Supplemental Material

Appendix 1. MEDLINE (flexible sigmoidoscopy) search strategy

#1 exp Colorectal Neoplasms/

#2 exp Colonic Neoplasms/

#3 exp Rectal Neoplasms/

#4 ((colorectal* or CRC or colon* or bowel* or intestine* or large intestine* or rectal or rectum or sigmoid or anal or anus) and (cancer or neoplasm* or malign* or tumor* or tumour* or carcinom* or sarcom* or adenocarcinom* or adeno?carcinom* or adenom* or lesion*)).mp.

#5 1 or 2 or 3 or 4

#6 exp Endoscopy, Gastrointestinal/

#7 exp Colonoscopy/

#8 exp Sigmoidoscopy/

#9 exp Proctoscopy/

#10 (endoscop* or proctoscop* or colonoscop* or sigmoidoscop* or rectosigmoidoscop* or proctosigmoidoscop* or COL or SIG or FSIG or (flex* adj3 sig*)).mp.

#11 6 or 7 or 8 or 9 or 10

#12 exp Mass Screening/

#13 exp Population Surveillance/

#14 (screen* or test* or (population* adj2 surveillance) or (early adj3 detect*) or (early adj3 prevent*)).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]

#15 12 or 13 or 14

#16 5 and 11 and 15

#17 randomized controlled trial.pt.

#18 controlled clinical trial.pt.

#19 randomized.ab.

#20 placebo.ab.

#21 clinical trial.sh.

#22 randomly.ab.

#23 trial.ti.

#24 17 or 18 or 19 or 20 or 21 or 22 or 23

#25 humans.sh.

#26 24 and 25

#27 16 and 26

Appendix 2. The Cochrane Library (flexible sigmoidoscopy) search strategy

#1 MeSH descriptor Colorectal Neoplasms explode all trees

#2 MeSH descriptor Colonic Neoplasms explode all trees

#3 MeSH descriptor Rectal Neoplasms explode all trees

#4 (colorectal* or CRC or colon* or bowel* or intestine* or large intestine* or rectal or rectum or sigmoid or anal or anus) and (cancer or neoplasm* or malign* or tumor* or tumour* or carcinom* or sarcom* or adenocarcinom* or adeno?carcinom* or adenom* or lesion*

#5 (#1 OR #2 OR #3 OR #4)

#6 MeSH descriptor Endoscopy explode all trees

#7 MeSH descriptor Colonoscopy explode all trees

#8 MeSH descriptor Sigmoidoscopy explode all trees

#9 MeSH descriptor Proctoscopy explode all trees

#10 (endoscop* or proctoscop* or colonoscop* or sigmoidoscop* or rectosigmoidoscop* or proctosigmoidoscop* or COL or SIG or FSIG) or (flex* near3 sig*)

#11 (#6 OR #7 OR #8 OR #9 OR #10)

#12 MeSH descriptor Mass Screening explode all trees

#13 MeSH descriptor Population Surveillance explode all trees

#14 (screen* or test*) or (population* near2 surveillance) or (early near3 detect*) or (early near3 prevent*)

#15 (#12 OR #13 OR #14)

#16 (#5 AND #11 AND #15)

Appendix 3: Characteristics of included studies (12-15)

Atkin 2010

Methods	574 general practices around 14 screening-centres in the UK were invited to participate, and 506 practices accepted the invitation. Recruitment and screening was performed November 1994 - March 1999. All eligible individuals in the participating general practices were screened for predefined exclusion criteria by their general practitioner, and the remaining received an information letter and questionnaire to establish interest in screening. Those who reported interest in screening were randomly assigned to the screening or control group in the ratio 1:2, respectively, by a central randomisation unit in blocks of 12. Randomisation was stratified according to household, trial centre and general practice. Persons in the control group were not contacted further. Follow-up was by public registries. At follow-up after median 11.2 years, six people in either group could not be traced. A further 234 persons in the screening group and 451 in the control group had emigrated.
Participants	Individuals aged 55 - 64 who responded with interest in screening and who did not meet any exclusion criteria: history of CRC, adenomas or inflammatory bowel disease; inability to provide informed consent; severe or terminal disease; life expectancy less than 5 years; sigmoidoscopy or colonoscopy within the previous 3 years. Persons reporting a strong family history of CRC or symptoms of CRC were also excluded and managed outside the trial.
Interventions	Flexible sigmoidoscopy once only with removal of small polyps and referring for full colonoscopy if they had polyps 10 mm or larger, three or more adenomas, adenomas with tubulovillous or villous histology, severe dysplasia or malignant disease, or 20 or more hyperplastic polyps above the distal rectum.
Outcomes	Compliance with screening, number referred for colonoscopy work-up, incidence of CRC (total, proximal and distal), yearly hazard rate, number needed to screen to prevent one colorectal cancer, all-cause mortality, mortality from CRC (intention-to-treat and per protocol), number needed to screen to prevent one death due to

