



**HAL**  
open science

## Clustering of recurrent events data applied to the re-admission of elderly people at hospital

Vincent Vandewalle, Genia Babykina, Jean-Baptiste Beuscart, Jesus A. Carretero Bravo, Fabien Visade

### ► To cite this version:

Vincent Vandewalle, Genia Babykina, Jean-Baptiste Beuscart, Jesus A. Carretero Bravo, Fabien Visade. Clustering of recurrent events data applied to the re-admission of elderly people at hospital. European Conference on Data Analysis 2022, Sep 2022, Naples, Italy. hal-03899727

**HAL Id: hal-03899727**

**<https://inria.hal.science/hal-03899727>**

Submitted on 15 Dec 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Clustering of recurrent events data applied to the re-admission of elderly people at hospital

Vincent Vandewalle

Joint work with Génia Babykina, Jean-Baptiste Beuscart, Jesús Á. Carretero Bravo, Fabien Visade

European Conference on Data Analysis 2022  
Thursday, September 15, 2022

UNIVERSITÉ  
CÔTE D'AZUR 

 Université  
de Lille

Evaluation des technologies de santé et des pratiques médicales  
**M&TricS**  
ULR 2694

*Inria*

 UCA | Universidad  
de Cádiz

1. Re-admission of elderly people data
2. Model-based clustering of counting process
3. Results on simulated data
4. Results on re-admission data
5. Conclusion and perspectives

1. Re-admission of elderly people data
2. Model-based clustering of counting process
3. Results on simulated data
4. Results on re-admission data
5. Conclusion and perspectives

## DAMAGE cohort (Deschasse et al., 2021)

- Prospective multi-centric cohort of patients of 75 years old or more
- Hospitalised in France (Hauts de France and Normandy regions)
- 3081 patients of whom 1531 patients have had at least one re-hospitalisation
- Socio-demographic, health, geriatric variables

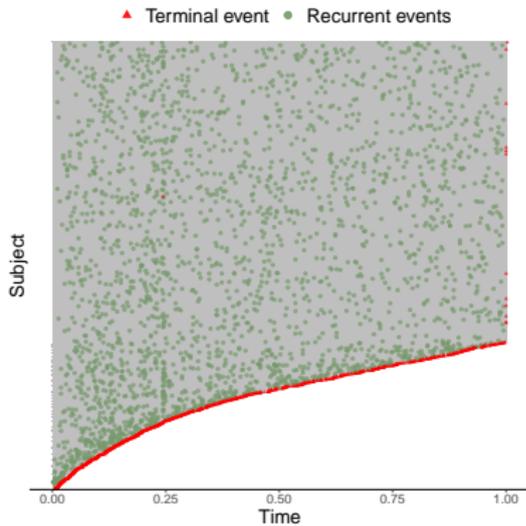
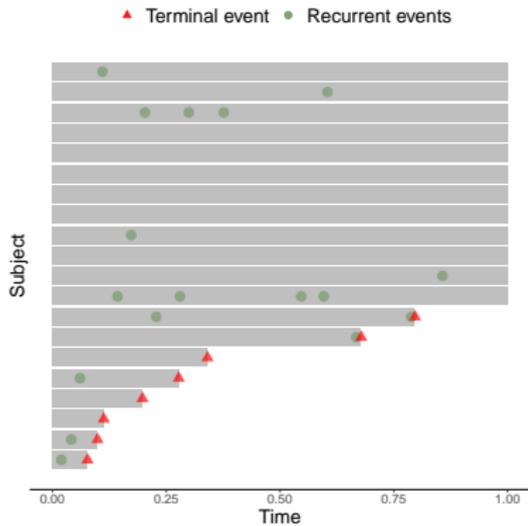
## Recurrent event considered

