

BNR Workshop, INI, Cambridge  
August 9, 2007

# Postulating monotonicity in nonparametric Bayesian regression

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Based on ongoing joint work with Olli Saarela (KTL)



- Motivation
- Previous approaches
- Unconstrained model: prior, illustration, MCMC
- Model with monotonicity constraints
- Illustration of the method with real epidemiological data
- Summary, conclusions

# Warning



- No mathematical results in this talk!

- In areas such as epidemiology, strong parametric assumptions are often imposed on the form of the regression function describing covariate effects.
- This is done as a modelling convention, typically without real support from contextual substantive arguments, evidence coming from earlier studies, or careful diagnostics afterwards.

# Motivation (2)



- Can one relax assumptions based on e.g. linearity/additivity or multiplicativity (proportional hazards, proportional odds)?
- Completely nonparametric estimation of regression surface may give a too complex ("noisy") picture of the true functional relationship as small disturbances in the data affect the function estimate.

- However: Often there are reasonable grounds to assume a monotonic relationship between a covariate and the considered response.
- (cf. remarks David Dunson made at the end of his talk on Monday: "In biostatistical applications, we actually often know a lot ...")

- For example, Arjas & Gasbarra (1994), Schell & Singh (1997) and Holmes & Heard (2003) have applied a monotonicity assumption coupled with a piecewise constant model with random change points for *curve estimation in one dimension*.
- Can one find computationally feasible generalisations to *multiple dimensions*, without making additional parametric assumptions?

- Consider a model for log hazard rate
$$\log(\lambda) = \theta(x_1, \dots, x_L) + \beta_1 z_1 + \dots + \beta_M z_M,$$
where  $x$  are factors to be handled non-parametrically (can be time scales or covariates) and  $z$  are factors for which linearity and additivity is assumed.
- Function  $\theta(x_1, \dots, x_L)$  is handled by applying a set of random change points for the covariate axes and assuming constancy of  $\theta$  within the resulting multivariate intervals/cells for  $(x_1, \dots, x_L)$ .



- This corresponds to a random classification of data by using rectangles/or boxes (= Cartesian products of intervals on the covariate axes).
- Assuming a constant hazard rate within each cell  $j$ , the log-likelihood contribution for observation  $i = 1, \dots, n$  is of the Poisson form
$$d_{ij}(\theta_j + \beta'z_i) - y_{ij} \exp(\theta_j + \beta'z_i),$$
where
  - $d_{ij}$  is event indicator, and
  - $y_{ij}$  is follow-up time in cell  $j$ .

- The random change point model applied here is motivated by
  - its computational simplicity
  - its straightforward extendibility to the multivariate case
  - the relative robustness of numerical probability evaluations such as predictive distributions (generally involving an integration of densities/intensities) w.r.t. to the smoothness properties of the functions involved in such models, and
  - the fact that, if needed, model averaging over non-smooth models will generally produce smooth reconstructions of the functional relationships considered (e.g., in terms of the pointwise posterior medians or means).

# Prior for change points



- A common pool of change points is allocated between the covariate axes; they are generally utilised where they produce the best fit to data.
- Distribution  $p(K)$ ,  $K = 0, \dots, K_{\text{MAX}}$  for the total number of change points can be used to control the smoothness of the function estimate.
- Each change point  $k$ ,  $k = 1, \dots, K$ , is allocated to one of the  $L$  covariate axes with prior probability  $p(a_k) = 1/L$ , with  $a_k = 1, \dots, L$ .

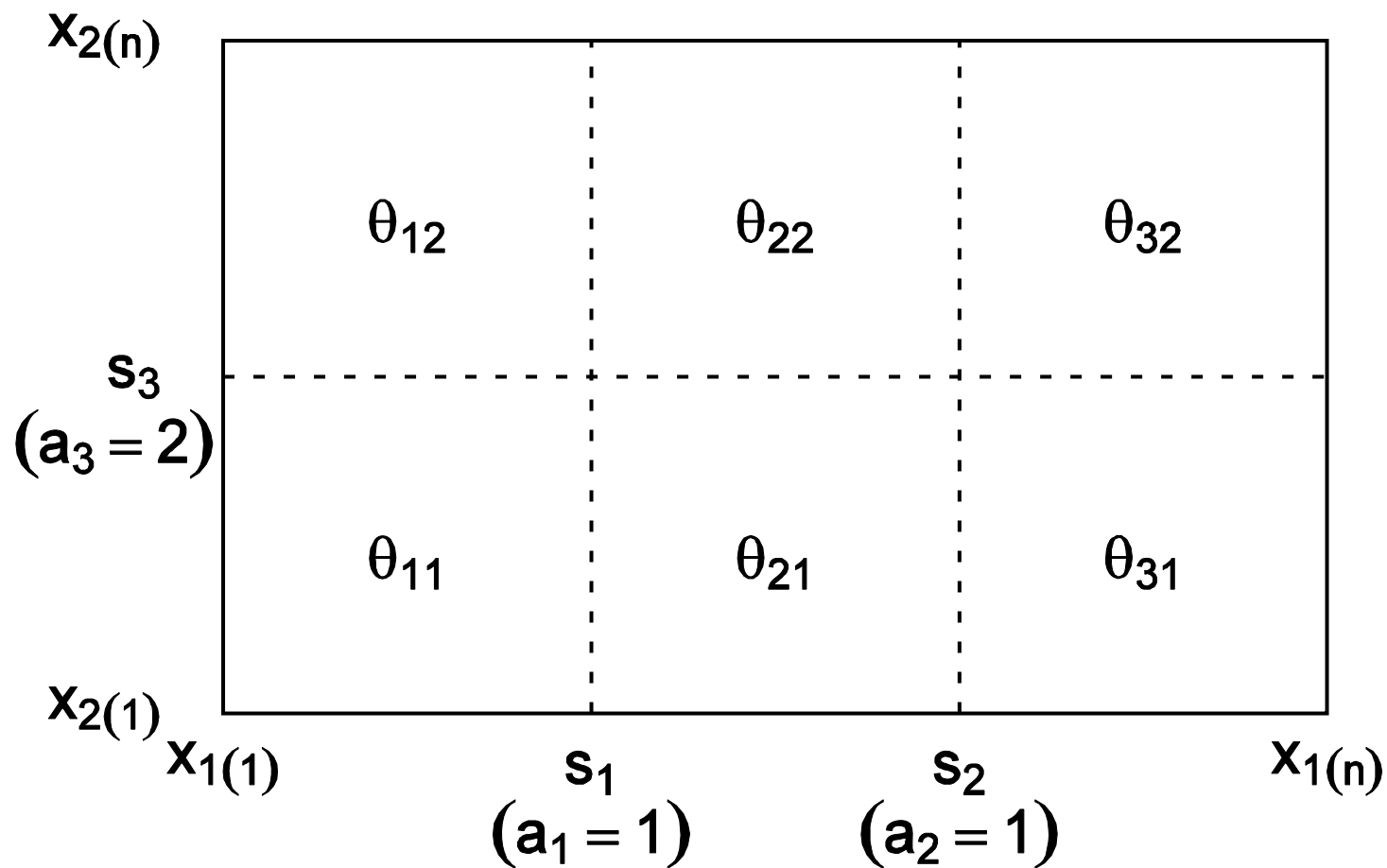
# Prior for change points (2)



- Prior for change point locations  $p(s_1, \dots, s_K \mid a_1, \dots, a_K, K)$ ?
- Given total number and allocation, locations of  $K_l$  points allocated for axis  $l$  can be distributed as
  - order statistics of  $K_l$  points uniformly distributed on  $[x_{l(1)}, x_{l(n)}]$ , or
  - even-numbered order statistics of  $2K_l + 1$  points uniformly distributed on  $[x_{l(1)}, x_{l(n)}]$ . This alternative places the step positions further away from each other, avoiding too many short steps (Green, 1995).

# Illustration

$$L = 2, K = 3$$



- Four types of moves
  1. Propose to add a new, or remove an existing change point and propose new values for related  $\theta$  parameters.
  2. Propose to change location of an existing change point and propose new values for related  $\theta$  parameters.
  3. Update the values of parameters  $\theta$
  4. Update the values of parameters  $\beta$

- Proposal for parameter  $\theta_j$  in a class  $j$  is  $N(\log(\sum_i d_{ij} / \sum_i y_{ij} \exp(\beta' z_i)), 1 / \sum_i d_{ij})$ , which corresponds to the maximum likelihood estimator for log rate parameter.
- If  $\sum_i d_{ij} = 0$ ,  $\theta_j$  is not defined.
- This proposal is independent of the current state of the chain; no Jacobian term needed in the Metropolis-Hastings acceptance ratio (cf. Dellaportas et al., 2002).

# Monotonic restrictions



- Back to the example with  $L = 2$  and  $K = 3$ ;  
Assuming isotonic effect for both axes,

resulting  
partial  
ordering:

	$\theta_{11}$	$\theta_{21}$	$\theta_{31}$	$\theta_{12}$	$\theta_{22}$	$\theta_{32}$
$\theta_{11}$	=	$\leq$	$\leq$	$\leq$	$\leq$	$\leq$
$\theta_{21}$	$\geq$	=	$\leq$		$\leq$	$\leq$
$\theta_{31}$	$\geq$	$\geq$	=			$\leq$
$\theta_{12}$	$\geq$			=	$\leq$	$\leq$
$\theta_{22}$	$\geq$	$\geq$		$\geq$	=	$\leq$
$\theta_{32}$	$\geq$	$\geq$	$\geq$	$\geq$	$\geq$	=



# How to apply monotonicity?



1. Sample from the unconstrained model and extract monotonic part from the resulting posterior sample (Holmes & Heard, 2003).
2. Use the unconstrained model as a proposal and incorporate monotonic constraints in the prior for  $\theta$ . Moves which violate monotonicity are rejected.
3. Construct a monotonic proposal.

# Applying monotonicity (2)



- Alternatives 1 and 2 are easy to implement because sampling from the unconstrained model is computationally straightforward.
- However, it is less clear whether use of the unconstrained model will generally result in good mixing in the space of monotonic submodels.
- It is not obvious how to construct good monotonic proposal distributions, particularly in higher dimensions.

# Applying monotonicity (3)



- The number of  $\theta$  parameters in our "piecewise constant" model is  
 $(K_1 + 1) \dots (K_L + 1)$ ,  
where  $K_l$  is the number of change points allocated on axis  $l$ .
- For example, when a new change point is proposed on axis 1, the number of proposed new  $\theta$  parameters needed for such a move is  
 $2(K_2 + 1) \dots (K_L + 1)$ .

- A good monotonic proposal distribution would be such that acceptance probability for birth/death moves for change points does not suffer when  $L$  (= # covariates in  $\theta$ ) increases.
- Further work is needed here.

# Question



- Is this BNR?

- A cohort of 4369 men aged 54-77 from southern and western Finland examined in 1992-1993 and free of CVD at the time of examination.
- Prospective follow-up for CVD events (coronary heart disease + ischaemic stroke) to the end of year 1999 .
- 568 first CVD events were recorded during the follow-up.

# Illustration (2)



- Consider here three risk factors; age and non-HDL cholesterol (isotonic effect assumed for CVD risk) and HDL cholesterol (antitonic effect assumed for CVD risk).
- Is there evidence of nonlinearity/non-additivity when the factors are considered pairwise with the nonparametric model?

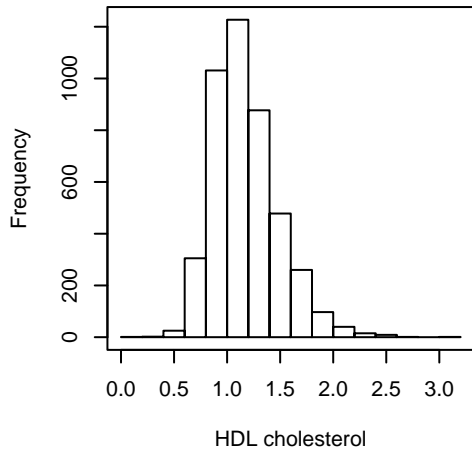
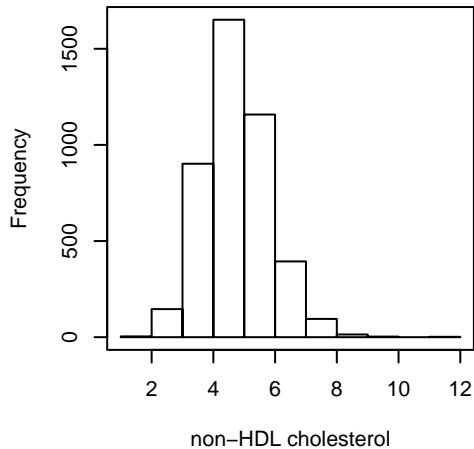
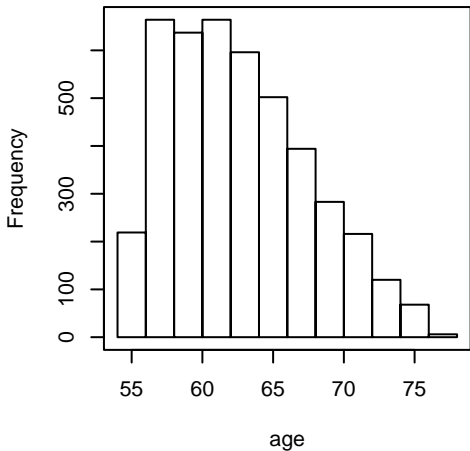
# Different models



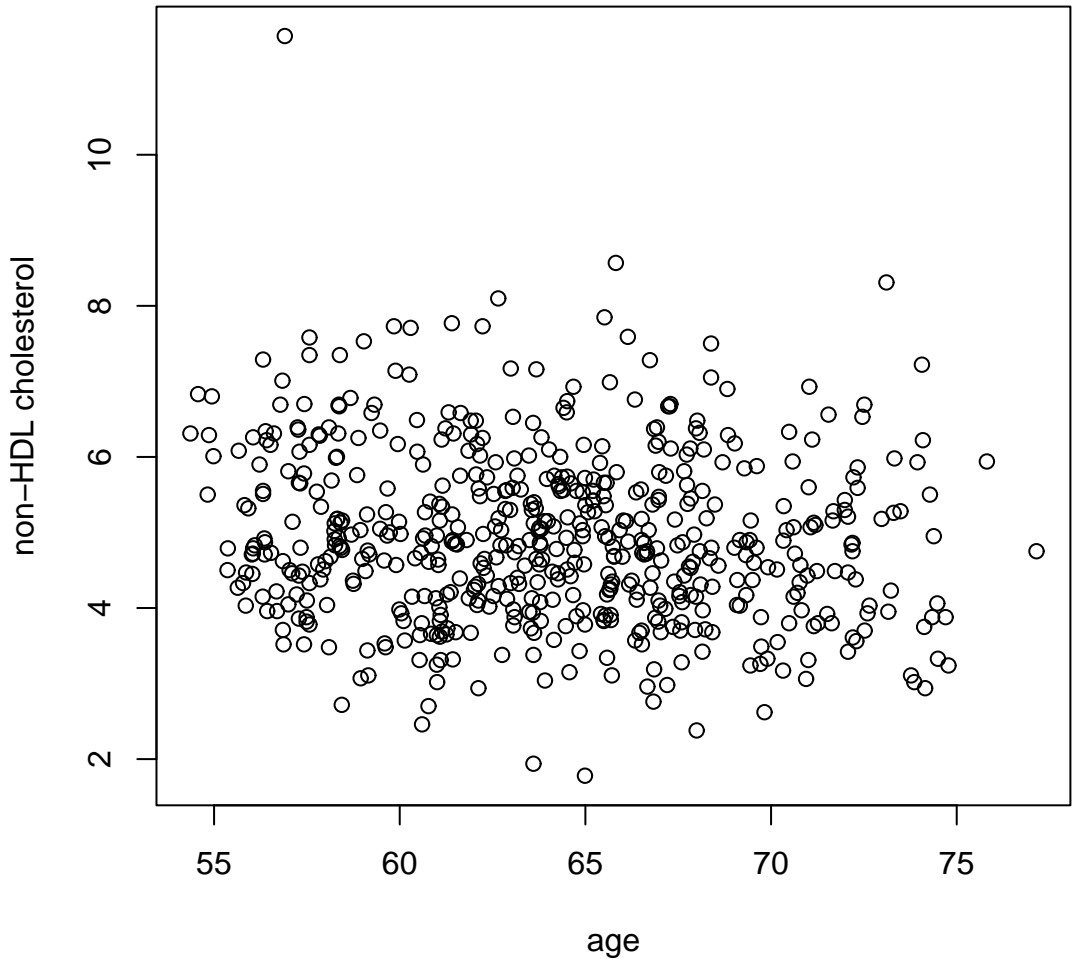
1. Unconstrained model for age and non-HDL
2. Unconstrained model for ranks of age and non-HDL
3. Constrained model for age and non-HDL
4. Constrained model for ranks of age and non-HDL
  
5. Unconstrained model for age and HDL
6. Unconstrained model for ranks of age and HDL
7. Constrained model for age and HDL
8. Constrained model for ranks of age and HDL
  
9. Unconstrained model for non-HDL and HDL
10. Unconstrained model for ranks of non-HDL and HDL
11. Constrained model for non-HDL and HDL
12. Constrained model for ranks of non-HDL and HDL



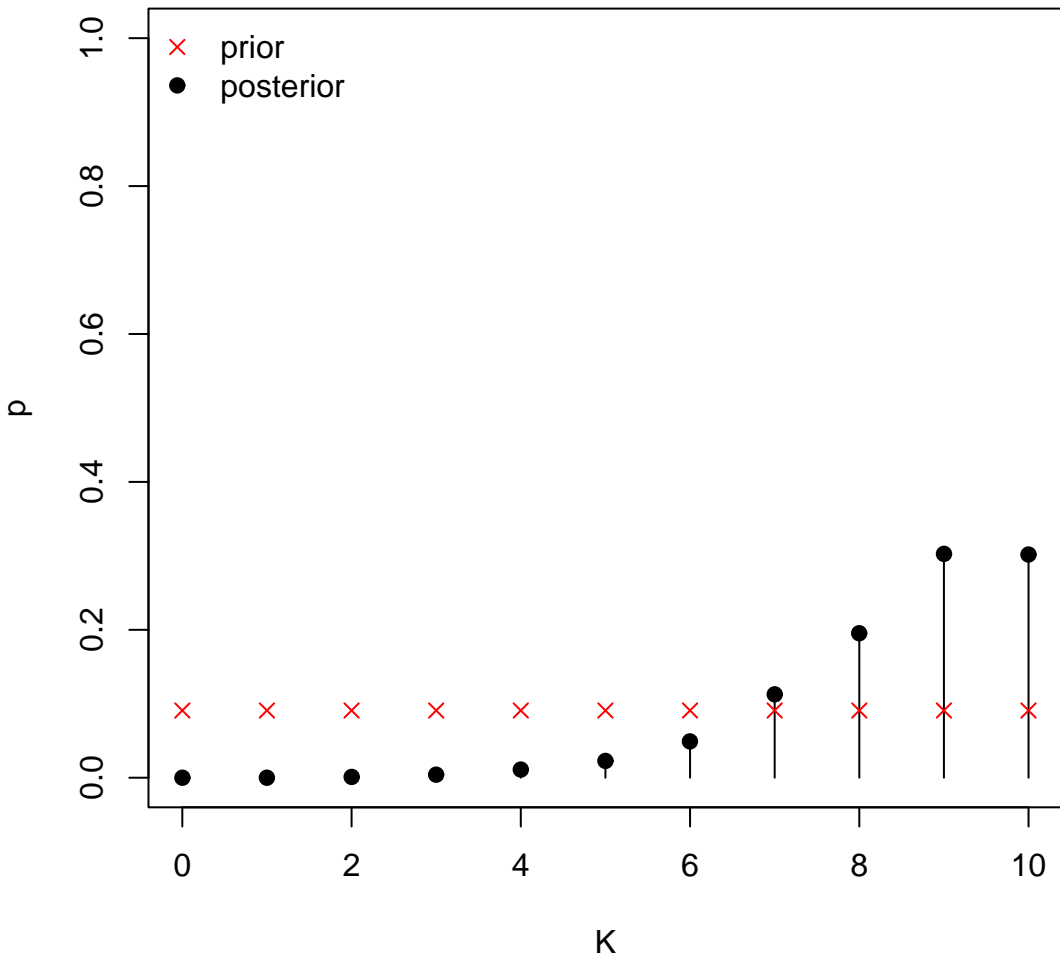
## Histograms; N=4369



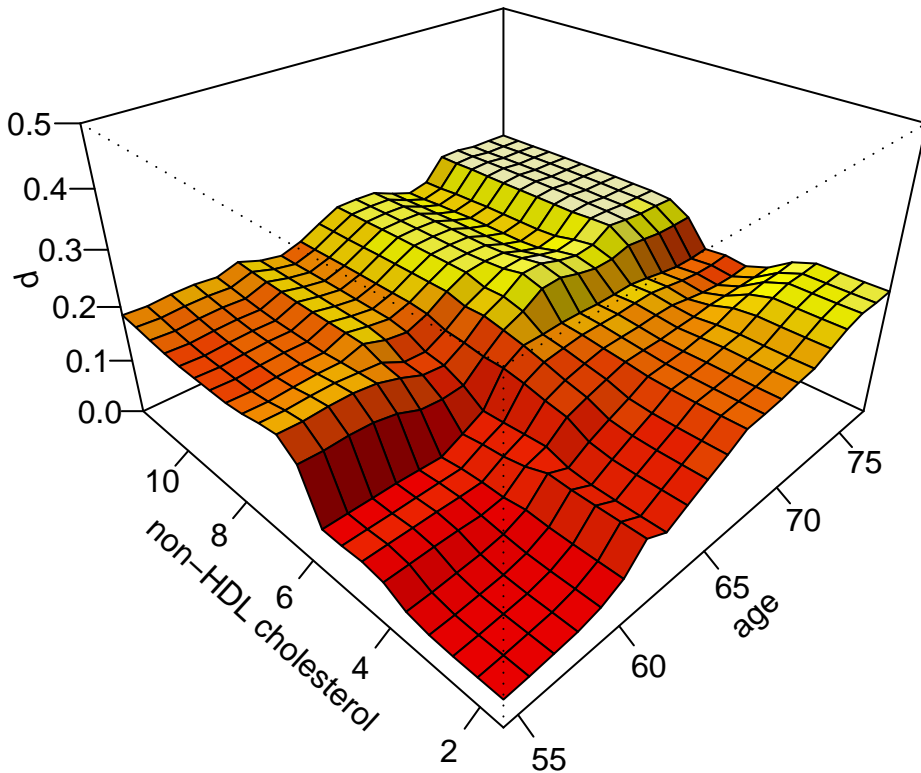
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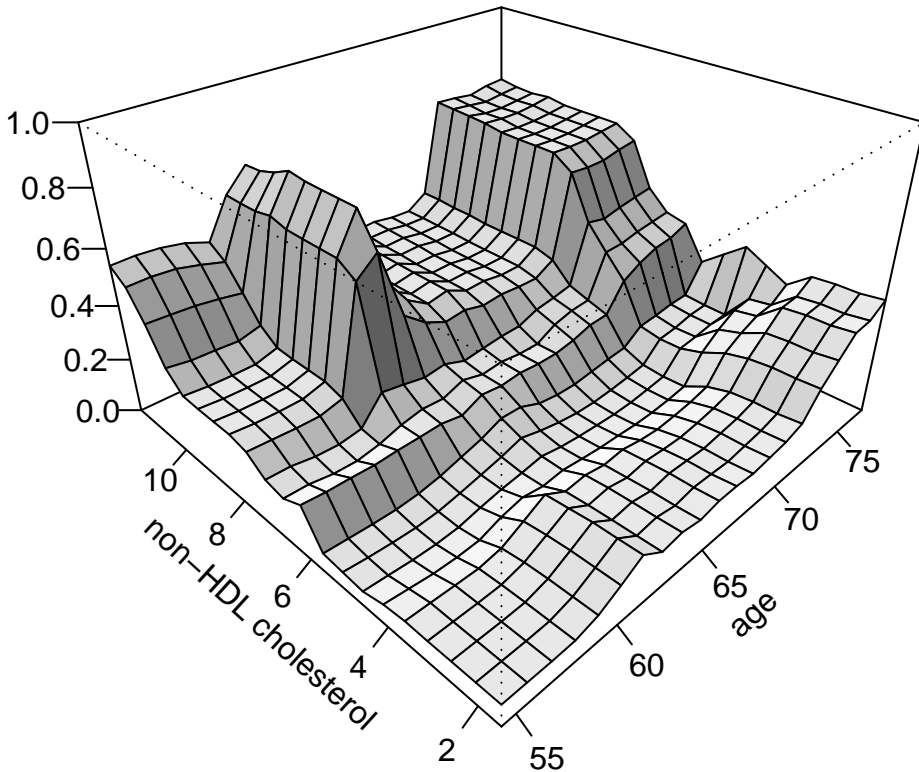
# 1. Unconstrained model for age and non-HDL: Total number of change points



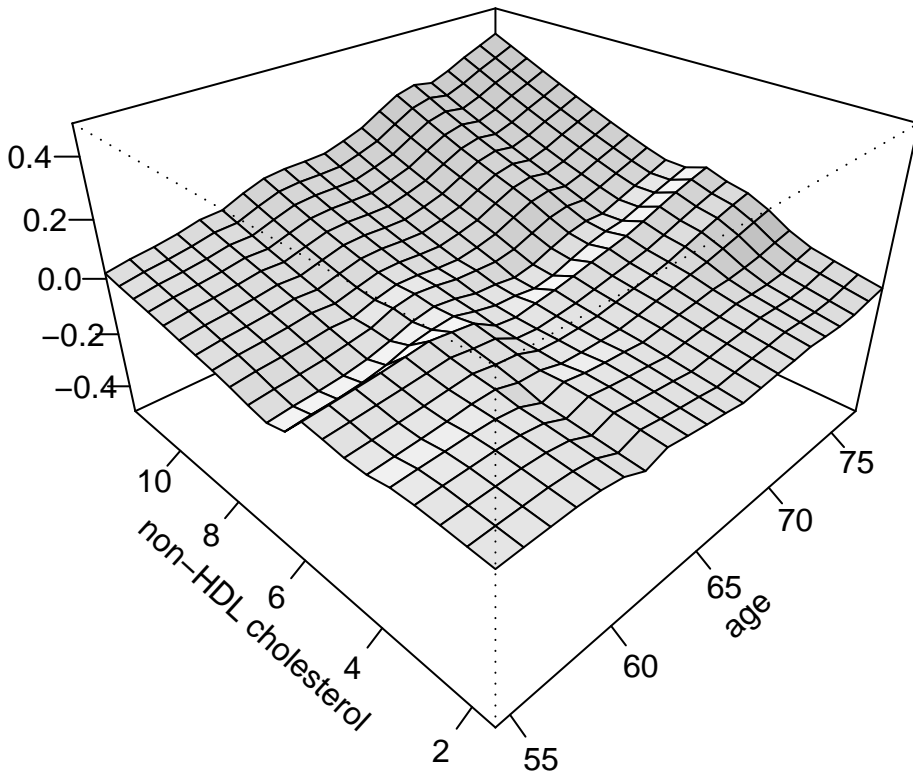
# 1. Unconstrained model for age and non-HDL: Posterior median 7 year risk



