

# A Joint Survival-Longitudinal Modelling Approach for the Dynamic Prediction of Rehospitalization in Telemonitored Chronic Heart Failure Patients

Edmund Njeru Njagi\*

Joint work with Dimitris Rizopoulos, Geert Molenberghs, Paul Dendale, and Koen Willekens

*\* Interuniversity Institute for Biostatistics and statistical Bioinformatics, Universiteit Hasselt, Belgium*

# Chronic Heart Failure

- Inability of heart to pump enough for body needs.
- Compensatory mechanisms.
- Problems (decompensation).

# Rehospitalization and Telemonitoring

- Rehospitalization rates high.
- Remote monitoring after discharge.
- Predict rehospitalization.

# Data

- Chronic heart failure (CHF) study.
- Focus on 80 patients telemonitored for 6 months.
- Daily measurements.

## Data Continued

- Diastolic, and Systolic Blood Pressure,
- Heart Rate, and Weight.
- Day when patient rehospitalized.

- Various methods based on cut-offs.
- Predict rehospitalizations using whole history?
- Performance of the predictions?

# Step 1:

- Joint model for time-to-rehospitalization and marker.
- Model for hazard, given marker.
- Time-varying covariate.

# Challenges

- Longitudinal not at every event time.
- Censoring.
- Longitudinal with error.



## Step 2:

- Conditional survival probabilities.
- $\text{Prob}(T_i^* \geq t + \Delta t | T_i^* > t)$  e.g.  $t + \Delta t = 20 + 5$
- Equivalently,  $\text{Prob}\{T_i^* \in (t, t + \Delta t] | T_i^* > t\}$

## Step 2 Continued:

- Confidence intervals for these estimates.
- Additional information for intervention decisions.

## Step 3 Continued:

- Quantify predictive performance.
- Based on Area Under ROC curve (AUC) ideas.

## Step 3 Continued:

- For given  $t$  and given  $\Delta t$  ( $AUC(t)$ ).
- For range of  $t$ 's and given  $\Delta t$  (D.D.I.)
- D.D.I. Dynamic discrimination index.

## Step 3 Continued:

- Logic:

$$\text{Prob}[\pi_i(t+\Delta t|t) < \pi_j(t+\Delta t|t) | \{T_i^* \in (t, t+\Delta t]\} \cap \{T_j^* > t+\Delta t\}]$$

# Model

- Time to first rehospitalization:

$$h_i(t|\mathcal{M}_i(t), \mathbf{w}_i) = \rho t^{\rho-1} \exp\{\gamma_0 + \gamma' \mathbf{w}_i + \alpha m_i(t)\},$$

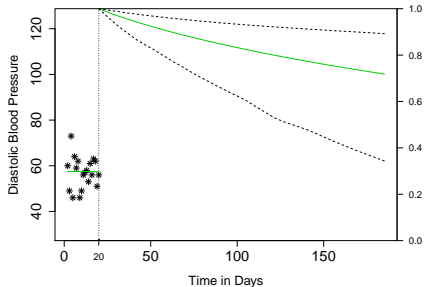
- Longitudinal DBP:

$$y_i(t) = m_i(t) + \varepsilon_i(t) = \beta_0 + \beta_1 t + \mathbf{b}_{0i} + \varepsilon_i(t),$$

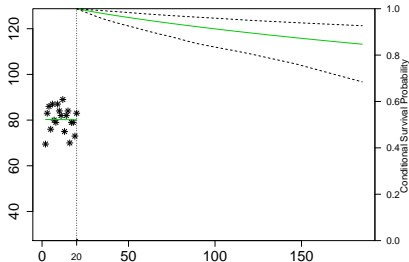
- “Non-informativeness”.

