

# Analysis of eGFR trajectories from Hong Kong Diabetes Registry

March 5, 2015

## 1 Description of data

### 1.1 Data overview

The data were comprised by two parts: the baseline data and the follow-up eGFR data. The baseline data, which were extracted from the Hong Kong Diabetes Registry(HKDR), included the information of clinical assessments and laboratory investigations at enrollment, and the well-defined complication outcomes censored to 31st, January 2009. As here we focused on the ESRD outcome, we only selected those Chinese patients with no history of ESRD which was defined according to the ICD-9 codes and eGFR <15. Therefore, we obtained a cohort consisted of 718 ESRD events and 8810 event-free patients at cersoring date. The follow-up data included all the creatinine records from enrollment to 2014, and the eGFR were corresponding calculated using the Chinese-modified MDRD formula.

```
> base_dat <- read.table("../data/ESRD1_Prospect_Cohort_718vs8810.csv",header=TRUE,sep=",");
> follow_dat <- read.table("../data/eGFR_19940714_20140630.csv",header=TRUE,sep=",");
> dim(base_dat);
```

```
[1] 9528 100
```

```
> names(base_dat);
```

[1]	"Obs_id"	"date"	"ETHNICOD"	"SEX_str"
[5]	"SEX"	"DOB"	"AGE"	"YEAR_DIA"
[9]	"AGE_ONSE"	"DMAGE"	"IDDM_UPD"	"FX"
[13]	"DAD_AF"	"MOM_AF"	"SIBLING1"	"SIBLING2"
[17]	"CHILD_A1"	"CHILD_A2"	"SMOKING_str"	"SMOKING"
[21]	"SMOKING_C"	"SMOKING_E"	"ALCOHOL_str"	"ALCOHOL"
[25]	"ALCOHOL_C"	"ALCOHOL_E"	"HEIGHT"	"WT"
[29]	"WAIST"	"HIP"	"SBP"	"DBP"
[33]	"BMI"	"WHR"	"HBA1C"	"FBG"
[37]	"TC"	"HDL"	"LDL"	"TG"
[41]	"ACR"	"RBC"	"HB"	"WBC"
[45]	"eGFR_BASE"	"FORM_D_A"	"FORM_DM"	"HOME_BLO"
[49]	"HOME_MON"	"HOME_FRE"	"ED_CHIRO"	"RETINO_B"
[53]	"NEURO_B"	"MICROALB_B"	"MACROALB_B"	"DEATH_HIST"

```

[57] "LLDs_Base"      "Hypert_Base"    "Oads_Base"      "Insulin_Base"
[61] "ACEIARB_Base"   "DEATH_END"      "DEATH_TIME"     "DEATH_DATE"
[65] "MI_HIST"        "MI_END"         "MI_TIME"        "CHF_HIST"
[69] "CHF_END"        "CHF_TIME"       "STK_HIST"       "STK_END"
[73] "STK_TIME"       "PVD_HIST"       "PVD_END"        "PVD_TIME"
[77] "CHD_HIST"       "CHD_END"        "CHD_TIME"       "CHD1_HIST"
[81] "CHD1_END"       "CHD1_TIME"      "CAN_HIST"       "CAN_END"
[85] "CAN_TIME"       "ESRD_HIST"      "ESRD_END"       "ESRD_TIME"
[89] "CVD_HIST"       "CVD_END"        "CVD_TIME"       "CKD_HIST"
[93] "CKD_END"        "CKD_TIME"       "ESRD1_HIST"     "ESRD1_END"
[97] "ESRD1_TIME"    "ANY_HIST"       "ANY_END"        "ANY_TIME"

```

```
> head(base_dat);
```

	Obs_id	date	ETHNICOD	SEX_str	SEX	DOB	AGE	YEAR_DIA	AGE_ONSE
1	1	2002-10-22	C	F	0	7/8/1940	62	2002	62
2	2	1996-10-04	C	M	1	13/3/1939	57	1995	56
3	3	1996-08-02	C	M	1	5/3/1935	61	1983	48
4	4	2001-03-16	C	M	1	1927	74	1980	53
5	5	1997-05-20	C	M	1	12/7/1924	73	1993	69
6	6	1999-03-23	C	F	0	7/5/1922	77	1991	69

	DMAGE	IDDM_UPD	FX	DAD_AF	MOM_AF	SIBLING1	SIBLING2	CHILD_A1	CHILD_A2
1	0	N	0	0	0	0	4	0	3
2	1	N	0	0	0	0	3	0	0
3	13	N	1	0	0	1	4	0	0
4	21	N	0	0	0	0	0	0	5
5	4	N	1	0	0	0	3	1	5
6	8	N	2	0	0	2	4	0	4

	SMOKING_str	SMOKING	SMOKING_C	SMOKING_E	ALCOHOL_str	ALCOHOL	ALCOHOL_C
1	N	0	0	0	N	0	0
2	E	1	0	1	C	2	1
3	C	2	1	1	E	1	0
4	E	1	0	1	E	1	0
5	N	0	0	0	N	0	0
6	N	0	0	0	N	0	0

	ALCOHOL_E	HEIGHT	WT	WAIST	HIP	SBP	DBP	BMI	WHR	HBA1C	FBG
1	0	1.450	55.5	81.0	93.5	131.0	73.5	26.39715	0.8663102	6.8	5.6
2	1	1.785	68.3	87.5	94.0	140.0	90.0	21.43603	0.9308510	6.3	5.0
3	1	1.590	46.4	69.0	82.0	140.0	68.0	18.35370	0.8414634	9.8	5.3
4	1	1.550	52.3	81.0	87.0	128.5	55.5	21.76899	0.9310345	6.2	9.3
5	0	1.535	62.6	86.5	92.5	125.0	70.0	26.56792	0.9351351	6.9	7.2
6	0	1.445	51.4	83.0	96.0	197.5	95.0	24.61656	0.8645833	5.6	8.7

