4+"
## [1] 0.8187308
## [1] "conditional on M1-,M2-,M4+"
## [1] 0.8187308
## [1] "conditional on M1+,M2+,M4-"
## [1] 0.8187308
## [1] "conditional on M1-,M2+,M4-"
## [1] 0.8187308
## [1] "conditional on M1+,M2-,M4-"
## [1] 0.8187308
## [1] "conditional on M1-,M2-,M4-"
## [1] 0.8187308
## [1] "marginal hr 0.816539324456875"
## [1] "M4"
## [1] "conditional on M1+,M2+,M3+"
## [1] 0.7046881
## [1] "conditional on M1-,M2+,M3+"
## [1] 0.7046881
## [1] "conditional on M1+,M2-,M3+"
## [1] 0.7046881
## [1] "conditional on M1-,M2-,M3+"
## [1] 0.7046881
## [1] "conditional on M1+,M2+,M3-"
## [1] 0.7046881
## [1] "conditional on M1-,M2+,M3-"
## [1] 0.7046881
## [1] "conditional on M1+,M2-,M3-"
## [1] 0.7046881
## [1] "conditional on M1-,M2-,M3-"

```

```
## [1] 0.7046881
## [1] "marginal hr 0.706779019594594"
```

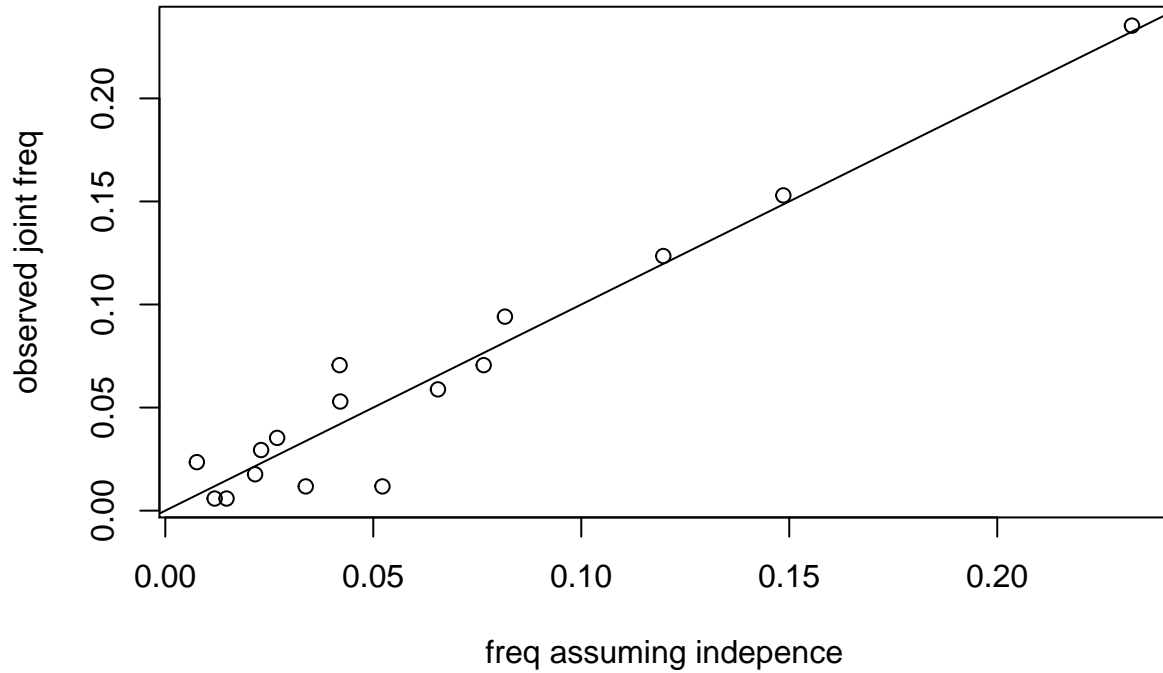


Table 1: simulation input

stratum	STRAT1	STRAT2	STRAT3	STRAT4	freq	n	med
M1-M2-M3-M4-	POSITIVE	T3/T4	IC0/1	<=20 WEEKS	0.235	57	2.836
M1-M2-M3-M4+	POSITIVE	T3/T4	IC0/1	>20 WEEKS	0.059	15	4.025
M1-M2-M3+M4-	POSITIVE	T3/T4	IC2/3	<=20 WEEKS	0.124	30	3.464
M1-M2-M3+M4+	POSITIVE	T3/T4	IC2/3	>20 WEEKS	0.012	3	4.916
M1-M2+M3-M4-	POSITIVE	<=T2	IC0/1	<=20 WEEKS	0.094	24	6.313
M1-M2+M3-M4+	POSITIVE	<=T2	IC0/1	>20 WEEKS	0.029	6	8.958
M1-M2+M3+M4-	POSITIVE	<=T2	IC2/3	<=20 WEEKS	0.053	12	7.710
M1-M2+M3+M4+	POSITIVE	<=T2	IC2/3	>20 WEEKS	0.006	3	10.941
M1+M2-M3-M4-	NEGATIVE	T3/T4	IC0/1	<=20 WEEKS	0.153	36	3.829
M1+M2-M3-M4+	NEGATIVE	T3/T4	IC0/1	>20 WEEKS	0.071	18	5.433
M1+M2-M3+M4-	NEGATIVE	T3/T4	IC2/3	<=20 WEEKS	0.071	18	4.676
M1+M2-M3+M4+	NEGATIVE	T3/T4	IC2/3	>20 WEEKS	0.018	3	6.636
M1+M2+M3-M4-	NEGATIVE	<=T2	IC0/1	<=20 WEEKS	0.012	3	8.521
M1+M2+M3-M4+	NEGATIVE	<=T2	IC0/1	>20 WEEKS	0.006	3	12.092
M1+M2+M3+M4-	NEGATIVE	<=T2	IC2/3	<=20 WEEKS	0.035	9	10.408
M1+M2+M3+M4+	NEGATIVE	<=T2	IC2/3	>20 WEEKS	0.024	6	14.769

## simulate invigor011 power

### sim without strata