	CRC.	
Notes	Compliance to screening reported as 71% (40674/57237) in the screening population. On the population-level, compliance will be lower due to the two-step invitation procedure.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Sequentially numbered randomization was done centrally in blocks of 12 and with the added constraint of no more than three consecutive allocations to one group within or across blocks.
Allocation concealment (selection bias)	Low risk	Central randomisation procedure
Blinding (performance bias and detection bias) All outcomes	Low risk	Outcomes were obtained from or confirmed by public registries. A second analysis as CRC as an underlying cause of death was obtained after blinded verification of death certificates by an independent expert coder who had access to clinical information when available
Incomplete outcome data (attrition bias) All outcomes	Low risk	Six people in each group could not be traced. 658 people had emigrated
Selective reporting (reporting bias)	Low risk	All relevant outcomes were reported on
Other bias	Low risk	No other threats to validity detected
Schoen 2012		
Methods	Eligible individuals were invited to participate in the trial by mass mailing. People who reported interest in screening provided written informed consent and	

	completed a baseline questionnaire before randomisation which was performed in blocks stratified according to screening centre, age and sex. A total of 154,900 people were enrolled from 1993 through 2001; 77,445 to the intervention group and 77,455 to the control group. All cancers and deaths were primarily assessed through a annually mailed questionnaire to all participants and subsequently verified from medical records and through linkage to public registries. Deaths that were potentially related to colorectal cancer were reviewed in a blinded fashion. CRC deaths included deaths due to CRC and its treatment.
Participants	Individuals 55 to 74 years of age with no prior history of prostate, lung, colorectal or ovarian cancer. Other exclusion criteria were: ongoing treatment of any type of cancer except basal-cell or squamous-cell skin cancer and, beginning in 1996, flexible sigmoidoscopy, colonoscopy or barium enema in the previous 3 years.
Interventions	Participants in the intervention group were offered a flexible sigmoidoscopy at baseline and at 3-5 years. Participants in the control group were not offered any screening and continued to receive "care as usual". The screening interventions were conducted at ten screening centres. A positive test result was defined as a finding of a polyp or a mass. Biopsies were not routinely performed, but individuals with a positive test were referred to their general practitioner for decisions regarding diagnostic follow-up.
Outcomes	CRC mortality, CRC incidence, all-cause mortality, staging, physical complications due to screening and follow-up colonoscopy
Notes	Carcinoid tumours were included as colorectal cancers 46.5% of participants in the control group had a flexible sigmoidoscopy or colonoscopy during the screening phase of the study. The rate of routine colonoscopy after the screening phase was 47.7% in the intervention group and 48.0% in the control group.
Risk of bias	
Bias	Authors' judgement Support for judgement

Random sequence generation (selection bias)	Low risk	Volunteers who responded to an invitation through mass-mailing were randomised using a central block-randomisation process stratified according to screening centre, age and gender
Allocation concealment (selection bias)	Low risk	Central randomisation process
Blinding (performance bias and detection bias) All outcomes	Low risk	Death review group unaware of group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Vital status was known for 99.9% of participants, and compliance with the annual study update questionnaire was 93.8%
Selective reporting (reporting bias)	Unclear risk	No reports of adverse effects due to colonoscopy follow-up
Other bias	Low risk	No other threats to validity detected

Segnan 2011

Methods	Participants were recruited in a two-step procedure between June 1995 and May 1999. Eligible individuals first received an interest-in-screening questionnaire by mail designed to assess eligibility for and interest in screening. Responders who reported interest in screening, were randomised 1:1 into an intervention group or a control group. The control group was not contacted further. In three regions, randomisation was on an individual basis, and in the other three regions, a cluster randomisation model was adopted with the general practice as the cluster unit. Follow-up data was obtained from local hospital discharge records, pathology department files, population cancer registries and regional mortality registries. Death certificates were retrieved of all patients diagnosed with CRC during follow-up and supplemented with clinical information

	when available. Median follow-up for incidence was 10.5 years and for mortality 11.4 years.
Participants	Individuals aged 55-64 in 6 regions in Italy. People were excluded if they reported a history of CRC, colorectal adenomas, inflammatory bowel disease, colorectal endoscopy in the previous two years, had two or more first degree relatives with CRC or had a medical condition that would preclude benefit from screening.
Interventions	Flexible sigmoidoscopy once only and referral for colonoscopy if: Polyp > 5 mm, inadequate bowel preparation and at least one polyp, 3 or more adenomas, adenomas with villous component greater than 20% or high-grade dysplasia or CRC at the prevalent screening procedure. In addition, attenders were referred for colonoscopy if clinically indicated, judged by the physician who performed the screening procedure.
Outcomes	CRC incidence, CRC mortality, all-cause mortality
Notes	Compliance with screening reported by the authors was 58.3% (of those who reported interest in screening). On the population-level, compliance will be lower due to the two-step invitation procedure. Cluster randomisation was not accounted for in the statistical analyses, and intra-cluster correlation was not computed.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number sequence
Allocation concealment (selection bias)	Low risk	Allocation concealment was secured by using a computer-generated allocation algorithm
Blinding (performance bias and detection bias) All outcomes	Low risk	The independent investigators who assessed outcomes were blinded to group allocation

