## SEMI-PARAMETRIC RELATIVE RISK MODEL FOR CORRELATED BINARY DATA

#### ANIKO SZABO

Based on the exchangeability and marginal compatibility assumptions, we propose the following semiparametric model to describe  $\lambda_k(z), k = 0, \dots, N$  as a function of covariates z:

$$\lambda_k(z) = \mu_k \times \theta(\beta' z)^k, k = 0, \dots, N, \tag{1}$$

where  $\theta(\beta'z)$  is a known function with range [0,1]; and  $\mu_k$  is a non-parametric baseline vector of joint probabilities.

Since  $\lambda_1$  equals the marginal probability of a response  $\pi$ , model (1) can be interpreted as a multiplicative model for it:

$$\pi(z) = \mu_1 \times \theta(\beta' z).$$

Here  $\mu_1$  is the maximal marginal probability that can be achieved by the model, since  $\theta(.) \leq 1$ . It can also be interpreted as the probability of response for  $z = z_1$  for which  $\theta(\beta' z_1) = 1$  (potentially in limit).

We will allow two options: having  $\mu_1$  as a fixed pre-defined constant, or estimating it from the data.

#### 1. Initial setup

"../R/SPreg.R" 1a

require(CorrBin)

File defined by 1ab, 2, 3b, 4, 5.

## 1.1. Exchangeable model.

$$p_{r,n} = \binom{n}{r} \sum_{j=0}^{n-r} (-1)^j \binom{n-r}{j} \lambda_{r+j} = \binom{n}{r} \sum_{s=r}^n (-1)^{(s-r)} \binom{n-r}{s-r} \lambda_s, \tag{2}$$

$$\lambda_k = \sum_{j=0}^{n-k} \frac{\binom{n-k}{j} p_{n-j,n}}{\binom{n}{n-j}} = \sum_{r-k}^n \frac{\binom{n-k}{n-r} p_{r,n}}{\binom{n}{r}},\tag{3}$$

"../R/SPreg.R" 1b=

```
# lambda-to-p weight matrix, rows:r, cols:s
# (-1)^(s-r)*choose(n,r)*choose(n-r,s-r)

weight_mat <- function(n){
    s <- r <- 0:n
    res <- outer(r, s, function(x,y)(-1)^(y-x)*choose(n,x)*choose(n-x,y-x))
    res
}

p_from_lambda <- function(lambda.vec, n){
    H <- weight_mat(n)
    c(H %*% lambda.vec[1:(n+1)])
}

# p-to-lambda weight matrix, rows:k, cols:r
# (choose(n-k, n-r)/choose(n,r)</pre>
```

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```
weight_mat2 <- function(n){
    k <- r <- 0:n
    res <- outer(k, r, function(x,y)choose(n-x, n-y)/choose(n,y))
    res
}

lambda_from_p <- function(p.vec, n=length(p.vec)-1){
    H <- weight_mat2(n)
    c(H %*% p.vec)
}

File defined by lab, 2, 3b, 4, 5.</pre>
```

## 2. Defining the model

Parameter estimation is based on the maximization likelihood estimator with respect to likelihood function of observed data. Under the marginal compatibility assumption, the parameters  $\lambda$  are independent of cluster sizes. The likelihood function based on the observed data is written as follows:

$$L = \prod_{i=1}^{I} f_i \log p_{r_i, n_i}(z_i), \tag{4}$$

where p(r,n)(z) is the probability of observing r responses in a cluster of size n given covariates z, that can be calculated from (1) using the connection between  $\lambda$ s and probabilities in (2), and  $f_i$  are observation weights.