# Conditional Survival Probabilities, Day 20

Subject 1



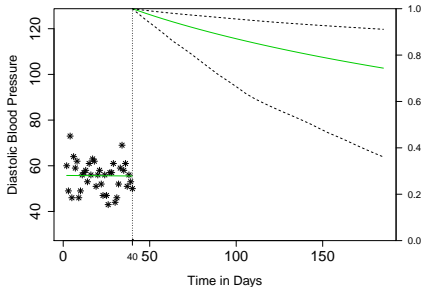
Subject 2



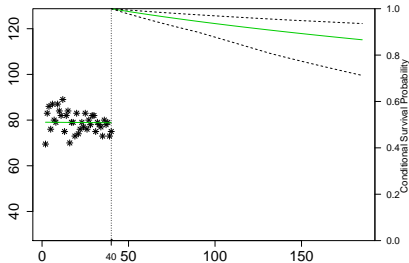
Conditional survival probabilities at each of the remaining time points till study end.

# Conditional Survival Probabilities, Day 40

Subject 1



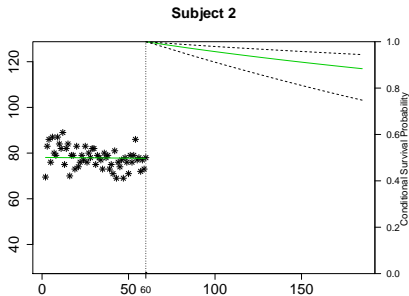
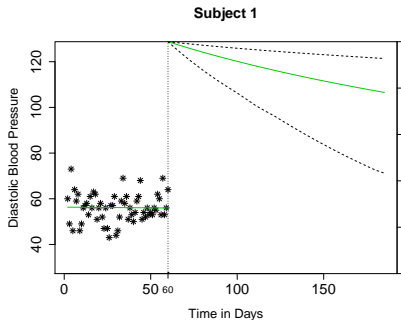
Subject 2



Conditional survival probabilities at each of the remaining time points till study end.



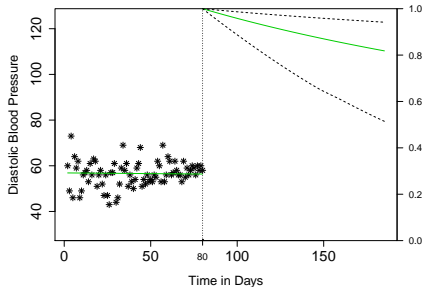
# Conditional Survival Probabilities, Day 60



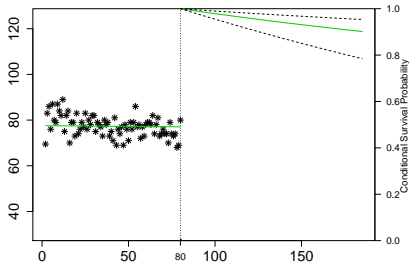
Conditional survival probabilities at each of the remaining time points till study end.