```
## [1] "finding 1000 input files when looking for r1"
## [1] "modification interval: 1.7 min"
## [1] "will add file name to the returned data"
```

Table 2: power of stratified: 78.4 unstratified: 81

var	n	mean	sd	min	25%	50%	75%	max
n	20000	246.000	0.000	246.000	246.000	246.000	246.000	246.000
nevent	20000	192.000	0.000	192.000	192.000	192.000	192.000	192.000
p_s	20000	0.051	0.120	0.000	0.001	0.006	0.039	1.000
delta_p	20000	-0.007	0.042	-0.558	-0.006	0.000	0.000	0.459

## sim with with strata

```
## [1] "finding 1000 input files when looking for r1"
## [1] "modification interval: 1.7 min"
## [1] "will add file name to the returned data"
```

Table 3: power of stratified: 78.3 unstratified: 73.4

var	n	mean	sd	min	25%	50%	75%	max
n	20000	246.000	0.000	246.000	246.000	246.000	246.000	246.000
nevent	20000	192.000	0.000	192.000	192.000	192.000	192.000	192.000
p_s	20000	0.052	0.122	0.000	0.001	0.006	0.039	1.000
delta_p	20000	0.010	0.058	-0.501	0.000	0.001	0.013	0.605

## try different collapsing strategy

### requiring 10 events per stratum

```
## [1] "finding 1000 input files when looking for r1"
## [1] "modification interval: 3.4 min"
## [1] "will add file name to the returned data"

## [1] "finding 1000 input files when looking for r2"
## [1] "modification interval: 3.4 min"
## [1] "will add file name to the returned data"
```

Table 4: collapse groups based on event/patient number: power of stratified: 78.6 / 78.5 ; unstratified: 73.4

var	n	mean	sd	min	25%	50%	75%	max
n	20000	246.000	0.000	246.000	246.000	246.000	246.000	246.000
nevent	20000	192.000	0.000	192.000	192.000	192.000	192.000	192.000
p_s	20000	0.052	0.121	0.000	0.001	0.006	0.039	1.000
p_cE	20000	0.050	0.119	0.000	0.000	0.006	0.038	0.997
n_strata_cE	20000	8.047	0.352	6.000	8.000	8.000	8.000	9.000
minStrataSize_cE	20000	14.777	0.979	12.000	15.000	15.000	15.000	18.000
p_cN	20000	0.051	0.119	0.000	0.001	0.006	0.038	0.999
n_strata_cN	20000	9.000	0.000	9.000	9.000	9.000	9.000	9.000
minStrataSize_cN	20000	12.000	0.000	12.000	12.000	12.000	12.000	12.000
delta_pE	20000	-0.001	0.021	-0.315	-0.002	0.000	0.001	0.190
delta_pN	20000	-0.001	0.020	-0.276	-0.001	0.000	0.001	0.180

Table 5: remove small strata based on event/patient number: power  
of stratified: 74.3 / 74.3 ; unstratified: 73.4

var	n	mean	sd	min	25%	50%	75%	max
n	20000	246.000	0.000	246.000	246.000	246.000	246.000	246.00
nevent	20000	192.000	0.000	192.000	192.000	192.000	192.000	192.00
p_s	20000	0.052	0.121	0.000	0.001	0.006	0.039	1.00
p_cE	20000	0.060	0.128	0.000	0.001	0.009	0.052	1.00
n_strata_cE	20000	4.000	0.000	4.000	4.000	4.000	4.000	4.00
minStrataSize_cE	20000	36.000	0.000	36.000	36.000	36.000	36.000	36.00
p_cN	20000	0.060	0.128	0.000	0.001	0.009	0.052	1.00
n_strata_cN	20000	4.000	0.000	4.000	4.000	4.000	4.000	4.00
minStrataSize_cN	20000	36.000	0.000	36.000	36.000	36.000	36.000	36.00
delta_pE	20000	0.008	0.052	-0.526	0.000	0.001	0.010	0.51
delta_pN	20000	0.008	0.052	-0.526	0.000	0.001	0.010	0.51

### different number of minE

```
## [1] "finding 1000 input files when looking for r1"
## [1] "modification interval: 4 min"
## [1] "will add file name to the returned data"
```

### power changes as threshold number