```
"../R/SPreg.R" 2≡
```

```
#' Fit semi-parametric relative risk model
#,
#'@rdname sprr
"", "Oparam formula a one-sided formula of the form \code{cbind(r, s) ~ predictors} where \code{r} and \code
#'@param data an optional matrix or data frame containing the variables in the formula \code{formula}. E
#'@param subset an optional vector specifying a subset of observations to be used.
#'Cparam weight an optional vector specifying observation weights.
#'@param link
                   a link function for the binomial distribution, the inverse of which models the covaria
#'@param mu1
                   an optional value between 0 and 1 giving the maximal predicted marginal probability. I
                   an optional list with elements named \code{beta}, \code{q}, and/or \code{mu1} giving s
#'Oparam control a list with parameters controlling the algorithm.
#'Oreturn an object of class \code{sprr} with the fitted model.
#' @importFrom stats terms model.matrix
#' Semi-parametric relative risk model
sprr <- function(formula, data, subset, weights, link="cloglog", mu1=NULL, start=NULL, control=list(eps=0
    fam <- binomial(link=link)</pre>
    model_fun <- fam$linkinv
    ⟨ Create model matrix from formula and data 3a⟩
    \langle Fit \ model \ 6 \rangle
    mt <- attr(mf, "terms")</pre>
    res <- list(coefficients = beta_new, q=q_new, niter = iter, loglik=logl,
                link = link, call = mc, terms = mt,
                xlevels = .getXlevels(mt, mf),
                data_object=list(model_matrix=mm, resp=Y, n=rowSums(Y), weights=weights),
                model_fun=model_fun)
```

```
class(res) <- "sprr"</pre>
               res
           }
File defined by 1ab, 2, 3b, 4, 5.
\langle Create \ model \ matrix \ from \ formula \ and \ data \ 3a \rangle \equiv
              if (missing(formula) || (length(formula) != 3L))
                    stop("'formula' missing or incorrect")
              if (missing(data))
                    data <- environment(formula)</pre>
               mc <- match.call(expand.dots = FALSE)</pre>
               m <- match(c("formula", "data", "subset", "weights"), names(mc), OL)</pre>
               m \leftarrow mc[c(1L,m)]
               if (is.matrix(eval(m$data, parent.frame())))
                    m$data <- as.data.frame(data)
               m[[1L]] <- quote(stats::model.frame)</pre>
               mf <- eval(m, parent.frame())</pre>
               # extract and check response variable
               Y <- model.response(mf)
               if (ncol(Y) != 2) stop("The response variable should be a 2-column matrix")
               # create model matrix
               mm <- model.matrix(formula, data=mf)</pre>
               # extract weights
               weights <- as.vector(model.weights(mf))</pre>
               if (!is.null(weights) && !is.numeric(weights))
                    stop("'weights' must be a numeric vector")
               if (!is.null(weights) && any(weights < 0))
                    stop("negative weights not allowed")
```

Using the model (1), and the 1-to-1 relationship equation (2), for cluster size N

$$p_{r,N}(z) = \binom{N}{r} \sum_{j=0}^{N-r} (-1)^j \binom{N-r}{j} \mu_{r+j} \theta(\beta' z)^{r+j}$$

$$= \sum_{y=r}^N \binom{y}{r} \theta(\beta' z)^r (1 - \theta(\beta' z))^{y-r} q_y.$$
(5)

Then for other cluster sizes, using marginal compatibility,

$$p_{r,n}(z) = \sum_{s=0}^{N} h(r, s, n, N) p_{s,N}(z).$$

2.1. **Model predictions and likelihood.** We define internal functions that calculate the model-based predicted values for a set of parameters, and the log-likelihood.

```
"../R/SPreg.R" 3b\equiv
```

Fragment referenced in 2.

```
pred_lp <- function(beta, data_object){
    lp <- data_object$model_matrix %*% beta</pre>
```

```
c(1p)
           }
           pred_theta <- function(beta, data_object, model_fun){</pre>
               lp <- pred_lp(beta, data_object)</pre>
               theta <- model_fun(lp)
               theta
           }
           pred_lambda <- function(beta, q, data_object, model_fun){</pre>
               lp <- data_object$model_matrix %*% beta</pre>
               theta <- model_fun(lp)
               N \leftarrow length(q)-1
               lambda_N <- lambda_from_p(q)</pre>
               th <- sapply(0:N, function(k)theta^k)
               lambda <- apply(th, 1, function(t)t * lambda_N)</pre>
               rownames(lambda) <- 0:N
               t(lambda)
           }
           pred_pvec <- function(beta, q, data_object, model_fun){</pre>
              11 <- pred_lambda(beta, q, data_object, model_fun)</pre>
              cs <- data_object$n
              pp <- lapply(seq_along(cs),</pre>
                             function(i){res <- p_from_lambda(ll[i,], n=cs[i]);</pre>
                                          names(res) <- 0:cs[i];</pre>
                                          res})
              pp
           }
           pred_p <- function(beta, q, data_object, model_fun){</pre>
              pvec <- pred_pvec(beta, q, data_object, model_fun)</pre>
              rvec <- data_object$resp[,1]</pre>
              pp <- sapply(seq_along(rvec), function(i)pvec[[i]][rvec[i]+1])</pre>
              pp
           }
           loglik <- function(beta, q, data_object, model_fun){</pre>
               p <- pred_p(beta=beta, q=q, data_object = data_object, model_fun=model_fun)
               w <- data_object$weights
               if (is.null(w)) 11 <- sum(log(p))</pre>
               else ll \leftarrow sum(ifelse(w==0, 0, w*log(p)))
           }
File defined by 1ab, 2, 3b, 4, 5.
```

2.2. **Methods for the sprr class.** First, define a printing method which does not show the saved data and model matrix