Incomplete outcome data (attrition bias) All outcomes	Low risk	280 (1.6%) individuals in the intervention group and 324 (1.9%) in the control group could not be traced
Selective reporting (reporting bias)	Low risk	All relevant outcomes were reported
Other bias	Low risk	No other threats to validity detected

Holme 2014

Methods	Eligible participants were individually centrally randomised to the screening group or control group between January 1999 and December 2000 (55-64-year age group) and in 2001 (50-54-year age group). In the screening group, there was a further 1:1 randomisation to either flexible sigmoidoscopy only or FOBT combined with flexible sigmoidoscopy. Of those selected, 1415 were excluded due to prior colorectal cancer, emigration, or death, and 3 could not be traced in the population registry. Follow-up was registry based and participants in the control group were never contacted.
Participants	All residents aged 55-64 living in the city of Oslo and Telemark County, Norway by November 1998 and all residents aged 50-54 living in the same cities by the end of the year 2000. Individuals with a history of CRC were excluded.
Interventions	Flexible sigmoidoscopy once only or flexible sigmoidoscopy combined with immunologic FOBT. During the endoscopic screening procedure, all detected lesions were biopsied. A positive screening test qualifying for full colonoscopy work-up and polypectomy was defined as any polyp 10 mm or more in diameter, any histologically verified adenoma irrespective of size, carcinoma or a positive FOBT.
Outcomes	Incidence of CRC, incidence of rectosigmoid CRC, incidence of neoplastic lesions, incidence of high-risk adenomas, mortality from CRC, mortality from all causes, stage of CRC, compliance with screening, rate and compliance of colonoscopy work-up.

Notes	Adherence with screening was 63%.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was done independently according to social security number by the National Bureau of Statistics
Allocation concealment (selection bias)	Low risk	Central randomisation process
Blinding (performance bias and detection bias) All outcomes	Low risk	Outcomes were obtained from public registries by a person not involved in the trial
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of lost to follow-up or censoring data
Selective reporting (reporting bias)	Low risk	All relevant outcomes were reported
Other bias	Low risk	No other threats to validity detected

Appendix 4: Raw Data

Atkin (12)

	Screened		Controls	
Year	NAR	Died from CRC	NAR	Died from CRC
1	57099	1	112939	12
2	56700	14	112130	26
3	56300	12	111321	35
4	55813	17	110320	42
5	55325	12	109319	44
6	54745	17	108113	28
7	54164	15	106907	47
8	53487	21	105552	71
9	52809	24	104196	65
10	51891	24	102397	59
11	50972	20	100597	72
12	25486	15	50299	51

Schoen (14)

	Screened		Controls	
Year	NAR	Died from CRC	NAR	Died from CRC
1	77445	6	77445	6
2	77107	16	77011	22
3	76510	17	76563	23
4	75912	21	76115	31
5	75218	23	75189	32
6	74523	25	74262	26
7	73638	27	73549	29
8	72753	31	72835	29
9	71413	32	71349	30
10	70073	16	69863	34
11	61186	18	61074	34
12	52298	10	52285	22
13	39364	10	39301	23

Holme (13)

	Screened	Controls

Year	NAR	Died from CRC	NAR	Died from CRC
1	20572	1	78220	7
2	20388	6	77499	20
3	20204	5	76777	23
4	20010	6	76025	29
5	19816	7	75272	26
6	19614	3	74497	28
7	19411	9	73722	28
8	19178	7	72883	26
9	18945	11	72044	43
10	18697	2	71086	35
11	18448	3	70127	54
12	12052	5	43822	44
13	5656	4	17517	8

Segnan (15)

	Screened		Controls	
Year	NAR	Died from CRC	NAR	Died from CRC
1	17136	2	17136	3
2	17021	2	17010	3
3	16906	6	16884	5
4	16788	7	16753	6
5	16671	5	16623	8
6	16540	6	16493	9
7	16410	6	16363	6
8	16271	7	16222	7
9	16133	5	16081	7
10	15421	6	15319	8
11	14710	13	14557	21

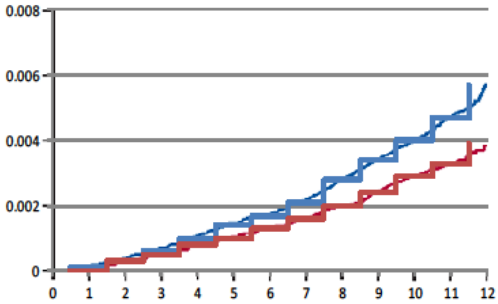
NAR is number at risk

CRC is colorectal cancer

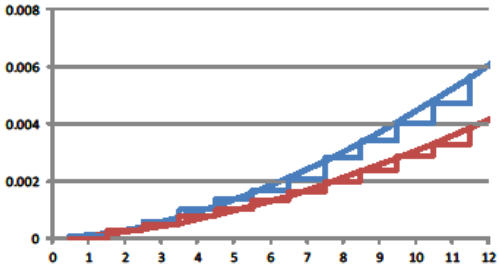
Appendix 5: Figures of Overall Colorectal-Cancer Mortality