	TC	HDL	LDL	TG	ACR	RBC	HB	WBC	eGFR_BASE	FORM_D_A	FORM_DM
1	5.40	1.10	3.73	1.26	0.17	4.45	13.8	8.4	72.61830	Y	Y
2	6.20	1.04	4.60	1.19	138.01	4.40	13.8	9.3	80.16108	N	N
3	4.60	1.56	2.80	0.53	0.77	4.51	14.0	5.4	141.57826	N	N
4	6.09	1.11	4.58	0.88	9.43	3.85	11.9	6.9	57.68408	Y	Y
5	4.40	1.25	2.70	0.87	0.63	5.00	15.5	4.5	100.98319	Y	Y
6	4.20	1.22	2.60	0.74	1.12	NA	NA	NA	101.95334	Y	Y

	HOME_BLO	HOME_MON	HOME_FRE	ED_CHIRO	RETINO_B	NEURO_B	MICROALB_B	MACROALB_B
1	1	1	3	N	0	0	0	0
2	4	0	NA	N	1	1	0	1
3	2	1	5	N	0	0	0	0
4	1	1	3	N	1	0	1	0
5	1	1	3	N	0	1	0	0
6	1	1	3	N	0	0	0	0

	DEATH_HIST	LLDs_Base	Hypert_Base	Oads_Base	Insulin_Base	ACEIARB_Base
1	0	0	1	0	0	1
2	0	0	0	1	0	0
3	0	0	0	1	0	0
4	0	0	1	1	0	0
5	0	0	1	1	0	1
6	0	1	1	1	0	1

	DEATH_END	DEATH_TIME	DEATH_DATE	MI_HIST	MI_END	MI_TIME	CHF_HIST	CHF_END
1	0	6.277892	2009-01-31	0	0	6.277892	0	0
2	0	12.325804	2009-01-31	0	0	12.325804	0	1
3	0	12.498289	2009-01-31	0	0	12.498289	0	0
4	1	3.444216	2004-08-25	0	0	3.444216	0	1
5	0	11.701574	2009-01-31	0	0	11.701574	0	0
6	0	9.861739	2009-01-31	0	0	9.861739	0	0

	CHF_TIME	STK_HIST	STK_END	STK_TIME	PVD_HIST	PVD_END	PVD_TIME	CHD_HIST
1	6.2778919	0	0	6.277892	0	0	6.2778919	0
2	1.5414100	0	0	12.325804	0	0	12.3258042	0
3	12.4982888	0	0	12.498289	0	0	12.4982888	0
4	0.5393566	0	0	3.444216	1	1	0.1916496	0
5	11.7015743	0	0	11.701574	0	0	11.7015743	0
6	9.8617385	0	0	9.861739	0	0	9.8617385	1

	CHD_END	CHD_TIME	CHD1_HIST	CHD1_END	CHD1_TIME	CAN_HIST	CAN_END
1	0	6.2778919	0	0	6.2778919	0	0
2	0	12.3258042	0	0	12.3258042	0	0
3	0	12.4982888	0	0	12.4982888	0	0
4	0	3.4442163	0	0	3.4442163	0	0
5	0	11.7015743	0	0	11.7015743	0	0
6	1	0.1943874	1	1	0.1943874	0	0

	CAN_TIME	ESRD_HIST	ESRD_END	ESRD_TIME	CVD_HIST	CVD_END	CVD_TIME
1	6.277892	0	0	6.277892	0	0	6.2778919
2	12.325804	0	0	12.325804	0	0	12.3258042
3	12.498289	0	0	12.498289	0	0	12.4982888
4	3.444216	0	0	3.444216	1	1	0.1916496
5	11.701574	0	0	11.701574	0	0	11.7015743
6	9.861739	0	0	9.861739	1	1	0.1943874

	CKD_HIST	CKD_END	CKD_TIME	ESRD1_HIST	ESRD1_END	ESRD1_TIME	ANY_HIST
1	0	0	6.2778919	0	0	6.277892	0
2	0	0	12.3258042	0	0	12.325804	0
3	0	0	12.4982888	0	0	12.498289	0
4	1	1	0.1533196	0	0	3.444216	1
5	0	0	11.7015743	0	0	11.701574	0

6	0	0	9.8617385	0	0	9.861739	1
	ANY_END	ANY_TIME					
1	0	6.2778919					
2	1	1.5414100					
3	0	12.4982888					
4	1	0.1533196					
5	0	11.7015743					
6	1	0.1943874					

The outcomes of interest were named as "ESRD1\_HIST"(0 represents no ESRD history), "ESRD1\_END"(endpoint censored to 2009) and "ESRD1\_TIME"(follow-up period).

```
> table(base_dat$ESRD1_HIST);
```

```
0
9528
```

```
> table(base_dat$ESRD1_END);
```

```
0    1
8810 718
```

```
> dim(follow_dat);
```

```
[1] 391551      4
```

```
> head(follow_dat);
```

	Obs_id	test_date	F_eGFR0	creatinine
1	1	2002-08-20	80.6474	84
2	1	2002-08-24	97.9131	71
3	1	2002-08-31	73.5245	91
4	1	2002-10-08	91.8750	75
5	1	2002-10-22	72.5693	92
6	1	2003-12-01	81.4311	83

