```
                        _____

                        Genstat Twenty-fourth Edition
                        Genstat Procedure Library Release PL33
                        _____
```

```
   1  SET [WORKINGDIRECTORY='C:/Varie/GenStat'; DIAGNOSTIC=messages]
   2  JOB
```

End of job.

```
                        _____

                        Genstat Twenty-fourth Edition
                        Genstat Procedure Library Release PL33
                        _____
```

```
   1  SET [WORKINGDIRECTORY='C:/Varie/GenStat'; DIAGNOSTIC=messages]
```

```
 6936
 6937  "filter the dataset to CIK and LD recipients"
 6938  RESTRICT eGFR_EPI2021, pz_categoria, mese, don_quality_score, don_eta, ric_CIT, C[1], C[2],
\
 6939   ric_eta, ric_sesso, ric_PRA; CONDITION=pz_categoria.IN.!T('CIK recipient','LD
recipient')
 6940
 6941  "generate continuous variable time"
 6942  DELETE [REDEFINE=yes] cmese2
 6943  CALCULATE cmese2 = !(#mese)
 6944
 6945  "Random Coefficient Regression"
 6946  DELETE [REDEFINE=yes] _vcs, _vcst, _cst, _effs, _effst, _sigma2, _cinit
 6947  "Calculating the Initial Values"
 6948  VCOMPONENTS [FIXED=pz_categoria * cmese2 + don_quality_score + don_eta + ric_CIT + C[2]\
 6949   + ric_eta + ric_sesso + ric_PRA; SPLINE=pz_categoria.cmese2; FACTORIAL=9] id/cmese2;
CONSTRAINTS=positive
 6950  REML [PRINT=*; MAXCYCLE=30; FMETHOD=automatic; PTERMS=pz_categoria.cmese2;
PSE=differences;\
 6951   METHOD=AI] eGFR_EPI2021
 6952  VKEEP [SIGMA2 = _sigma2] id/cmese2; COMPONENT = _vcs,_vcst; EFFECTS=_tes,_test
 6953  CALC _vcs,_vcst = _vcs,_vcst / _sigma2
 6954  VARIATE _effs,_effst; VALUE=_tes,_test
 6955  CALC _cst = CORR(_effs;_effst)*SQRT(_vcs*_vcst)
 6956  VARIATE [VALUE=_vcs,_cst,_vcst] _cinit
 6957  "Fit the model and check it"
 6958  VCOMPONENTS [FIXED=pz_categoria * cmese2 + don_quality_score + don_eta + ric_CIT + C[2]\
 6959   + ric_eta + ric_sesso + ric_PRA; SPLINE=pz_categoria.cmese2; FACTORIAL=9] RANDOM=id/cmese2
 6960  VSTRUCTURE [TERMS=id/cmese2; CORRELATE=unrest; FORM=whole; CINITIAL=_cinit]
 6961  REML [PRINT=model,components,deviance; MAXCYCLE=30; FMETHOD=automatic;\
 6962   PTERMS=pz_categoria.cmese2; PSE=differences; METHOD=AI] eGFR_EPI2021; SAVE=wsave
```

REML variance components analysis

Response variate: eGFR_EPI2021
Fixed model: Constant + cmese2 + pz_categoria + cmese2.pz_categoria + don_quality_score
+ don_eta + ric_CIT + C['volume_attivitàDEC_centrotx'] + ric_eta + ric_sesso + ric_PRA
Random model: id + id.cmese2
Spline model: Spline(cmese2).pz_categoria
Number of units: 244 (260 units excluded due to zero weights or missing values)

Residual term has been added to model

Sparse algorithm with AI optimisation
All covariates centred
Analysis is subject to the restriction on eGFR_EPI2021

Covariance structures defined for random model

Correlated terms:

    Set Correlation across terms
      1 Unstructured

    Set Terms   Covariance model within term
      1 id   Identity
      1 id.cmese2   Identity

Estimated variance components

Random term   component   s.e.
Spline(cmese2).pz_categoria
                                         0.69   1.76

Estimated parameters for covariance models

Random term(s)	Factor	Model(order)	Parameter	Estimate	s.e.
id + id.cmese2	Across terms	Unstructured	v_11	4.200	1.110
			v_21	-0.03919	0.02537
			v_22	0.003364	0.001217
	Within terms	Identity	-	-	-

Note: the covariance matrix for each term is calculated as G or R where
 var(y) = Sigma2(ZGZ'+R), i.e.   relative to the residual variance, Sigma2.