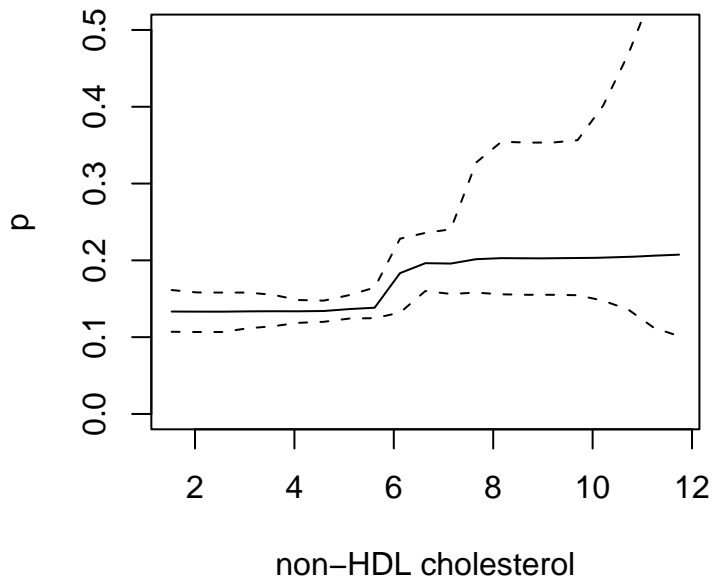
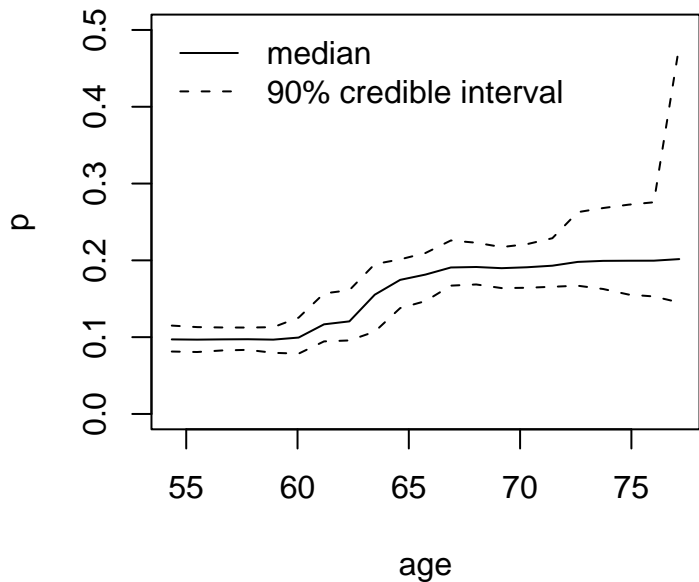
# 1. Unconstrained model for age and non-HDL: Length of 90% credible interval



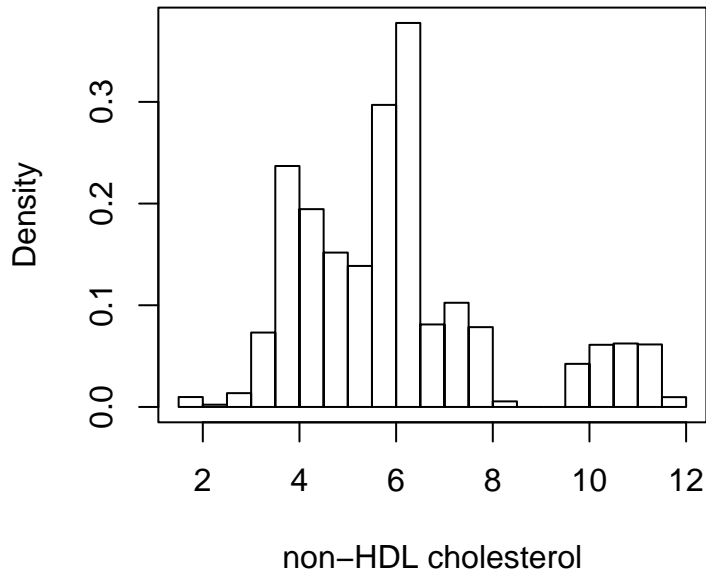
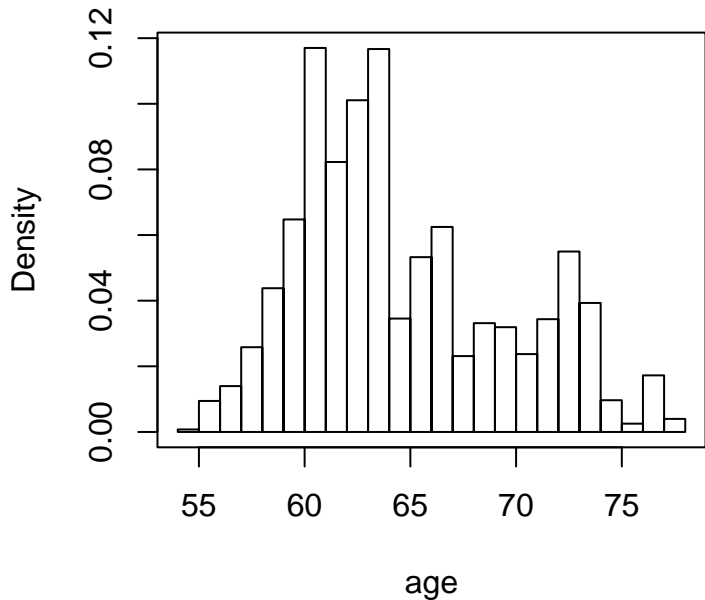
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# 1. Unconstrained model for age and non-HDL: One-dimensional projections

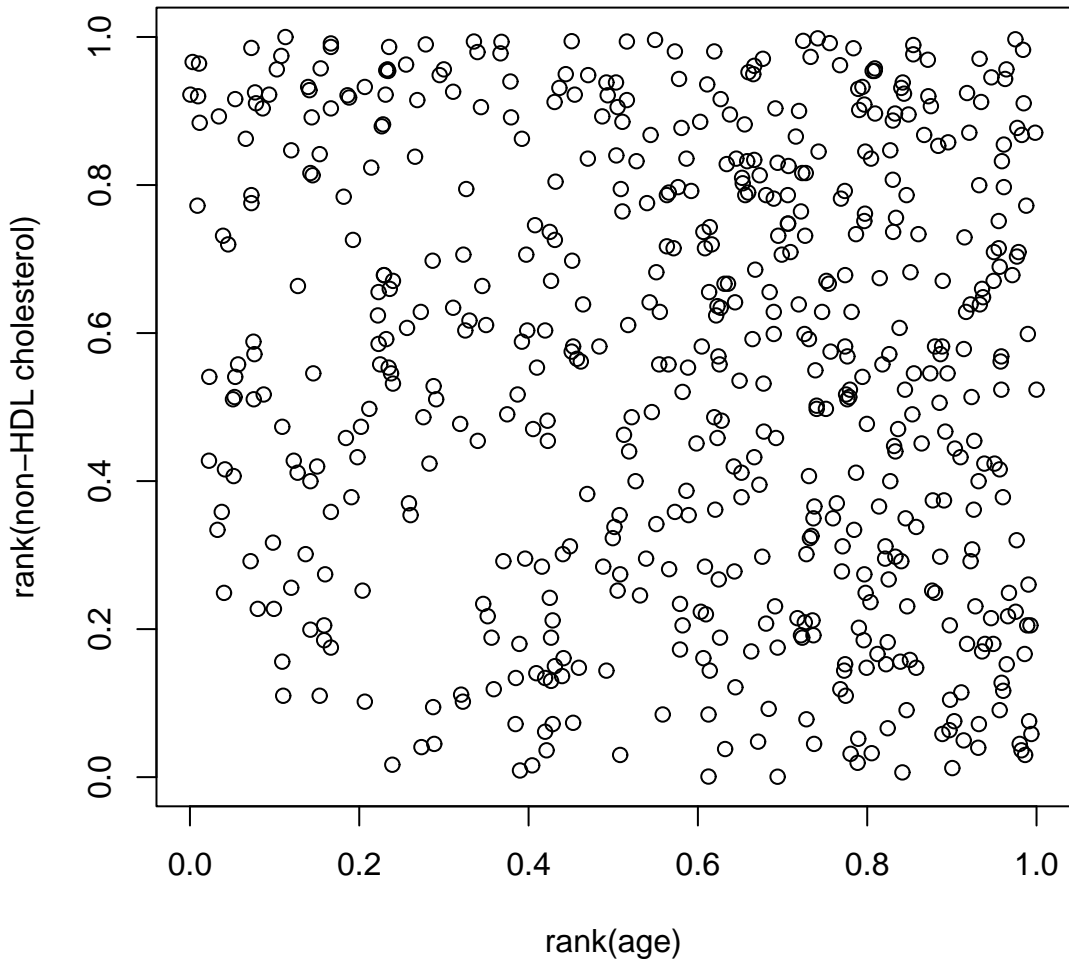


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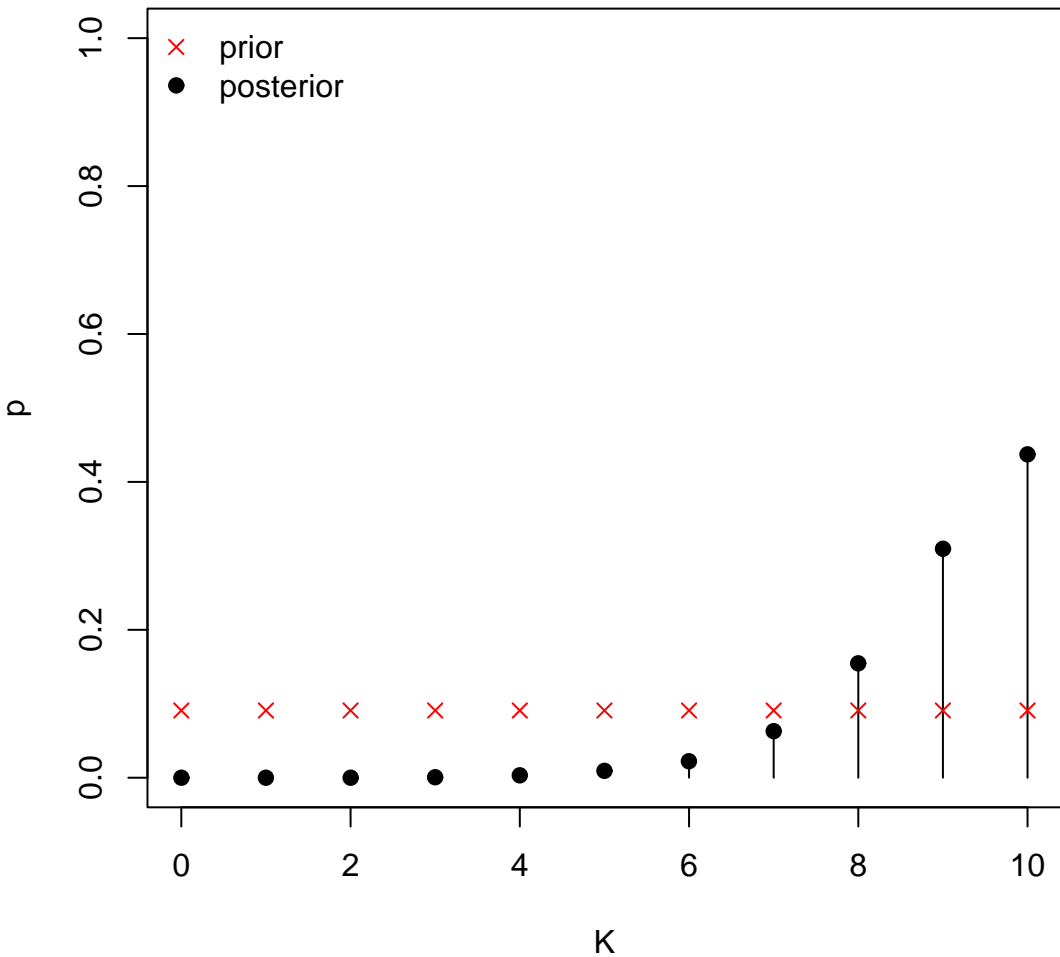




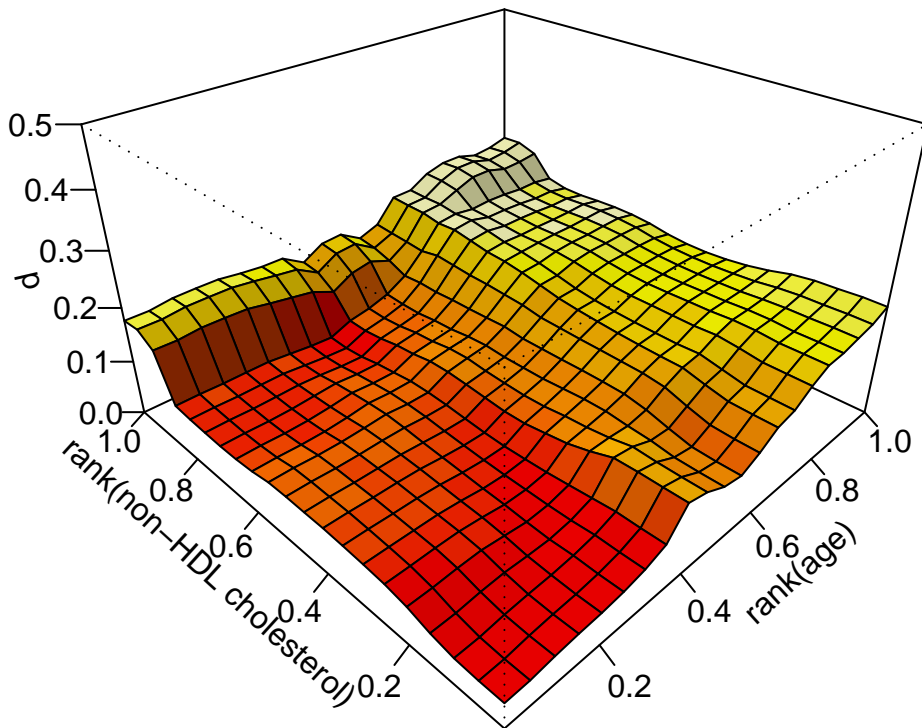
## 2. Unconstrained model for ranks of age and non-HDL: Distribution of events by covariates



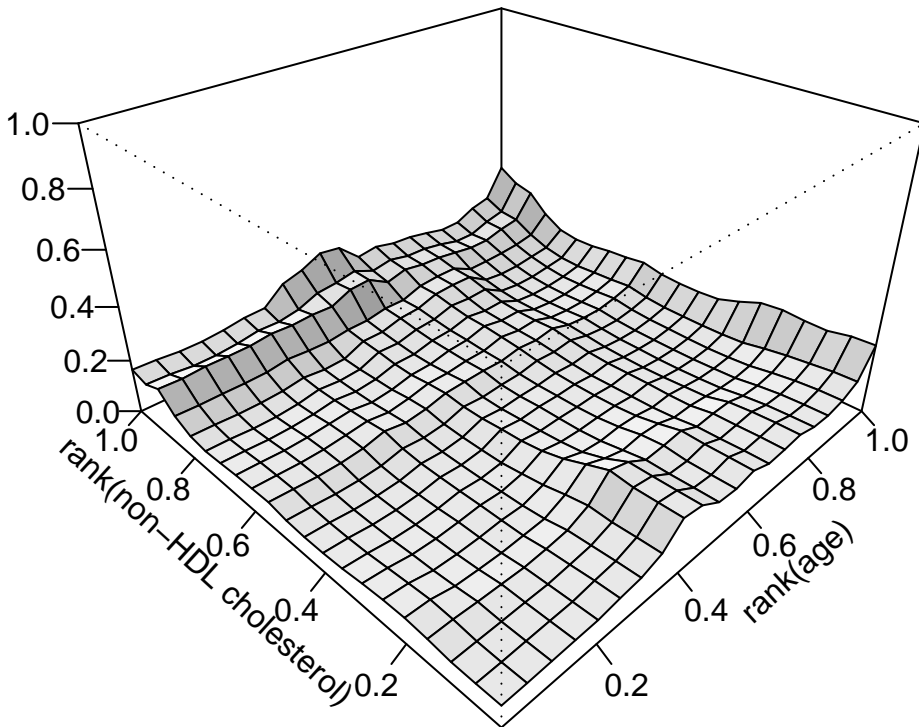
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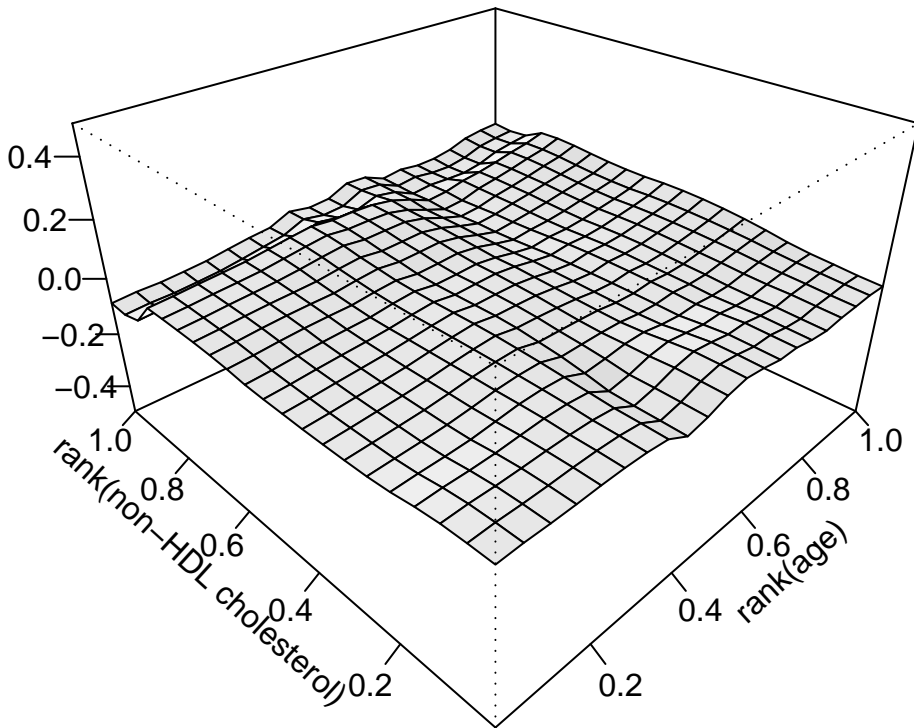
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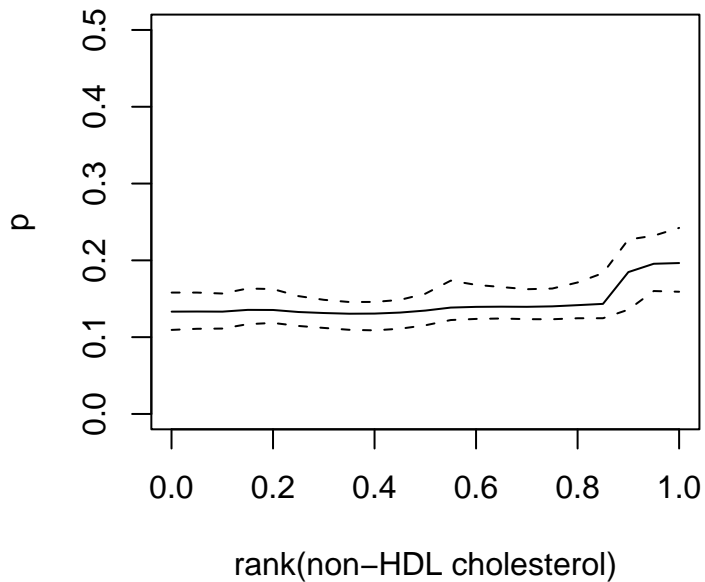
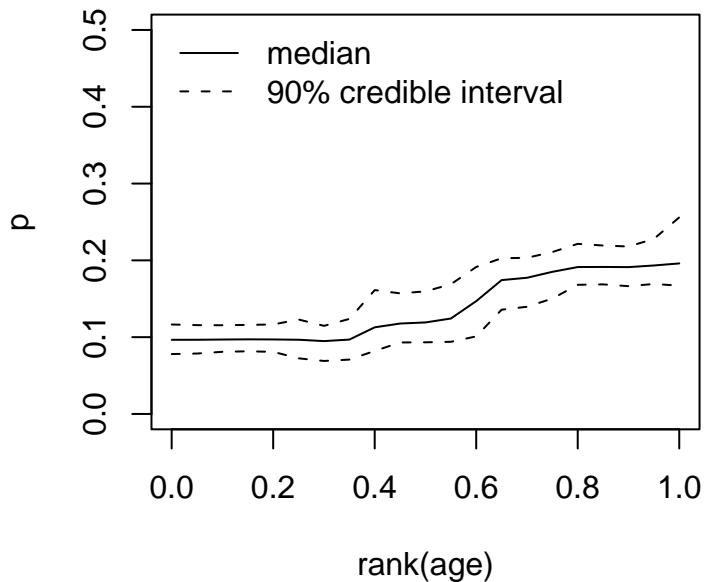
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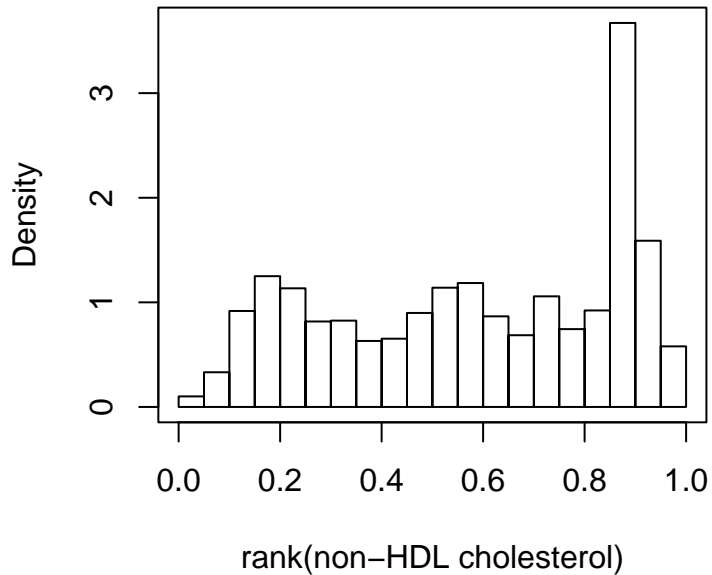
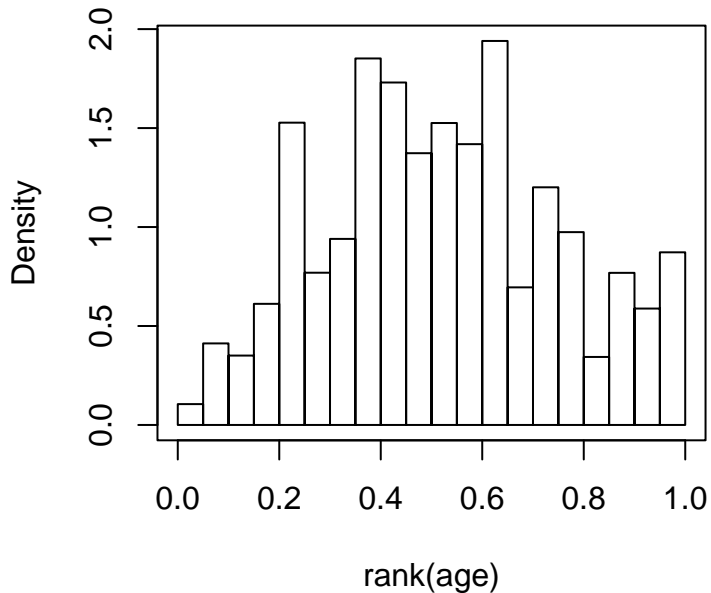
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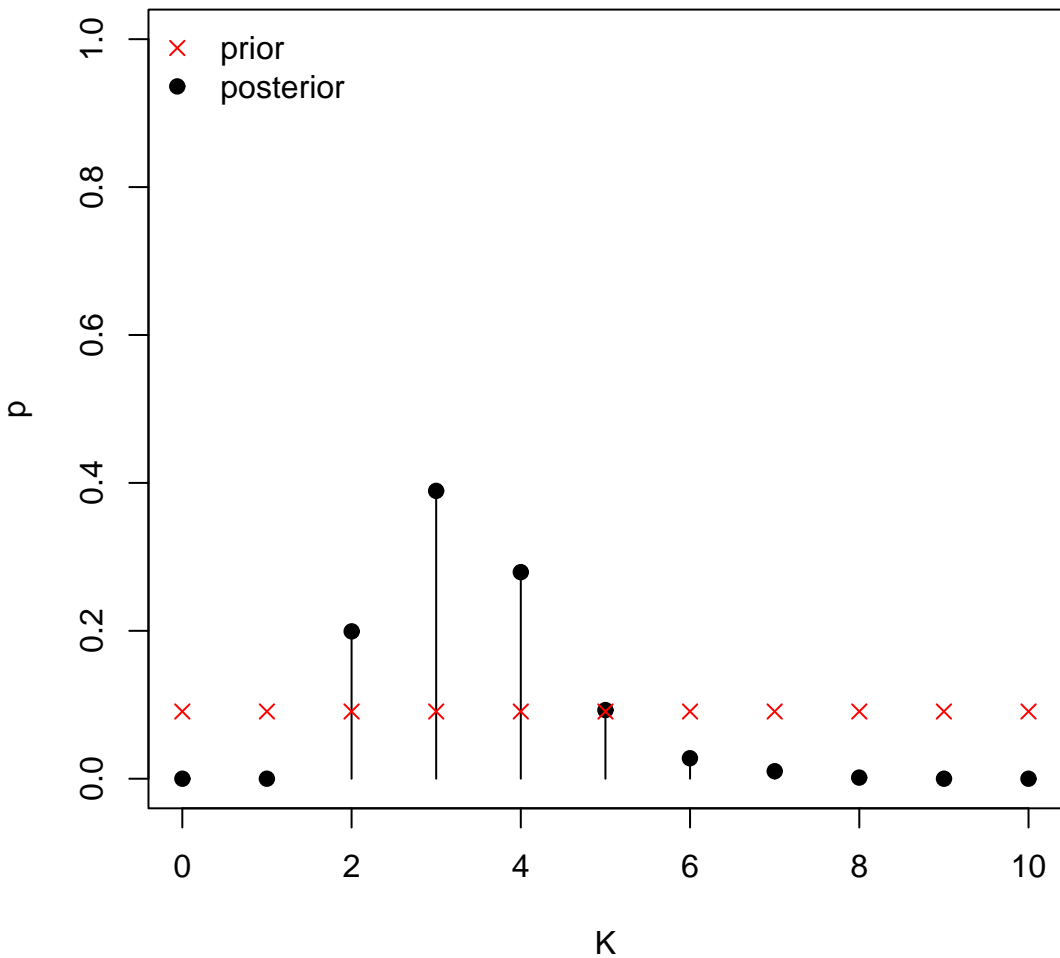
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## 2. Unconstrained model for ranks of age and non-HDL: Distributions for change point positions