We merged the baseline data and the follow-up eGFR data according to the id of subject:

```
> result_merge <- data_merge(base_dat,follow_dat,base_id="Obs_id",follow_id="Obs_id");
> merged_dat <- result_merge$merged_dat;
> dim(merged_dat);
```

```
[1] 365475    104
```

We only selected those records between baseline and event/censoring dates,that said, those eGFR records before baseline or after event/censoring dates were removed. Moreover, we also calculated the follow-up age, duration of diabetes, and the backward time gap between event/censoring date and measurement date of eGFR, named "F\_AGE","F\_DMAGE" and "BW\_TIME", respectively.

```
> sub_dat <- record_filter(merged_dat,ftime_name="ESRD1_TIME");
> dim(sub_dat);
```

```
[1] 140665    107
```

```
> names(sub_dat);
```

```

[1] "Obs_id"      "date"        "ETHNICOD"    "SEX_str"
[5] "SEX"         "DOB"         "AGE"         "YEAR_DIA"
[9] "AGE_ONSE"    "DMAGE"       "IDDM_UPD"    "FX"
[13] "DAD_AF"      "MOM_AF"      "SIBLING1"    "SIBLING2"
[17] "CHILD_A1"    "CHILD_A2"    "SMOKING_str" "SMOKING"
[21] "SMOKING_C"   "SMOKING_E"   "ALCOHOL_str" "ALCOHOL"
[25] "ALCOHOL_C"   "ALCOHOL_E"   "HEIGHT"      "WT"
[29] "WAIST"       "HIP"         "SBP"         "DBP"
[33] "BMI"         "WHR"         "HBA1C"       "FBG"
[37] "TC"          "HDL"         "LDL"         "TG"
[41] "ACR"         "RBC"         "HB"          "WBC"
[45] "eGFR_BASE"   "FORM_D_A"    "FORM_DM"     "HOME_BLO"
[49] "HOME_MON"    "HOME_FRE"    "ED_CHIRO"    "RETINO_B"
[53] "NEURO_B"     "MICROALB_B"  "MACROALB_B"  "DEATH_HIST"
[57] "LLDs_Base"   "Hypert_Base" "Oads_Base"    "Insulin_Base"
[61] "ACEIARB_Base" "DEATH_END"   "DEATH_TIME"  "DEATH_DATE"
[65] "MI_HIST"     "MI_END"      "MI_TIME"     "CHF_HIST"
[69] "CHF_END"     "CHF_TIME"    "STK_HIST"    "STK_END"
[73] "STK_TIME"    "PVD_HIST"    "PVD_END"     "PVD_TIME"
[77] "CHD_HIST"    "CHD_END"     "CHD_TIME"    "CHD1_HIST"
[81] "CHD1_END"    "CHD1_TIME"   "CAN_HIST"    "CAN_END"
[85] "CAN_TIME"    "ESRD_HIST"   "ESRD_END"    "ESRD_TIME"
[89] "CVD_HIST"    "CVD_END"     "CVD_TIME"    "CKD_HIST"
[93] "CKD_END"     "CKD_TIME"    "ESRD1_HIST"  "ESRD1_END"
[97] "ESRD1_TIME"  "ANY_HIST"    "ANY_END"     "ANY_TIME"
[101] "Obs_id"      "test_date"   "F_eGFR0"     "creatinine"
[105] "F_AGE"       "F_DMAGE"     "BW_TIME"

```

## 1.2 Outcomes

For simplicity, we extracted those variables involved in this analysis, and removed those records with missing data. We first plotted the observed creatinine and eGFR values (Figure 1). From the figure, we can see there are some abnormal records, which may be due to measurement or typo errors.

```

> sub_var <- c("Obs_id", "date", "SEX", "ESRD1_END", "ESRD1_TIME", "test_date", "F_eGFR0",
+             "creatinine", "F_AGE", "F_DMAGE", "BW_TIME");
> nomiss_dat <- sub_dat[complete.cases(sub_dat[,sub_var]),];
> dim(nomiss_dat);

```

```
[1] 139126    107
```

```

> test_date <- as.Date(nomiss_dat$test_date);
> c(min(test_date), max(test_date));

```

```
[1] "1993-06-17" "2009-01-31"
```

```

> plot(test_date,nomiss_dat$F_eGFR0,xlim=c(min(test_date),max(test_date)),
+       xlab="date of measurement",ylab="eGFR");

> plot(test_date,nomiss_dat$creatinine,xlim=c(min(test_date),max(test_date)),
+       xlab="date of measurement",ylab="Creatinine");