# Conditional Survival Probabilities, Day 80

Subject 1

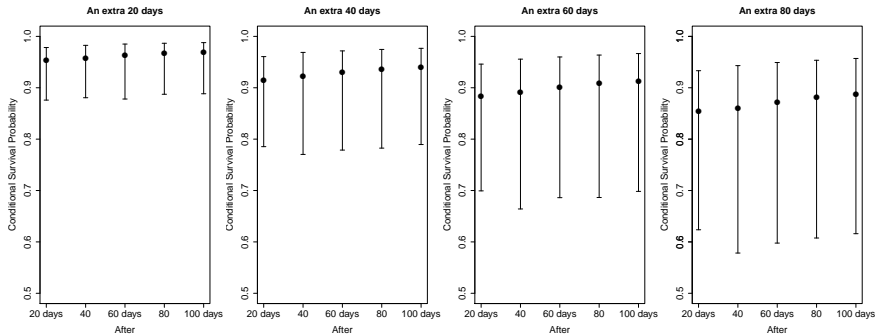


Subject 2



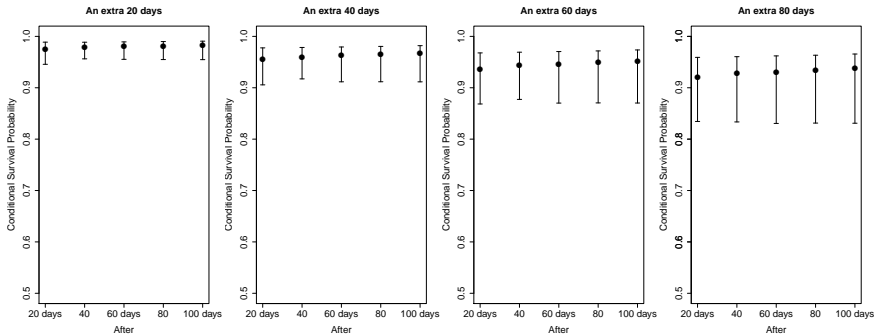
Conditional survival probabilities at each of the remaining time points till study end.

# Dynamic Updates of Survival Probabilities



Patient 1: Conditional surv. probs. of an extra 20, 40, 60 and 80 days, with each additional 20 days' measurements.

# Dynamic Updates of Survival Probabilities



Patient 2: Conditional surv. probs. of an extra 20, 40, 60 and 80 days, with each additional 20 days' measurements.

# Predictive Performance

$\Delta t$	$t$	AUC( $t$ )	DDI
2	14	0.6944	0.4875
	28	0.7429	
	42	0.9552	
	84	0.3770	
	168	0.0862	
4	14	0.6944	0.4949
	28	0.7714	
	42	0.8955	
	84	0.3770	
	168	0.0862	
8			0.5814
16			0.5745

# Predictive Performance



$\Delta t$	DDI
2	0.6698
4	0.6698
8	0.7433
16	0.6576





- The probabilities and their confidence intervals.
- Additional information to aid intervention decisions.
- Predictive performance quantified.



## More Work On:

- All markers simultaneously.
- Recurrent nature of the time-to-hospitalization.
- Consider more parameterizations, e.g. value plus slope.



-  Dendale, P., De Keulenaer, G., Troisfontaines, P., Weytjens, C. *et al.* (2011). Effect of a telemonitoring-facilitated collaboration between general practitioner and heart failure clinic on mortality and rehospitalization rates in severe heart failure: the TEMA-HF 1 (TElemonitoring in the MAnagement of Heart Failure) study. *European Journal of Heart Failure*, **14**, 333–340.
-  Njagi, E. N., Rizopoulos, D., Molenberghs, G., Dendale, P., and Willekens, K. (2013). A joint survival-longitudinal modelling approach for the dynamic prediction of rehospitalization in telemonitored chronic heart failure patients. *Statistical Modelling*, **13**, 179–198

-  Rizopoulos, D. (2010). JM: An R package for the joint modelling of longitudinal and time-to-event data. *Journal of Statistical Software*, **35**(9), 1–33.
-  Rizopoulos, D. (2011). Dynamic Predictions and Prospective Accuracy in Joint Models for Longitudinal and Time-to-Event Data. *Biometrics*, **67**, 819–829.
-  Rizopoulos, D. (2012a). *Joint Models for Longitudinal and Time-to-Event Data*. Boca Raton: Chapman and Hall/CRC.
-  Rizopoulos, D. (2012b). Package “JM”: R package version 1.0-0, URL <http://cran.r-project.org/web/packages/JM/JM.pdf>.

-  Tsiatis, A. and Davidian, M. (2004). Joint modeling of longitudinal and time-to-event data: an overview. *Statistica Sinica*, **14**, 809–834.
-  Verbeke, G., Molenberghs, G., and Rizopoulos, D. (2010). Random effects models for longitudinal data. *Longitudinal Research with Latent Variables*. K. van Montfort, H. Oud, and Al Satorra (Eds.). New York: Springer, pp. 37–96.

# Thank you for Your Attention.