```
else cat("No coefficients\n")
               if (length(x$q)){
                    cat("Baseline joint probabilities (mu):\n")
                    N \leftarrow length(x$q)-1
                    11 <- c(lambda_from_p(x$q))</pre>
                    names(11) \leftarrow 0:N
                    print.default(format(ll, digits = digits),
                        print.gap = 2, quote = FALSE)
               }
               else cat("No baseline joint probabilities\n")
              cat("Log-likelihood: ", format(x$loglik, digits=digits), "\n")
              invisible(x)
           }
File defined by 1ab, 2, 3b, 4, 5.
The prediction method will predict for a variety of scenarios:
      • Input data set:
          - the data used in the fitting;

    new data.

      • Results:
           -p_{r,n}(z): the probability of observing the given r responses with cluster size n, given z;
          -\{p_{n}(z)\}: the entire vector of response probabilities for cluster size n, given z (will be a list due
             to varying lengths);
          -\lambda_{1,n}(z): the marginal probability of response for cluster size n, given z;
          -\{\lambda_{\cdot,n}(z)\}: the entire vector of joint probabilities \lambda for cluster size n, given z;
          -\beta'z: the linear predictor value z;
          -\theta(\beta'z): the relative risk at predictor value z.
"../R/SPreg.R" 5=
           predict.sprr <- function(object, newdata=NULL,</pre>
                                             type=c("mean", "relrisk", "likelihood", "probvec", "lvec", "lp"),
                                             newn=NULL, ...){
             type <- match.arg(type)</pre>
             tt <- terms(object)</pre>
             if (!missing(newdata)){
               Terms <- delete.response(tt)</pre>
               m <- model.frame(Terms, newdata, xlev = object$xlevels)</pre>
               if (!is.null(cl <- attr(Terms, "dataClasses")))</pre>
                         .checkMFClasses(cl, m)
               mm <- model.matrix(Terms, m)</pre>
               data_object <- list(model_matrix=mm)</pre>
               if (!missing(newn)){
                   if (!(length(newn) == 1L || length(newn) == nrow(newdata)))
                      stop("'newn' should have length 1 or equal to the number of rows of 'newdata'")
                    data_object$n <- rep(newn, length=nrow(newdata))</pre>
                   }
             } else {
               data_object <- object$data_object</pre>
```

if (type=="likelihood"){
 if (!missing(newdata))

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```
stop("Type = 'likelihood' is not available for new data. Consider using type='probvec' to get vec
               pred <- pred_p(beta=object$coefficients, q=object$q,</pre>
                               data_object=data_object,
                               model_fun=object$model_fun)
            } else
            if (type %in% c("mean", "lvec")){
               11 <- pred_lambda(beta=object$coefficients, q=object$q,</pre>
                               data_object=data_object,
                               model_fun=object$model_fun)
               pred <- if (type=="mean") 11[,2] else 11</pre>
            } else
            if (type == "lp"){
               pred <- pred_lp(beta=object$coefficients, data_object=data_object)</pre>
            if (type == "relrisk"){
               pred <- pred_theta(beta=object$coefficients, data_object=data_object,</pre>
                                    model_fun=object$model_fun)
            if (type == "probvec"){
              if (!missing(newdata) && missing(newn))
                  stop("For prediction of probability vectors with new data, cluster sizes should be specified in 'n
              pred <- pred_pvec(beta=object$coefficients, q=object$q, data_object=data_object,</pre>
                                    model_fun=object$model_fun)
            return(pred)
File defined by 1ab, 2, 3b, 4, 5.
```