```

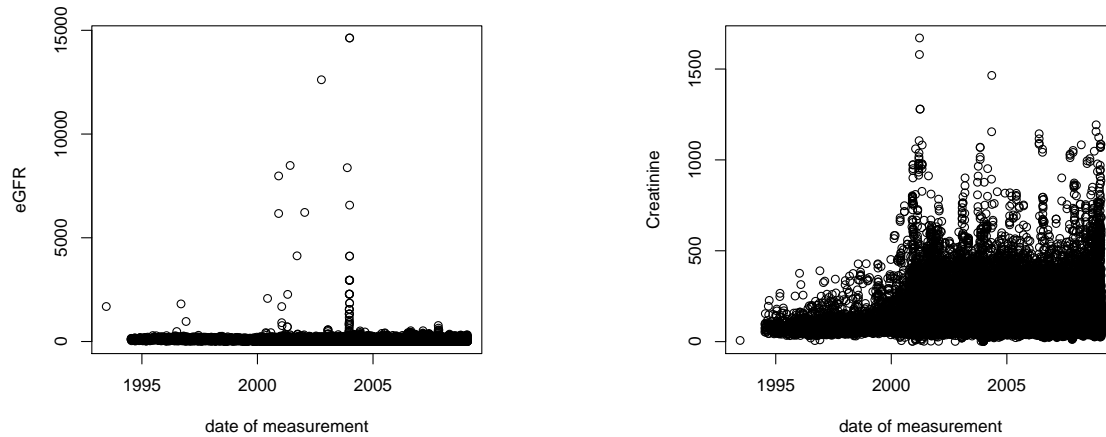


Figure 1: *Distribution of the raw data of eGFR and creatinine.*

We removed those records with  $\text{eGFR} \geq 300$ , which were considered to be errors. The updated distributions were shown in Figure 2.

```

> sub_nomiss <- nomiss_dat[which(nomiss_dat$F_eGFR0<300),];
> dim(sub_nomiss);

[1] 138970    107

> test_date <- as.Date(sub_nomiss$test_date);
> c(min(test_date),max(test_date));

[1] "1994-07-14" "2009-01-31"

> plot(test_date,sub_nomiss$F_eGFR0,xlim=c(min(test_date),max(test_date)),
+       xlab="date of measurement",ylab="eGFR");

> plot(test_date,sub_nomiss$creatinine,xlim=c(min(test_date),max(test_date)),
+       xlab="date of measurement",ylab="Creatinine");

```

As we here only focused on the patients developed ESRD, we extracted those subjects and plotted the distribution of eGFR.

```

> event_dat <- sub_nomiss[sub_nomiss$ESRD1_END==1,];
> dim(event_dat);

```

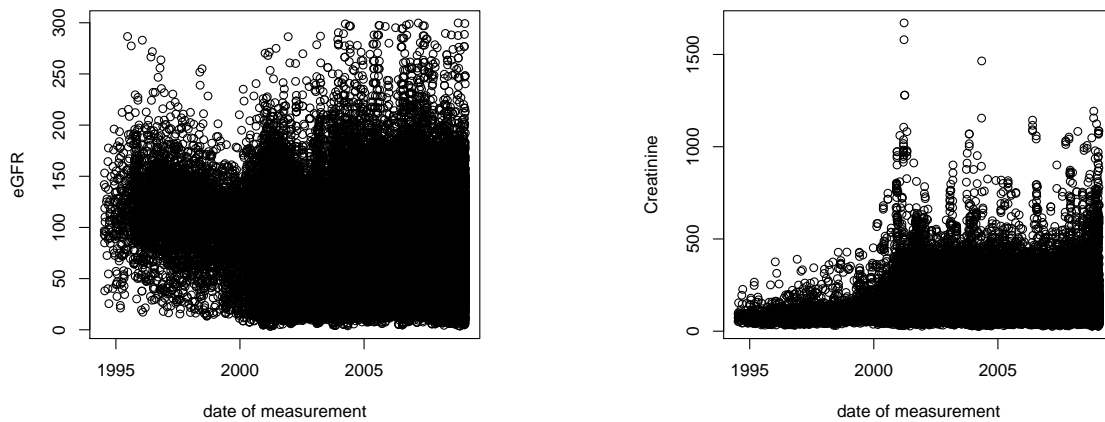


Figure 2: *Distribution of eGFR and creatinine after removing those records with eGFR greater than 300.*

```
[1] 12508    107

> length(unique(event_dat$Obs_id));

[1] 710

> dest_eGFR <- density(event_dat$F_eGFR0);

> plot(dest_eGFR,xlim=c(min(event_dat$F_eGFR0),max(event_dat$F_eGFR0)),xlab="eGFR",
+       ylab="Density",main="ESRD subjects");
```

As shown in Figure 3, the distribution is skewed. We thus did a log transformation of eGFR, and calculated the quadratic and cubic terms of backward period at the same time.

```
> event_dat <- transform(event_dat,log_eGFR=log(event_dat$F_eGFR0),
+                         time2=event_dat$BW_TIME^2,time3=event_dat$BW_TIME^3);
> dest_logeGFR <- density(event_dat$log_eGFR);

> plot(dest_logeGFR,xlim=c(min(event_dat$log_eGFR),max(event_dat$log_eGFR)),xlab="Ln(eGFR)",
+       ylab="Density",main="ESRD subjects");
```

We then summarized the number of measurement for each subject (Figure 4).

```
> num_stat <- table(table(event_dat$Obs_id));
> par(mar=c(5,4,1,2));
> plot(as.numeric(names(num_stat)),num_stat,type="h",lwd=3,xaxs="i",xlim=c(0,140),
+       xlab="No. of measurements",ylab="No. of subjects",yaxt="n");
> axis(side=2);
```

