

## Appendix 1: simulation code using R

```
# generating outcomes for binary data using OR as effect measure
# n: number of studies
# size: number of patients in control group in each study
# rat: pateint ratios between treatment and control groups size_ctr=size_tr*rat
# pc: probability in control group
# or: treatment effect
# With between study variance, tau: between-study SD

meta= function (n, size, rat, pc, or, tau) {

  log_or=log(or)

  log_or_hat = rnorm (n, log_or, tau*tau)
  or_hat = exp(log_or_hat)

  pt=(pc/(1-pc)*or_hat)/(1+(pc/(1-pc))*or_hat)

  out_ctr = rbinom (n, size*rat, pc)
  #size_tr=size/rat

  out_tr= rbinom (n, size, pt)

  n_ctr=rep(size*rat,n)
  n_tr=rep(size,n)

  non_out_ctr=n_ctr-out_ctr
  non_out_tr=n_tr-out_tr

  out_data=matrix (c(n_ctr,out_ctr,non_out_ctr,n_tr, out_tr, non_out_tr),ncol=6)

  return (out_data)

}
```

```
# Generating, combining and saving data sets
# m:number of sets to be generated

mydat = function (n, size, rat, pc, or,m, tau) {

  set.seed(2013)

  i=m

  while (i>0) {

    data=meta (n, size, rat, pc, or, tau)

    set_num=c(rep(i,n))

    study_num=c(1:n)

    index=matrix(c(set_num,study_num), ncol=2)

    data_new=cbind (index, data)

    if (i==m) { data_all=data_new}

    else { data_all=rbind(data_new, data_all)}

    i=i-1
  }

  return (data_all)
}
```

## Appendix 2: Impact of the treatment effect changes on bias in log OR scale

Number of studies = 5      Number of patients = 100      Group ratio = 1      Control arm probability = 0.001      Number of simulated data sets = 2500      Between-study SD = 0.5																
Methods	Positive Treatment Effect						No Treatment Effect				Positive Treatment Effect					
	Excluding BAZE studies						Including BAZE studies									
	Log OR =0.22		Log OR = 0.69		Log OR=1.61		OR = 0		OR = 0		Log OR =0.22		Log OR = 0.69		Log OR=1.61	
	$\bar{\beta}$	bias	$\bar{\beta}$	bias	$\bar{\beta}$	bias	Log OR	bias	Log OR	bias	$\bar{\beta}$	bias	$\bar{\beta}$	bias	$\bar{\beta}$	bias
IV Random effects	0.10	-0.12	0.38	-0.32	0.82	-0.79	0.01	0.01	<0.01	<0.01	0.03	-0.19	0.12	-0.57	0.45	-1.16
IV Fixed effects	0.10	-0.12	0.38	-0.32	0.82	-0.79	0.01	0.01	<0.01	<0.01	0.03	-0.19	0.14	-0.55	0.45	-1.16
M-H Radom effects	0.10	-0.12	0.38	-0.32	0.82	-0.79	0.01	0.01	<0.01	<0.01	0.03	-0.19	0.12	-0.57	0.45	-1.16
M-H Fixed effects	0.10	-0.12	0.38	-0.32	0.83	-0.78	0.01	0.01	<0.01	<0.01	0.03	-0.19	0.14	-0.55	0.49	-1.12
Peto	0.17	-0.05	0.63	-0.07	1.30	-0.31	0.01	0.01	<0.01	<0.01	0.04	-0.18	0.18	-0.52	0.65	-0.96
Methods	Negative Treatment Effect						No Treatment Effect				Negative Treatment Effect					
	Excluding BAZE studies						Including BAZE studies									
	Log OR = -0.22		Log OR = -0.69		Log OR= -1.61						Log OR = -0.22		Log OR = -0.69		Log OR= -1.61	
	$\bar{\beta}$	bias	$\bar{\beta}$	bias	$\bar{\beta}$	bias					$\bar{\beta}$	bias	$\bar{\beta}$	bias	$\bar{\beta}$	bias
IV Random effects	-0.13	-0.09	-0.35	-0.34	-0.76	-0.85					-0.01	-0.21	-0.04	-0.65	-0.06	-1.55
IV Fixed effects	-0.13	-0.09	-0.35	-0.34	-0.76	-0.85					-0.02	-0.20	-0.04	-0.65	-0.07	-1.54
M-H Radom effects	-0.13	-0.09	-0.35	-0.34	-0.76	-0.85					-0.01	-0.21	-0.04	-0.65	-0.06	-1.55
M-H Fixed effects	-0.13	-0.09	-0.35	-0.34	-0.76	-0.85					-0.02	-0.20	-0.04	-0.65	-0.07	-1.54
Peto	-0.23	0.01	-0.62	-0.07	-1.34	-0.27					-0.02	-0.20	-0.05	-0.64	-0.08	-1.53