Atkin Fig 2G (12)

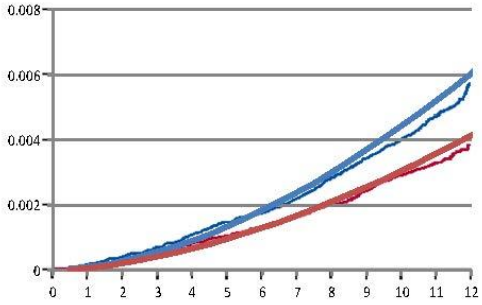
Original Figure-KM Overlay



KM-Weibull Overlay

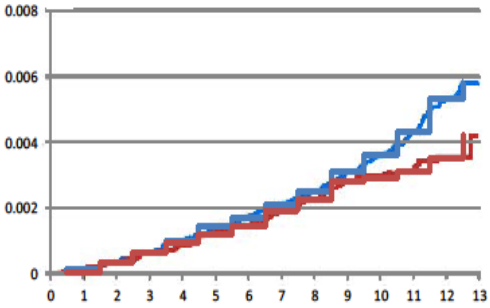


Original Figure-Weibull Overlay

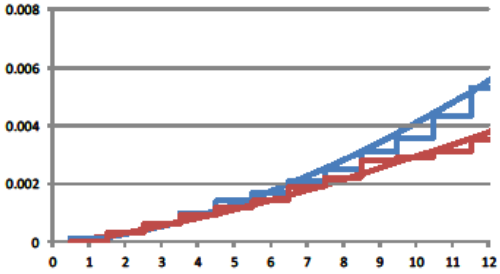


Holme Fig. 2B (13)

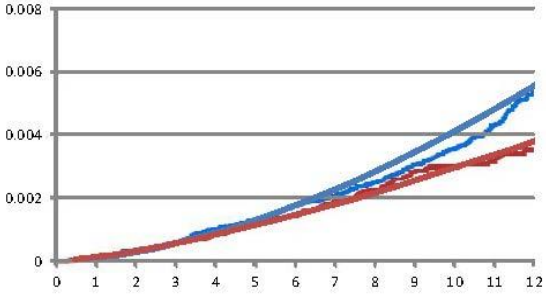
Original Figure-KM Overlay



KM-Weibull Overlay



Original Figure-Weibull Overlay

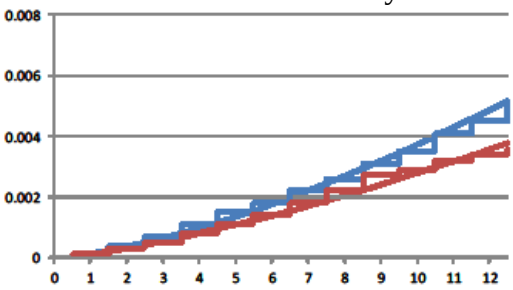


Schoen Fig. 1B (14)

Original Figure-KM Overlay

Raw data provided in publication

KM-Weibull Overlay

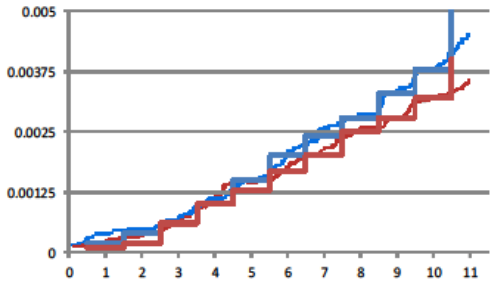


Original Figure-Weibull Overlay

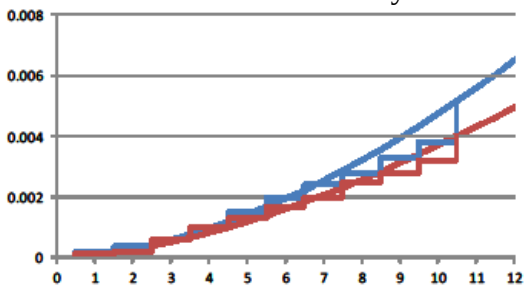
Raw data provided in publication

Segnan Fig. 2C (15)