Successive readmission to the hospital

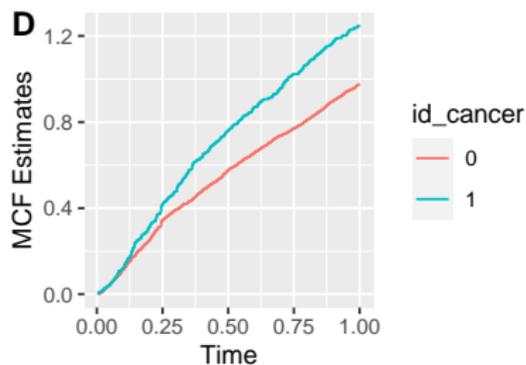
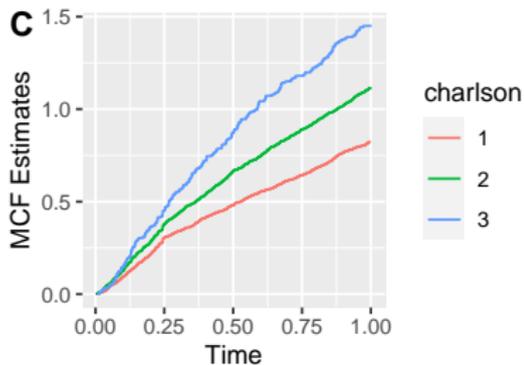
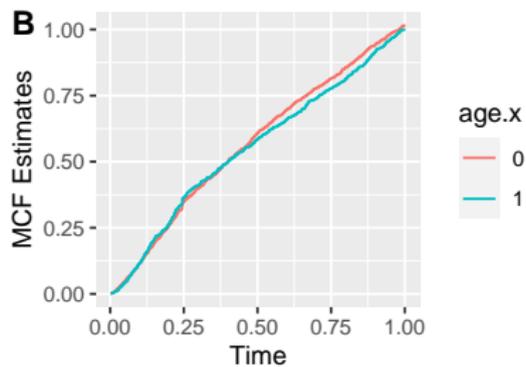
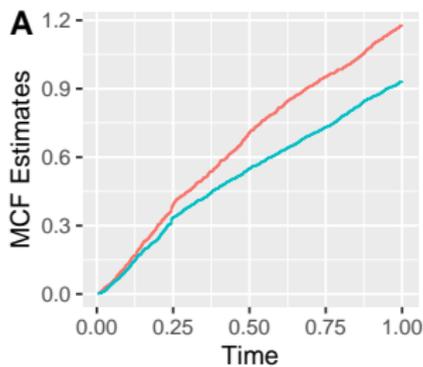
## Medical questions

- Is the readmission process correlated with some clinical variables?
- Is the intensity of the readmission process correlated with survival?

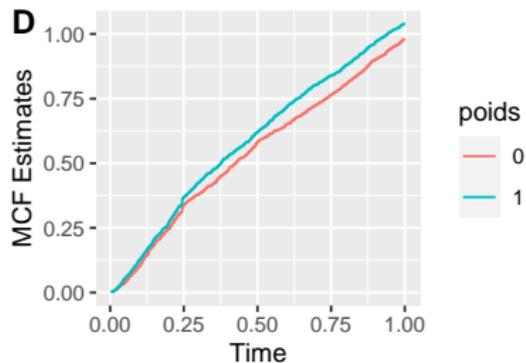
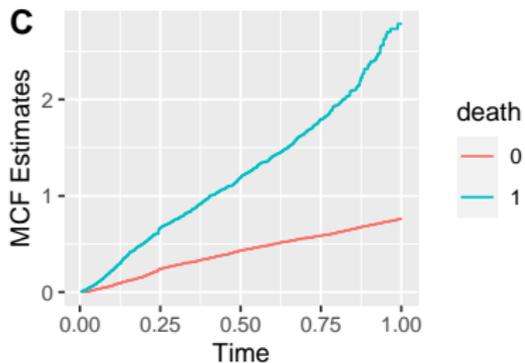
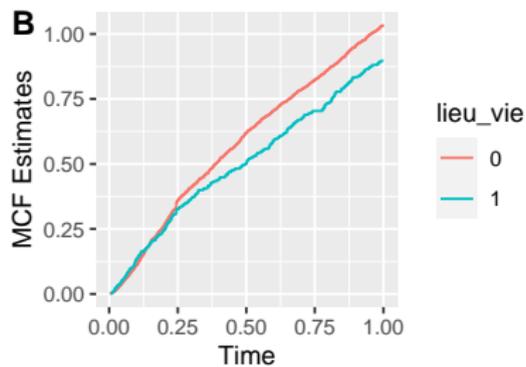
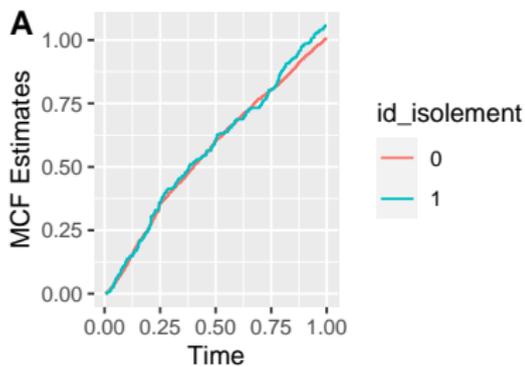
# Visualization of recurrent events