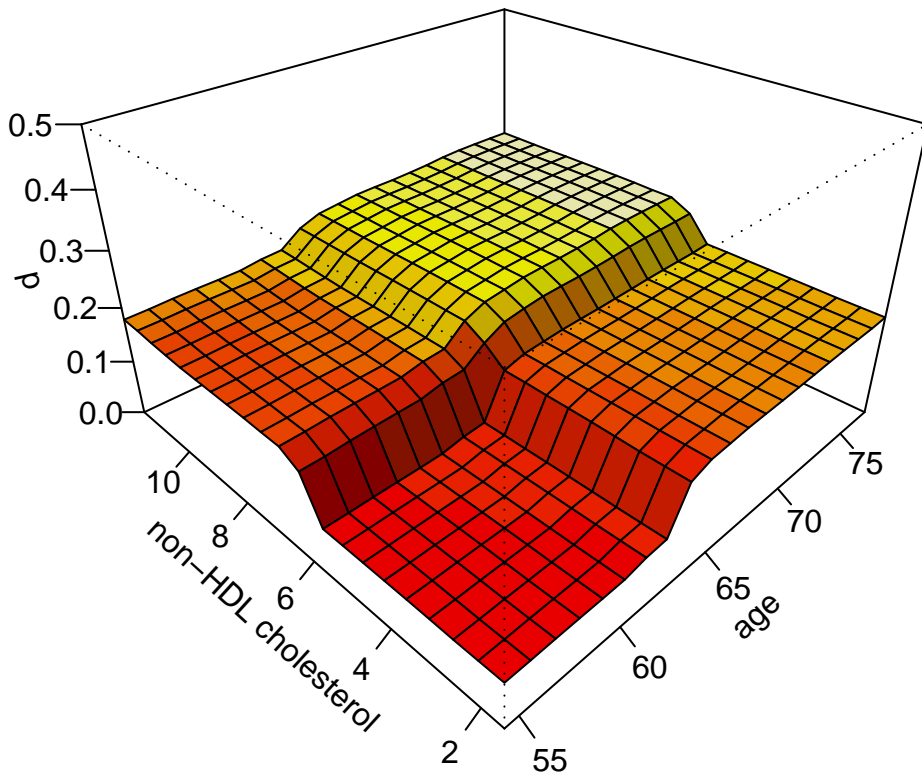


### 3. Constrained model for age and non-HDL: Total number of change points

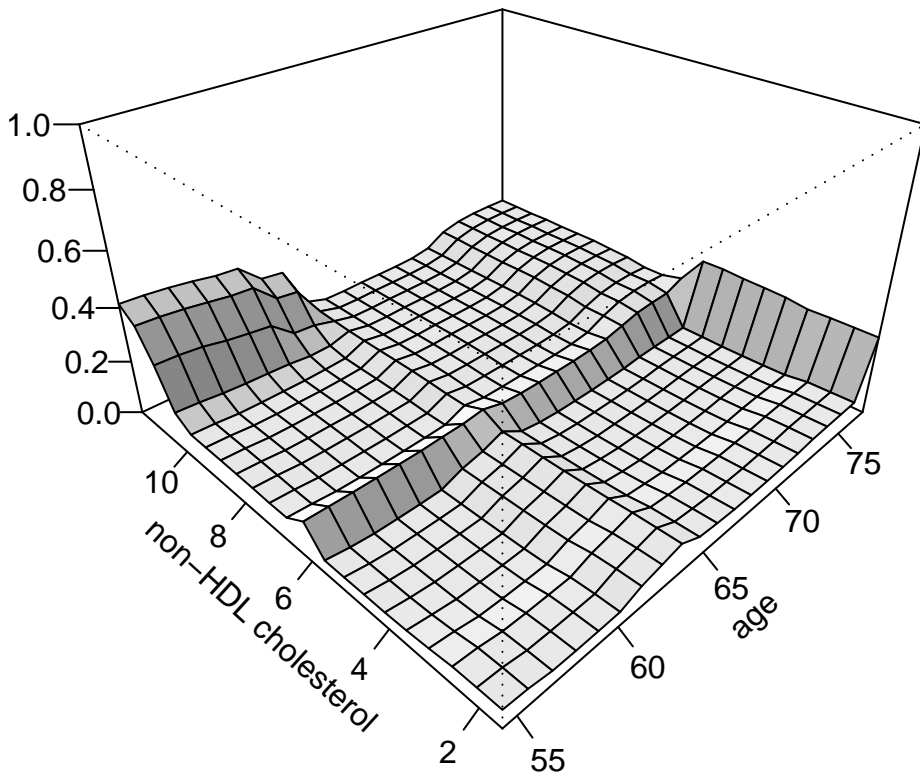




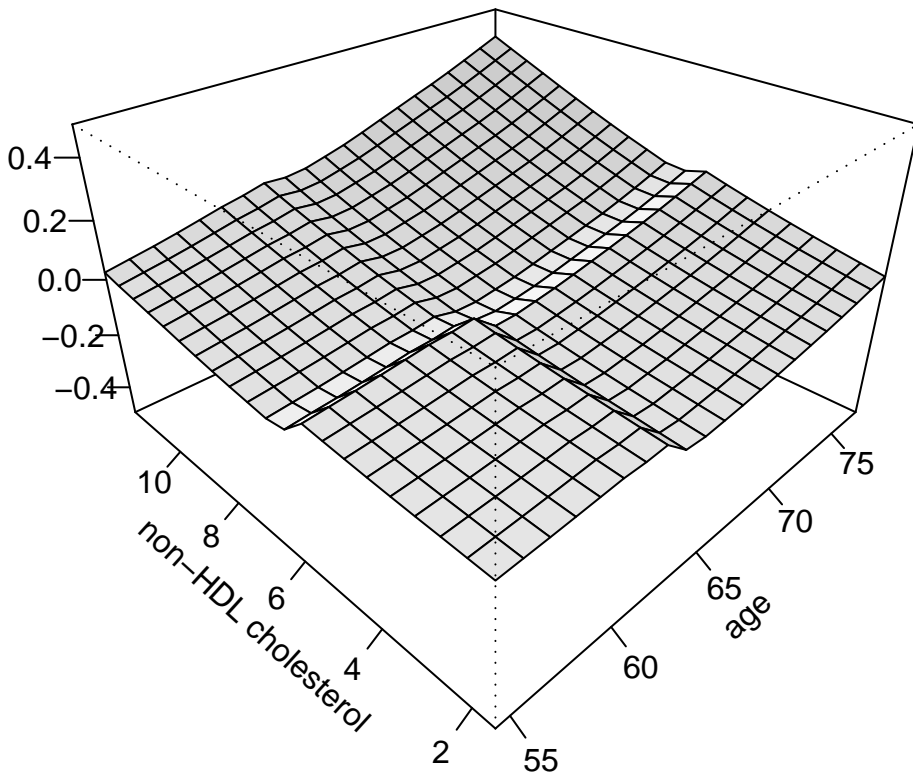
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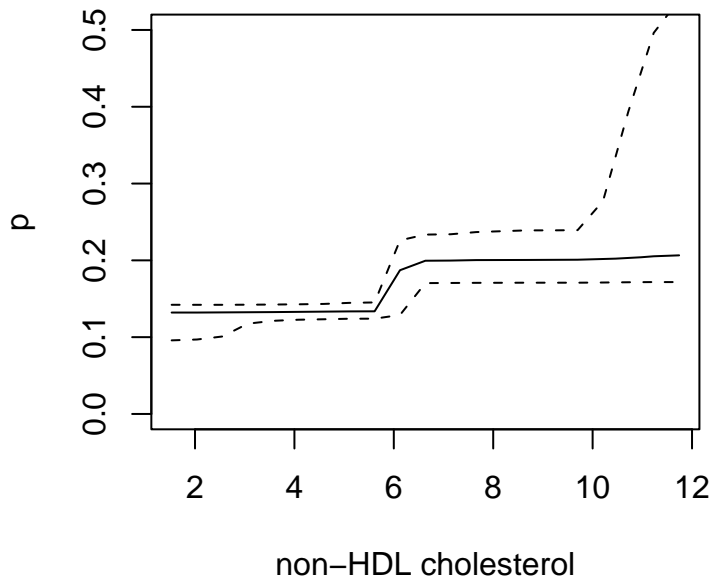
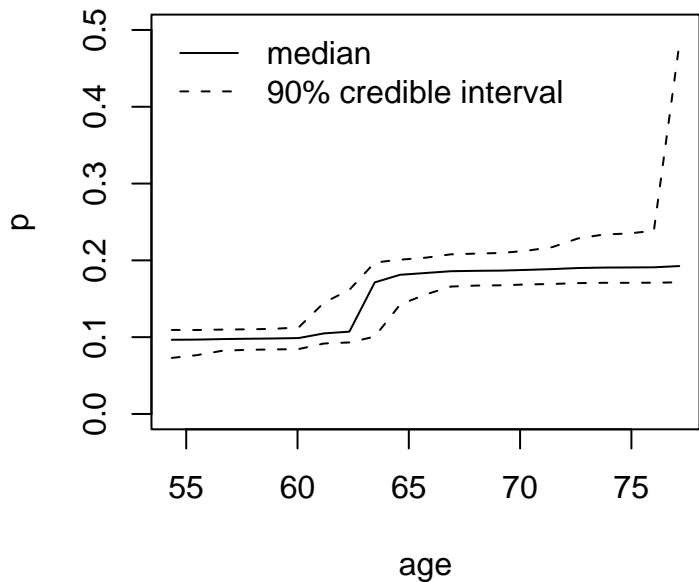
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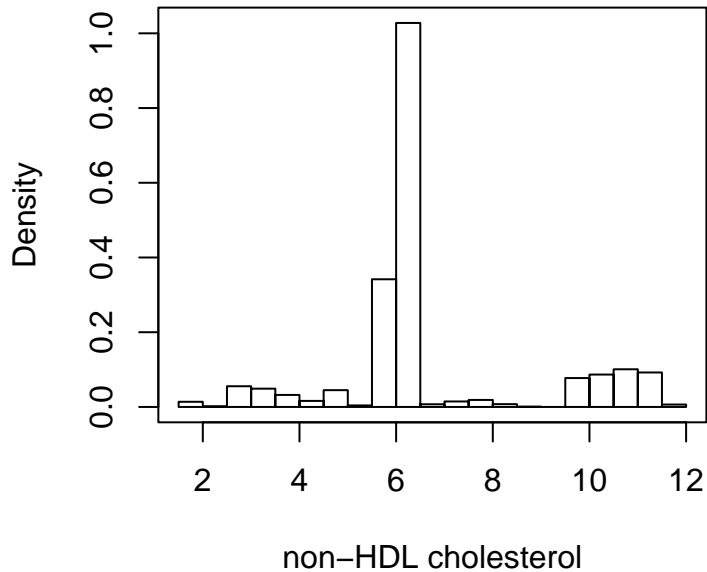
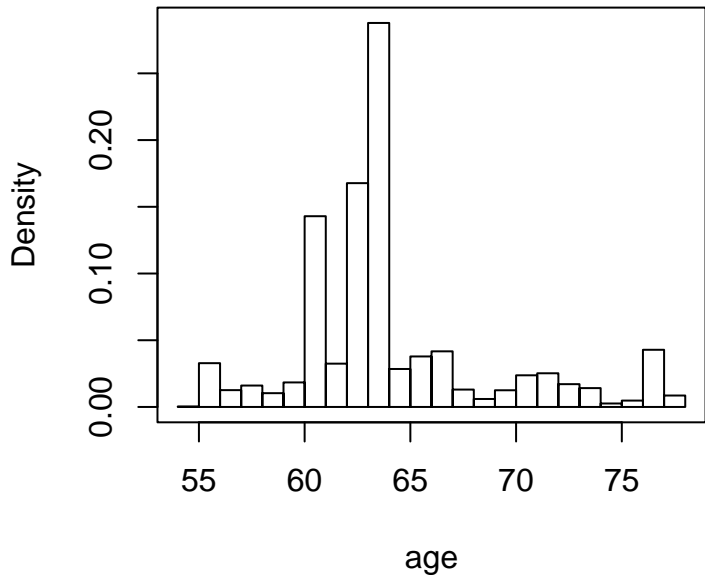
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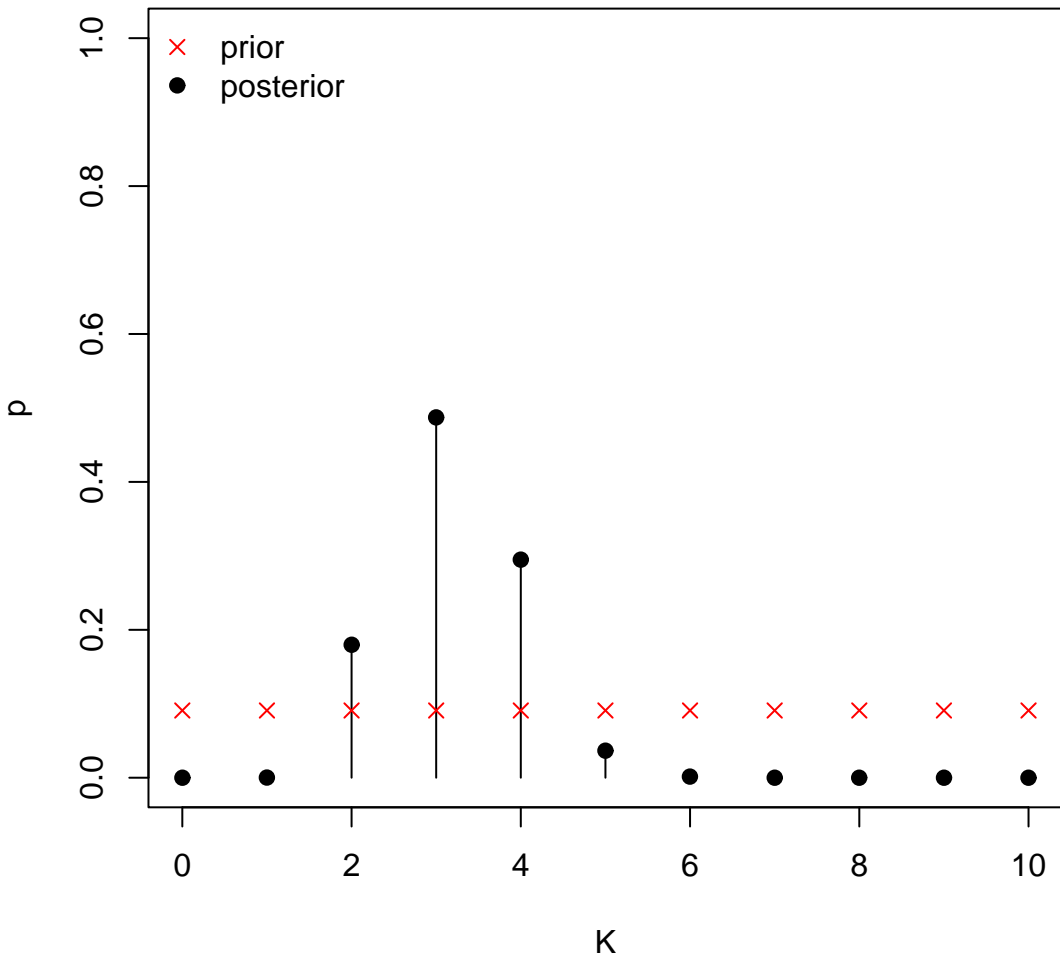
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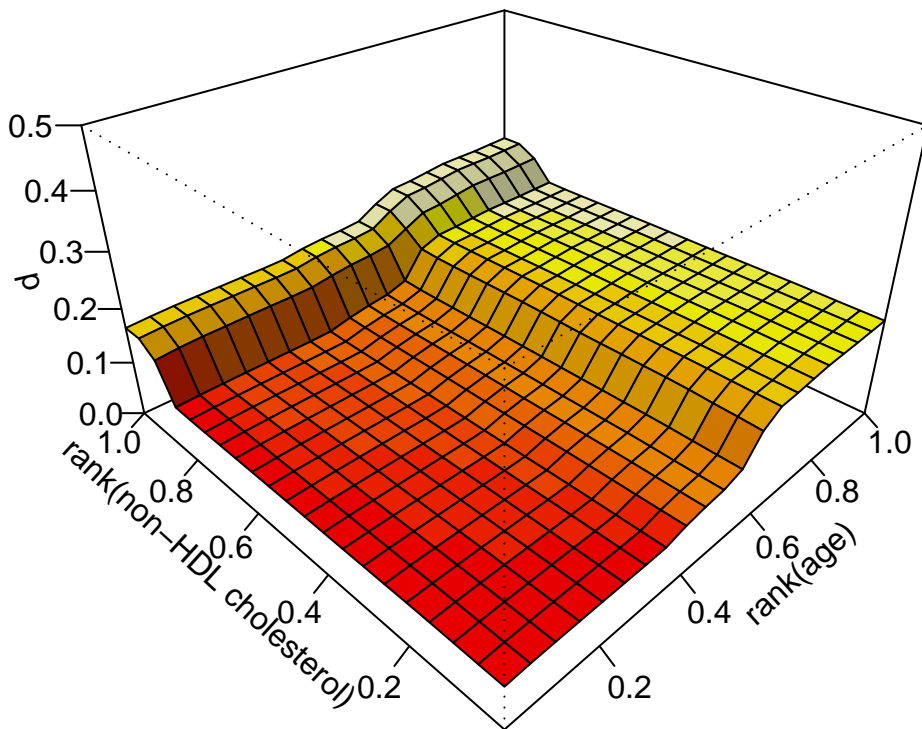
### 3. Constrained model for age and non-HDL: Distributions for change point positions



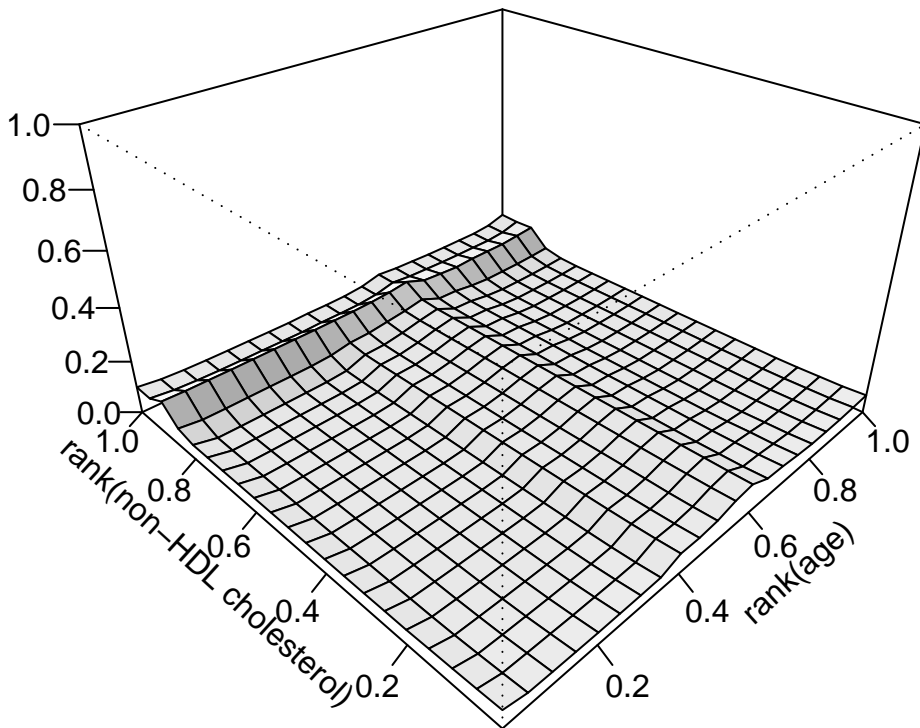
#### 4. Constrained model for ranks of age and non-HDL: Total number of change points



#### 4. Constrained model for ranks of age and non-HDL: Posterior median 7 year risk

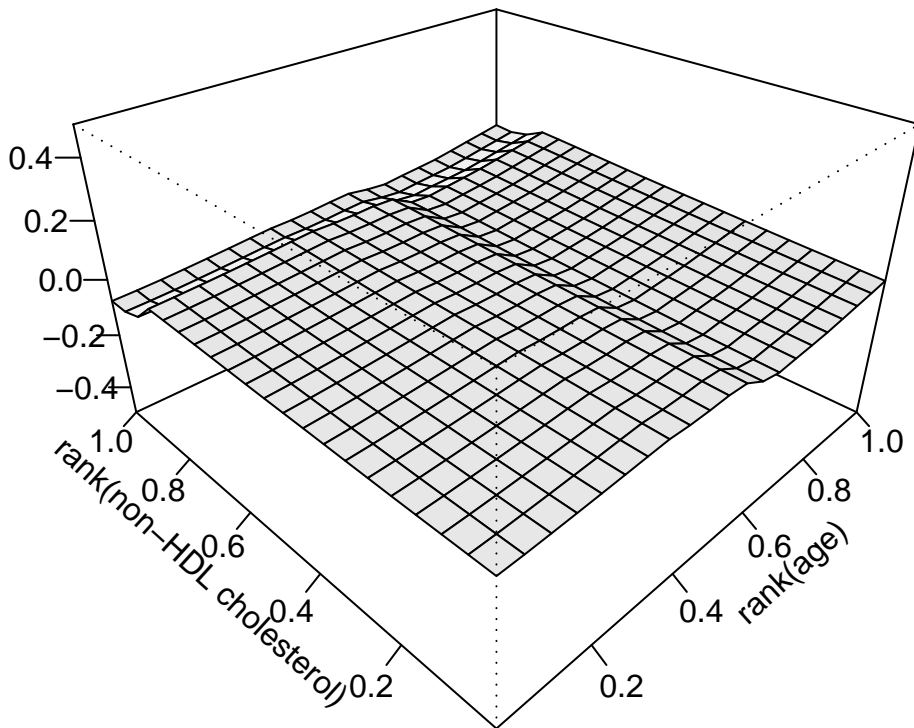


#### 4. Constrained model for ranks of age and non-HDL: Length of 90% credible interval

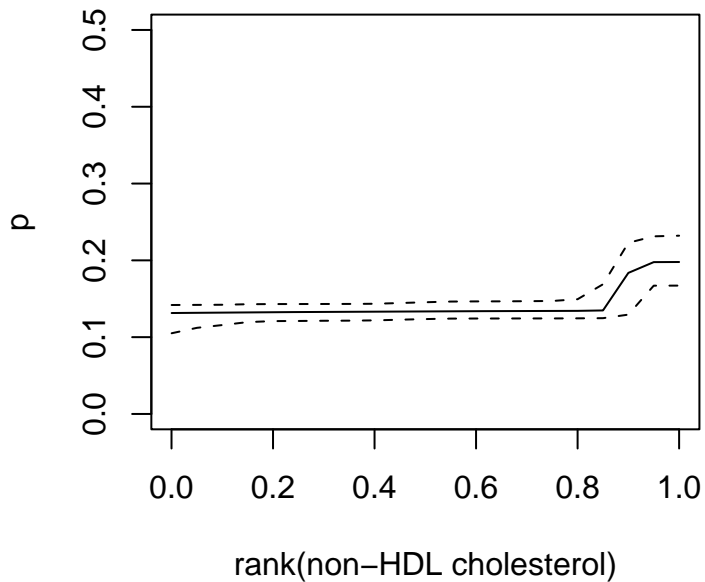
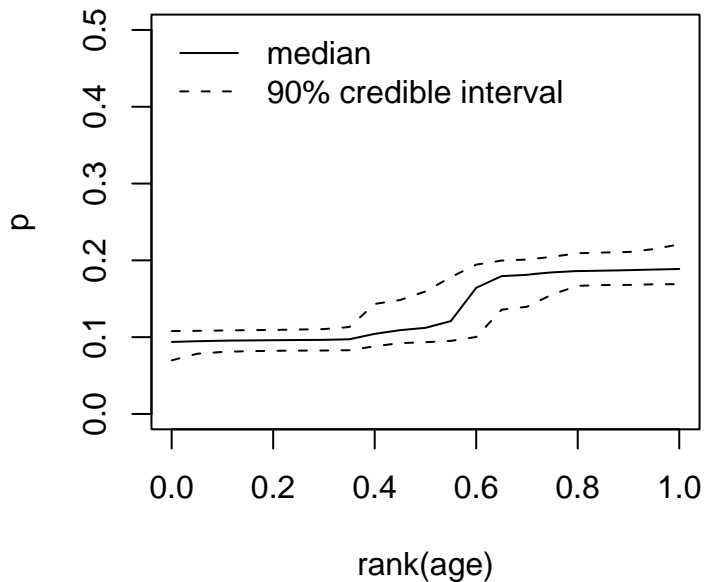