Residual variance model

Term	Model(order)	Parameter	Estimate	s.e.
Residual	Identity	Sigma2	70.04	8.07

Deviance: -2*Log-Likelihood

        Deviance   d.f.
   1501.89   228

Note: deviance omits constants which depend on fixed model fitted.

```
 6963  VPLOT
 6964
 6965
 6966  "calculate and save P value and text for the plot (The P value includes non linear spline
component)"
 6967  SCALAR [MODIFY = yes] IDENTIFIER = rdf
 6968  VKEEP [DF= rdf] pz_categoria.cmese2; EFFECTS=beta; SEDEFFECTS=se; NDF=ndf; DDF = ddf;
FSTATISTIC = f; WALD = w
 6969  CALC _Pval_f = CUF(f;ndf;ddf;0)
 6970  TXCONSTRUCT [TEXT=text_Plin_diff] 'P value for different slopes=', #_Pval_f; DECIMALS = 2
 6971
 6972
 6973  "Get the mean population curve via VPREDICT for the plot"
 6974  VPREDICT [PREDICTIONS = mgfr; SE = semgfr] pz_categoria,cmese2; LEVELS=!T('CIK
recipient','LD recipient'),!(1,2...60)
```

```
 6975  VTABLE TABLE= mgfr, semgfr; VARIATE = MGFR, SEMGFR; CLASSIFICATION = CAT
 6976
 6977  "Graph setting for the plot (colours, pattern of mean trajectories lines, axes settings"
 6978  CALC red  = RGB(212; 17; 89)
 6979   &  blue = RGB(26; 133; 255)
 6980  PEN [RESET=yes] 1,2; METHOD=line; COLOUR=#blue,#red; CFILL='match'; SYMBOLS='none';
THICK=2
 6981  YAXIS [RESET=yes] WINDOW=1; TITLE='mGFR (ml/min/1.73m~^{2})'; LOWER=0; UPPER=120;
MARKS=!(0,15,30,45,60,90,120 )
 6982  XAXIS [RESET=yes] WINDOW=1; TITLE='Months since transplant'; LOWER=0; UPPER=60;
MARKS=!(0,3,6,12,24,36,48,60)
 6983  FRAME [GRID=yx; RESET=yes] WINDOW=1; BOX=omit
 6984
 6985  "Calculations to plot Individual trajectories for recipients only"
 6986  SUBSET [pz_categoria .in. !T('CIK recipient','LD recipient'); SETLEVELS=yes] \
 6987       id,pz_categoria,eGFR_EPI2021,cmese2; iid,icat,iY,iX
 6988  TABULATE [CLASS=iid; PRINT=*] !(#icat); MEANS=tid "Get category for individuals"
 6989  VTABLE tid; idcat
 6990  GROUPS [REDEFINE=yes] idcat
 6991  CALC nidpen = NVALUES(idcat)
 6992  CALC idcolour = NEWLEVELS(idcat;!(blue,red))
 6993
 6994  "Calculations to plot 95% confidence intervals as coloured regions by reversin lower bound
and appending
-6995  to the upper bounds to define a region to be shaded "
 6996  SCALAR IDENTIFIER = t
 6997  CALC t = ABS(EDT(0.025; rdf; 0))
 6998  SORT [INDEX=CAT[1,2]] CAT[1,2],MGFR
 6999  CALC LB = MGFR - t * SEMGFR
 7000  CALC UB = MGFR + t * SEMGFR
 7001  CALC RLB,RCAT[1,2] = REVERSE(LB,CAT[1,2])
 7002  APPEND [AY] UB,RLB
 7003  APPEND [AX] CAT[2],RCAT[2]
 7004  APPEND [AP] CAT[1],RCAT[1]
 7005
 7006  "Make the plot"
 7007  DSTART
 7008  DGRAPH [WINDOW=1; KEYWINDOW=0] Y=MGFR; X=CAT[2]; PEN=CAT[1]; LAYER=3 "Mean lines"
 7009  PEN     1,2; METHOD=fill; JOIN=given; TAREA = 200
 7010  DGRAPH [WINDOW=1; KEYWINDOW=0; SCREEN=keep] Y=AY; X=AX; PEN=AP; LAYER=2 "95% Confidence
region"
 7011  PEN     1...nidpen; COLOUR=#idcolour; METHOD=line; SYMBOL='none'; THICK=0.9;
LINESTYLE='solid'; TLINE = 150
 7012  DGRAPH [WINDOW=1; KEYWINDOW=0; SCREEN=keep] Y=iY; X=iX; PEN=iid; LAYER=1 "Individuals
lines"
 7013  PEN     1,2; COLOUR=#blue,#red
 7014  DKEY   [WINDOW=6; NCOLUMNS=1; PENLABELS=!(1,2); BORDER=none; XLOFFSET=-6] \
 7015       !T('CIK recipient','LD recipients');  METHOD='none'
 7016  PEN 2; COLOUR=1; SYMBOL=0; ROTATION=0; SIZE=1; LABELS= text_Plin_diff
 7017  DGRAPH [WINDOW=1; KEYWINDOW=0; SCREEN=keep] 3; 30; PEN=2 "text"
 7018  DFINISH
```