# Correlation of the event with other variables (1/2)



# Correlation of the event with other variables (2/2)



# Goals of the proposed approach

## Identify cluster of patients

- Adapt the treatment to each cluster
- Avoid therapeutic obstinacy

## Assumptions

- Patients in a same cluster should follow the same recurrent events distribution
- The effect of covariates can be different in each cluster

## Proposal

Assume that the data come from a **mixture of counting processes** with **intensity depending on covariates**

1. Re-admission of elderly people data
2. Model-based clustering of counting process
3. Results on simulated data
4. Results on re-admission data
5. Conclusion and perspectives

## Mixtures in survival analysis on time to first event: Cox and extensions

- Different censoring schemes (Peng, 2000)
- Censored data with high-dimensional covariates (Bussy et al., 2019)

## Many applications in the analysis of recurrent events

Hospital readmissions, disease recurrences, repeated failures of industrial systems

## Extensions of Cox model with recurrence: counting point process setting

- Andersen-Gill model (Andersen and Gill, 1982)
- Frailty models (Aalen, 1988; Oakes, 1992)

## Mixtures of recurrent events

- Discrete-time duration model (McDonald and Rosina, 2001; Dean, Bauer, and Shanahan, 2014)
- Frailty-mixture models for recurrent event of *cure models* in health applications (Xu et al., 2012; Tawiah, McLachlan, and Ng, 2020).

Fully parametric mixture model based on the Andersen-Gill model with covariates

## Notations

- $(T_{ij})_{j \geq 1}$  : the times of successive events for  $i$  ( $i = 1, \dots, n$ )
- $N_i(t)$  the number of events occurred to individual  $i$
- $Z_i \in \{0, 1\}^K$  the cluster of  $i$  in binary coding
- $\{N_i(t)\}_{t \geq 0}$  given  $Z_{ik} = 1$  characterised by intensity  $\lambda_{ik}(t)$

$$\lambda_{ik}(t)dt = \mathbb{E} [dN_i(t) | \mathcal{F}(t-), \mathbf{X}_i(t), Z_{ik} = 1],$$

$\mathbf{X}_i(t)$  the covariate process and  $\mathcal{F}(t-)$  the filtration generated by the process

## Intensity of the process in cluster $k$

$$\lambda_{ik}(t) = \lambda_{0k}(t) \exp(\mathbf{X}_i \boldsymbol{\beta}_k^\top)$$

with baseline Weibull intensity  $\lambda_{0k}(t) = \gamma_{1k} \gamma_{2k} t^{\gamma_{2k}-1}$

## Likelihood of path $i$

$$p(\mathbf{t}_i | \mathbf{X}_i; \boldsymbol{\theta}) = \sum_{k=1}^K \pi_k \underbrace{\prod_{j=1}^{n_i} [\lambda_{ik}(t_{ij}, \boldsymbol{\theta}_k)] \times \exp\left(-\int_0^{\tau_i} \lambda_{ik}(u, \boldsymbol{\theta}_k) du\right)}_{p(\mathbf{t}_i | \mathbf{X}_i, Z_{ik}=1; \boldsymbol{\theta})}.$$

## EM algorithm

Starting from  $\boldsymbol{\theta}^{(0)}$ , alternate the following two steps until convergence

- **E-step** : update the class membership matrix at iteration  $h$

$$\rho_{ik}^{(h)} = \frac{\pi_k^{(h-1)} p(\hat{\boldsymbol{\theta}}_k^{(h-1)})}{\sum_{l=1}^K \pi_k^{(h-1)} p(\hat{\boldsymbol{\theta}}_k^{(h-1)})},$$

- **M-step** : update model parameter by maximizing the expectation of the log-likelihood

$$\hat{\boldsymbol{\theta}}_k^{(h)} = \underset{\boldsymbol{\theta}}{\operatorname{argmax}} \sum_{i=1}^n \rho_{ik}^{(h)} \log p(\mathbf{t}_i | \mathbf{X}_i, Z_{ik} = 1; \boldsymbol{\theta})$$