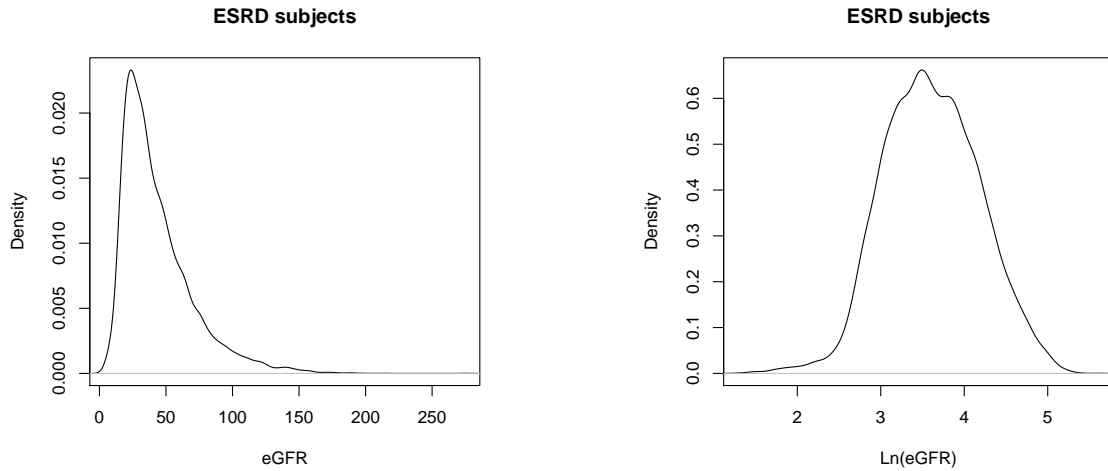


Figure 3: *Distribution of eGFR and  $\log(eGFR)$  for ESRD subjects.*

## 2 Analysis

### 2.1 Modelling using "lcmm" function

We first fit the model using the "lcmm" function, and specified "linear" as the link function. The "lcmm" with linear link function is similar with the "hlme" function, but the reason for using "lcmm" function is that the confidence interval of predict values can be obtained by using the corresponding prediction function.

```
> event_model <- lcmm(log_eGFR ~ BW_TIME+time2+time3+F_AGE+SEX+F_DMAGE,
+                      mixture =~ BW_TIME+time2+time3,
+                      random =~ BW_TIME,
+                      link="linear",subject="Obs_id",ng=3,data=event_dat);
```

Be patient, lcmm is running ...

The program took 792.07 seconds

```
> event_model;
```

```
General latent class mixed model
  fitted by maximum likelihood method
```

```
lcmm(fixed = log_eGFR ~ BW_TIME + time2 + time3 + F_AGE + SEX +
      F_DMAGE, mixture = ~BW_TIME + time2 + time3, random = ~BW_TIME,
      subject = "Obs_id", ng = 3, link = "linear", data = event_dat)
```

Statistical Model:

Dataset: event\_dat

Number of subjects: 710

Number of observations: 12508

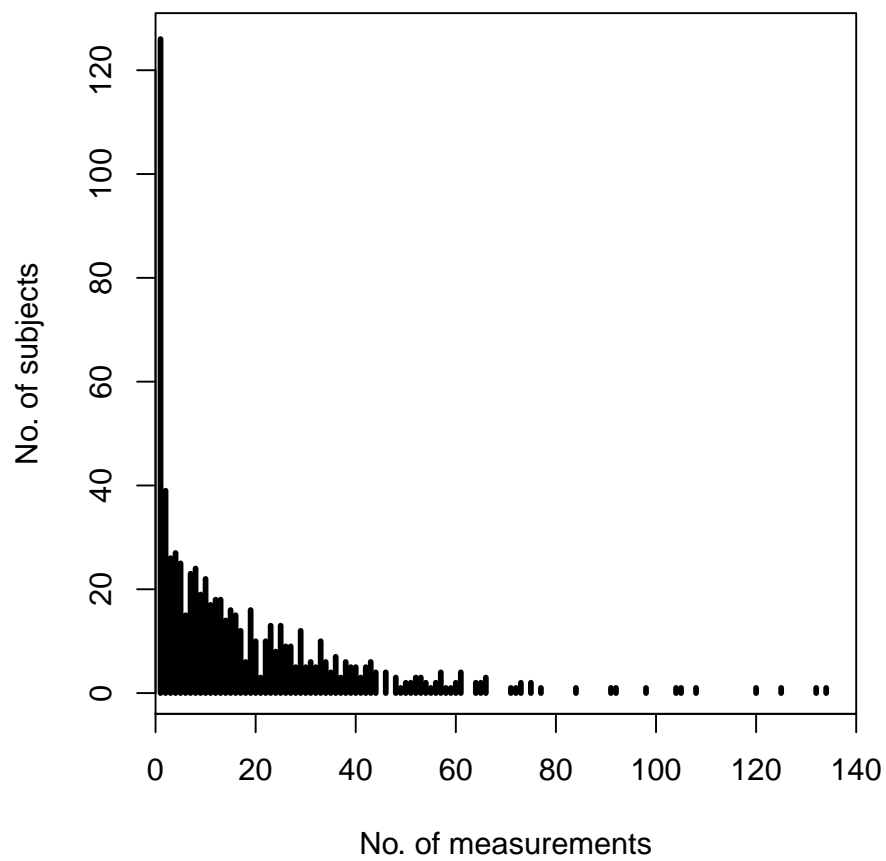


Figure 4: *Number of eGFR records for patients.*

```
Number of latent classes: 3
Number of parameters: 21
Link function: linear
```

Iteration process:

```
Convergence criteria satisfied
Number of iterations: 22
Convergence criteria: parameters= 3.7e-09
                      : likelihood= 8.9e-08
                      : second derivatives= 6.8e-13
```

Goodness-of-fit statistics:

```
maximum log-likelihood: -689.43
AIC: 1420.86
BIC: 1516.73
```

Now we can further investigate the posterior probabilities of subjects in each class (Figure 5 and 6).

```
> postprob(event_model);
```