P value for different slopes=0.48
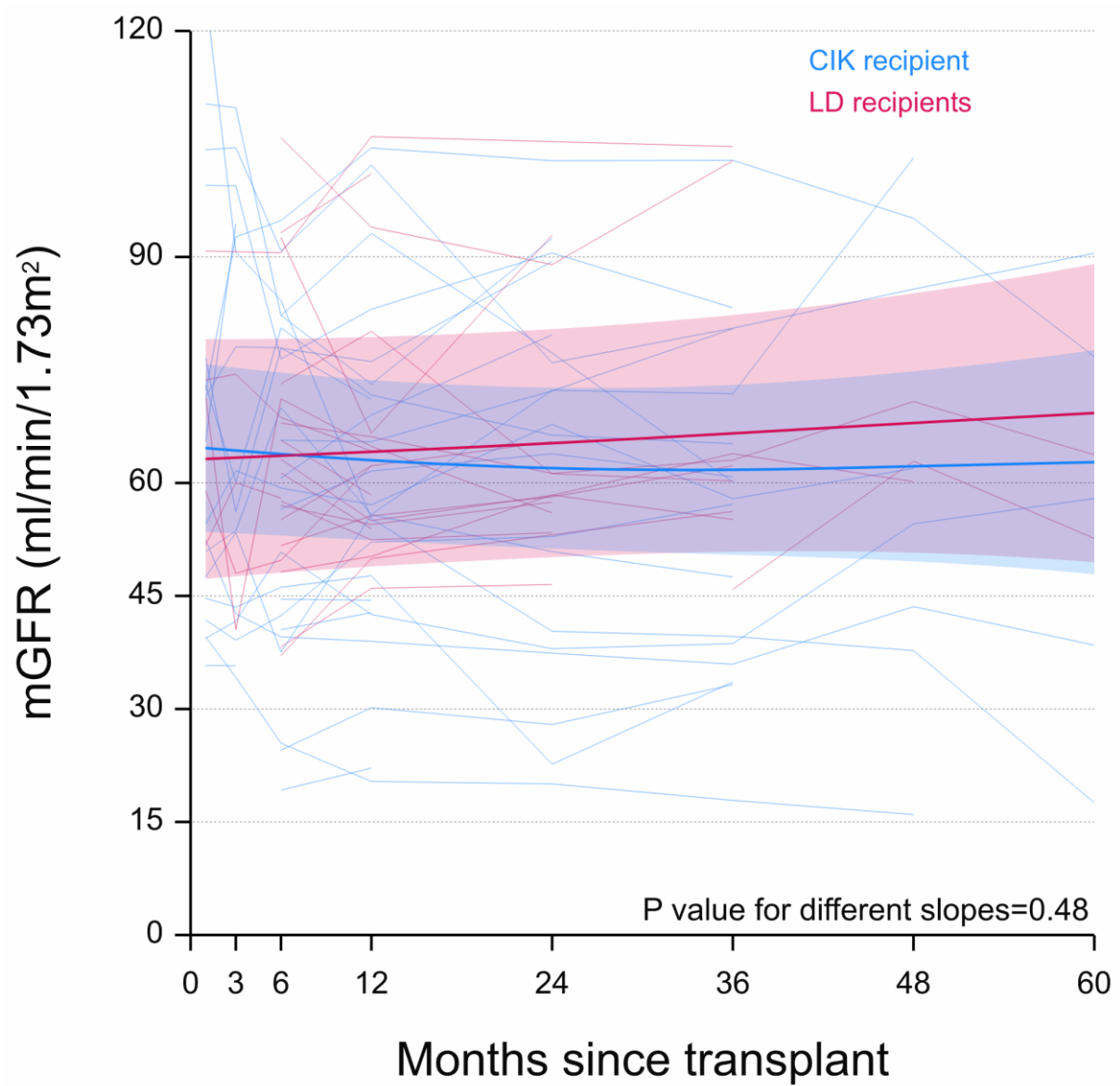
7019
 7020
 7021 "Print linear difference between CIK and LD eGFR slopes per year FROM THE REGRESSION TABLE
(NOT INCLUDING SPLINES)"
 7022 VRSETUP [SAVE = wsave]
 7023 VRFIT [PRINT=model] pz_categoria * cmese2 + don_quality_score + don_eta + ric_CIT + C[2]\
 7024   + ric_eta + ric_sesso + ric_PRA