# 3. FITTING THE MODEL VIA AN EM-MM ALGORITHM

We implement an algorithm called the Expectation Maximization Minorize-Maximize, abbreviated as EM MM, to estimate parameters. Catalina Stefanescu and Bruce W. Turnbull have proved that the marginal compatibility assumption is equivalent to assuming that clusters are from a sample of clusters sharing the same cluster size (the maximum cluster size N is a good choice and is used in our study), but some observations are completely missing at random, abbreviated as MCAR [?]. The expectation step in the EM MM algorithm can be performed based on the MCAR assumption. The estimation of the non-parametric backbone  $\mu_k$  will be done through the corresponding pdf  $q_t, t = 0, \ldots, N$ , because enforcing the complete monotonicity of  $\mu$  is much more demanding than enforcing  $\sum q_t = 1$ . Thus the set of parameters to be estimated is  $\phi = (q, \beta)$ , under the restrictions  $\sum_{y=0}^{N} q_y = 1$  and  $\frac{1}{N} \sum_{y=0}^{N} yq_y = \mu_1$ . In the EM setup, the missing data for each cluster i comes from its representation as a MCAR sample

In the EM setup, the missing data for each cluster i comes from its representation as a MCAR sample from a cluster of size N with  $s_i$  responses. So the complete data are  $\mathcal{D} = \{r_i, n_i, z_i; s_i\}_{i=1}^{I}$  and the observed data are  $\mathcal{D} = \{r_i, n_i, z_i; s_i\}_{i=1}^{I}$ . The complete data log-likelihood is

$$\log L_c(\phi \mid \mathcal{D}_c) = \sum_{i=1}^{I} f_i \log p_{s_i}(z_i) = \sum_{i=1}^{I} \sum_{s=0}^{N} f_i I(s_i = s) \log \left[ \sum_{y=s}^{N} {y \choose s} \theta(\beta' z_i)^s (1 - \theta(\beta' z_i))^{y-s} q_y \right].$$

Its expectation given the observed data and a current set of parameter estimates  $\phi^{(k)}$  is

$$E[\log L_c \mid \phi^{(k)}, \mathcal{D}] = \sum_{i=1}^{I} \sum_{s=0}^{N} f_i P(S_i = s \mid \phi^{(k)}, \mathcal{D}) \log \left[ \sum_{y=s}^{N} \binom{y}{s} \theta(\beta' z_i)^s (1 - \theta(\beta' z_i))^{y-s} q_y \right].$$

$$\langle Fit \ model \ 6 \rangle \equiv$$

$$\langle Define \ internal \ functions \ 9a \rangle$$

$$\langle Set \ initial \ values \ 9c \rangle$$

 $\diamondsuit$  Fragment referenced in 2.

3.1. **E-step.** Using the Bayes theorem,

$$e_{is}^{(k)} = P(s_i = s \mid \phi^{(k)}, \mathcal{D}) \propto h(r_i, s, n_i, N) P(S_i = s \mid \phi^{(k)}, \mathcal{D}),$$

where the coefficient of proportionality is chosen so that these values add up to 1 over  $s = 0, \dots, N$ , and

$$P(S_i = s \mid \phi^{(k)}, \mathcal{D}) = \sum_{y=s}^{N} {y \choose s} \theta(\beta^{(k)'} z_i)^s (1 - \theta(\beta^{(k)'} z_i))^{y-s} q_y^{(k)}.$$

3.2. **M-step.** The maximization step uses Minorize-Maximize to update the parameters  $\phi$ . We apply Jensen's inequality to bound from below the sum within the logarithm by assigning element-wise weights to each  $q_y$ , and transforming the log sum expression to obtain an update for parameters  $\phi$ .

$$\log \left[ \sum_{y=s}^{N} \binom{y}{s} \theta(\beta' z_{i})^{s} (1 - \theta(\beta' z_{i}))^{y-s} q_{y} \right] = \log \left[ \sum_{y=s}^{N} w_{iys}^{(k)} \frac{\binom{y}{s} \theta(\beta' z_{i})^{s} (1 - \theta(\beta' z_{i}))^{y-s} q_{y}}{w_{iys}^{(k)}} \right] \ge$$

$$\sum_{y=s}^{N} w_{iys}^{(k)} \log \left[ \frac{\binom{y}{s} \theta(\beta' z_{i})^{s} (1 - \theta(\beta' z_{i}))^{y-s} q_{y}}{w_{iys}^{(k)}} \right] =$$

$$\sum_{y=s}^{N} w_{iys}^{(k)} \log \left[ \binom{y}{s} \theta(\beta' z_{i})^{s} (1 - \theta(\beta' z_{i}))^{y-s} q_{y} \right] - \sum_{y=s}^{N} w_{iys}^{(k)} \log w_{iys}^{(k)}.$$