## BIC criterion

$$\text{BIC}(K) = \ell(\hat{\boldsymbol{\theta}}; K) - \frac{\nu_K}{2} \log n$$

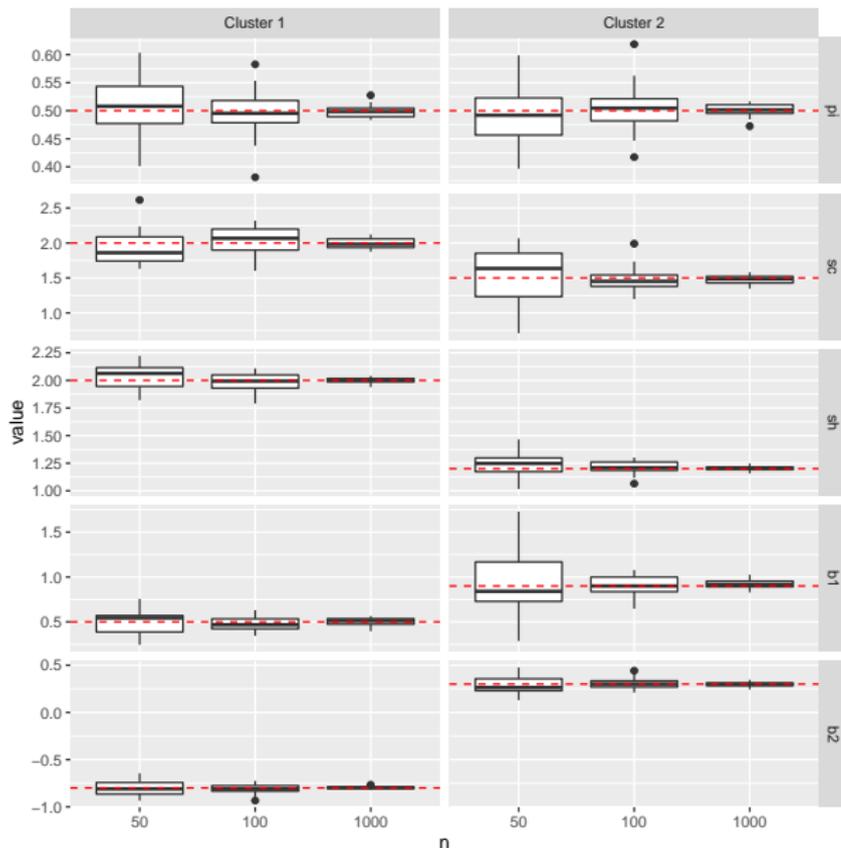
with  $\nu_K = K(d + 2)$ , and  $n$  the number of paths

## Remark

The choice of the covariates could also be performed using BIC

1. Re-admission of elderly people data
2. Model-based clustering of counting process
3. Results on simulated data
4. Results on re-admission data
5. Conclusion and perspectives

# Consistency of the parameters estimation



- 20 replicates
- Bayes error: 14.5%
- Consistency of the parameters estimation

1. Re-admission of elderly people data
2. Model-based clustering of counting process
3. Results on simulated data
4. Results on re-admission data
5. Conclusion and perspectives

# Output of the model

The variables `sex` and `age` are taken into account as covariates

BIC selects 2 clusters

Parameters of the clusters

	$\hat{\pi}_k$	$\hat{\gamma}_{1k}$	$\hat{\gamma}_{2k}$	$\hat{\beta}_{1k}$	$\hat{\beta}_{2k}$
Class 1	0.34	2.56	0.97	-0.16	-0.09
Class 2	0.66	0.58	0.85	-0.43	0.23

Distribution of the number of events given to the cluster (%)