          Response variate: eGFR_EPI2021
            Weight matrix: REML weights
             Fitted terms: Constant + pz_categoria + cmese2 + cmese2.pz_categoria +
don_quality_score + don_eta + ric_CIT + C['volume_attivitàDEC_centrotx'] + ric_eta + ric_sesso +
ric_PRA

 7025 VRKEEP [RDF = rrdf] pz_categoria.cmese2; ESTIMATES = rb_lin_diff; SE = rse_lin_diff; DDF
= ddf
 7026 CALC rt = ABS(EDT(0.025; rrdf; 0))
 7027 SCALAR [MODIFY=yes] zt
 7028 CALC zt = ABS(#rb_lin_diff$[2] / #rse_lin_diff$[2])
 7029 CALC _Pval_t = 2* CUT(zt;rrdf;0)
 7030 CALC erb_lin_diff = #rb_lin_diff$[2] * 12 * -1 "Difference in slopes per
ml/min/1.73m2/year CIK vs LD recipients"
 7031 CALC erse_lin_diff = #rse_lin_diff$[2]* 12
 7032 CALC erlb_lin_diff = erb_lin_diff - rt * erse_lin_diff
 7033 &   erub_lin_diff = erb_lin_diff + rt * erse_lin_diff
 7034 PRINT erb_lin_diff, erse_lin_diff, rt, erlb_lin_diff, erub_lin_diff; DECIMALS = 2

   erb_lin_diff   erse_lin_diff   rt   erlb_lin_diff   erub_lin_diff
          -2.02   2.21   1.97   -6.37   2.34

 7035 TXCONSTRUCT [TEXT=ertext_lin_diff] 'Adjusted linear diff. between CIK and LD recipients:',
#erb_lin_diff, \
 7036   ' (95%CI: ', #erlb_lin_diff, ' to ', #erub_lin_diff, '; P=', #_Pval_t, ')'; DECIMALS =
,1,,1,*,1,*,2,*
 7037 PRINT [IPRINT=*] ertext_lin_diff

            Adjusted linear diff. between CIK and LD recipients:-2.0 (95%CI: -6.4 to 2.3; P=0.36)