Therefore, the lower bound of the expected complete data log-likelihood function is:

$$E[\log L_{c}(\phi) \mid \phi^{(k)}, \mathcal{D}] \geq \sum_{i=1}^{I} \sum_{s=0}^{N} \sum_{y=s}^{N} f_{i} e_{is}^{(k)} w_{iys}^{(k)} \log \left[ \binom{y}{s} \theta(\beta' z_{i})^{s} (1 - \theta(\beta' z_{i}))^{y-s} \right] + \sum_{i=1}^{I} \sum_{s=0}^{N} \sum_{y=s}^{N} f_{i} e_{is}^{(k)} w_{iys}^{(k)} \log q_{y} - \sum_{i=1}^{I} \sum_{s=0}^{N} \sum_{y=s}^{N} f_{i} e_{is}^{(k)} w_{iys}^{(k)} \log w_{iys}^{(k)}, \quad (6)$$

where the last term does not actually depend on the parameters, and can be ignored. Also note that the terms containing  $\beta$  and q are separated, and can be maximized individually.

The weights at the  $k^{th}$  iteration are selected so that they add up to 1 and in the above equation equality holds for  $\phi = \phi^{(k)}$ ,

$$w_{iys}^{(k)} = \frac{\binom{y}{s} \theta(\beta^{(k)'} z_i)^s (1 - \theta(\beta^{(k)'} z_i))^{y-s} q_y^{(k)}}{\sum_{\gamma=s}^{N} \binom{\gamma}{s} \theta(\beta^{(k)'} z_i)^s (1 - \theta(\beta^{(k)'} z_i))^{\gamma-s} q_\gamma^{(k)}}.$$
 (7)

3.3. Implementation of E-step. In (6) we only need

$$e_{is}^{(k)}w_{iys}^{(k)} = \frac{f_i h(r_i, s, n_i, N) a_{iys}^{(k)}}{\sum_{t=0}^{N} \sum_{\gamma=t}^{N} h(r_i, t, n_i, N) a_{i\gamma t}^{(k)}},$$

where  $a_{iys}^{(k)} = \binom{y}{s} \theta(\beta^{(k)'} z_i)^s (1 - \theta(\beta^{(k)'} z_i))^{y-s} q_y^{(k)}$  and the denominator is just a normalizing constant.  $\langle Setup \ for \ E\text{-step 8a} \rangle \equiv$ 

```
# replace each cluster with N(N-1)/2 clusters of size N
new <- cbind(s=rep(0:N, each=N+1), y=rep(0:N, times=N+1))
new <- new[new[,"s"] <= new[,"y"],]

rep_idx <- rep(1:nrow(Y), each=nrow(new))
Y2 <- cbind(1:nrow(Y), Y)[rep_idx,]
colnames(Y2) <- c("i", "resp","nonresp")
mm2 <- mm[rep_idx,,drop=FALSE]

rep_idx2 <- rep(1:nrow(new), times=nrow(Y))
Ycomb <- cbind(Y2, new[rep_idx2,])</pre>
```

Fragment referenced in 6.

3.4. Implementation of the M-step. The first term in (6) corresponds to a weighted binomial likelihood with y as the cluster size, s as the number of successes, a link function  $\theta^{-1}$ , and weights  $f_i e_{is}^{(k)} w_{iys}^{(k)}$ , so  $\beta$  can be updated using logistic regression.

```
\langle M\text{-step for beta 8c} \rangle \equiv
```

Fragment referenced in 6.

```
mod <- glm(cbind(Ycomb[,"s"], Ycomb[,"y"]-Ycomb[,"s"]) ~ mm2+0, family=fam, weights=ew, start=beta_ol
beta_new <- coef(mod)</pre>
```

Fragment referenced in 6.