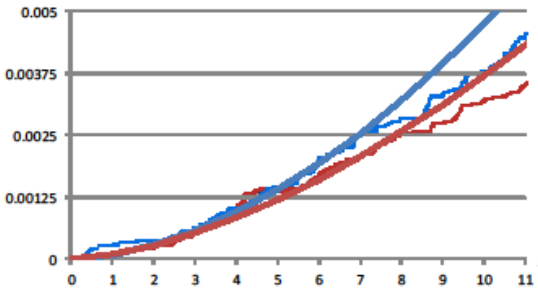
Original Figure-KM Overlay



KM-Weibull Overlay



Original Figure-Weibull Overlay



Appendix 6: Code used to perform MCMC procedure in SAS for the individual Weibull curves

```
%macro oneStudy(dataset,output);

   proc mcmc data=&dataset outpost=&output nmc=1000000 thin=10 seed=11111111
        monitor=(_parms_ surv_t surv_c surv_d);
   ods select PostSummaries;
   ods output PostSummaries=ds PostIntervals=is;
   array surv_t[360];
   array surv_c[360];
    array surv_d[360];
   parms (alpha0 alpha1) 1 (beta0 beta1) 0;
   prior beta: ~ normal(0, var=10000);
   prior alpha: ~ gamma(0.001,is=0.001);

   begincnst;
     surv_t1 = 1;
     surv_c1 = 1;
       surv_d1 = 0;
   endcnst;

   beginprior;
     do midx = 1 to 360;
       surv_t[midx] = exp(-exp(beta1+beta0)*(midx/12)**alpha1);
       surv_c[midx] = exp(-exp(beta0)*(midx/12)**alpha0);
          surv_d[midx] = surv_t[midx] - surv_c[midx];
     end;
   endprior;

   lambda = beta0 + beta1*trtgrp;
    alphaw = alpha0 * (1-trtgrp) + alpha1 * trtgrp;
   /*******************************************************/
   /* (1) the logpdf and logsdf functions are not used  */
   /*******************************************************/
   /*     gamma =  exp(-lambda /alpha);
         llike = v*logpdf('weibull', t, alpha, gamma) +
               (1-v)*logsdf('weibull', t, alpha, gamma);
   */
   /*******************************************************/
   /* (2) the simplified likelihood formula is used    */
   /*******************************************************/
   llike  = nsub*(dead*(log(alphaw) + (alphaw-1)*log(time) + lambda) -
          exp(lambda)*(time**alphaw));
   model general(llike);
 run;
 %mend;
```