Posterior classification:

```
class1 class2 class3
N 259.00 306.0 145.00
% 36.48 43.1 20.42
```

Posterior classification table:

```
--> mean of posterior probabilities in each class
      prob1 prob2 prob3
class1 0.7869 0.1750 0.0381
class2 0.1761 0.7035 0.1204
class3 0.0333 0.1632 0.8034
```

Posterior probabilities above a threshold (%):

```
      class1 class2 class3
prob>0.7 66.02 47.39 68.28
prob>0.8 55.21 37.91 57.24
prob>0.9 37.07 25.49 48.28
```

```
> plot_ppr(event_model);
```

```
> ng <- event_model$ng;
```

```
> post_pr <- event_model$pprob;
```

```
> pairs(post_pr[,2+1:ng],pch=16,col=1:ng,cex=1.5,gap=0);
```

We built a data set for prediction to plot the estimated trajectories. Here the median age 65, median DM duration 12 and sex as male were used. The function "plot\_predictY" incorporated the prediction function "predictY" in LCMM package (Figure 7).

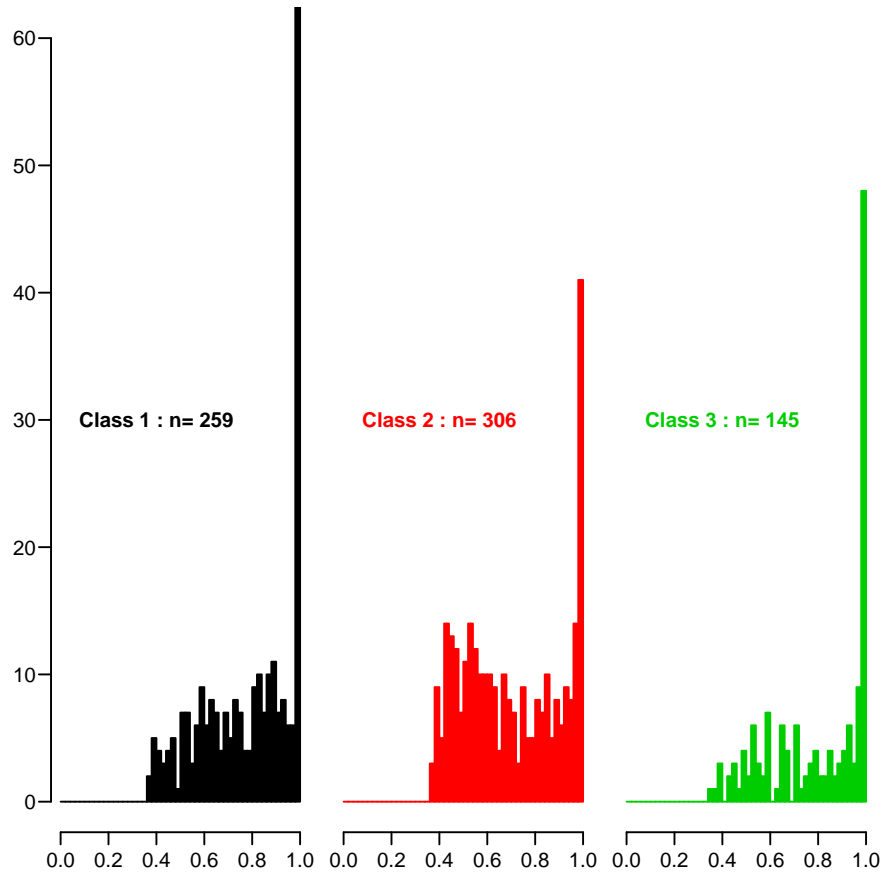


Figure 5: *Posterior probabilities of 3 classes for the ESRD model.*

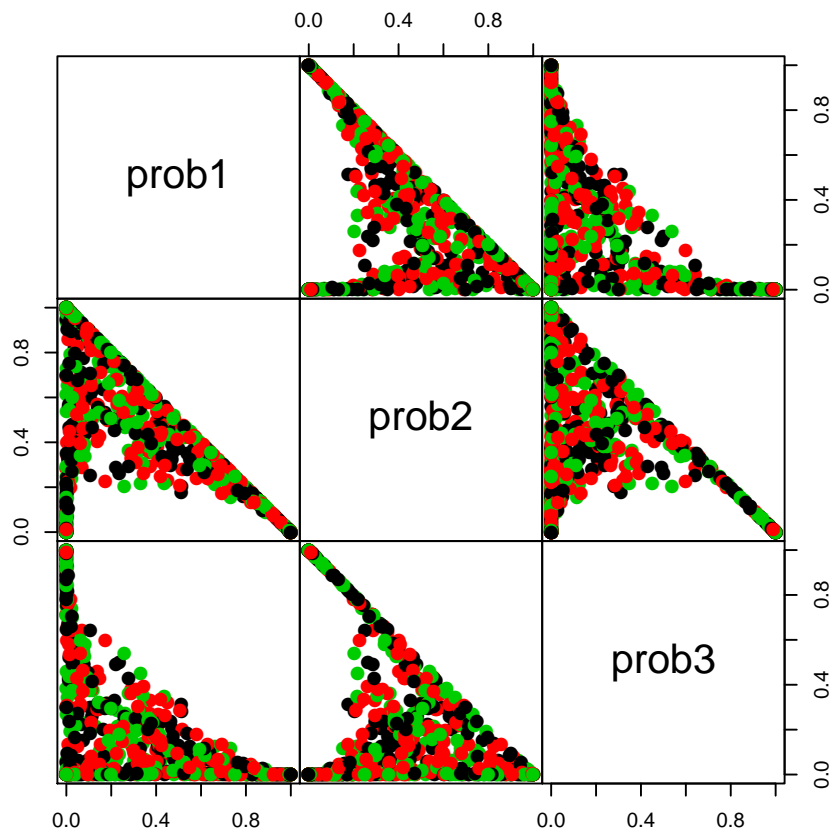


Figure 6: *Pairwise posterior probabilities from the fitted model using "lcm". It seems the discrimination between classes is bad.*

```

> adjust_var <- event_model$Xnames[-c(1:4)];
> x <- seq(ceiling(min(event_dat$BW_TIME)),0,by=1);
> plotdata <- data.frame(cbind(1,x,x^2,x^3));
> plotdata <- cbind(plotdata,round(65+x,0),1,round(12+x,0));
> names(plotdata) <- c(event_model$Xnames[1:4],adjust_var);
> plotdata

```

	intercept	BW_TIME	time2	time3	F_AGE	SEX	F_DMAGE
1	1	-12	144	-1728	53	1	0
2	1	-11	121	-1331	54	1	1
3	1	-10	100	-1000	55	1	2
4	1	-9	81	-729	56	1	3
5	1	-8	64	-512	57	1	4
6	1	-7	49	-343	58	1	5
7	1	-6	36	-216	59	1	6
8	1	-5	25	-125	60	1	7
9	1	-4	16	-64	61	1	8
10	1	-3	9	-27	62	1	9
11	1	-2	4	-8	63	1	10
12	1	-1	1	-1	64	1	11
13	1	0	0	0	65	1	12

```

> stat_pred <- plot_predictY(event_model,ctrl_model=NULL,event_dat,plotdata,id_name="Obs_id");

```

## 2.2 Modelling using "hlme" function

We also tried to model the eGFR trajectories using "hlme" function. From the introduction of the package, it seems that the confidence intervals of prediction were not provided.

```

> event_hlme <- hlme(log_eGFR ~ BW_TIME+time2+time3+F_AGE+SEX+F_DMAGE,
+                    mixture =~ BW_TIME+time2+time3,
+                    random =~ BW_TIME,
+                    subject="Obs_id",ng=3,data=event_dat);

```

Be patient, hlme is running ...  
The program took 636.35 seconds

```

> event_hlme;

```

Heterogenous linear mixed model  
fitted by maximum likelihood method

```

hlme(fixed = log_eGFR ~ BW_TIME + time2 + time3 + F_AGE + SEX +
      F_DMAGE, mixture = ~BW_TIME + time2 + time3, random = ~BW_TIME,
      subject = "Obs_id", ng = 3, data = event_dat)