The second term is a multinomial likelihood for q with the usual restriction  $\sum_{y=0}^{N} q_y = 1$ , and an additional restriction for the mean  $\sum_{y=0}^{N} yq_y = N\mu_1$ . Rewriting the second term of (6) with  $c_y^{(k)} = \sum_{i=1}^{I} \sum_{s=0}^{N} f_i e_{is}^{(k)} w_{iys}^{(k)}$  and including the equality constraints via a Lagrangian, we need to maximize

$$F(q, \alpha_1, \alpha_2) = \sum_{y=0}^{N} c_y^{(k)} \log q_y - \alpha_1 (\sum_{y=0}^{N} q_y - 1) - \alpha_2 (\sum_{y=0}^{N} y q_y - N \mu_1).$$

Taking partial derivatives, and setting them to 0, we can show that the solution is

$$q_y^{(k)} = \frac{c_y^{(k)}}{1+ry} / \left[ \sum_{x=0}^N \frac{c_x^{(k)}}{1+rx} \right], \tag{8}$$

where  $r = \hat{\alpha}_2/\hat{\alpha}_2$  is the solution of the equation

$$f(r) = \sum_{x=0}^{N} \frac{c_x^{(k)}(x - N\mu_1)}{1 + rx} = 0.$$
(9)

To ensure  $q_y \ge 0$  for all y = 0, ..., N, we need  $r > -\frac{1}{N}$ . We reparameterize it as  $r = -\frac{1}{N} + \exp(\rho)$  to enforce the constraint.

 $\langle Define internal functions 9a \rangle \equiv$ 

```
mean_constrained_probs <- function(cc, m=NULL){
   if (is.null(m)) return(cc/sum(cc))
   N <- length(cc) - 1
   r_eq <- Vectorize(function(rho){i <- 0:N; sum(cc * (i - m)/(1+(exp(rho)-1/N)*i))})
   rho <- uniroot(r_eq, interval=c(-10, 10), extendInt="yes")
   r <- exp(rho$root) - 1/N
   q <- cc / (1 + r * (0:N))
   q <- q/sum(q)
   q
}</pre>
```

Fragment referenced in 6.

Fragment referenced in 6.

```
⟨ M-step for q 9b⟩ ≡

c_vec <- tapply(ew, list(y=Ycomb[,"y"]), sum, simplify=TRUE)
    if (is.null(mu1))
        q_new <- mean_constrained_probs(c_vec)
    else
        q_new <- mean_constrained_probs(c_vec, N*mu1)
</pre>
```

3.5. **Initial values.** The initial values for  $\beta$  can be selected using linear regression on transformed estimates of the marginal probabilities:

$$\theta^{-1} \left( \frac{\pi(z)}{\mu_1} \right) = \beta' z$$

For q, we will get the marginally compatible estimate for the pooled dataset, ensure a minimal probability of 0.01 at each value, then shift it to have mean  $\mu_1$ .

 $\langle Set \ initial \ values \ 9c \rangle \equiv$ 

```
N <- max(rowSums(Y))
if (is.null(start$beta)){
  p0 <- (Y[,1] + 0.5)/(Y[,1] + Y[,2]+ 1)</pre>
```

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```
if (is.null(mu1) && is.null(start$mu1))
      lp0 <- fam$linkfun(pmin(1-.Machine$double.eps, p0))</pre>
   else if (!is.null(mu1))
      lp0 <- fam$linkfun(pmin(1-.Machine$double.eps, p0/mu1))</pre>
   else if (!is.null(start$mu1))
      lp0 <- fam$linkfun(pmin(1-.Machine$double.eps, p0/start$mu1))</pre>
   if (is.null(weights))
       lm0 \leftarrow lm.fit(x=mm, y=lp0)
   else
       lm0 <- lm.wfit(x=mm, y=lp0, w=weights)</pre>
   beta_new <- coef(lm0)</pre>
} else {
   beta_new <- start$beta
if (is.null(start$q)){
   pooled <- CBData(data.frame(Trt = "All", NResp = Y[,1], ClusterSize = rowSums(Y)), trt="Trt",</pre>
                      clustersize="ClusterSize", nresp="NResp")
   est <- mc.est(pooled)
   q0 <- est$Prob[est$ClusterSize == N]</pre>
   if (is.null(mu1) && is.null(start$mu1))
       q_new <- mean_constrained_probs(pmax(q0, 0.01))</pre>
    else if (!is.null(mu1))
       q_new <- mean_constrained_probs(pmax(q0, 0.01), N*mu1)</pre>
    else if (!is.null(start$mu1))
       q_new <- mean_constrained_probs(pmax(q0, 0.01), N*start$mu1)</pre>
} else {
  q_new <- start$q</pre>
  if (!is.null(start$mu1))
     q_new <- mean_constrained_probs(q_new, N*start$mu1)</pre>
```

Fragment referenced in 6.