Appendix 7: Code used to generate random effects Weibull model

```
### R file to call WinBUGS

require(BRugs)

meanvec <- c(0,0)
prec2mat <- structure(.Data=c(0.01,0,0,0.01), .Dim=c(2,2))
comega0 <- structure(.Data=c(100,0,0,100), .Dim=c(2,2))
domega0 <- structure(.Data=c(100,0,0,100), .Dim=c(2,2))
Rmat <- structure(.Data=c(0.01,0,0,0.01), .Dim=c(2,2))

model.file <- "metaWeibullOct2014.txt"

### CRC data
dat <- read.csv("metaAnalysisDataNov4.csv")[1:98,1:5]
dat$t <- dat$t + 1   #recode trt/ctrl as 2/1 not 1/0
dat$time <- dat$time-0.5 # match convention from SAS Weibull of events in mid-interval

### prepare more for MCMC
### give n's for everything
NS <- 4; N <- 98 ### 4 studies, 98 data lines, 2 treatments
data.list <- pairlist(s=1.0*dat$s, r=1.0*dat$d, n=1.0*dat$n,
                      t=1.0*dat$t, b=1.0*rep(1,nrow(dat)),
                      time=1.0*dat$time, dt=1.0*rep(1,nrow(dat)),
                      mean=meanvec, prec2=prec2mat, R=Rmat,
                      N=1.0*N, NS=1.0*NS)
dput(data.list, "data.fileCRC.txt")

### edit CRC data since the structures get messed up.
options(BRugsVerbose=TRUE)
modelCheck(model.file)
modelData("data.fileCRCedit.txt")
modelCompile()
modelGenInits()
modelUpdate(5000)
samplesSet(c("cmean","tmean","dmean","cmeanstudy","tmeanstudy","dstudy",
           "tphi","tlambda","cphi","clambda","domega","comega","cphistudy","clambdastudy",
           "tphistudy","tlambdastudy"))
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)
modelUpdate(numUpdates=5000,thin=10)

outtest <- samplesHistory('*',plot=FALSE)
#outtest <- samplesHistory('*',plot=TRUE) # use this to see trace plots

par(mfrow=c(3,2))
for(i in 1:58){plot(outtest[[i]],type='l')}
```

```
### make a plot just to look at things
# control group phi values (overall then study-specific)
boxplot(outtest[c("cphi","cphistudy[1]","cphistudy[2]","cphistudy[3]")])
abline(h=median(unlist(outtest["cphi"])))
abline(v=1.5)

# treatment group phi values (overall then study-specific)
boxplot(outtest[c("tphi","tphistudy[1]","tphistudy[2]","tphistudy[3]")])
abline(h=median(unlist(outtest["tphi"])))
abline(v=1.5)

# control group lambda values (overall then study-specific)
boxplot(log='y',outtest[c("clambda","clambdastudy[1]","clambdastudy[2]","clambdastudy[3]")])
abline(h=median(unlist(outtest["clambda"])))
abline(v=1.5)

# treatment group lambda values (overall then study-specific)
boxplot(log='y',outtest[c("tlambda","tlambdastudy[1]","tlambdastudy[2]","tlambdastudy[3]")])
abline(h=median(unlist(outtest["tlambda"])))
abline(v=1.5)

# difference in nu values (overall then study-specific)
boxplot(outtest[c("dmean[1]","dstudy[1,1]","dstudy[2,1]","dstudy[3,1]")])
abline(h=median(unlist(outtest["dmean[1]"])))
abline(v=1.5)
abline(h=0)

# difference in theta values (overall then study-specific)
boxplot(outtest[c("dmean[2]","dstudy[1,2]","dstudy[2,2]","dstudy[3,2]")])
abline(h=median(unlist(outtest["dmean[2]"])))
abline(v=1.5)
abline(h=0)

### get inference on the parms
outparms <- matrix(unlist(outtest[c("cphi","cphistudy[1]","cphistudy[2]","cphistudy[3]",
                                    "tphi","tphistudy[1]","tphistudy[2]","tphistudy[3]",
                                    "clambda","clambdastudy[1]","clambdastudy[2]","clambdastudy[3]",
                                    "tlambda","tlambdastudy[1]","tlambdastudy[2]","tlambdastudy[3]",
                                    "dmean[1]","dstudy[1,1]","dstudy[2,1]","dstudy[3,1]",
                                    "dmean[2]","dstudy[1,2]","dstudy[2,2]","dstudy[3,2]")]),ncol=24)
mysummary <- function(x){
        c(mean=mean(x),sd=sd(x),median=median(x),q25=as.numeric(quantile(x,pr=.25)),q75=as.numeric(quantil
e(x,pr=.75)),
        l95cl=as.numeric(quantile(x,pr=.025)),u95cl=as.numeric(quantile(x,pr=.975)))
}

apply(outparms,2,mysummary)


### longer run with just some params
set.seed(54321)
options(BRugsVerbose=TRUE)
modelCheck(model.file)
modelData("data.fileCRCedit.txt")
modelCompile()
```

```
modelGenInits()
modelUpdate(5000)

samplesSet(c("tphi","tlambda",
             "cphi","clambda"))
modelUpdate(numUpdates=50000)
outtest <- samplesHistory('*',plot=FALSE)
#outtest <- samplesHistory('*',plot=TRUE) # use this to see trace plots