```

Statistical Model:  
Dataset: event\_dat  
Number of subjects: 710

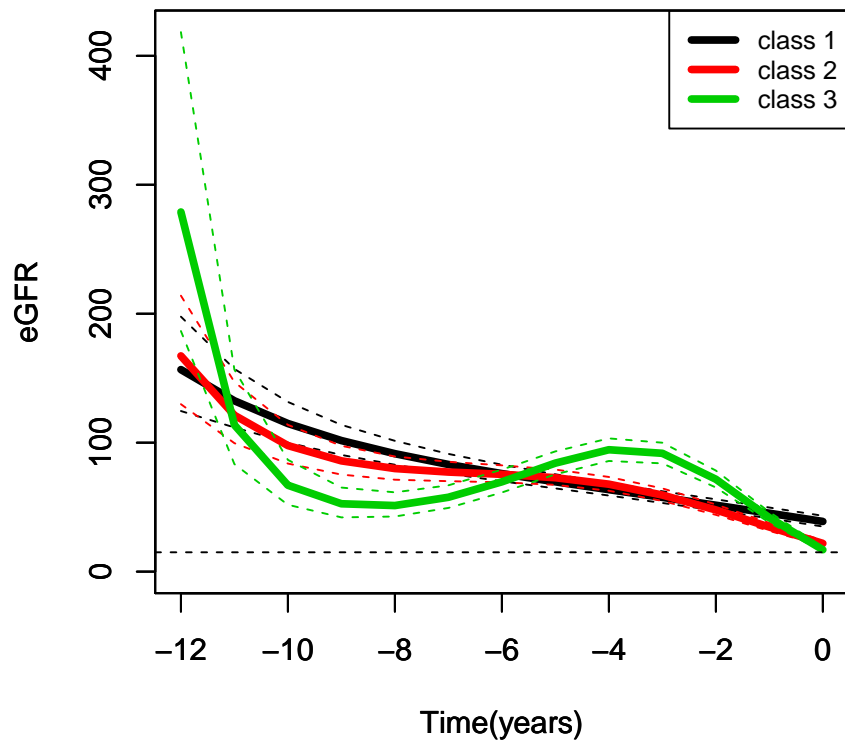


Figure 7: Mean trajectories of eGFR for the three latent classes of subjects developing ESRD. The horizontal dashed line represents eGFR is equal to 15

```

Number of observations: 12508
Number of latent classes: 3
Number of parameters: 21

Iteration process:
  Convergence criteria satisfied
  Number of iterations: 22
  Convergence criteria: parameters= 6.9e-10
                        : likelihood= 1.4e-08
                        : second derivatives= 7.9e-14

Goodness-of-fit statistics:
  maximum log-likelihood: -689.43
  AIC: 1420.86
  BIC: 1516.73

> postprob(event_hlme);

Posterior classification:
  class1 class2 class3
N 145.00  306.0 259.00
%  20.42  43.1  36.48

Posterior classification table:
--> mean of posterior probabilities in each class
      prob1 prob2 prob3