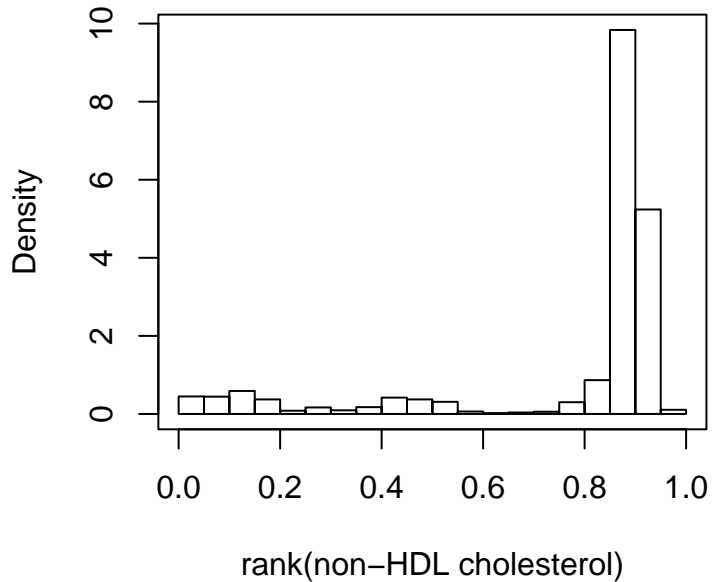
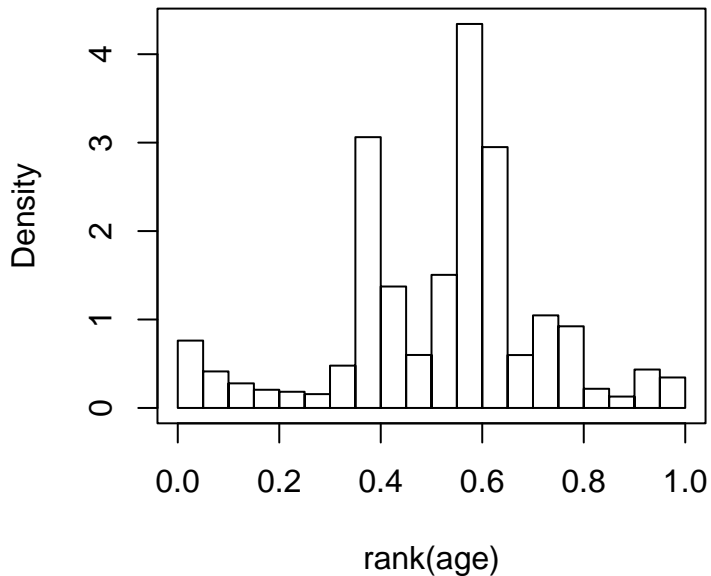
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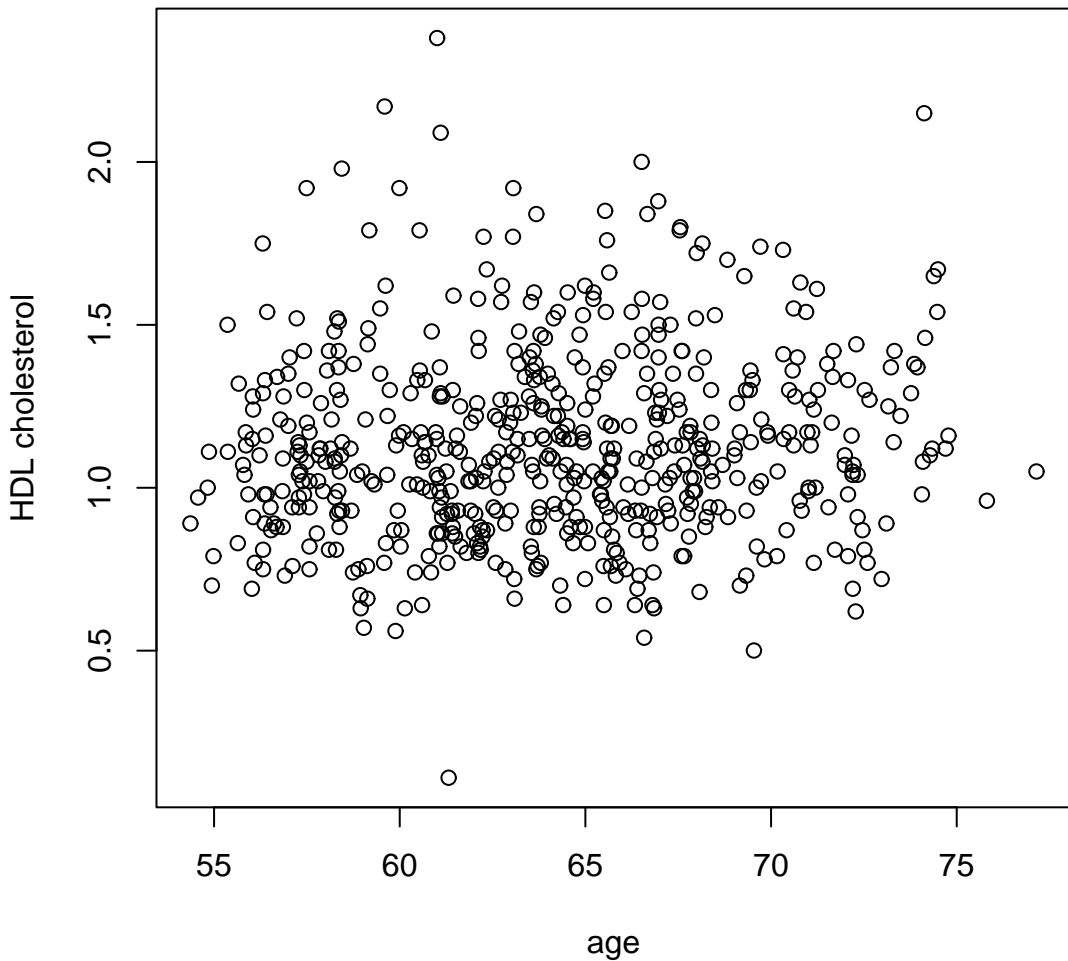
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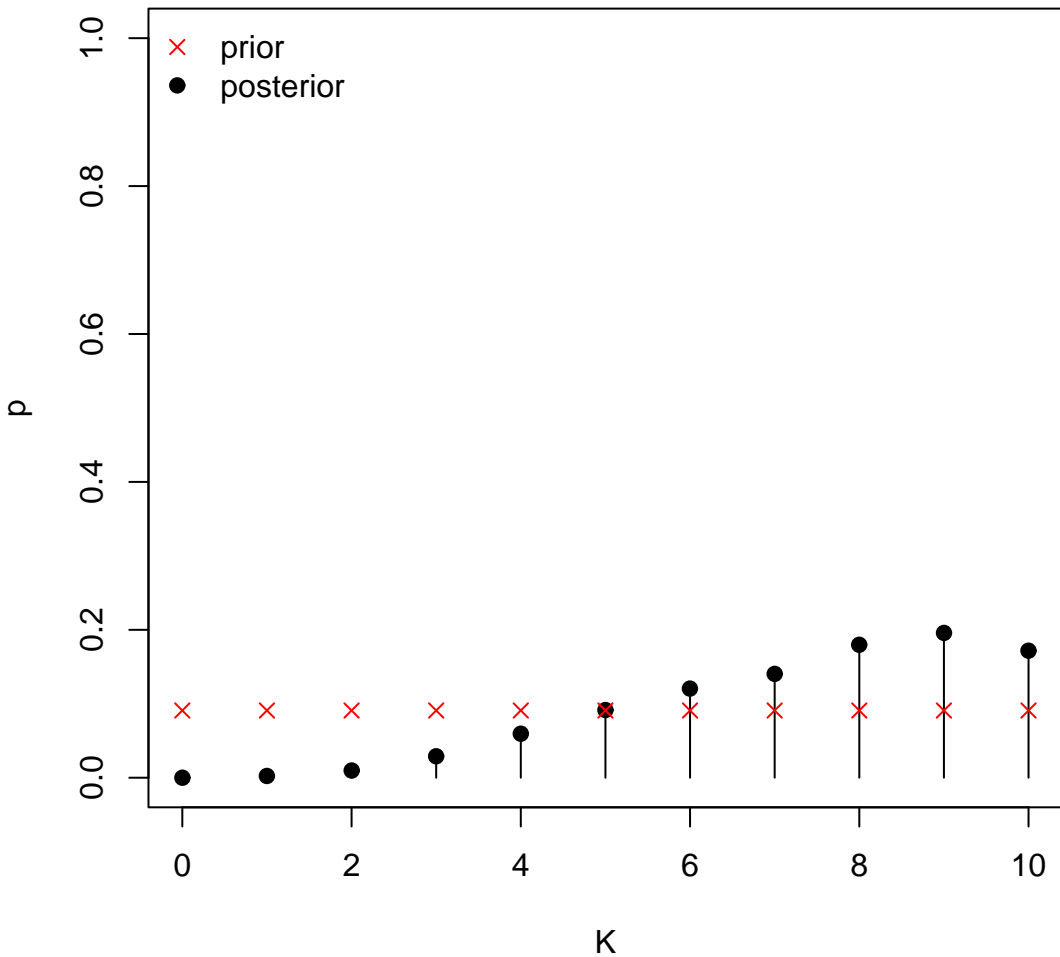
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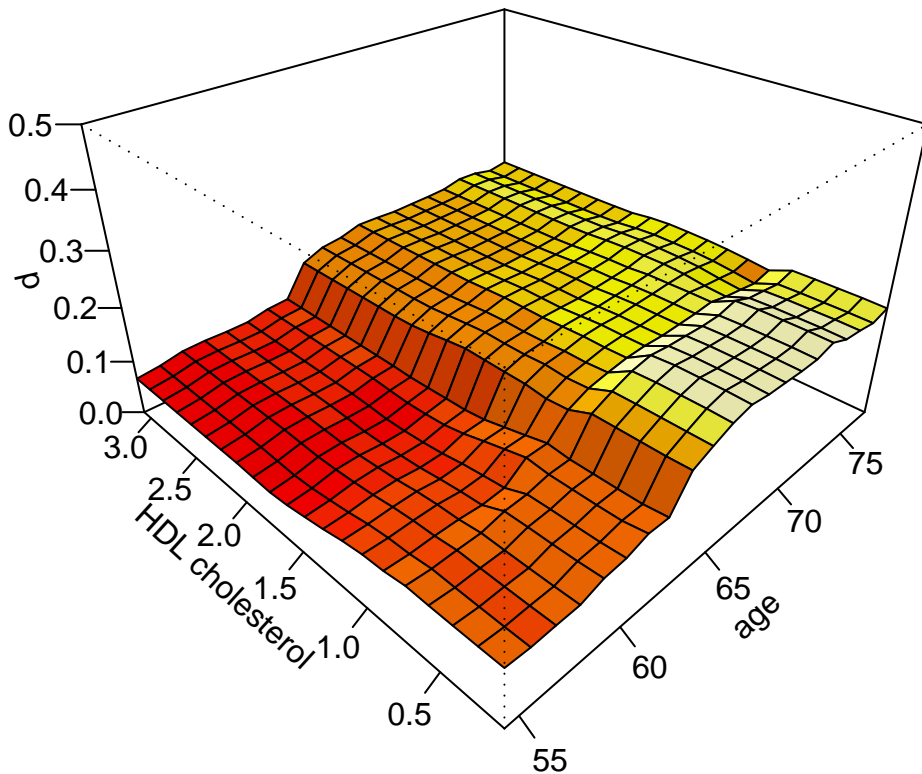
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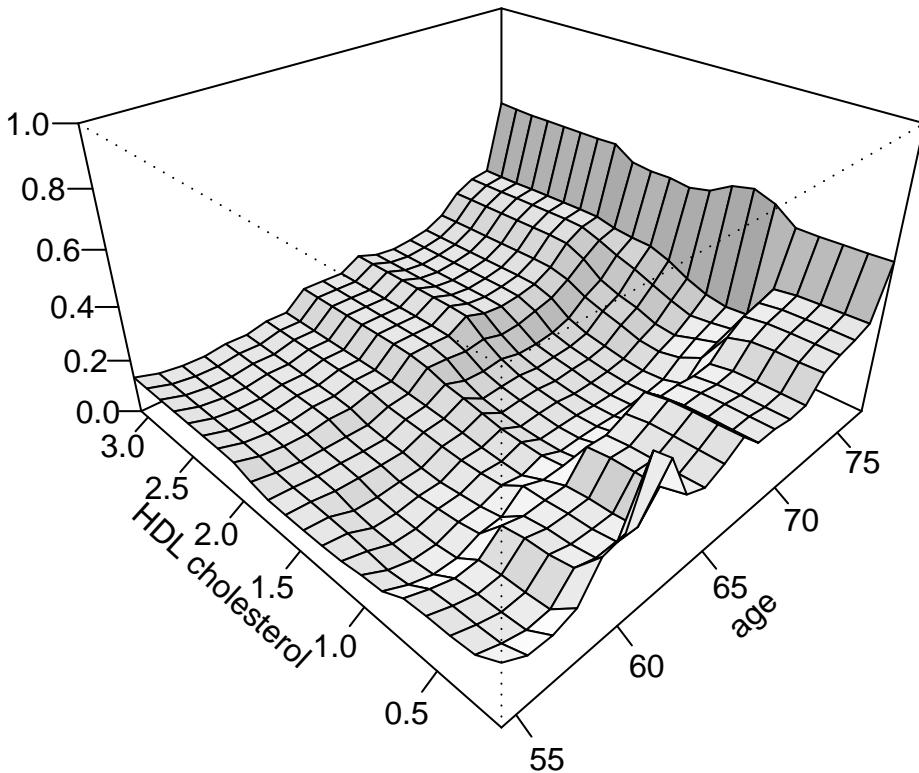
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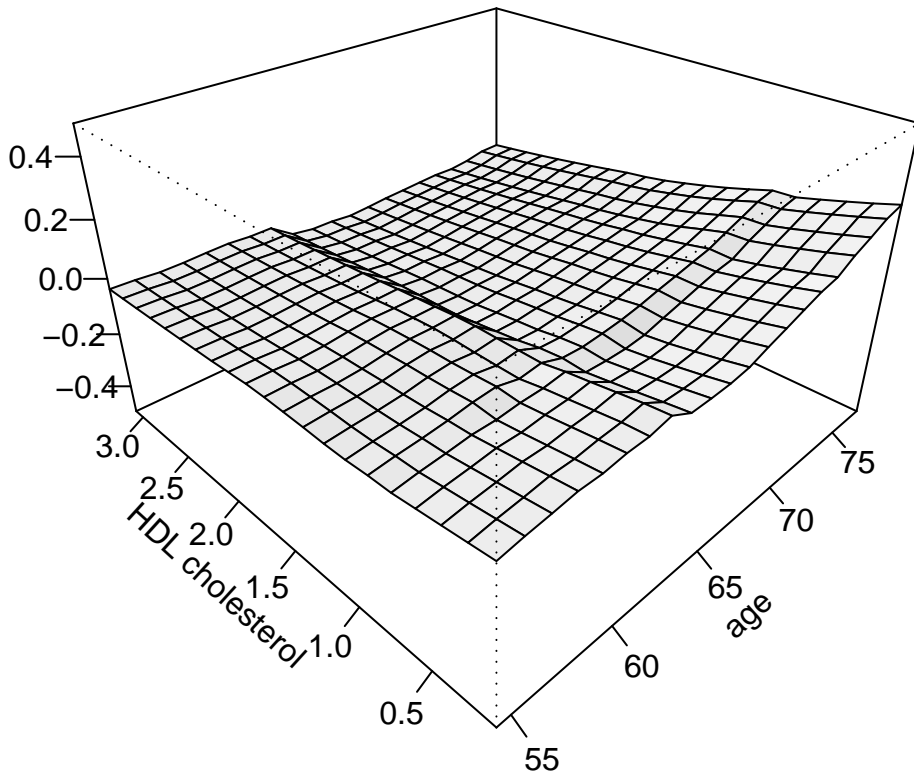
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## 5. Unconstrained model for age and HDL: Length of 90% credible interval

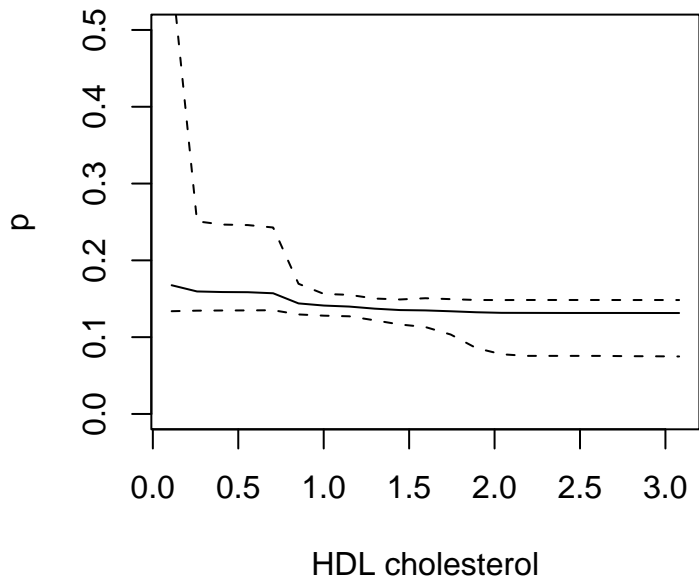
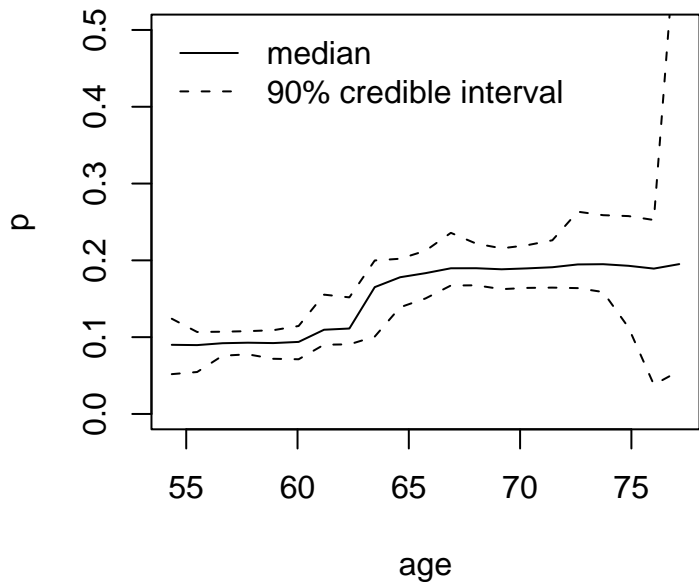


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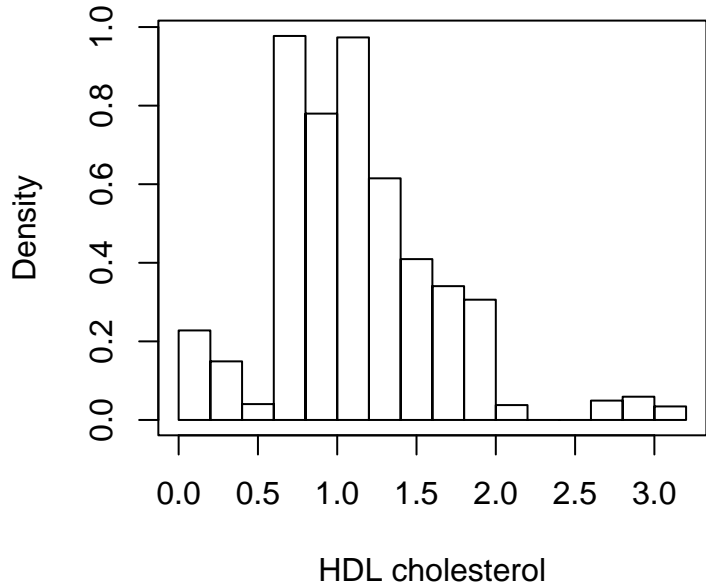
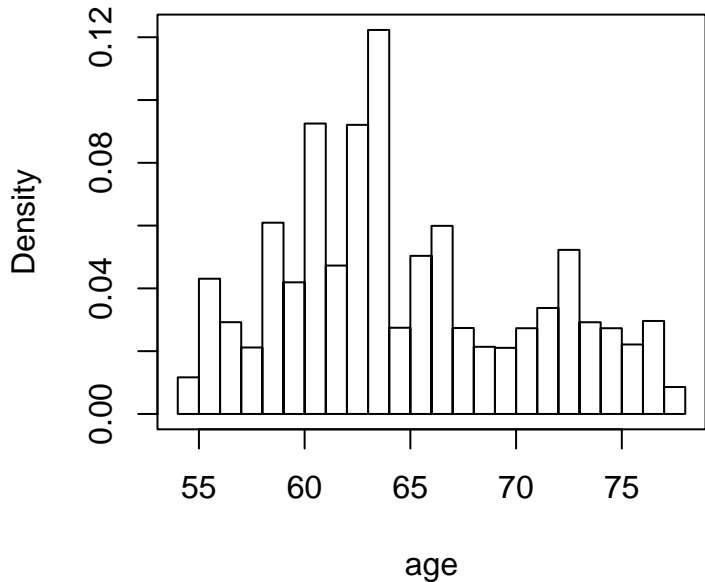




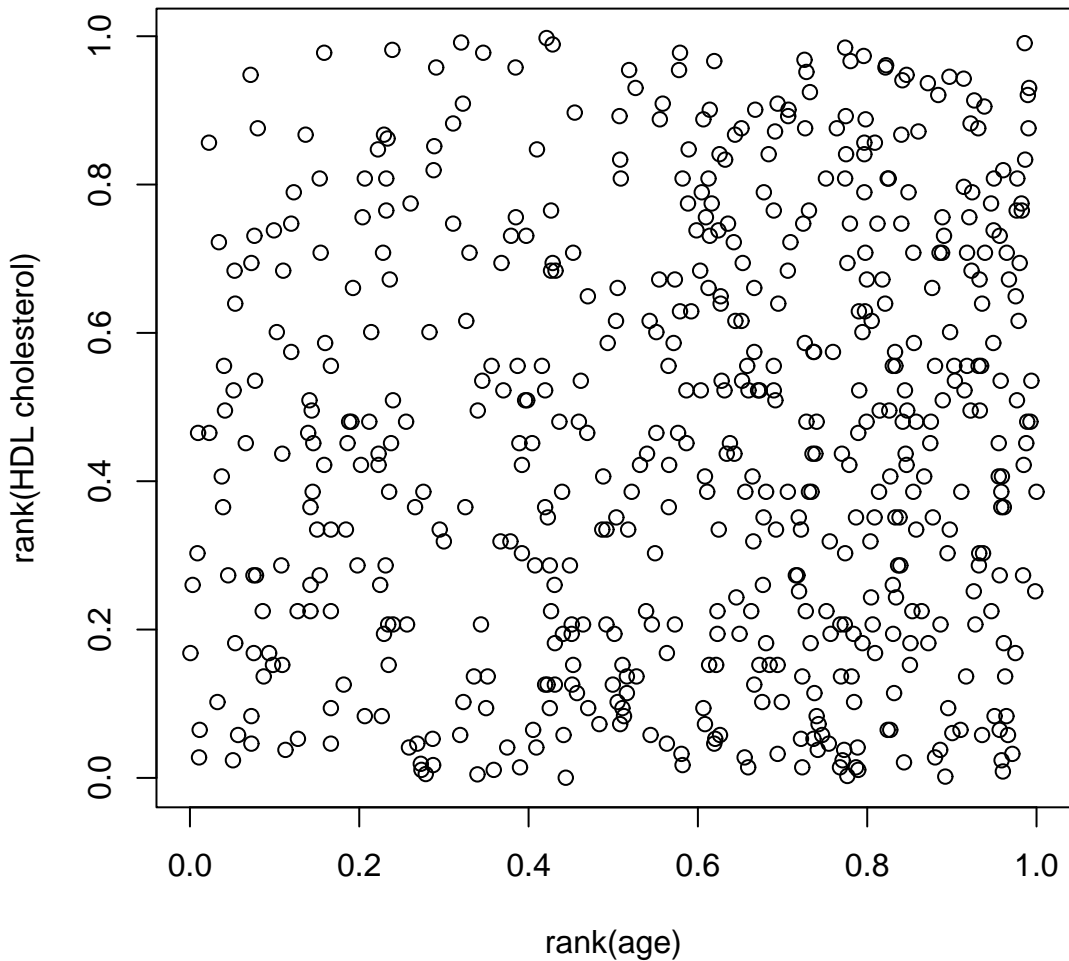
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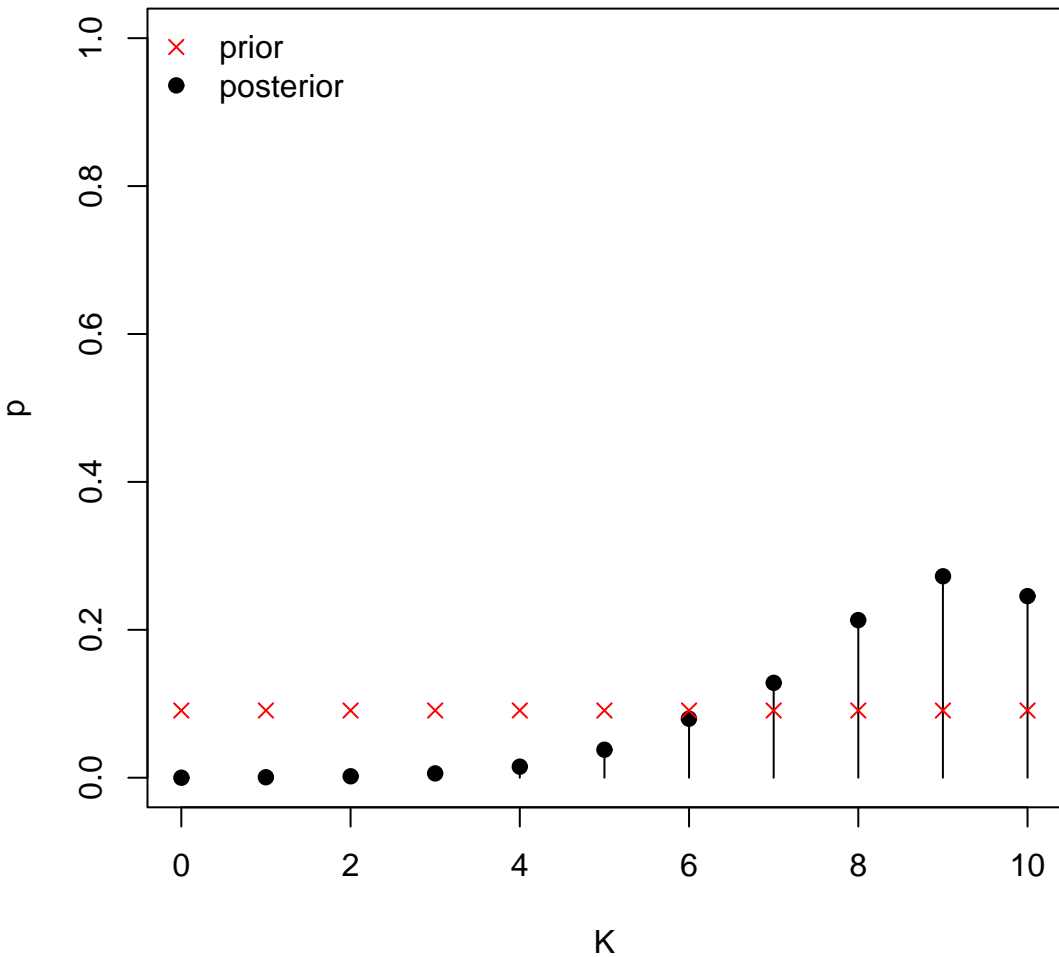
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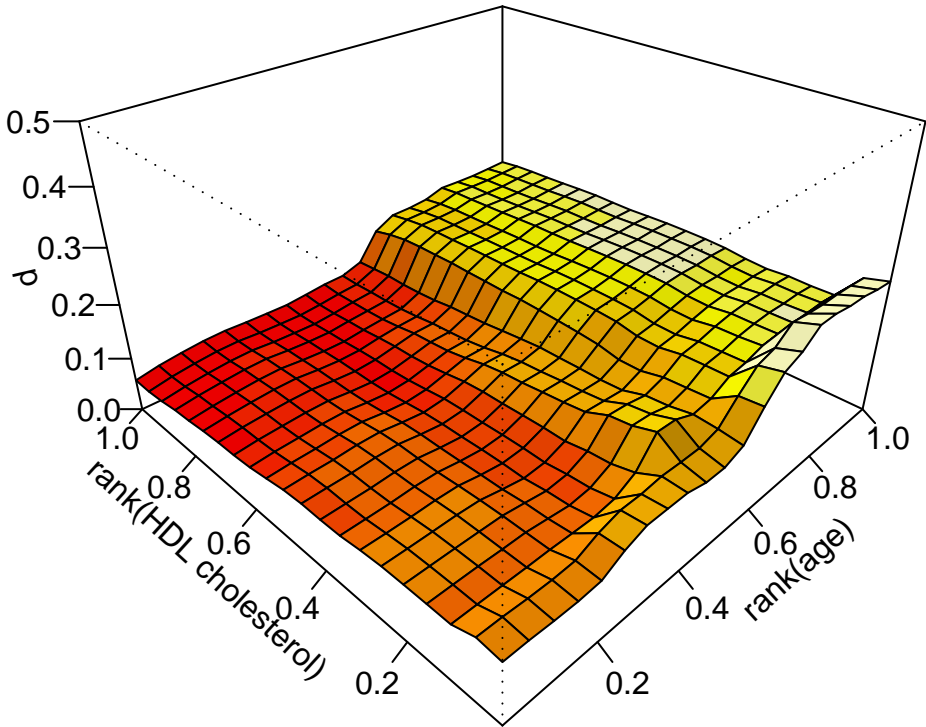
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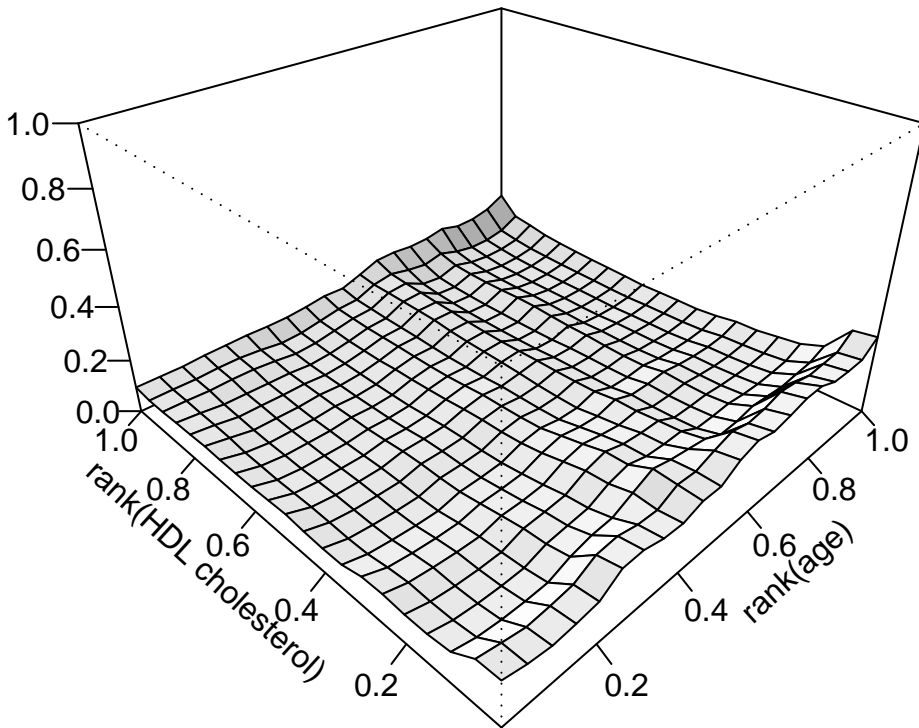
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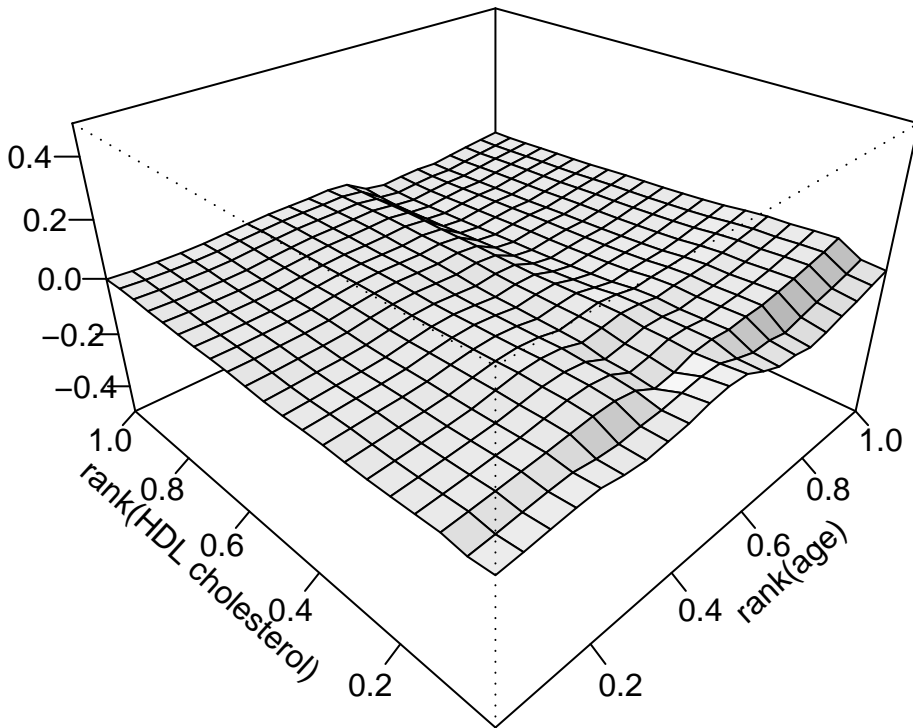
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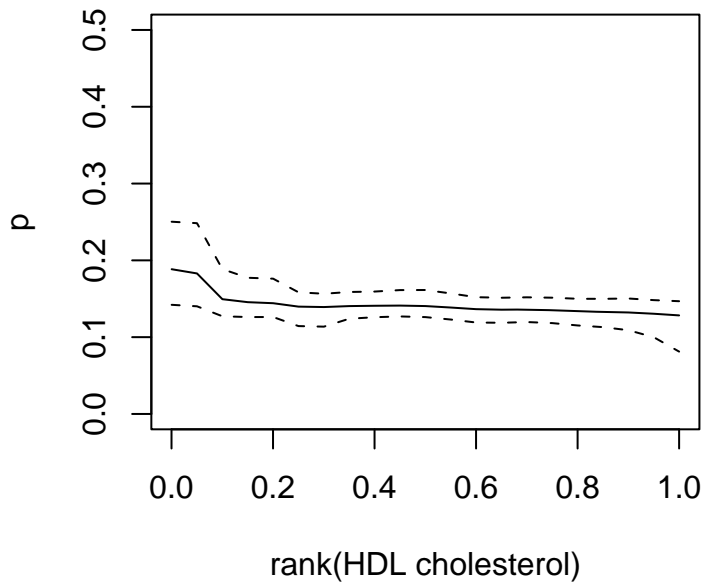
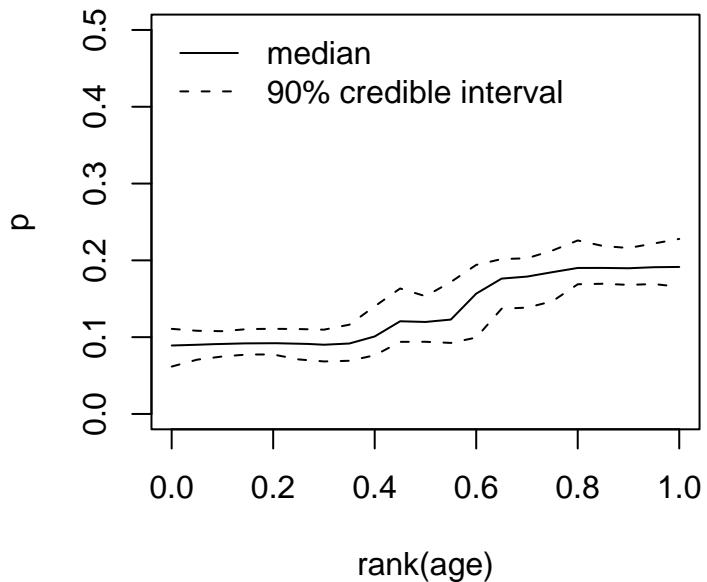
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## 6. Unconstrained model for ranks of age and HDL: Difference to proportional hazards model