Note:

- 1)  $\bar{\beta}$ : mean of estimates of log OR
- 2) bias\_log OR = (log OR) -  $\bar{\beta}$  when log OR < 0; bias =  $\bar{\beta}$  - (log OR), when log OR >= 0
- 3) negative (-) bias indicate under estimating of treatment effect; positive bias indicates over estimating of treatment effect

### Appendix 3a: Impact of the treatment effect changes on RMSE

Number of studies = 5	Number of patients = 100		Group ratio = 1	Control arm probability = 0.001	Number of simulated data sets = 2500			Between-study SD = 0.5
Methods	Excluding BAZE studies				Including BAZE studies			
	OR = 1	OR 0.8	OR =0.5	OR = 0.2	OR = 1	OR 0.8	OR =0.5	OR = 0.2
IV Random effects	0.38	0.41	0.59	0.91	0.13	0.26	0.61	1.51
IV Fixed effects	0.38	0.41	0.59	0.91	0.13	0.26	0.61	1.50
M-H Radom effects	0.38	0.41	0.59	0.91	0.13	0.26	0.61	1.50
M-H Fixed effects	0.38	0.40	0.59	0.90	0.13	0.26	0.61	1.50
Peto	0.39	0.61	0.63	0.60	0.15	0.28	0.62	1.46

### Appendix 3b: Impact of the treatment effect changes on width of 95% CI

Number of studies = 5	Number of patients = 100		Group ratio = 1	Control arm probability = 0.001	Number of simulated data sets = 2500			Between-study SD = 0.5
Methods	Excluding BAZE studies				Including BAZE studies			
	OR = 1	OR 0.8	OR =0.5	OR = 0.2	OR = 1	OR 0.8	OR =0.5	OR = 0.2
IV Random effects	6.05	6.08	6.35	6.23	3.42	3.45	3.47	3.48
IV Fixed effects	6.00	6.02	6.10	6.21	3.40	3.41	3.42	3.45
M-H Radom effects	6.05	6.08	6.35	6.23	3.42	3.45	3.47	3.48
M-H Fixed effects	6.00	6.02	6.10	6.21	3.40	3.41	3.42	3.45
Peto	7.28	7.31	7.42	7.53	3.50	3.50	3.50	3.50

Appendix 3c: Impact of the treatment effect changes on coverage of 95% CI

Number of studies = 5	Number of patients = 100		Group ratio = 1	Control arm probability = 0.001	Number of simulated data sets = 2500			Between-study SD = 0.5
Methods	Excluding BAZE studies				Including BAZE studies			
	OR = 1	OR 0.8	OR =0.5	OR = 0.2	OR = 1	OR 0.8	OR =0.5	OR = 0.2
IV Random effects	100	96.5	91.9	86.1	100	100	100	96.1
IV Fixed effects	100	96.5	91.9	86.1	100	100	100	95.4
M-H Radom effects	100	96.5	91.9	86.1	100	100	100	96.1
M-H Fixed effects	100	96.5	91.9	86.1	100	100	100	95.4
Peto	99.6	96.3	91.0	83.5	100	100	100	96.0