 7038
 7039

```
1053  SUBSET [pz_categoria .in. !T('CIK recipient','LD recipient'); SETLEVELS=yes] \
1054        id, _d, _t, pz_categoria, don_quality_score, ric_CIT; r_id, r_d, r_t,
r_pz_categoria, r_don_quality_score, r_ric_CIT
1055  FACTOR [MODIFY=yes; REFERENCELEVEL = 2] r_pz_categoria
1056
1057  CALC n = NVALUES(r_d)
1058  VARIATE [NVALUES = n] CENSOR
1059  RESTRICT CENSOR; r_d.EQ.1
1060  CALC CENSOR = 0
1061  RESTRICT CENSOR
1062  RESTRICT CENSOR; r_d.EQ.0
1063  CALC CENSOR=1
1064  RESTRICT CENSOR
1065  PRINT n


          n
      56.00


1066  CALC r_mese = r_t * 12
1067  FSPREADSHEET [BOOK=0]
CENSOR,r_d,r_don_quality_score,r_id,r_pz_categoria,r_ric_CIT,r_t,r_mese
1068
1069  "Prepare setting and text for the Kaplan-Meier plot"
1070  CALC red  = RGB(212; 17; 89)
1071   &  blue = RGB(26; 133; 255)
1072  PEN [RESET=yes] 1,2; METHOD=line; COLOUR=#blue,#red; CFILL='match'; SYMBOLS='none';
THICK=2
1073  YAXIS [RESET=yes] WINDOW=1; TITLE='Transplant Survival (%)'; LOWER=0; UPPER=1;
MARKS=!(0,.2,.4,.6,.8,1 ); LABELS=!T('0','20','40','60','80','100')
1074  XAXIS [RESET=yes] WINDOW=1; TITLE='Months since transplant'; LOWER=0; UPPER=60;
MARKS=!(0,3,6,12,24,36,48,60)
1075  FRAME [GRID=yx; RESET=yes] WINDOW=1; BOX=omit
1076  RSTEST [METHOD=logrank] TIME=r_mese; CENSOR=CENSOR; GROUPS=r_pz_categoria; TESTS= LOGR


Test statistics for equality of survival curves for r_pz_categoria

                            Statistic    d.f.     probability
                Log-rank        1.161       1          0.281

1077  CALC _lrpval = LOGR['logrank']$[3]
1078  TXCONSTRUCT [TEXT=text_logrank] 'Log-rank test, P value=', #_lrpval; DECIMALS = *,2
1079
1080  "Kaplan-Meier Plot"
1081  DSTART
1082  KAPLANMEIER [PRINT=graph; XUPPER=60; KEYWINDOW=0; WINDOW=1;\
1083   PLOT=reference]\
1084   TIME=r_mese; CENSOR=CENSOR.ne.0; GROUPS=r_pz_categoria
1085  DKEY   [WINDOW=7; NCOLUMNS=1; PENLABELS=!(1,2); BORDER=none; XLOFFSET=12; TPOSITION =
'inside'] \
1086        !T('CIK recipient','LD recipients');  METHOD='none'
1087  PEN 2; COLOUR=1; SYMBOL=0; ROTATION=0; SIZE=1; LABELS= text_logrank
1088  DGRAPH [WINDOW=1; KEYWINDOW=0; SCREEN=keep] 0.3; 30; PEN=2
1089  DFINISH
```
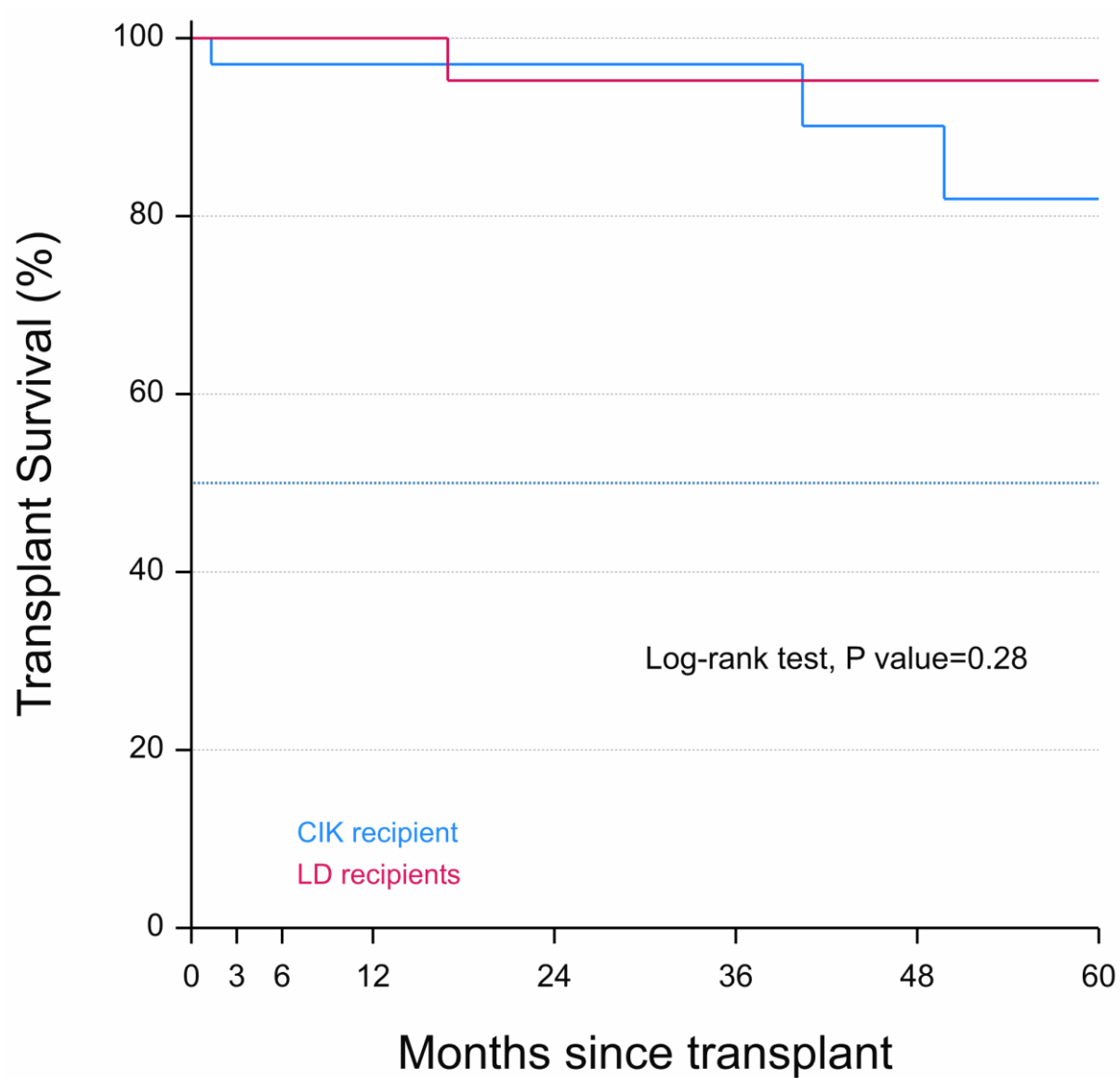
```
1090
1091   "Crude Cox PH Model"
1092   RPROPORTION [PRINT=_2lo; TIMES=r_mese; CENSORED=CENSOR; _2LOGLIKELIHOOD=llhd; ESTIMATES=
cbHR; SE=cbse] r_pz_categoria
```