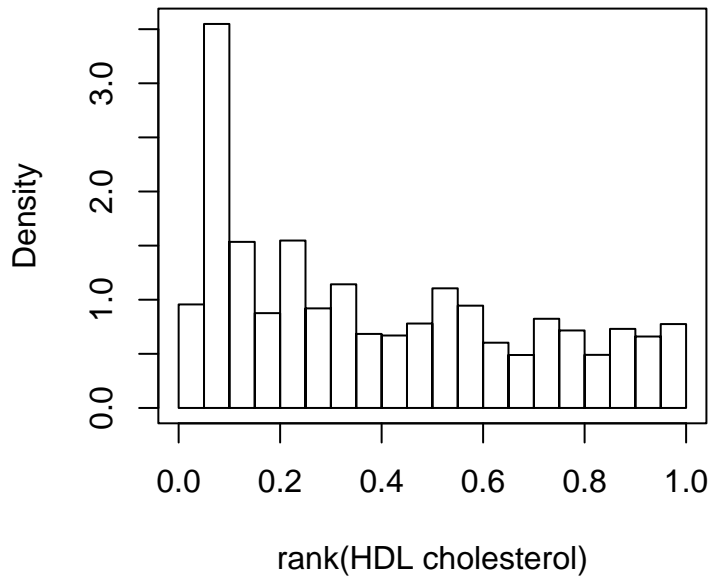
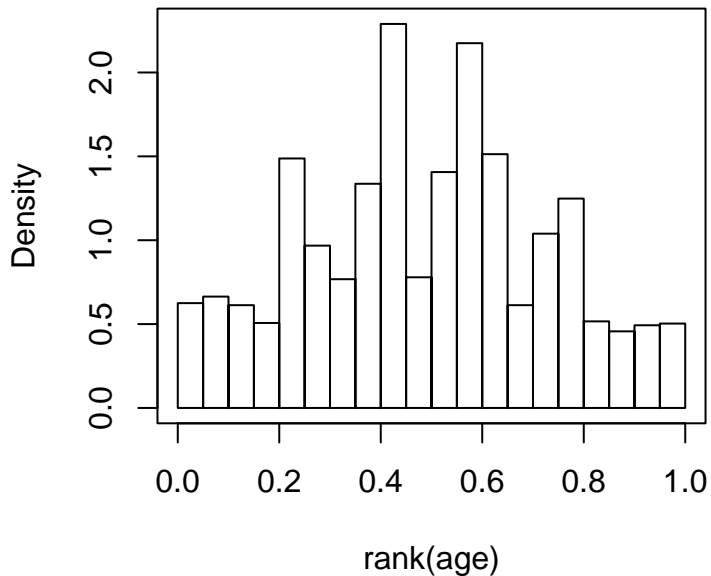


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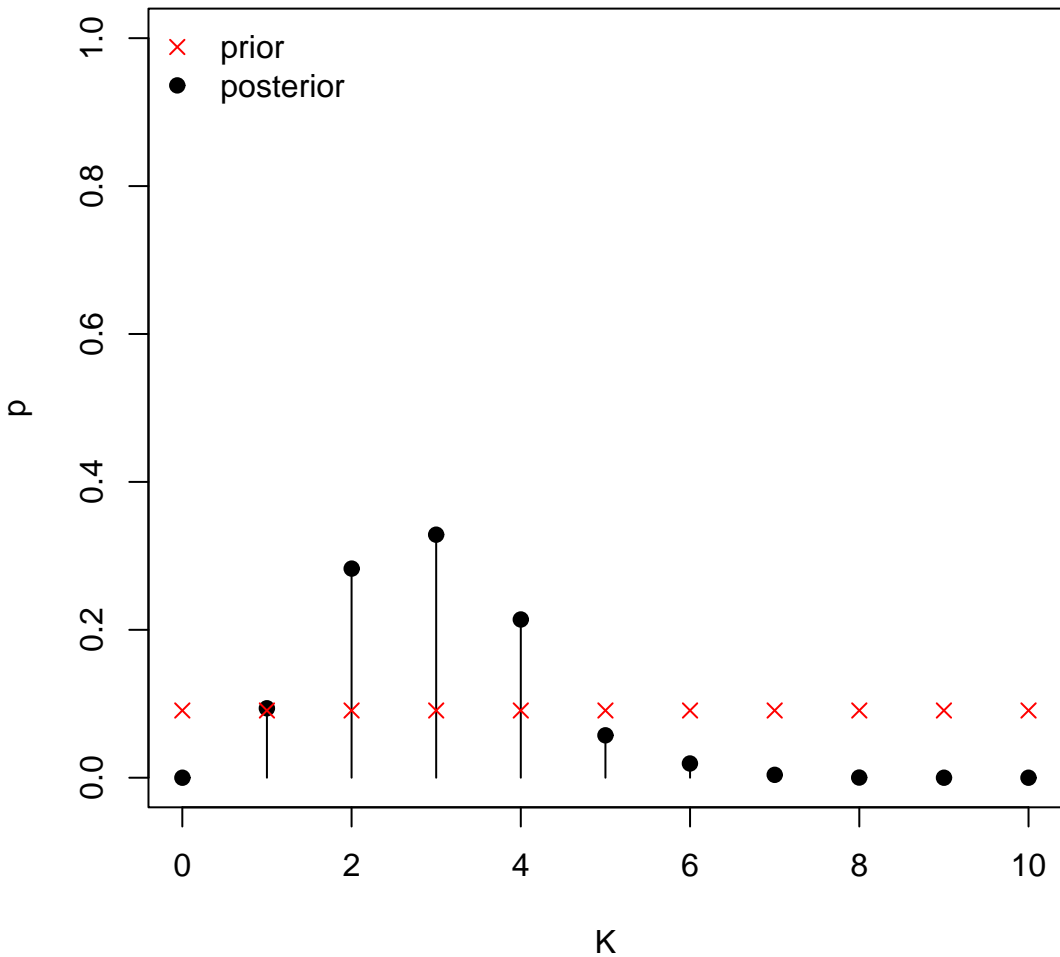




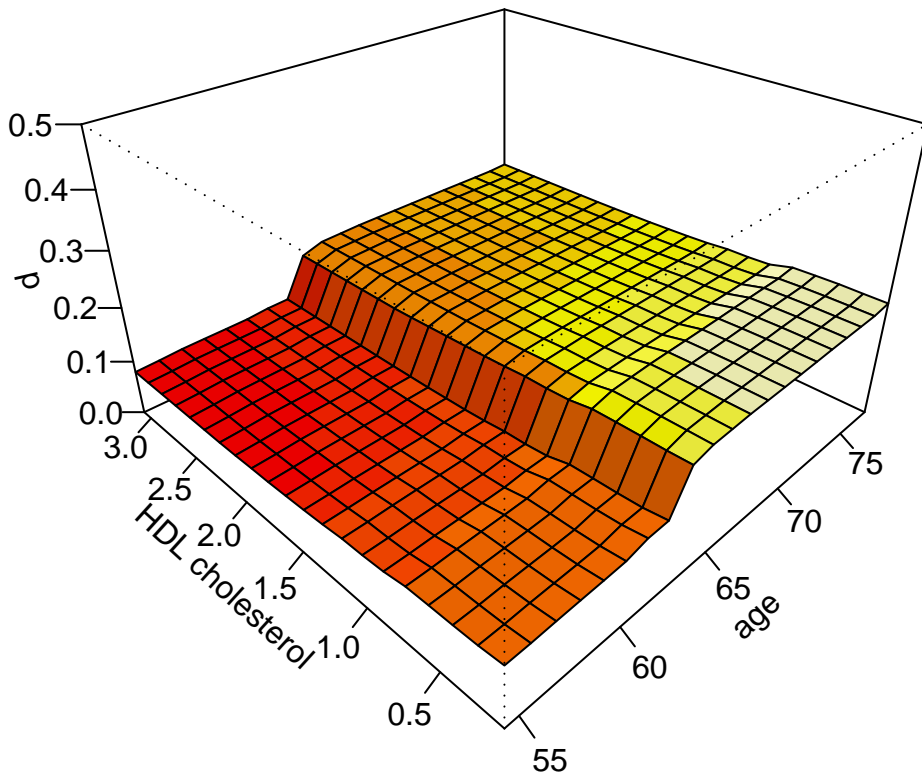
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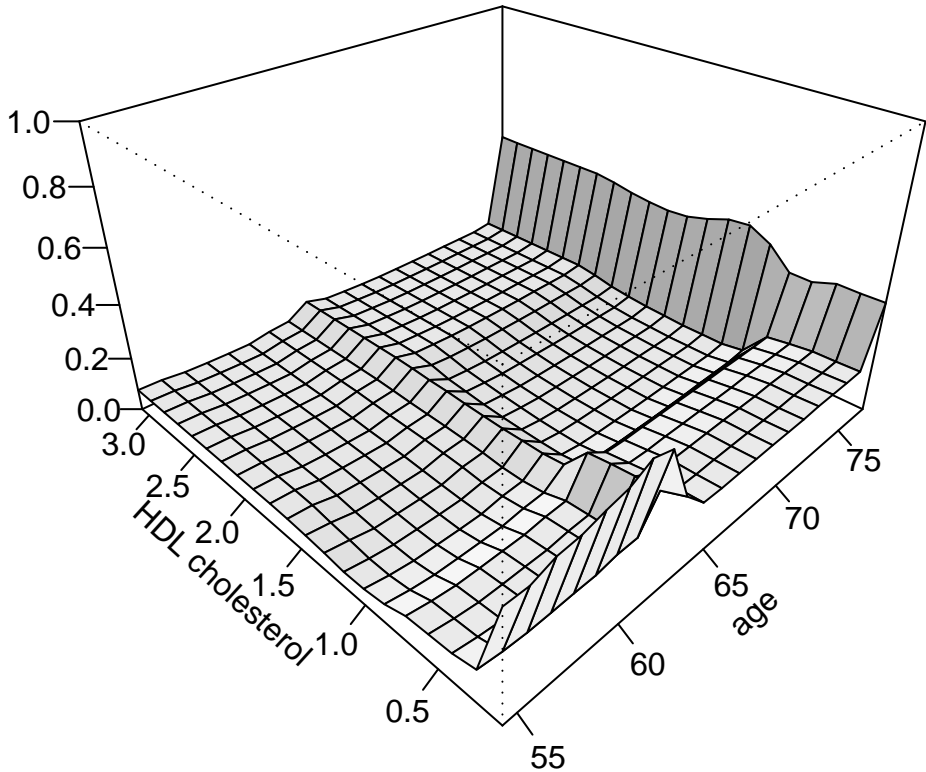
## 7. Constrained model for age and HDL: Total number of change points



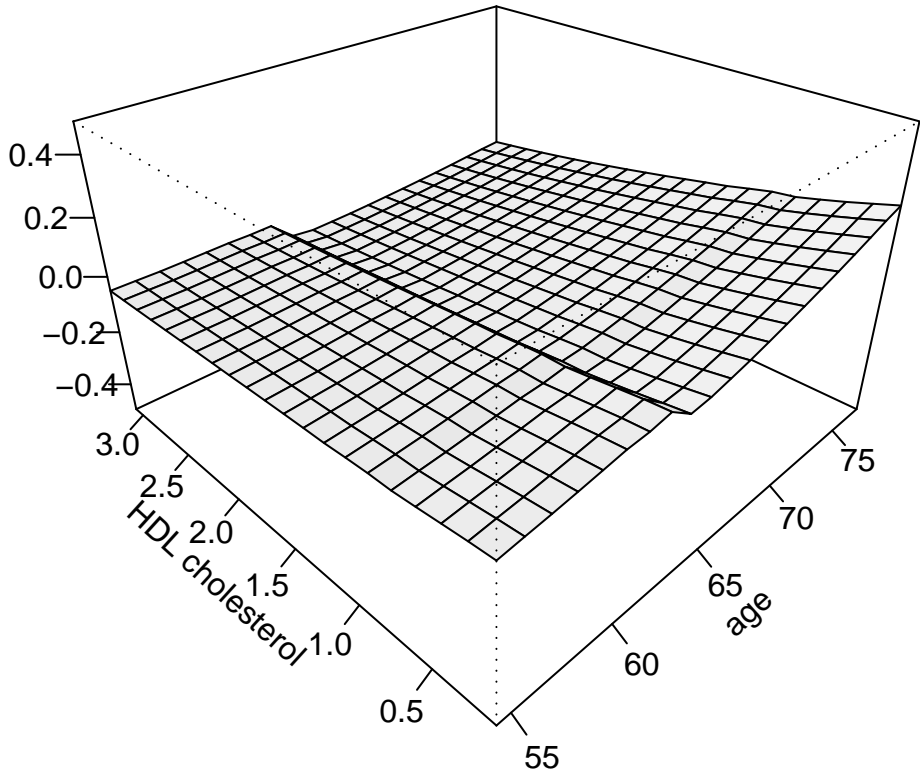
## 7. Constrained model for age and HDL: Posterior median 7 year risk



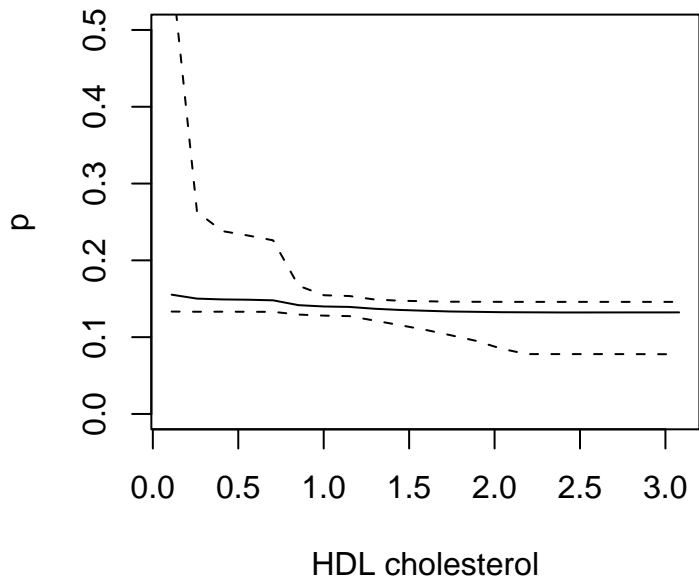
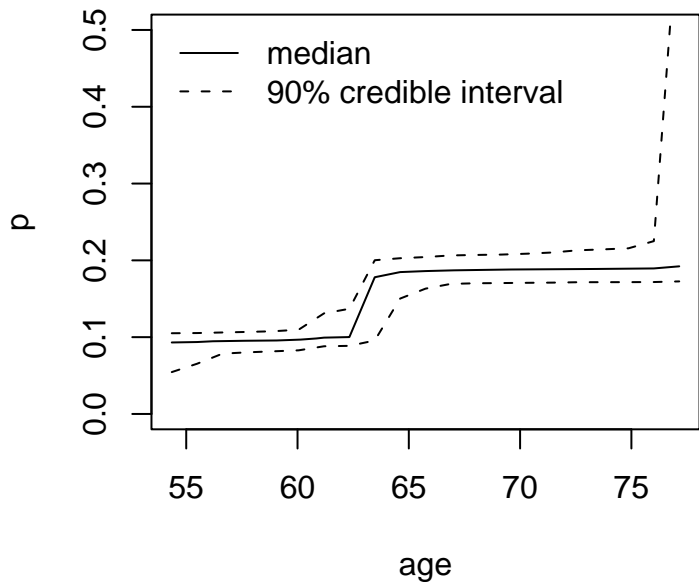
## 7. Constrained model for age and HDL: Length of 90% credible interval



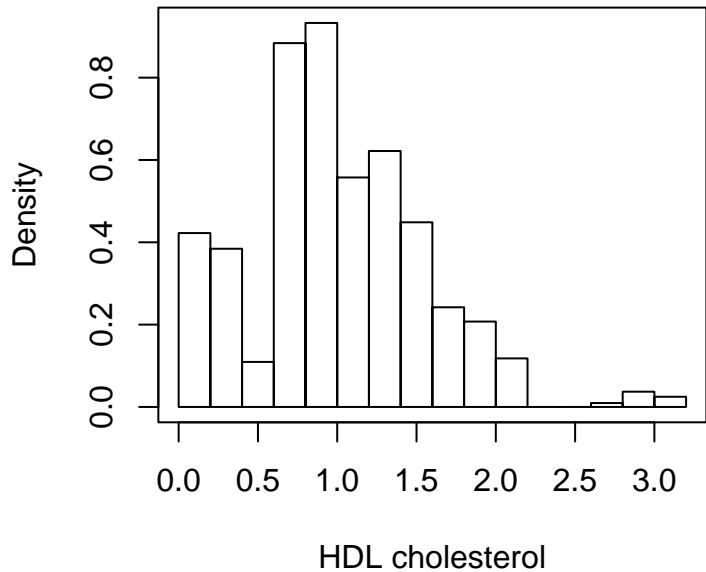
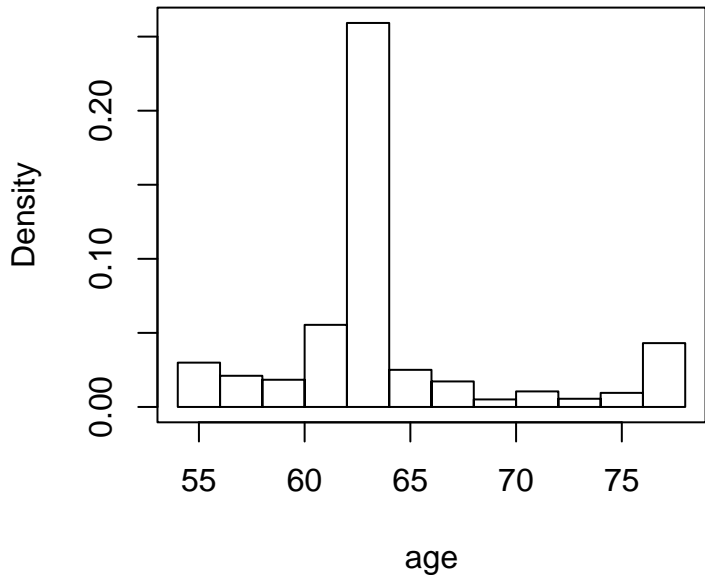
## 7. Constrained model for age and HDL: Difference to proportional hazards model



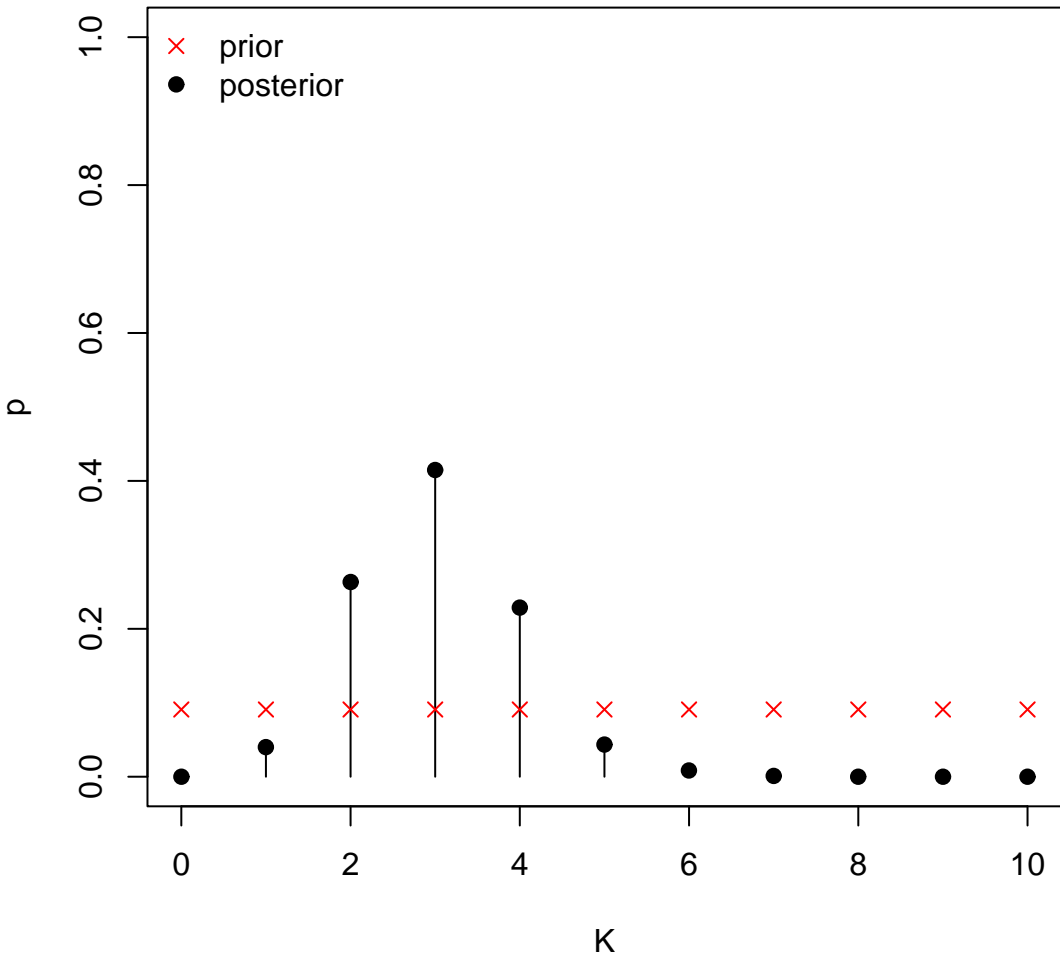
## 7. Constrained model for age and HDL: One-dimensional projections