### save just the parms needed for LTTB paper
write.csv(outtest[c("cphi","clambda","tphi","tlambda")],file="outsimmetaCRCOct2014.csv")




ma_data = read.csv("outsimmetaCRCOct2014.csv", header=TRUE)
names(ma_data) <- c('iteration','cphi','clambda','tphi','tlambda')
nsim <- 1000
nyrs <- 40 # to get a sensible ub for ci need 50 maybe or 60
nmos <- nyrs*12

# Define the survival and risk and RRR and ARR, for each month and for each nsim simulations. #
tvec = (1:nmos)/12
surv_c = array(NA, c(nsim,nmos))
surv_t = array(NA, c(nsim,nmos))
risk_c = array(NA, c(nsim,nmos))
risk_t = array(NA, c(nsim,nmos))
arrpost = array(NA, c(nsim,nmos))
rrrpost = array(NA, c(nsim,nmos))
for (i in 1:nsim){
for (j in 1:nmos){
surv_t[i,j] = exp(-((tvec[j])/(ma_data$tlambda[i]))^(ma_data$tphi[i]))
surv_c[i,j] = exp(-((tvec[j])/(ma_data$clambda[i]))^(ma_data$cphi[i]))
}}
for (i in 1:nsim){
for (j in 1:nmos){
risk_c[i,j] = 1-surv_c[i,j]
risk_t[i,j] = 1-surv_t[i,j]
rrrpost[i,j] = (1-surv_t[i,j])/(1-surv_c[i,j])
arrpost[i,j] = (surv_t[i,j])-(surv_c[i,j])
}}


# post processing #
logit <- function(x) log(x/(1-x))
invlogit <- function(x) exp(x)/(1+exp(x))


risk_control_mean = array(NA, nyrs)
risk_control_sd = array(NA, nyrs)
risk_control_logit_mean = array(NA, nyrs)
risk_control_logit_sd = array(NA, nyrs)
risk_control_logit_lb = array(NA, nyrs)
risk_control_logit_ub = array(NA, nyrs)
risk_control_lb = array(NA, nyrs)
```

```
risk_control_ub = array(NA, nyrs)

risk_trt_mean = array(NA, nyrs)
risk_trt_sd = array(NA, nyrs)
risk_trt_logit_mean = array(NA, nyrs)
risk_trt_logit_sd = array(NA, nyrs)
risk_trt_logit_lb = array(NA, nyrs)
risk_trt_logit_ub = array(NA, nyrs)
risk_trt_lb = array(NA, nyrs)
risk_trt_ub = array(NA, nyrs)

rrr_mean = array(NA, nyrs)
rrr_sd = array(NA, nyrs)
rrr_log_mean = array(NA, nyrs)
rrr_log_sd = array(NA, nyrs)
rrr_log_lb = array(NA, nyrs)
rrr_log_ub = array(NA, nyrs)
rrr_lb = array(NA, nyrs)
rrr_ub = array(NA, nyrs)

arr_mean = array(NA, nyrs)
arr_sd = array(NA, nyrs)
arr_lb = array(NA, nyrs)
arr_ub = array(NA, nyrs)

nnt_mean = array(NA, nyrs)
nnt_sd = array(NA, nyrs)
nnt_lb = array(NA, nyrs)
nnt_ub = array(NA, nyrs)

#for each year calculate the risk for trewatment and control, and RRR and ARR. #
#also, find their SD and 95% CI #

for (i in 1:nyrs){

risk_control_mean[i] = mean(risk_c[,tvec==i])
risk_control_sd[i] = sd(risk_c[,tvec==i])
risk_control_logit_mean[i] = mean(logit(risk_c[,tvec==i]))
risk_control_logit_sd[i] = sd(logit(risk_c[,tvec==i]))
risk_control_logit_lb[i] = risk_control_logit_mean[i] - 1.96*risk_control_logit_sd[i]
risk_control_logit_ub[i] = risk_control_logit_mean[i] + 1.96*risk_control_logit_sd[i]
risk_control_lb[i] = invlogit(risk_control_logit_lb[i])
risk_control_ub[i] = invlogit(risk_control_logit_ub[i])

risk_trt_mean[i] = mean(risk_t[,tvec==i])
risk_trt_sd[i] = sd(risk_t[,tvec==i])
risk_trt_logit_mean[i] = mean(logit(risk_t[,tvec==i]))
risk_trt_logit_sd[i] = sd(logit(risk_t[,tvec==i]))
risk_trt_logit_lb[i] = risk_trt_logit_mean[i] - 1.96*risk_trt_logit_sd[i]
risk_trt_logit_ub[i] = risk_trt_logit_mean[i] + 1.96*risk_trt_logit_sd[i]
risk_trt_lb[i] = invlogit(risk_trt_logit_lb[i])
risk_trt_ub[i] = invlogit(risk_trt_logit_ub[i])

rrr_mean[i] = mean(rrrpost[,tvec==i])
rrr_sd[i] = sd(rrrpost[,tvec==i])
rrr_log_mean[i] = mean(log(rrrpost[,tvec==i]))
```

```
rrr_log_sd[i] = sd(log(rrrpost[,tvec==i]))
rrr_log_lb[i] = rrr_log_mean[i] - 1.96*rrr_log_sd[i]
rrr_log_ub[i] = rrr_log_mean[i] + 1.96*rrr_log_sd[i]
rrr_lb[i] = exp(rrr_log_lb[i])
rrr_ub[i] = exp(rrr_log_ub[i])


arr_mean[i] = mean((risk_c-risk_t)[,tvec==i])
arr_sd[i] = sd((risk_c-risk_t)[,tvec==i])
arr_lb[i] = arr_mean[i] - 1.96*arr_sd[i]
arr_ub[i] = arr_mean[i] + 1.96*arr_sd[i]

nnt_mean[i] = mean((1/(risk_c-risk_t))[,tvec==i])
nnt_sd[i] = sd((1/(risk_c-risk_t))[,tvec==i])
nnt_lb[i] = nnt_mean[i] - 1.96*nnt_sd[i]
nnt_ub[i] = nnt_mean[i] + 1.96*nnt_sd[i]

}


risk_control_values = data.frame(risk_control_mean, risk_control_sd, risk_control_logit_mean,
risk_control_logit_sd, risk_control_logit_lb, risk_control_logit_ub, risk_control_lb, risk_control_ub)
risk_control_values
risk_trt_values = data.frame(risk_trt_mean, risk_trt_sd, risk_trt_logit_mean, risk_trt_logit_sd, risk_trt_logit_lb,