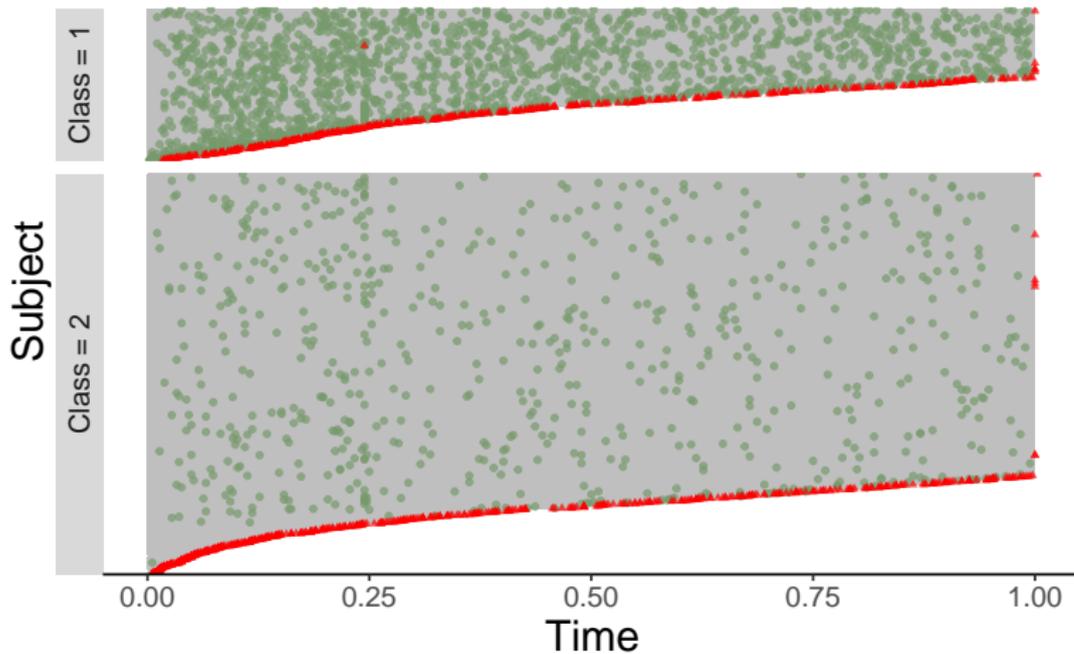
	1	2	3	4	5	6	7	8	9
Class 1	0	29	44	16	7.3	1.9	1.2	0.6	0.2
Class 2	70	30	0.1	0	0	0	0	0	0

Interpretation with respect to other covariates

	age.x	sex	death
Class 1	30%	63%	54%
Class 2	31%	67%	25%

# Visualisation of the clusters

▲ Terminal event ● Recurrent events



1. Re-admission of elderly people data
2. Model-based clustering of counting process
3. Results on simulated data
4. Results on re-admission data
5. Conclusion and perspectives

## Conclusion

- Able to detect different recurrence types in the data
- Not uniquely based on the number of event but also on the variation of the intensity
- Additional interpretation of the re-admission process

## Perspectives

- Make depend the prior probability on baseline covariates
- Perform prognosis of the patient cluster
- Study how to integrate the information on the patient cluster at baseline to medical practices

-  Aalen, Odd O (1988). “Heterogeneity in survival analysis”. In: *Statistics in medicine* 7.11, pp. 1121–1137.
-  Andersen, Per Kragh and Richard D Gill (1982). “Cox’s regression model for counting processes: a large sample study”. In: *The annals of statistics*, pp. 1100–1120.
-  Bussy, Simon et al. (2019). “C-mix: A high-dimensional mixture model for censored durations, with applications to genetic data”. In: *Statistical methods in medical research* 28.5, pp. 1523–1539.
-  Dean, Danielle O, Daniel J Bauer, and Michael J Shanahan (2014). “A discrete-time Multiple Event Process Survival Mixture (MEPSUM) model.”. In: *Psychological methods* 19.2, p. 251.
-  Deschasse, G. et al. (2021). “Development of a predictive score for mortality at 3- and 12-month after discharge from an acute geriatric unit as a trigger for advanced care planning”. In.
-  McDonald, John W and Alessandro Rosina (2001). “Mixture modelling of recurrent event times with long-term survivors: Analysis of Hutterite birth intervals”. In: *Statistical Methods and Applications* 10.1, pp. 257–272.

-  Oakes, David (1992). “Frailty models for multiple event times”. In: *Survival analysis: State of the art*. Springer, pp. 371–379.
-  Peng, Fengchun (2000). “A mixture-model approach to the analysis of survival data”. In: *Generalized Linear Models: A Bayesian Perspective*. CRC Press. Chap. 15.
-  Tawiah, Richard, Geoffrey J McLachlan, and Shu Kay Ng (2020). “Mixture cure models with time-varying and multilevel frailties for recurrent event data”. In: *Statistical methods in medical research* 29.5, pp. 1368–1385.
-  Xu, Ying et al. (2012). “Estimation of summary protective efficacy using a frailty mixture model for recurrent event time data”. In: *Statistics in medicine* 31.29, pp. 4023–4039.