## 7. Constrained model for age and HDL: Distributions for change point positions

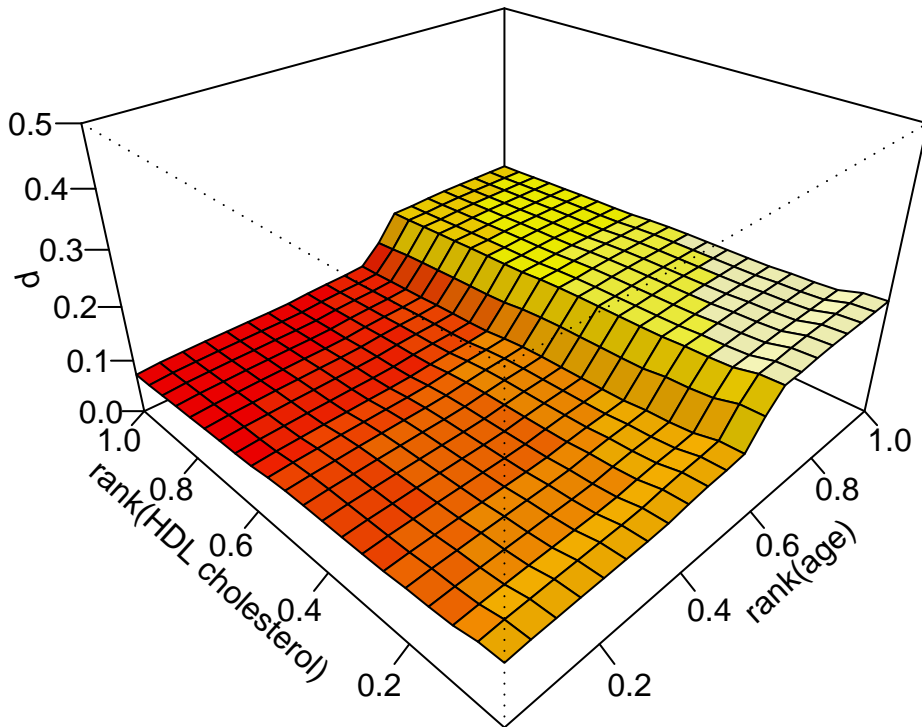


## 8. Constrained model for ranks of age and HDL: Total number of change points

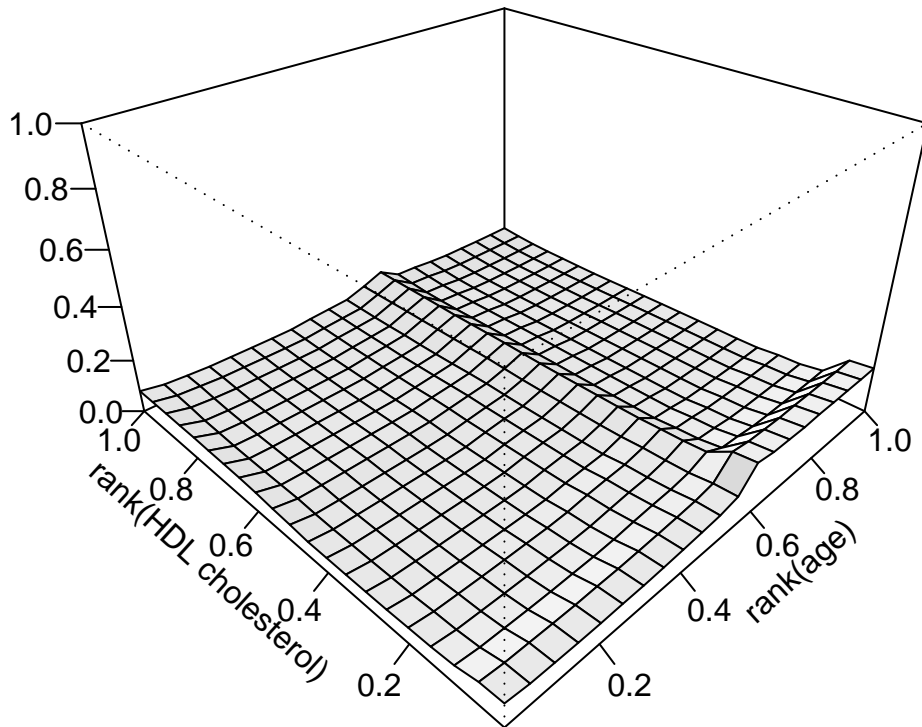




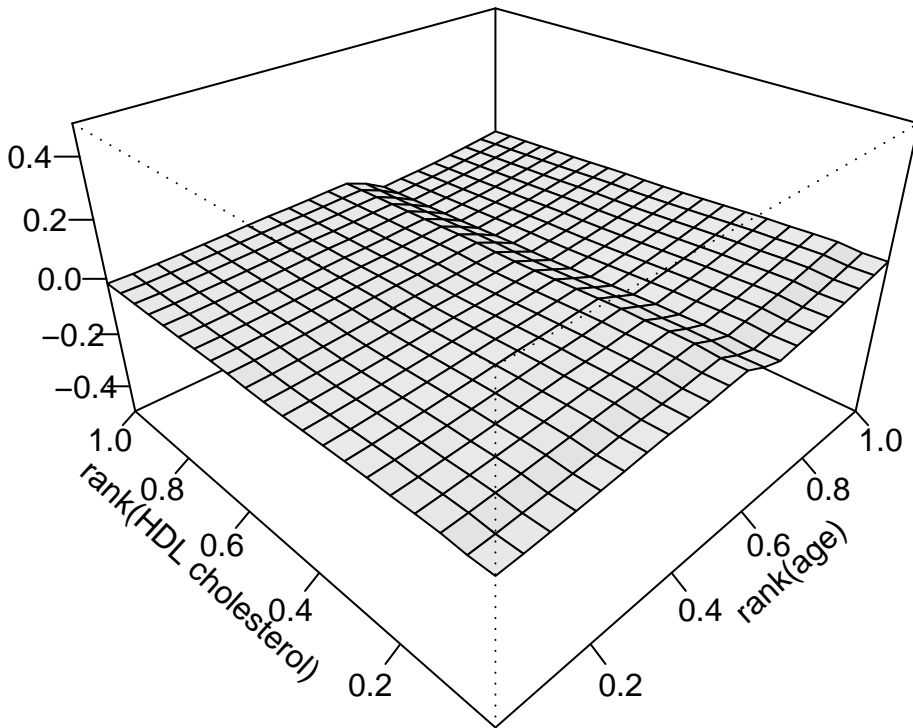
## 8. Constrained model for ranks of age and HDL: Posterior median 7 year risk



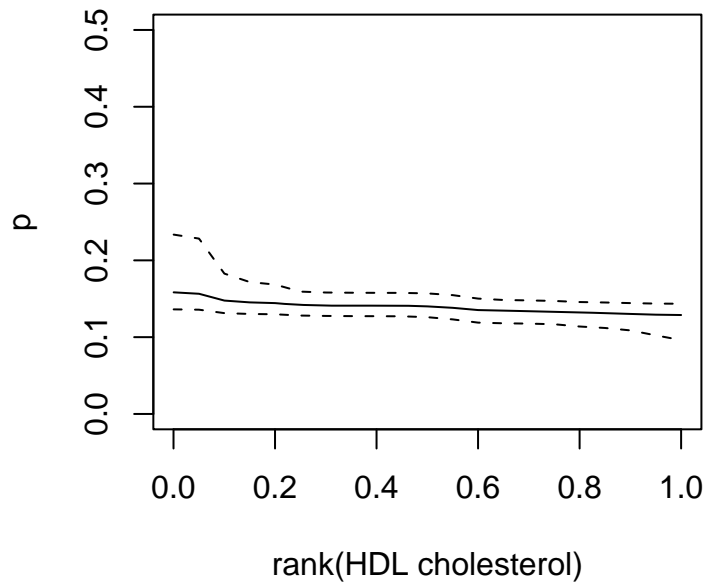
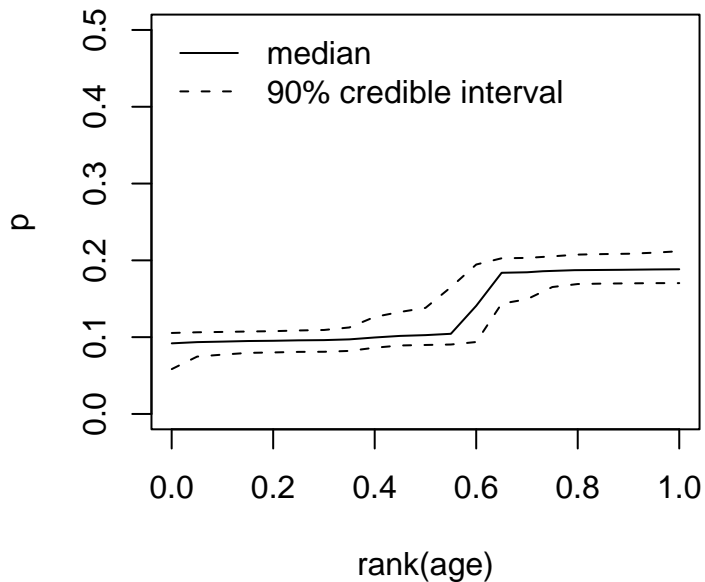
## 8. Constrained model for ranks of age and HDL: Length of 90% credible interval



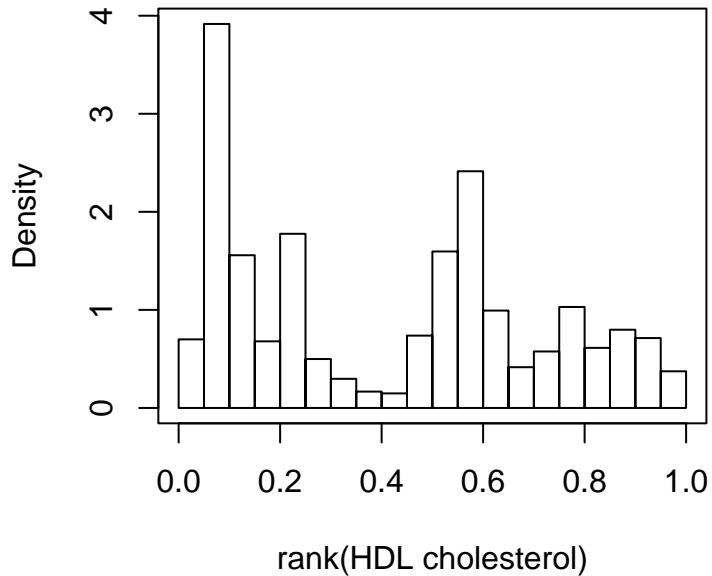
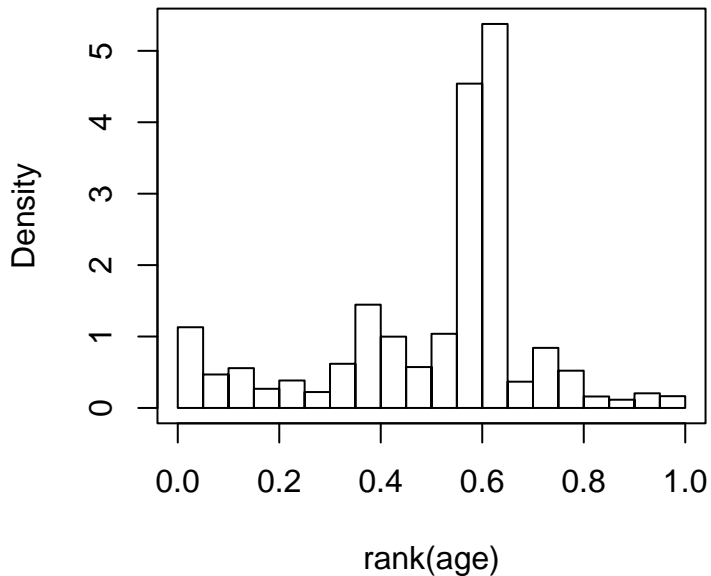
## 8. Constrained model for ranks of age and HDL: Difference to proportional hazards model



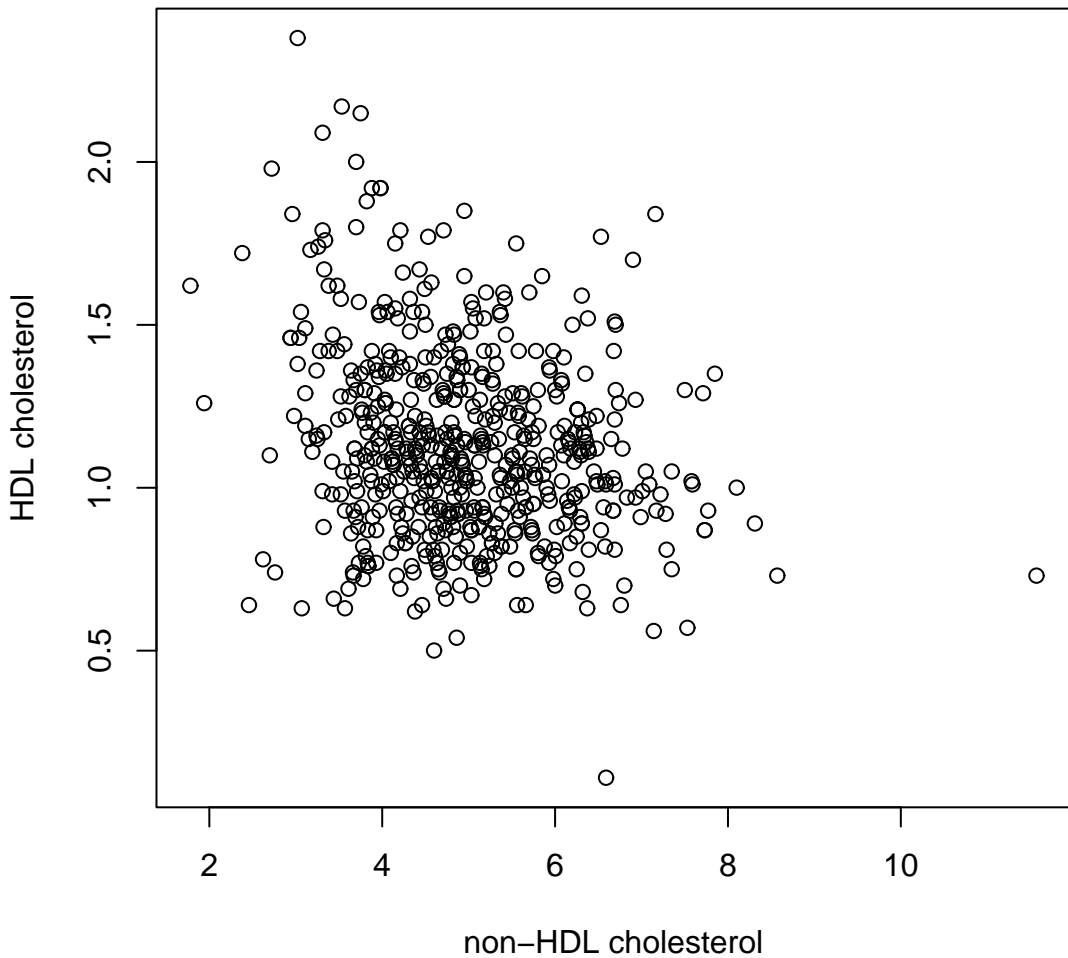
## 8. Constrained model for ranks of age and HDL: One-dimensional projections



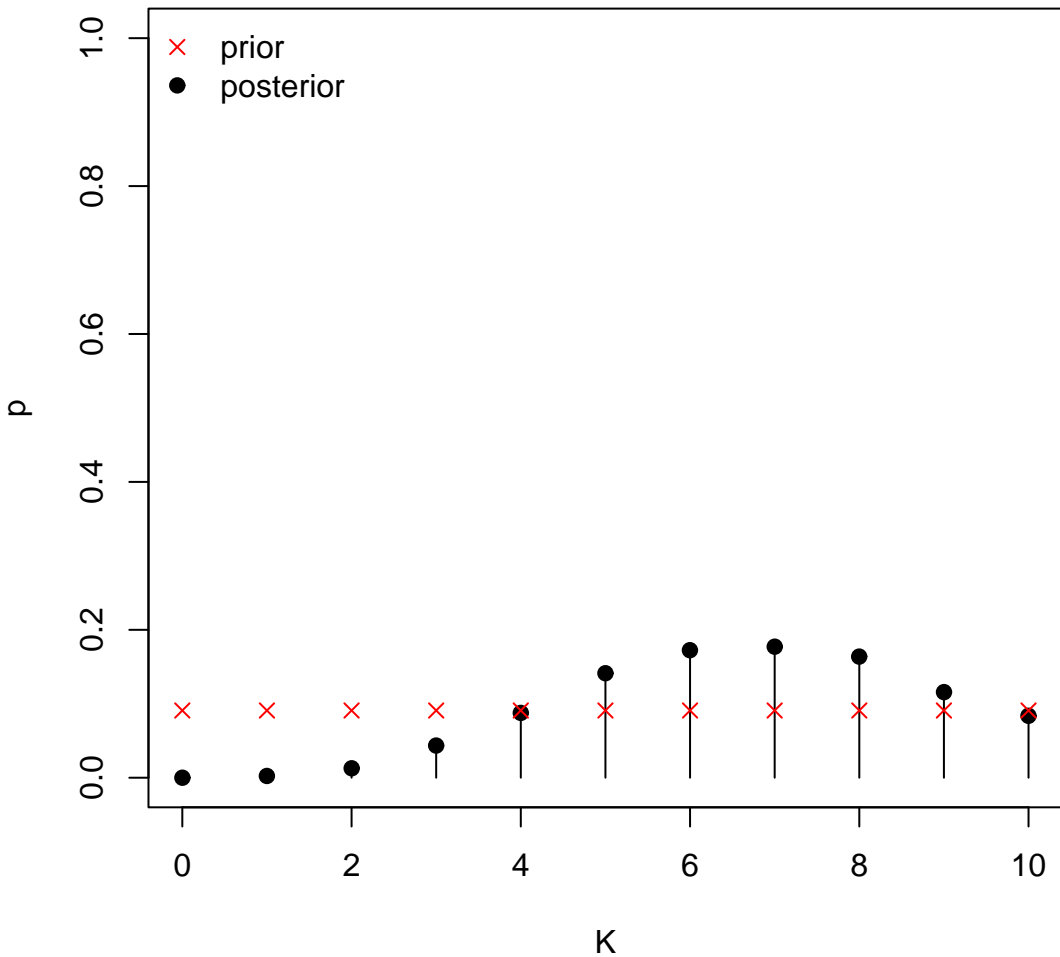
## 8. Constrained model for ranks of age and HDL: Distributions for change point positions



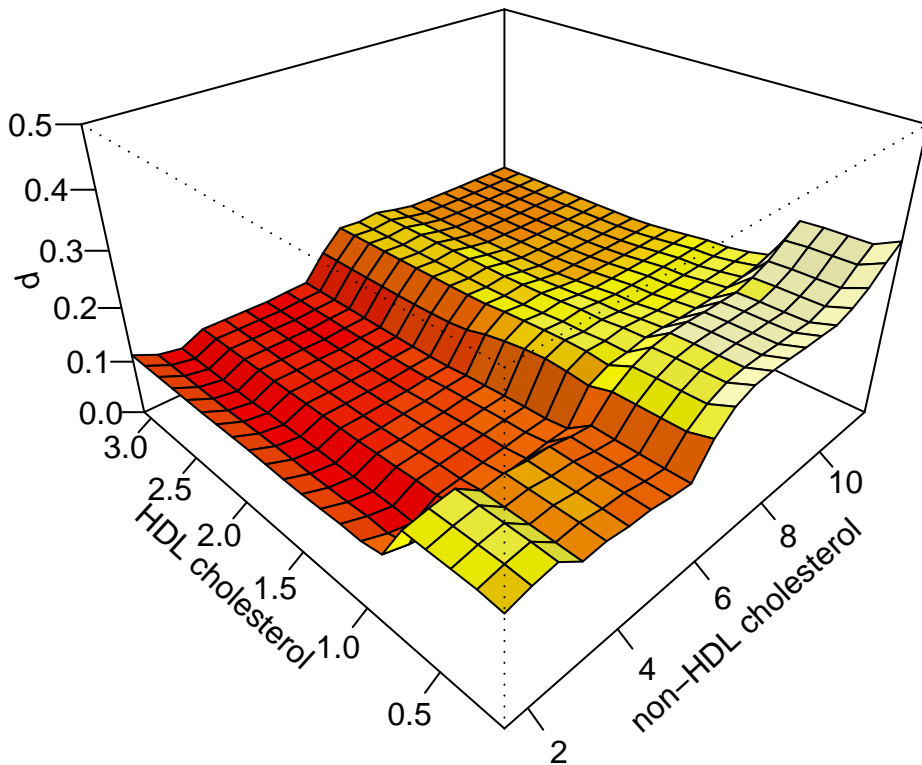
## 9. Unconstrained model for non-HDL and HDL: Distribution of events by covariates



## 9. Unconstrained model for non-HDL and HDL: Total number of change points

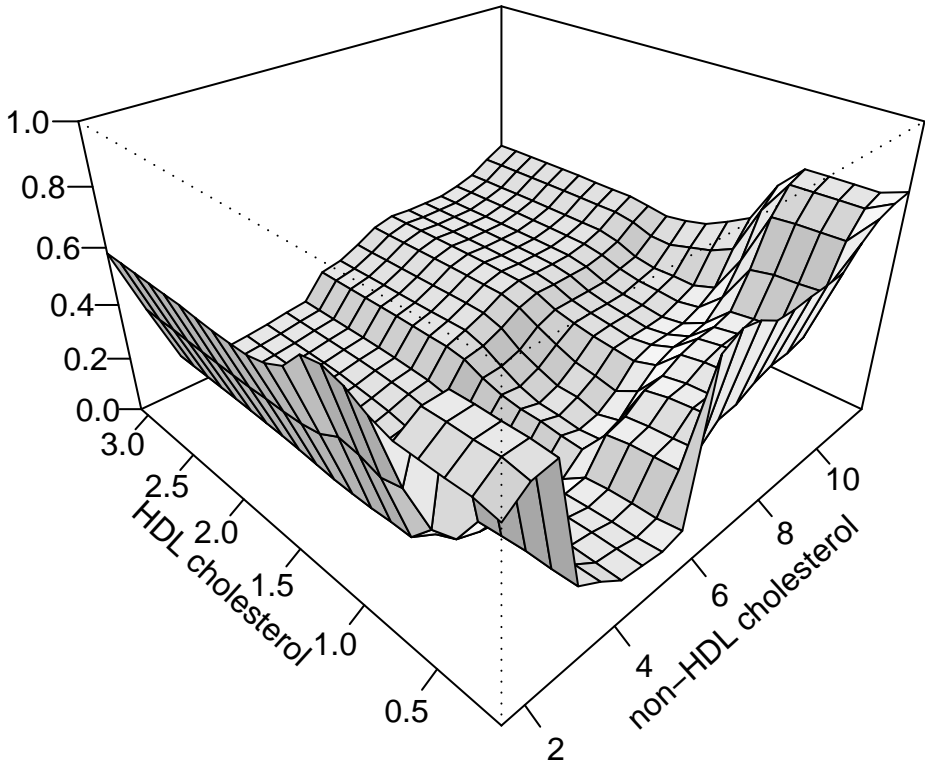


## 9. Unconstrained model for non-HDL and HDL: Posterior median 7 year risk

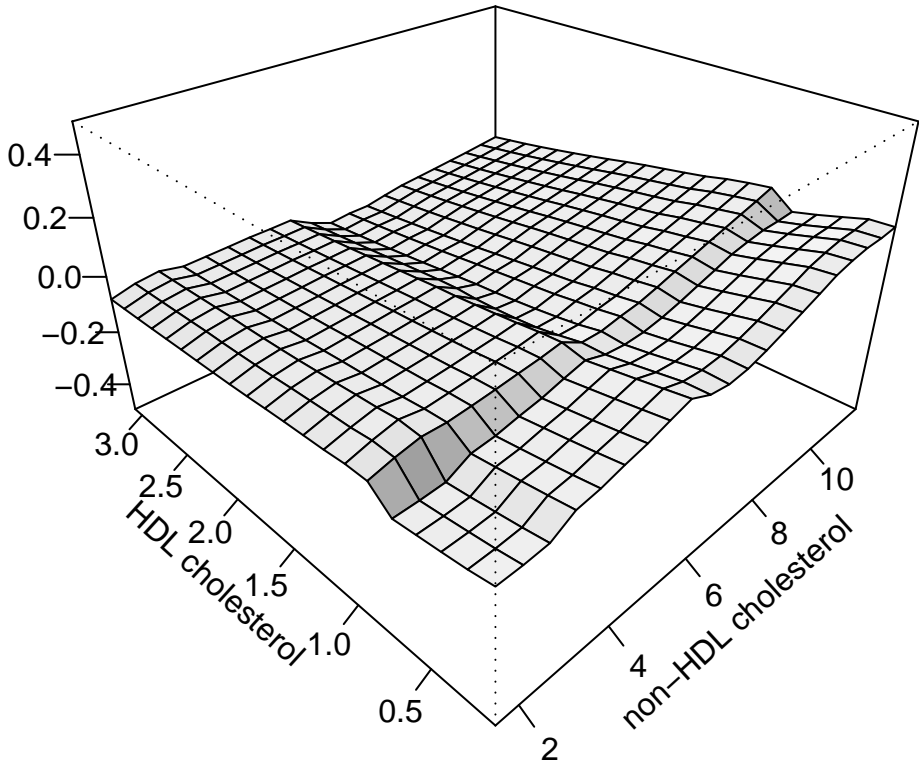




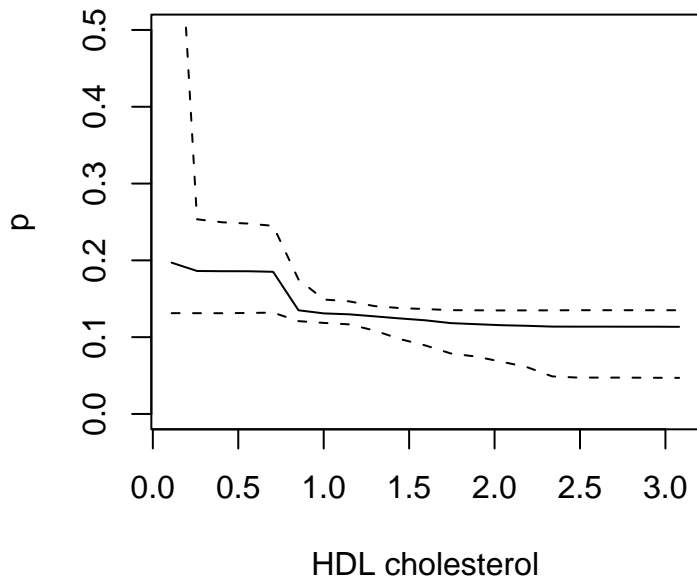
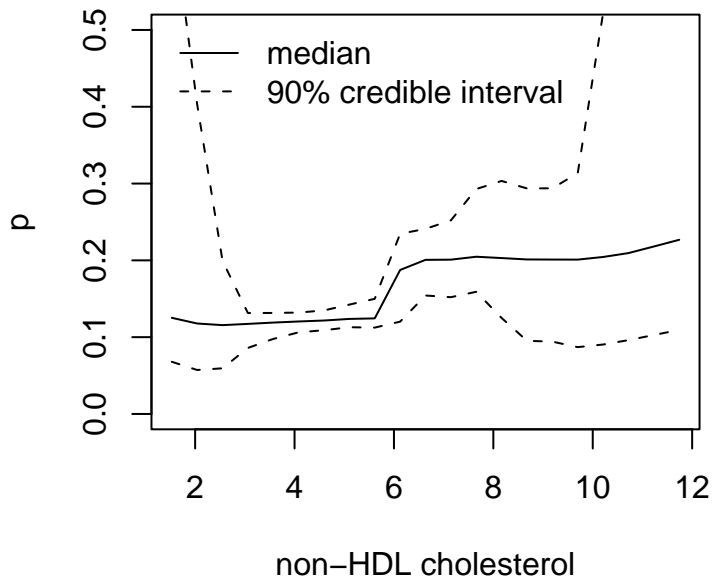
## 9. Unconstrained model for non-HDL and HDL: Length of 90% credible interval