Cox's proportional hazards model

```
-2 x log-likelihood: 31.220
d.f. in fitted model: 1
```

```
1093   DELETE [REDEFINE=yes] cHR, lbcHR, ubcHR, cZ, cpval
1094   SCALAR [MODIFY=yes] cHR, lbcHR, ubcHR, cZ, cpval
1095   CALC  cHR = exp(cbHR$[1])
1096   CALC  lbcHR = exp(cbHR$[1] - 1.96 * cbse$[1])
1097   &     ubcHR = exp(cbHR$[1] + 1.96 * cbse$[1])
1098   &     cZ = ABS(cbHR$[1]/cbse$[1])
1099   &     cpval = 2* (1 - CLNORMAL(#cZ;0;1))
1100
1101   TXCONSTRUCT [TEXT=crude_hr] 'Crude HR:', #cHR, \
1102     ' (95%CI: ', #lbcHR, ' to ', #ubcHR, '; P=', #cpval, ')'; DECIMALS = 2
1103   PRINT [IPRINT=*] crude_hr
```

        Crude HR:3.13 (95%CI: 0.35 to 28.10; P=0.31)

```
1104
1105   "Adjuted Cox PH Model"
1106   RPROPORTION [PRINT=_2lo; TIMES=r_mese; CENSORED=CENSOR; _2LOGLIKELIHOOD=llhd; ESTIMATES=
abHR; SE=abse] r_pz_categoria+r_don_quality_score+r_ric_CIT
```

Cox's proportional hazards model

```
-2 x log-likelihood: 22.875
d.f. in fitted model: 3
```

```
change: -8.345 on -2 d.f.
chi-square probability: 0.015
```

```
1107   DELETE [REDEFINE=yes] aHR, lbaHR, ubaHR, aZ, apval
1108   SCALAR [MODIFY=yes] aHR, lbaHR, ubaHR, aZ, apval
1109   CALC  aHR = exp(abHR$[3])
1110   CALC  lbaHR = exp(abHR$[3] - 1.96 * abse$[3])
1111   &     ubaHR = exp(abHR$[3] + 1.96 * abse$[3])
1112   &     aZ = ABS(abHR$[3]/abse$[3])
1113   &     apval = 2 * (1 - CLNORMAL(#aZ;0;1))
1114
1115   TXCONSTRUCT [TEXT=adjusted_hr] 'Adjusted HR:', #aHR, \
1116     ' (95%CI: ', #lbaHR, ' to ', #ubaHR, '; P=', #apval, ')'; DECIMALS = 2
1117   PRINT [IPRINT=*] adjusted_hr
```

        Adjusted HR:2.24 (95%CI: 0.12 to 43.41; P=0.59)