risk_trt_logit_ub, risk_trt_lb, risk_trt_ub)
risk_trt_values
rrr_values = data.frame(rrr_mean, rrr_sd, rrr_log_mean, rrr_log_sd, rrr_log_lb, rrr_log_ub, rrr_lb, rrr_ub)
rrr_values
arr_values = data.frame(arr_mean, arr_sd, arr_lb, arr_ub)
arr_values
nnt_values = data.frame(nnt_mean, nnt_sd, nnt_lb, nnt_ub)
nnt_values


## LAGTIME ##

##### First time ARR reaches 0.0001
ltt1b <- apply(arrpost,1,function(x){
        tvec <- (1:nmos)/12
        gtx <- (tvec>0)  # do not look in first x yrs
        out <- ((tvec[gtx])[((x)[gtx])>0.0001])[1]
        if(is.na(out)) out <- nyrs
        if(out>nyrs) out <- nyrs
        return(out)
})

##### First time ARR reaches 0.0002
ltt2b <- apply(arrpost,1,function(x){
        tvec <- (1:nmos)/12
        gtx <- (tvec>0)  # do not look in first x yrs
        out <- ((tvec[gtx])[((x)[gtx])>0.0002])[1]
        if(is.na(out)) out <- nyrs
        if(out>nyrs) out <- nyrs
        return(out)
})
```

```
##### First time ARR reaches 0.0003333
ltt3b <- apply(arrpost,1,function(x){
        tvec <- (1:nmos)/12
        gtx <- (tvec>0)  # do not look in first x yrs
        out <- ((tvec[gtx])[((x)[gtx])>0.0003333])[1]
        if(is.na(out)) out <- nyrs
        if(out>nyrs) out <- nyrs
        return(out)
})

##### First time ARR reaches 0.0005
ltt5b <- apply(arrpost,1,function(x){
        tvec <- (1:nmos)/12
        gtx <- (tvec>0)  # do not look in first x yrs
        out <- ((tvec[gtx])[((x)[gtx])>0.0005])[1]
        if(is.na(out)) out <- nyrs
        if(out>nyrs) out <- nyrs
        return(out)
})

##### First time ARR reaches 0.001
ltt10b <- apply(arrpost,1,function(x){
        tvec <- (1:nmos)/12
        gtx <- (tvec>0)  # do not look in first x yrs
        out <- ((tvec[gtx])[((x)[gtx])>0.001])[1]
        if(is.na(out)) out <- nyrs
        if(out>nyrs) out <- nyrs
        return(out)
})

##### First time ARR reaches 0.002
ltt20b <- apply(arrpost,1,function(x){
        tvec <- (1:nmos)/12
        gtx <- (tvec>0)  # do not look in first x yrs
        out <- ((tvec[gtx])[((x)[gtx])>0.002])[1]
        if(is.na(out)) out <- nyrs
        if(out>nyrs) out <- nyrs
        return(out)
})

quantile(ltt1b,pr=c(.01,.025,.05,.1,.25,.5,.75,.9,.95,.975,.99))
quantile(ltt2b,pr=c(.01,.025,.05,.1,.25,.5,.75,.9,.95,.975,.99))
quantile(ltt5b,pr=c(.01,.025,.05,.1,.25,.5,.75,.9,.95,.975,.99))
quantile(ltt10b,pr=c(.01,.025,.05,.1,.25,.5,.75,.9,.95,.975,.99))
quantile(ltt20b,pr=c(.01,.025,.05,.1,.25,.5,.75,.9,.95,.975,.99))


ltt1b_mean = mean(ltt1b)
ltt1b_log_mean = mean(log(ltt1b))
ltt1b_log_sd = sd(log(ltt1b))
ltt1b_log_lb = ltt1b_log_mean - 1.96*ltt1b_log_sd
ltt1b_log_ub = ltt1b_log_mean + 1.96*ltt1b_log_sd
ltt1b_lb = exp(ltt1b_log_lb)
ltt1b_ub = exp(ltt1b_log_ub)

ltt2b_mean = mean(ltt2b)
```

```
ltt2b_log_mean = mean(log(ltt2b))
ltt2b_log_sd = sd(log(ltt2b))
ltt2b_log_lb = ltt2b_log_mean - 1.96*ltt2b_log_sd
ltt2b_log_ub = ltt2b_log_mean + 1.96*ltt2b_log_sd
ltt2b_lb = exp(ltt2b_log_lb)
ltt2b_ub = exp(ltt2b_log_ub)

ltt3b_mean = mean(ltt3b)
ltt3b_log_mean = mean(log(ltt3b))
ltt3b_log_sd = sd(log(ltt3b))
ltt3b_log_lb = ltt3b_log_mean - 1.96*ltt3b_log_sd
ltt3b_log_ub = ltt3b_log_mean + 1.96*ltt3b_log_sd
ltt3b_lb = exp(ltt3b_log_lb)
ltt3b_ub = exp(ltt3b_log_ub)

ltt5b_mean = mean(ltt5b)
ltt5b_log_mean = mean(log(ltt5b))
ltt5b_log_sd = sd(log(ltt5b))
ltt5b_log_lb = ltt5b_log_mean - 1.96*ltt5b_log_sd
ltt5b_log_ub = ltt5b_log_mean + 1.96*ltt5b_log_sd
ltt5b_lb = exp(ltt5b_log_lb)
ltt5b_ub = exp(ltt5b_log_ub)



ltt10b_mean = mean(ltt10b)
ltt10b_log_mean = mean(log(ltt10b))
ltt10b_log_sd = sd(log(ltt10b))
ltt10b_log_lb = ltt10b_log_mean - 1.96*ltt10b_log_sd
ltt10b_log_ub = ltt10b_log_mean + 1.96*ltt10b_log_sd
ltt10b_lb = exp(ltt10b_log_lb)
ltt10b_ub = exp(ltt10b_log_ub)

ltt20b_mean = mean(ltt20b)
ltt20b_log_mean = mean(log(ltt20b))
ltt20b_log_sd = sd(log(ltt20b))
ltt20b_log_lb = ltt20b_log_mean - 1.96*ltt20b_log_sd
ltt20b_log_ub = ltt20b_log_mean + 1.96*ltt20b_log_sd
ltt20b_lb = exp(ltt20b_log_lb)
ltt20b_ub = exp(ltt20b_log_ub)

lttb = data.frame(ltt10b_mean, ltt10b_lb, ltt10b_ub, ltt20b_mean, ltt20b_lb, ltt20b_ub)
lttb
lttb_small = data.frame(ltt2b_mean, ltt2b_lb, ltt2b_ub, ltt5b_mean, ltt5b_lb, ltt5b_ub, ltt10b_mean, ltt10b_lb,
ltt10b_ub)
lttb_small
```