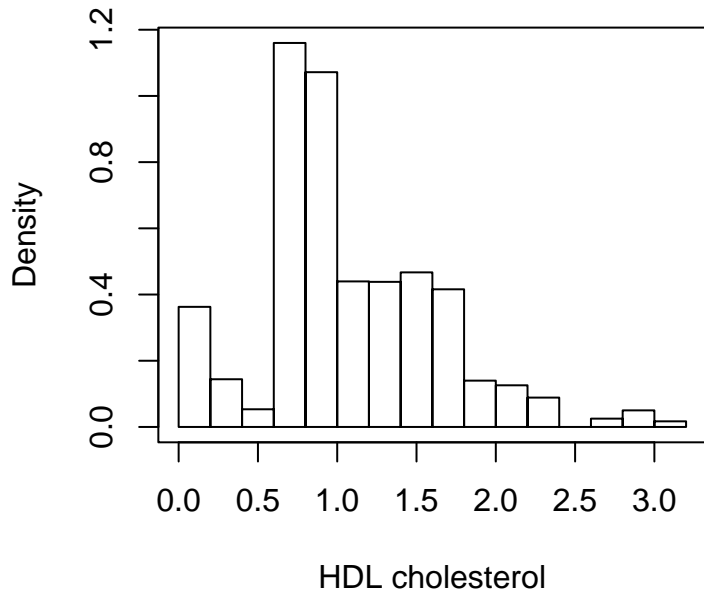
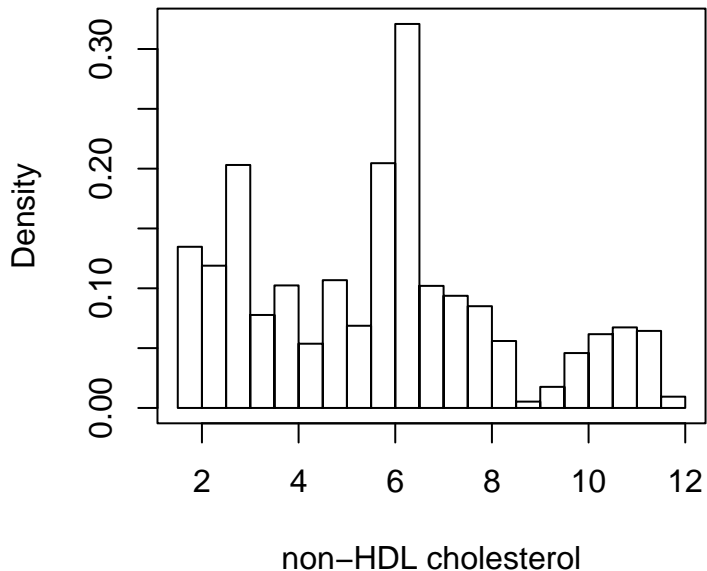
## 9. Unconstrained model for non-HDL and HDL: Difference to proportional hazards model



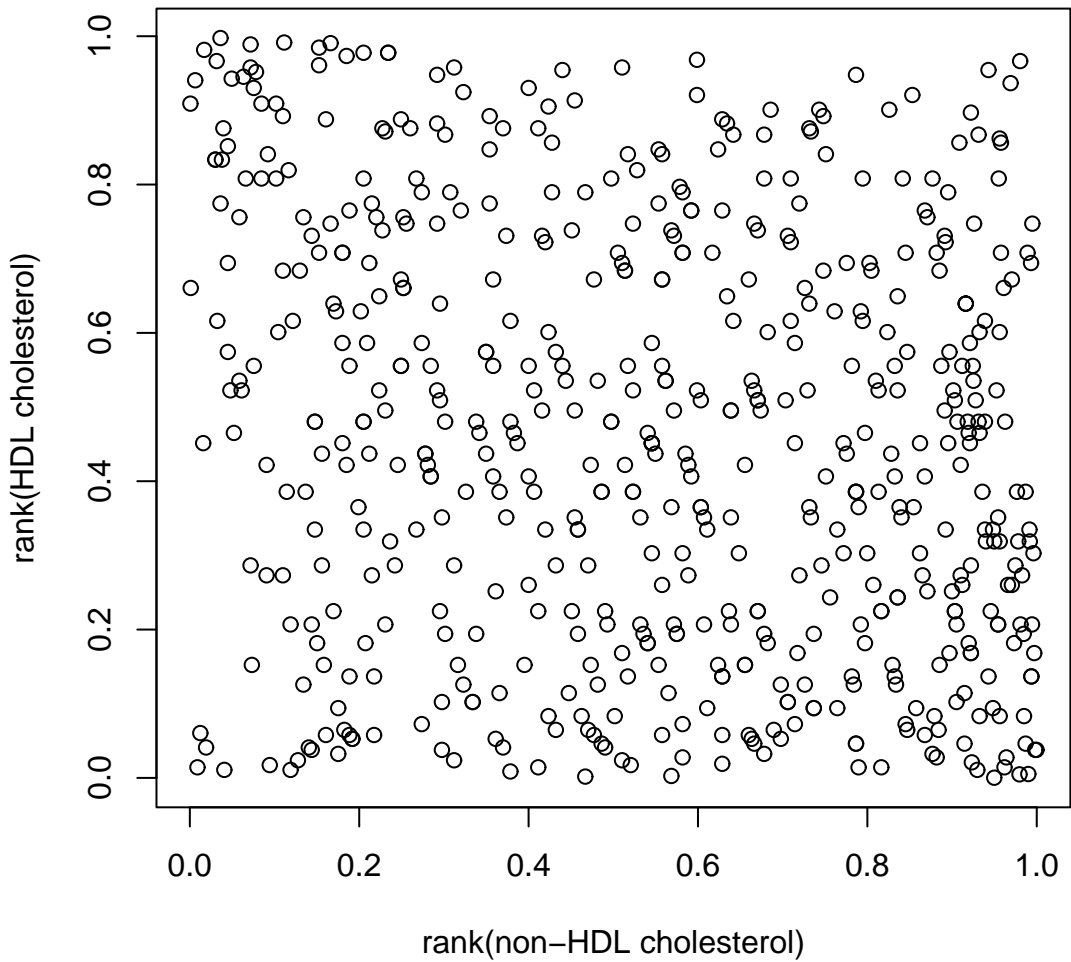
## 9. Unconstrained model for non-HDL and HDL: One-dimensional projections



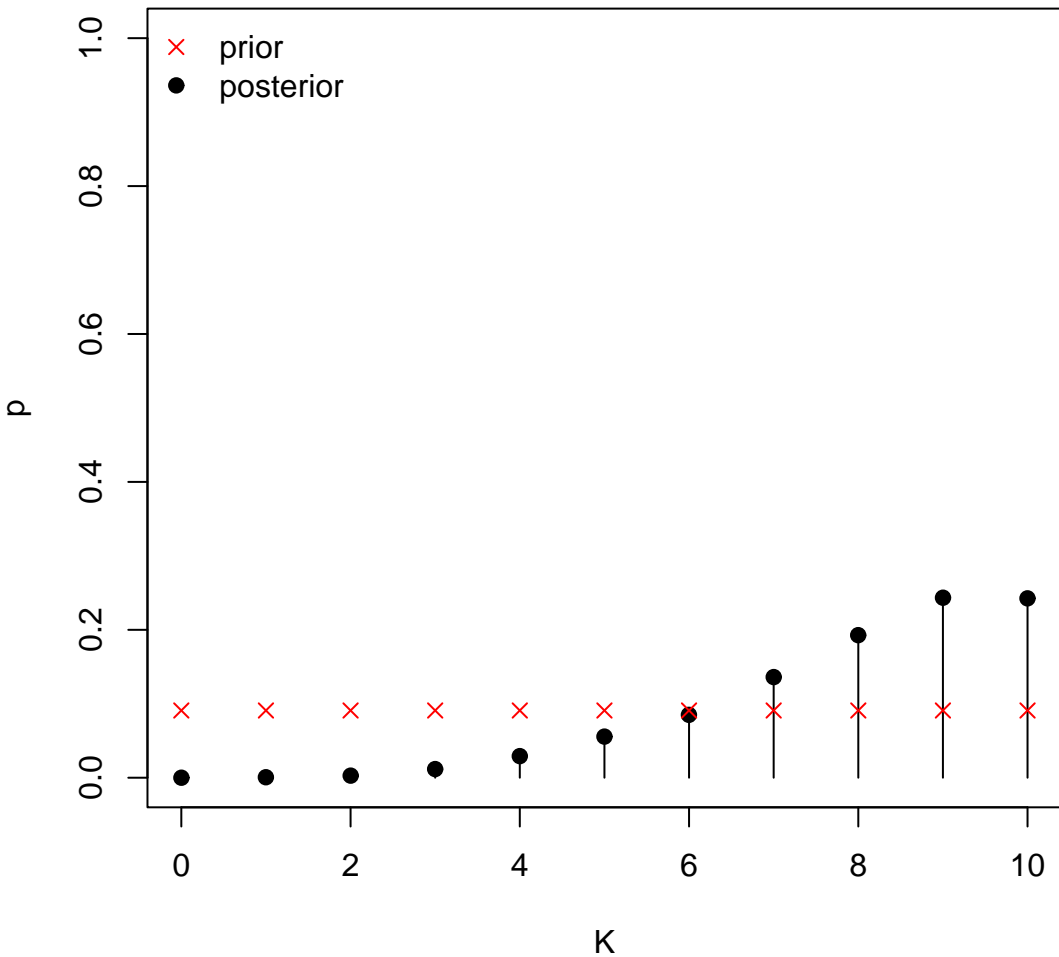
## 9. Unconstrained model for non-HDL and HDL: Distributions for change point positions



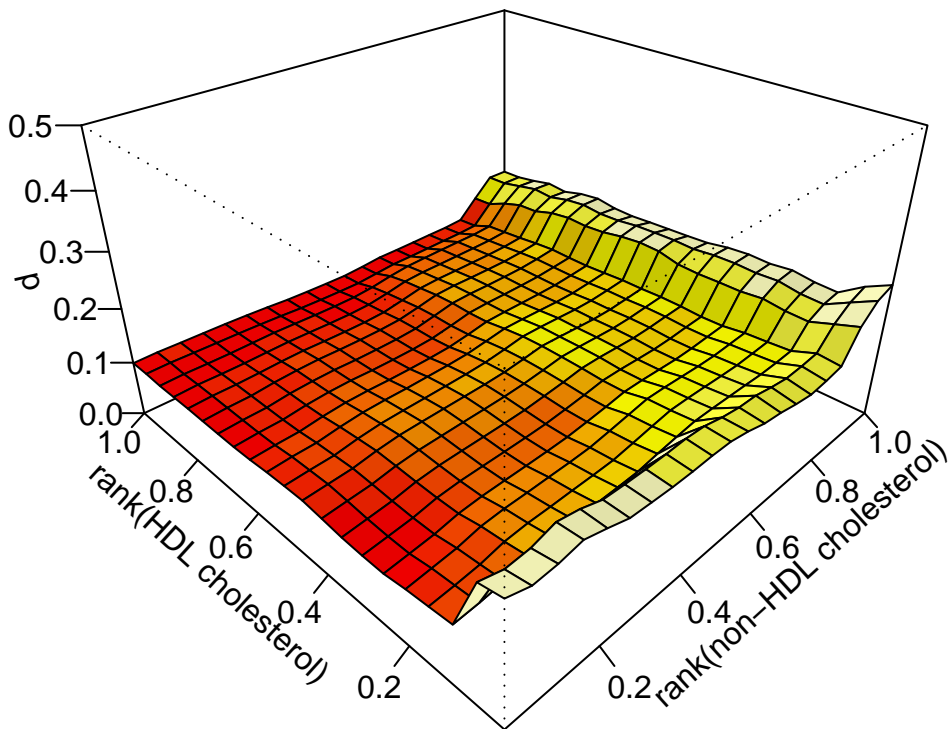
# 10. Unconstrained model for ranks of non-HDL and HDL: Distribution of events by covariates



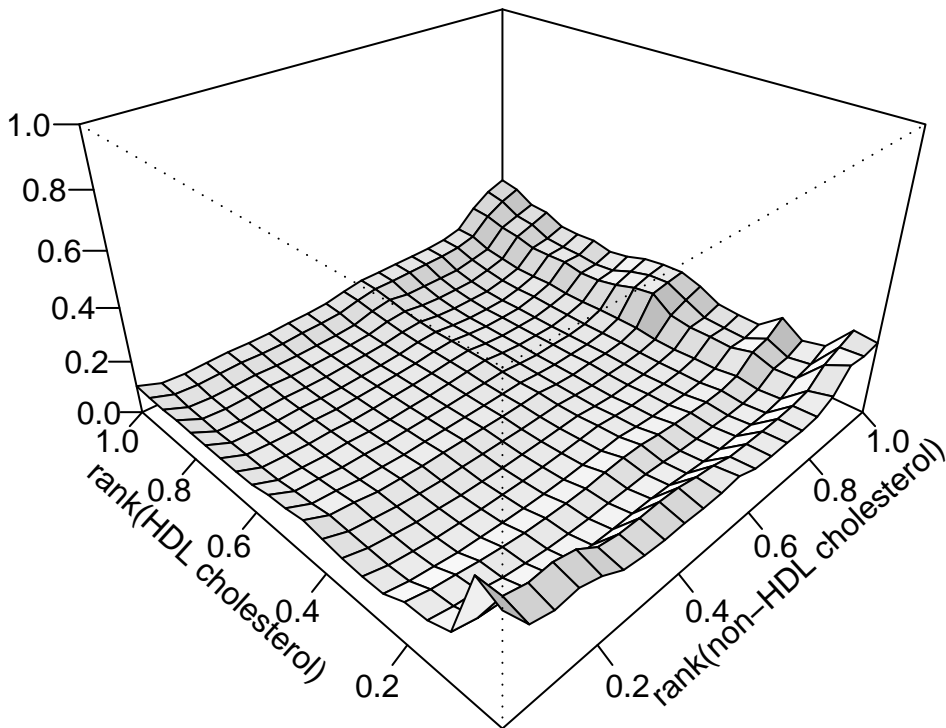
# 10. Unconstrained model for ranks of non-HDL and HDL: Total number of change points



# 10. Unconstrained model for ranks of non-HDL and HDL: Posterior median 7 year risk

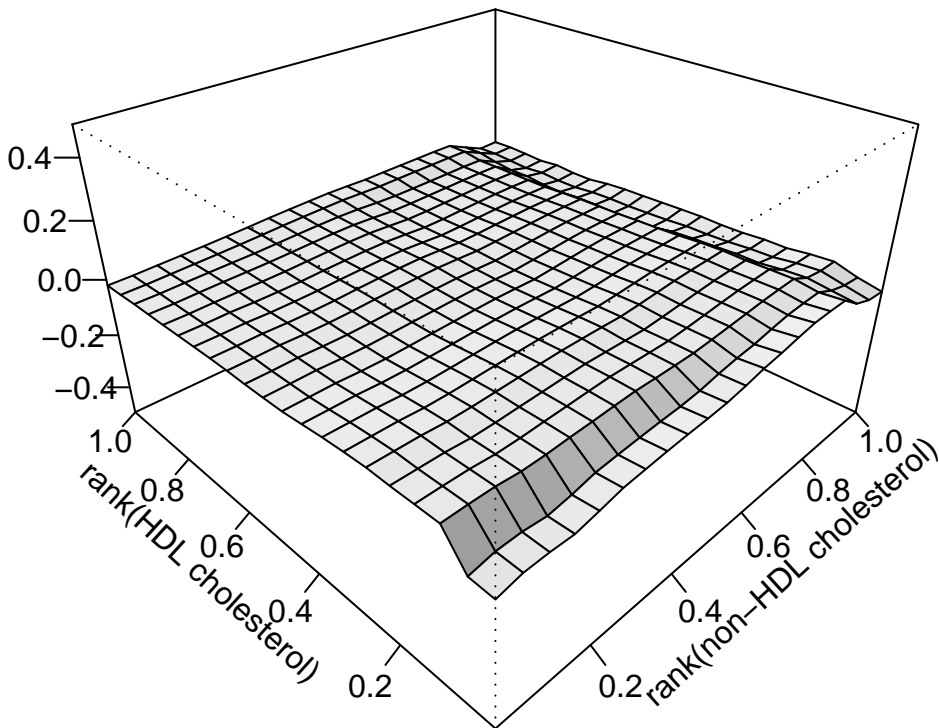


## 10. Unconstrained model for ranks of non-HDL and HDL: Length of 90% credible interval

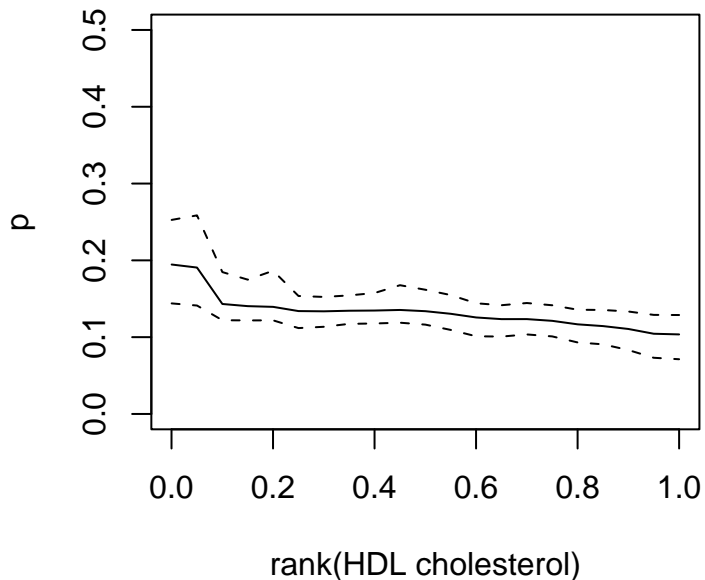
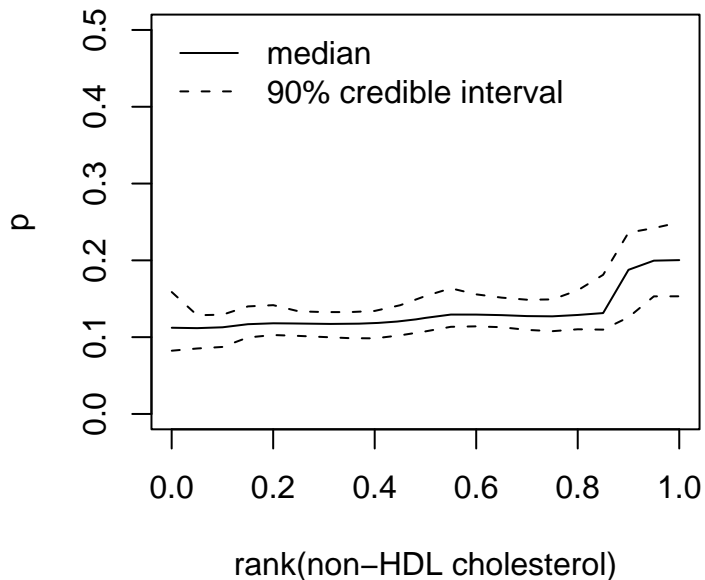




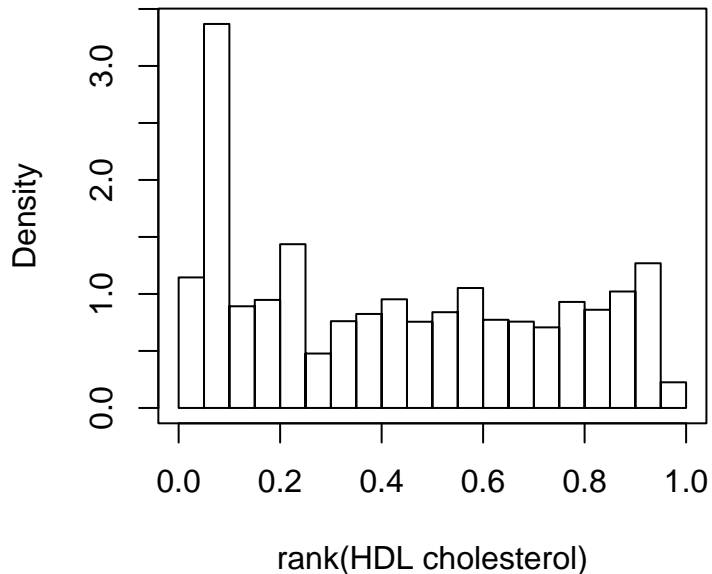
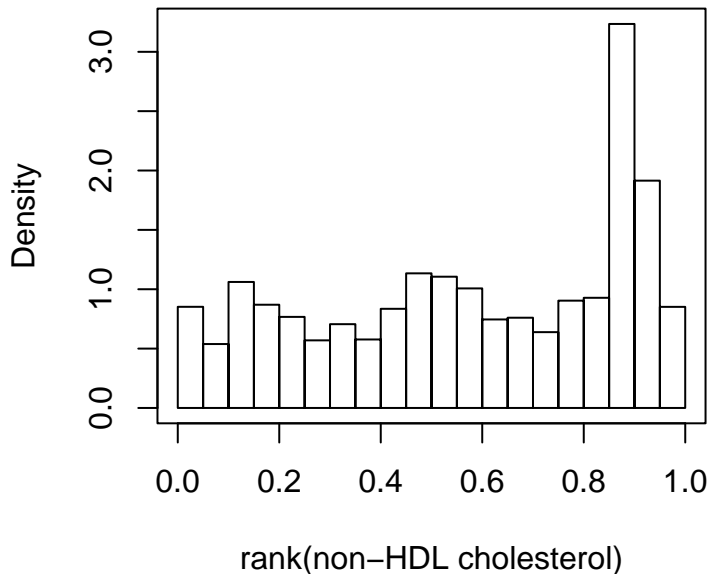
## 10. Unconstrained model for ranks of non-HDL and HDL: Difference to proportional hazards model



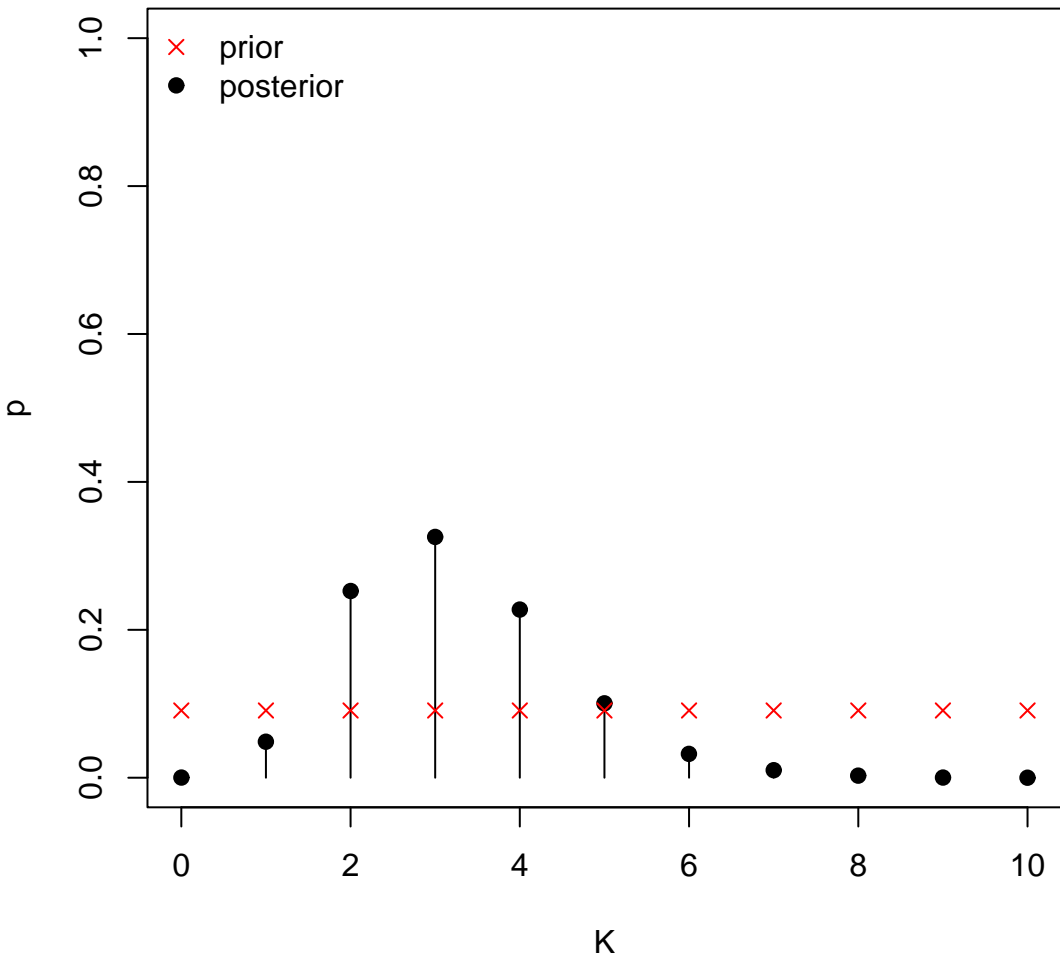
## 10. Unconstrained model for ranks of non-HDL and HDL: One-dimensional projections



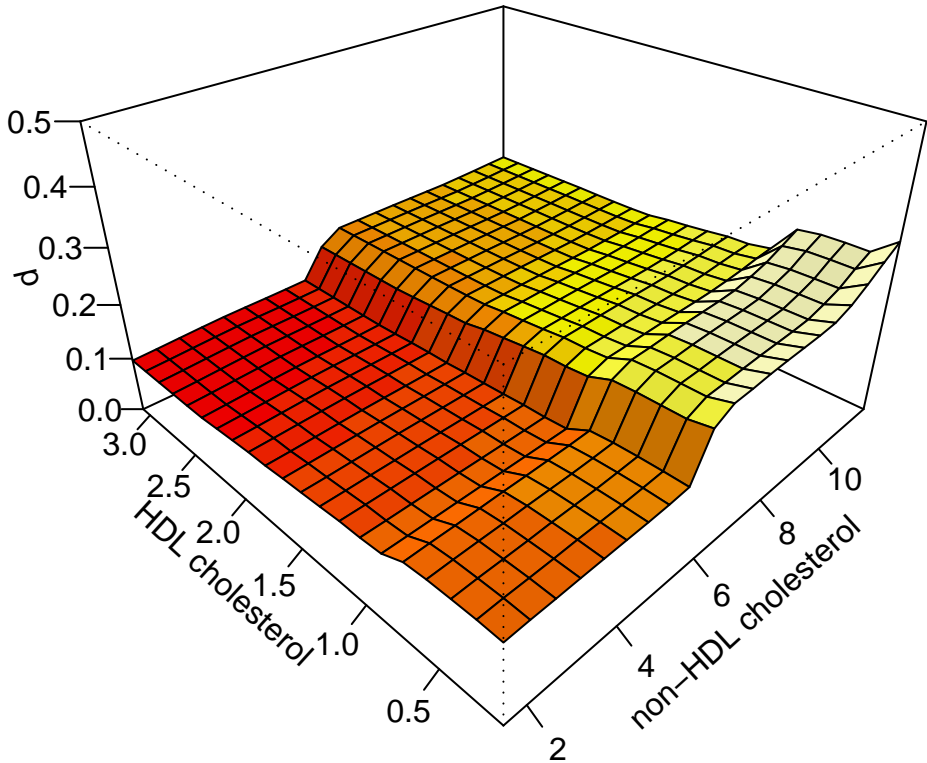
## 10. Unconstrained model for ranks of non-HDL and HDL: Distributions for change point positions