class1 0.8034 0.1632 0.0333
class2 0.1204 0.7035 0.1761
class3 0.0381 0.1750 0.7869

Posterior probabilities above a threshold (%):
      class1 class2 class3
prob>0.7  68.28  47.39  66.02
prob>0.8  57.24  37.91  55.21
prob>0.9  48.28  25.49  37.07

> post_pr <- event_hlme$postprob;
>

> ng <- event_model$ng;
> pairs(post_pr[,2+1:ng],pch=16,col=1:ng,cex=1.5,gap=0);

> plot.predict.hlme(event_hlme,plotdata,var.time="BW_TIME",legend.loc="topright");

```

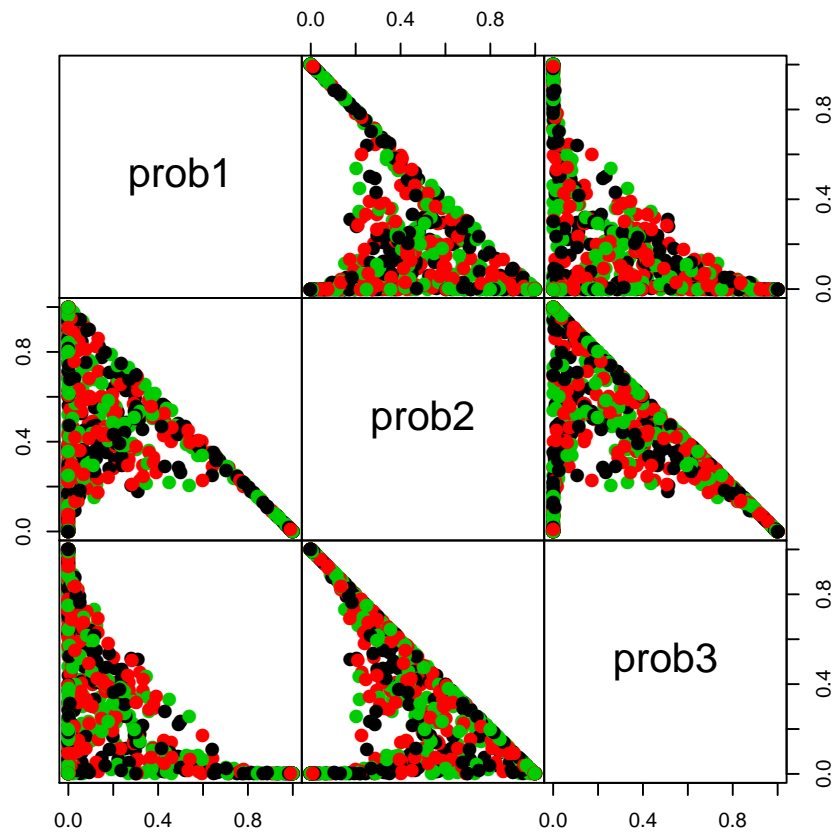


Figure 8: *Pairwise posterior probabilities from the fitted model using "hlme".*

### Class-specific mean latent process predicted trajectory

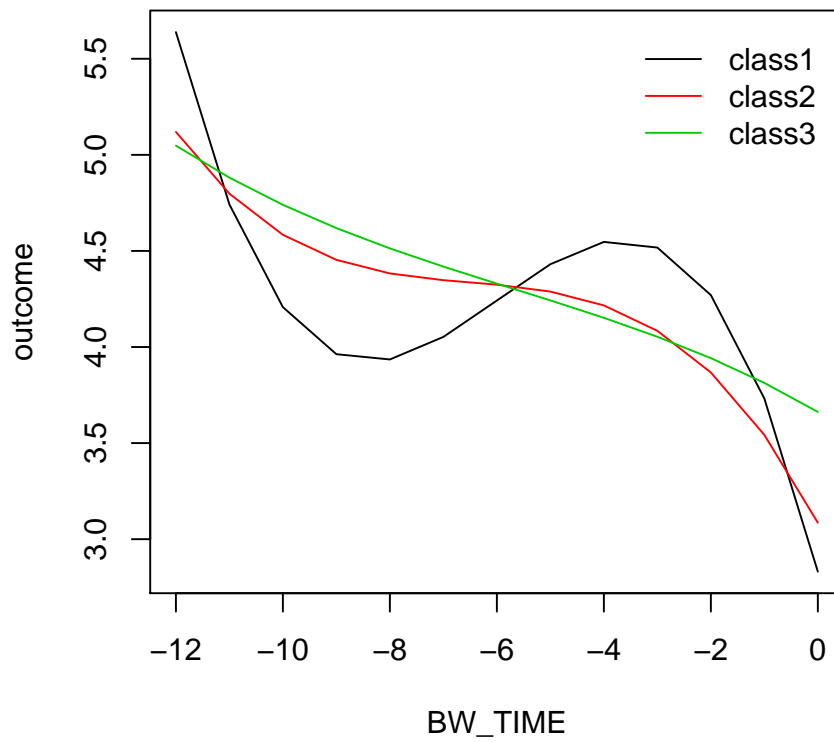


Figure 9: Mean trajectories of eGFR for the three latent classes of subjects developing ESRD. Model was fitted using the "hlme" function; The horizontal dashed line represents eGFR is equal to 15