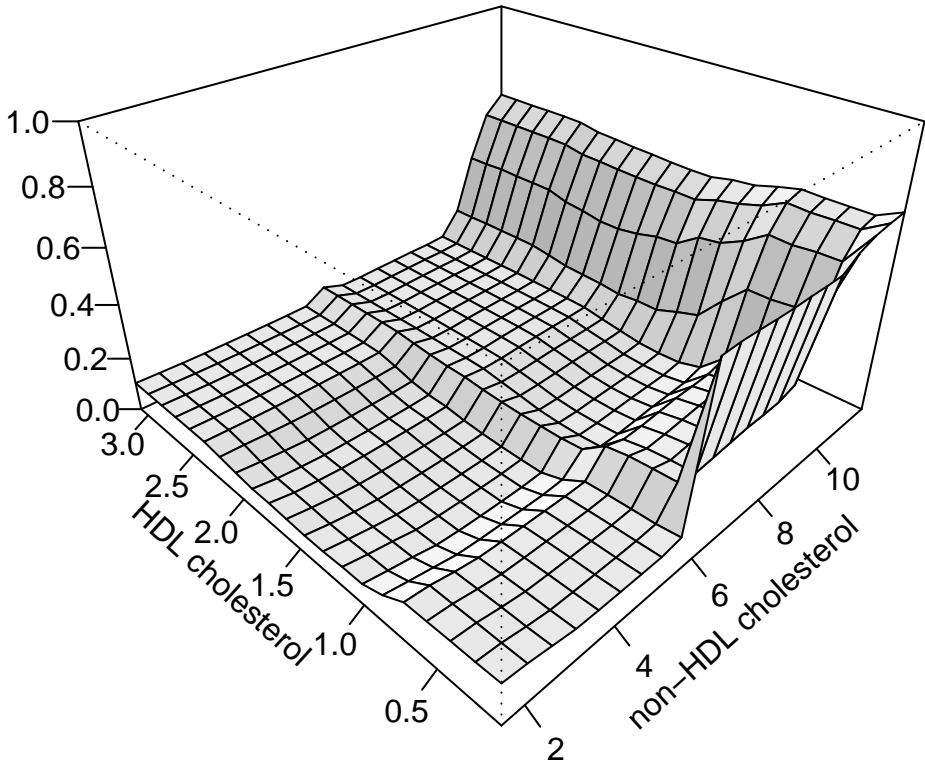
# 11. Constrained model for non-HDL and HDL: Total number of change points



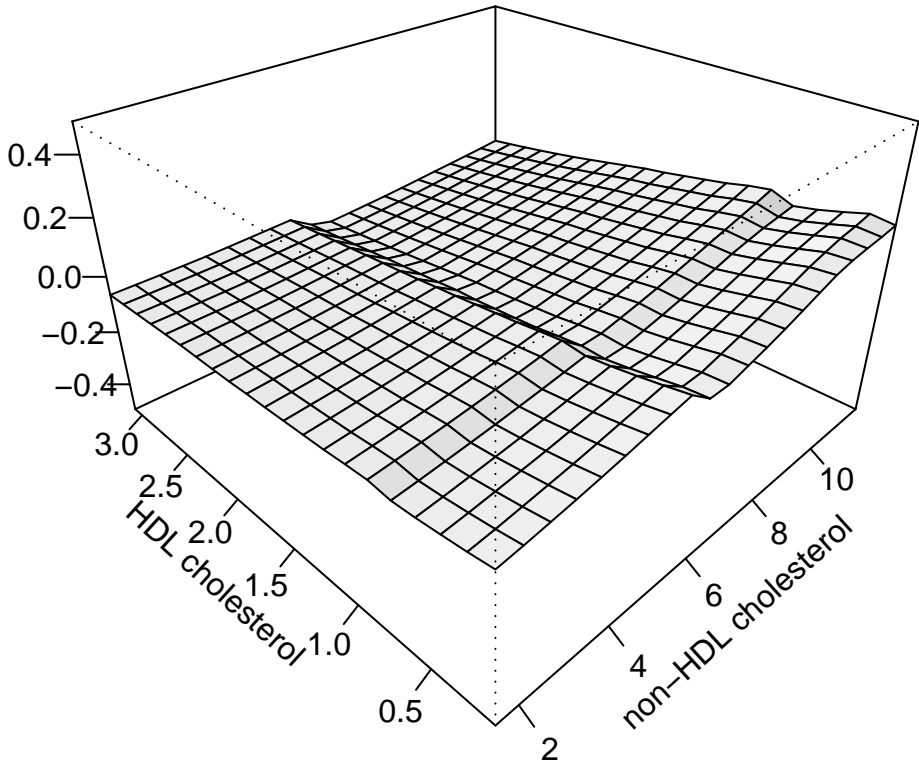
## 11. Constrained model for non-HDL and HDL: Posterior median 7 year risk



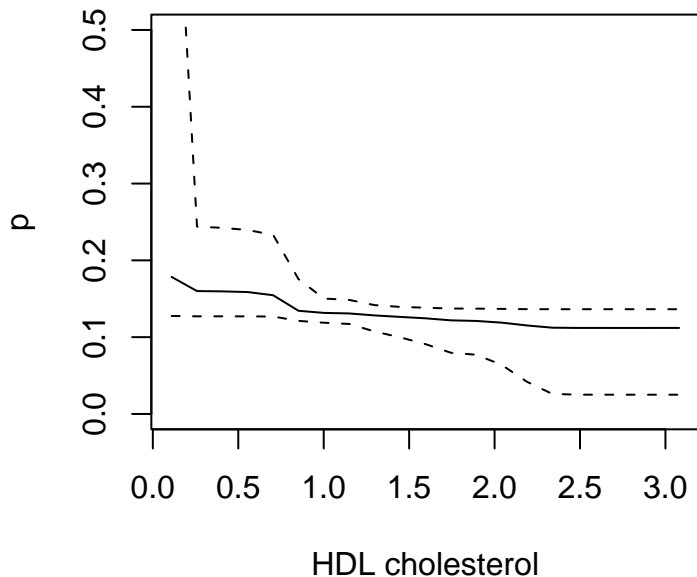
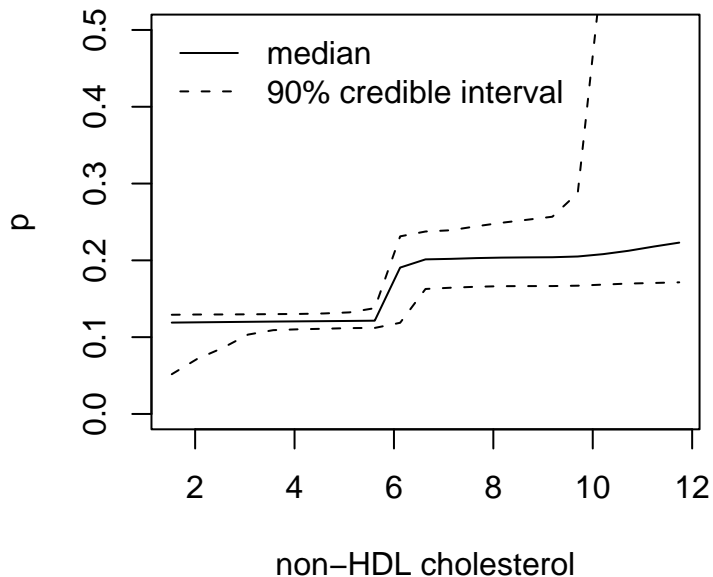
# 11. Constrained model for non-HDL and HDL: Length of 90% credible interval



## 11. Constrained model for non-HDL and HDL: Difference to proportional hazards model

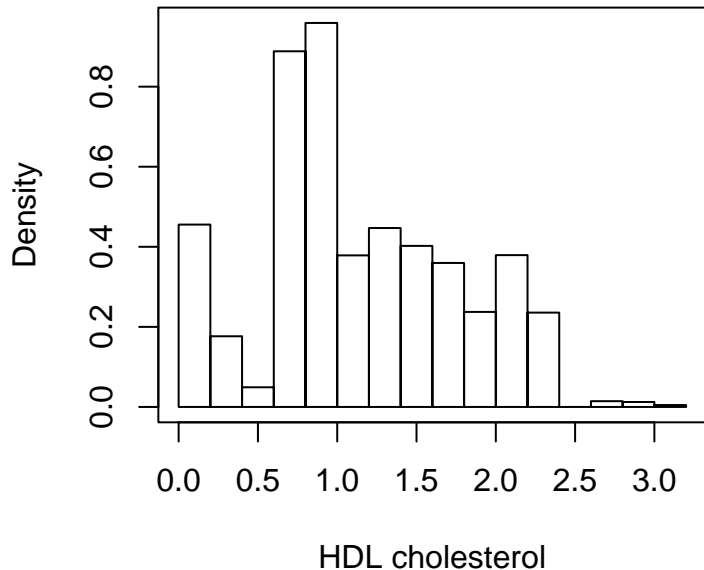
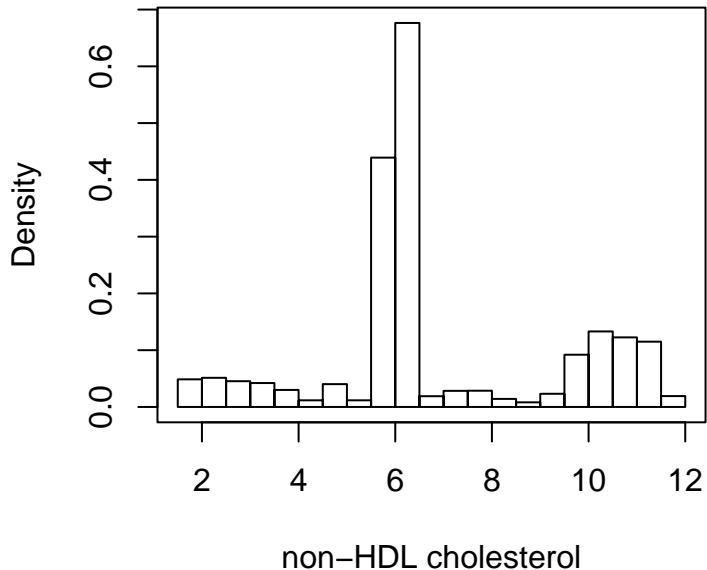


## 11. Constrained model for non-HDL and HDL: One-dimensional projections

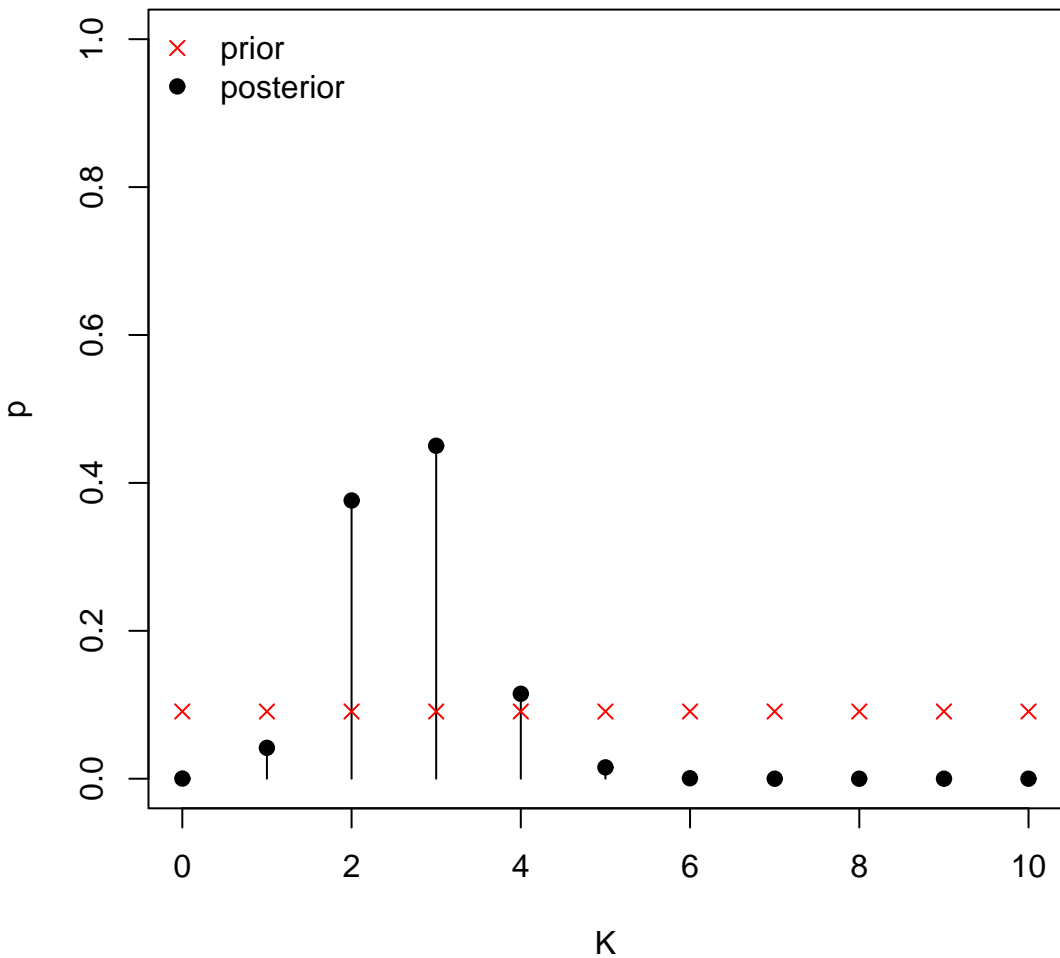




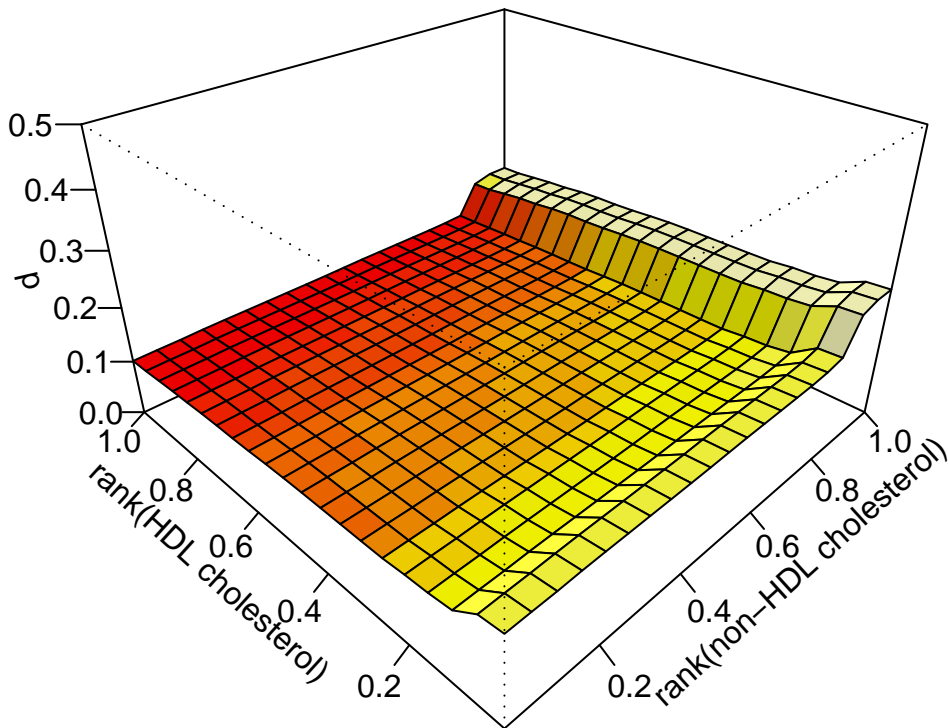
## 11. Constrained model for non-HDL and HDL: Distributions for change point positions



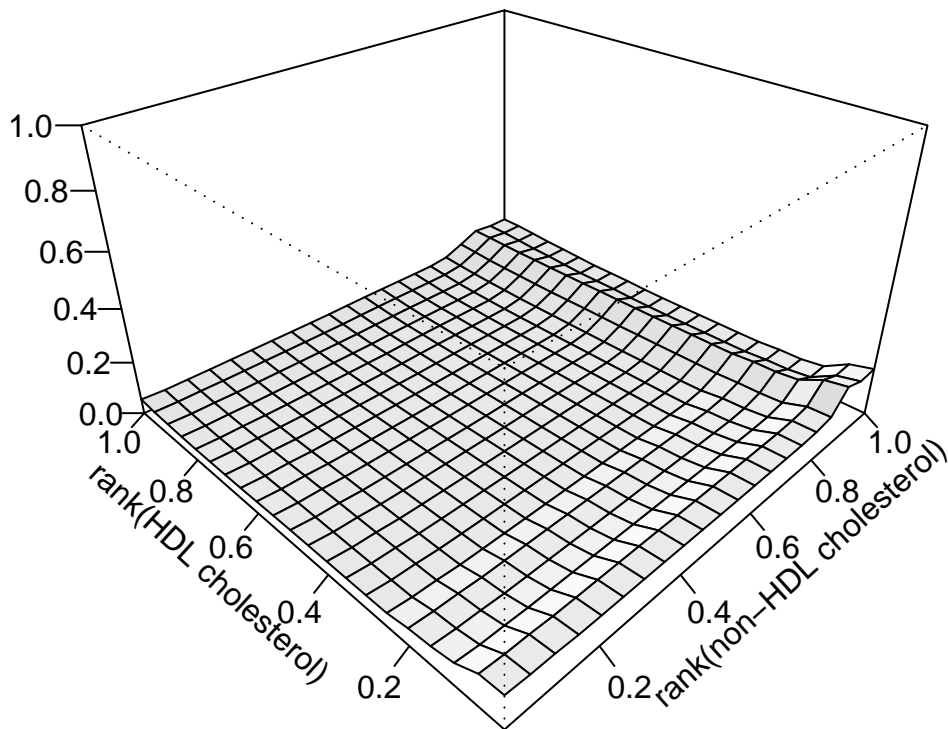
## 12. Constrained model for ranks of non-HDL and HDL: Total number of change points



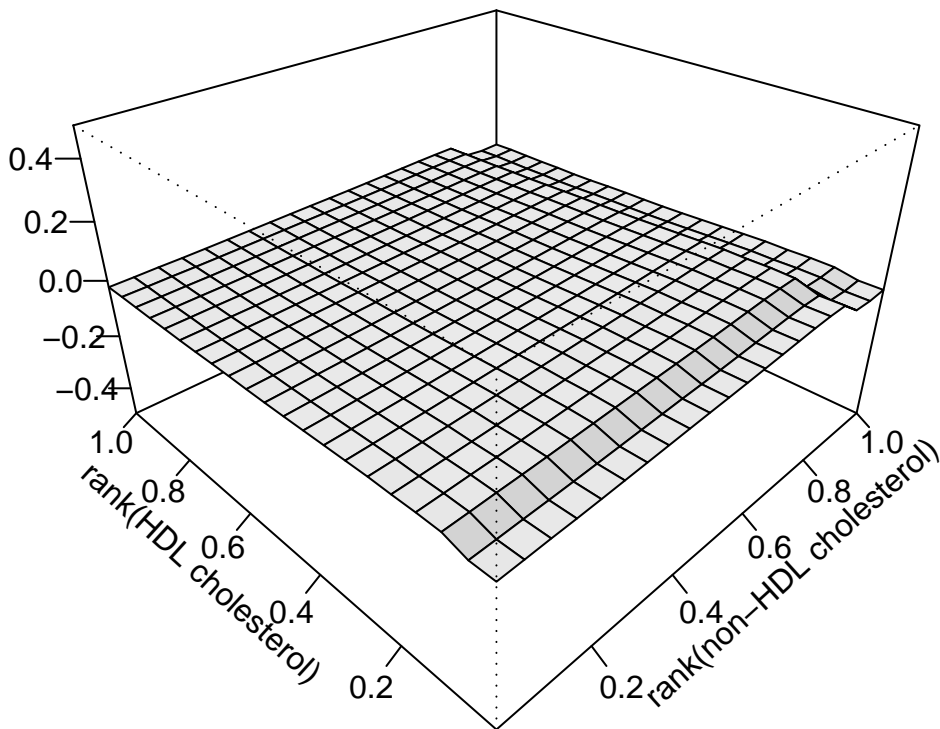
## 12. Constrained model for ranks of non-HDL and HDL: Posterior median 7 year risk



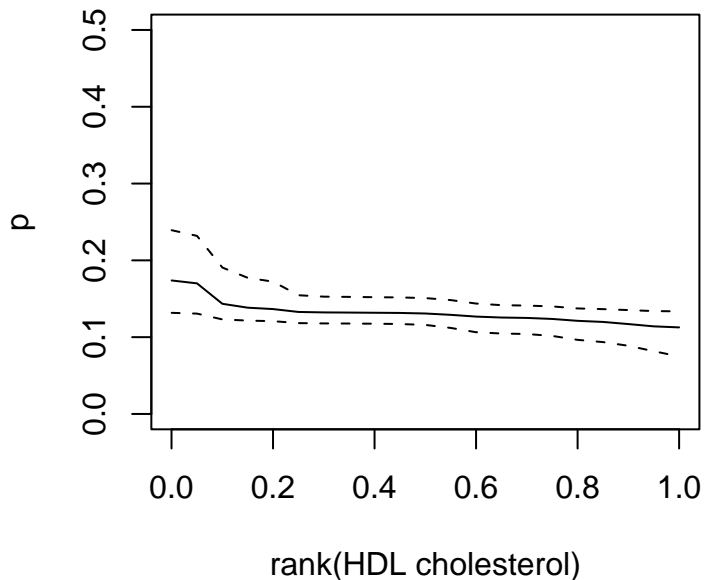
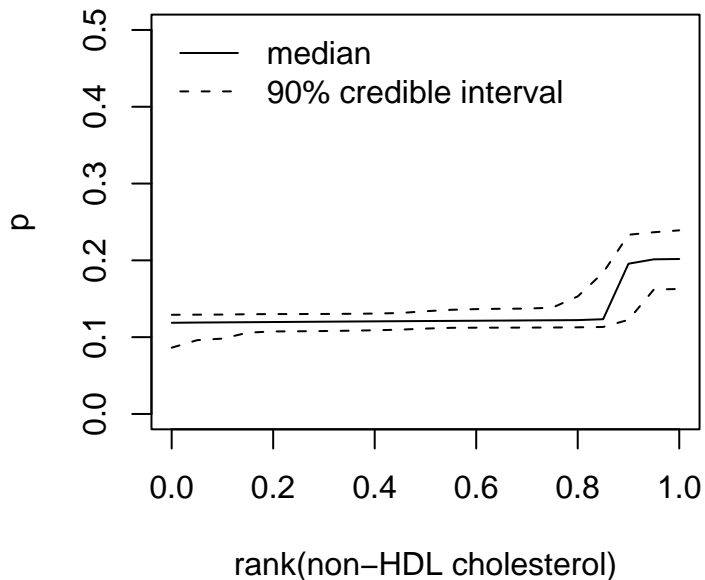
## 12. Constrained model for ranks of non-HDL and HDL: Length of 90% credible interval



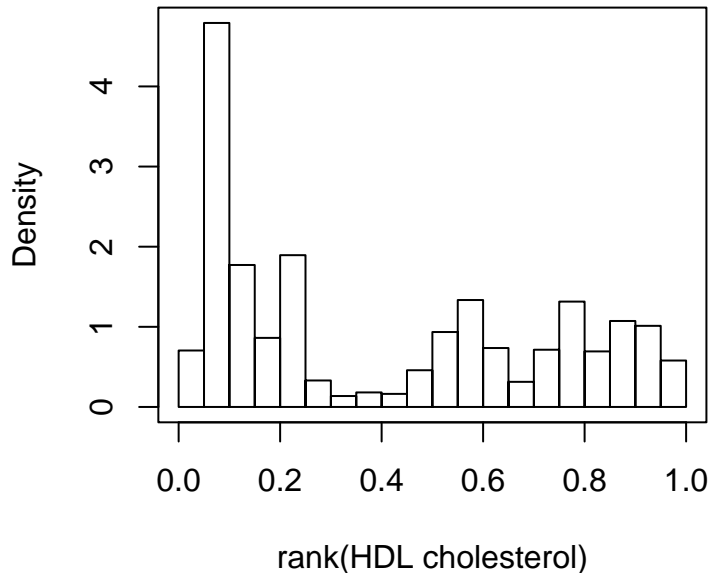
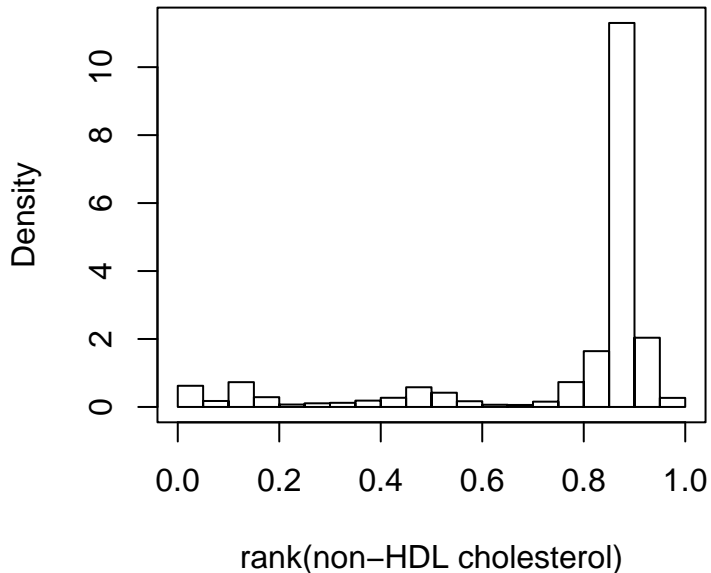
## 12. Constrained model for ranks of non-HDL and HDL: Difference to proportional hazards model



## 12. Constrained model for ranks of non-HDL and HDL: One-dimensional projections



## 12. Constrained model for ranks of non-HDL and HDL: Distributions for change point positions



- In the study of biostatistical/epidemiological problems there is a lot of uncritical use of parametric models.
- The resulting parameter estimates may then not "mean anything real".
- Structural model assumptions are likely to influence the results of empirical data analysis much more strongly than, e.g., specifying a particular type of prior in a Bayesian model.



# Summary, conclusions (2)



- The Bayesian approach to statistical inference adds a great deal of freedom in specifying statistical models for data analysis, by allowing one to think more freely about the structural properties of the models that seem plausible, such as
  - hierarchical or modular structures,
  - natural restrictions in the parameter space,
  - dependencies/conditional independencies,
  - making a distinction between the model describing the underlying state variables and the measurement model,
  - etc.

- The results from data analysis can often be given in terms of probabilities, then involving an integration with respect to the "unobservables" in the model.
  - This leads to relative robustness of such results with respect to the smoothness properties of the functions being used in the models ("Even very simple models may be O.K.!).
  - If needed, averaging over non-smooth functions will generally produce smooth reconstructions of the functional relationships that are considered.

# Summary, conclusions (4)



- In situations where it can be applied, an assumed monotonicity property of the regression function with respect to covariates has a strong stabilizing effect on the estimates.
- Sometimes mathematically / computationally attractive properties of models are introduced at the cost of unrealistic description of the data. Relevance vs. elegance!
- Careful model diagnostics should be carried out!

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