Identification of frail individuals in a Veneto Local Health Unit: A proposal based on partially ordered sets

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Objectives

1. Counting **frail** subjects, with special care needs.
2. Identify a **common criterion** to define frail subjects.
3. Find algorithms to quickly detect those people also in emergency situations.
4. **Detecting** vulnerable individuals
5. Obtaining a **scale** level of fragility

Having an updated frail people list, the Local Health Unit can

- **Program** interventions and distributions of resources
- **Monitor** environmental risks

Definitions of frailty

Paradigms to define **frailty**:

Bio-psycho-social paradigm

"Frailty is a **dynamic** *state affecting an individual who experiences* **losses** *in one or more* **domains** *of human functioning (physical, psychological, social), which is caused by the influence of a* **range of variables** *and which increases the* **risk of adverse outcomes**.*"*
(Gobbens et al., 2010)

Biomedical paradigm

"Frailty can be defined as a physiologic state of increased **vulnerability** *to stressors that results from decreased* **physiologic reserves**, *and even dysregulation, of* **multiple physiologic systems**.*"*
(Fried et al., 2004)

Definitions of frailty

Frailty Index in relation to the accumulation of deficits

"An individual's frailty index score reflects the proportion of potential **deficits** *present in that person, and indicates the likelihood that frailty is present."*
(Rockwood & Mitnitski, 2007)
Rockwood and Mitnitsky considered symptoms, signs, diseases, and disabilities as deficits and they combined them in a **Frailty Index**.

Definitions of frailty

A unique definition does not exist in literature, however it is possible to highlight some common elements to describe frailty (Gobbens et al., 2010):

- Multidimensionality
- Continuity (degenerative process)
- Declining reserve capacity for dealing with stressor (less homeostasis).
- Increased susceptibility to adverse outcomes as death and emergency hospitalization
- Common in elderly

Operative definition

We have considered two operative frailty definitions currently used in Italy:

1. Frail people according to the **Adjusted Clinical Groups** (ACG) system, adopted in Veneto Region, The Johns Hopkins ACG System (2011);
2. Frail people according to the risk of adverse outcomes, **Combined Statistical Model** (MoSaiCo) adopted in Ravenna, (Falasca et al., 2011).

In addition, we have proposed a new approach to measure frailty, based on **partially ordered sets** (Poset).

Data and record linkage

Sources

- Healthcare databases of ULSS15 (Alta Padovana), years 2012, 2013 and 2014.
- Several dataflows have been used in the analysis, such as hospital discharge records, participation in the prescription charges, accident & emergency data, territorial drug prescriptions, home care services, mental health services data and outpatient data.

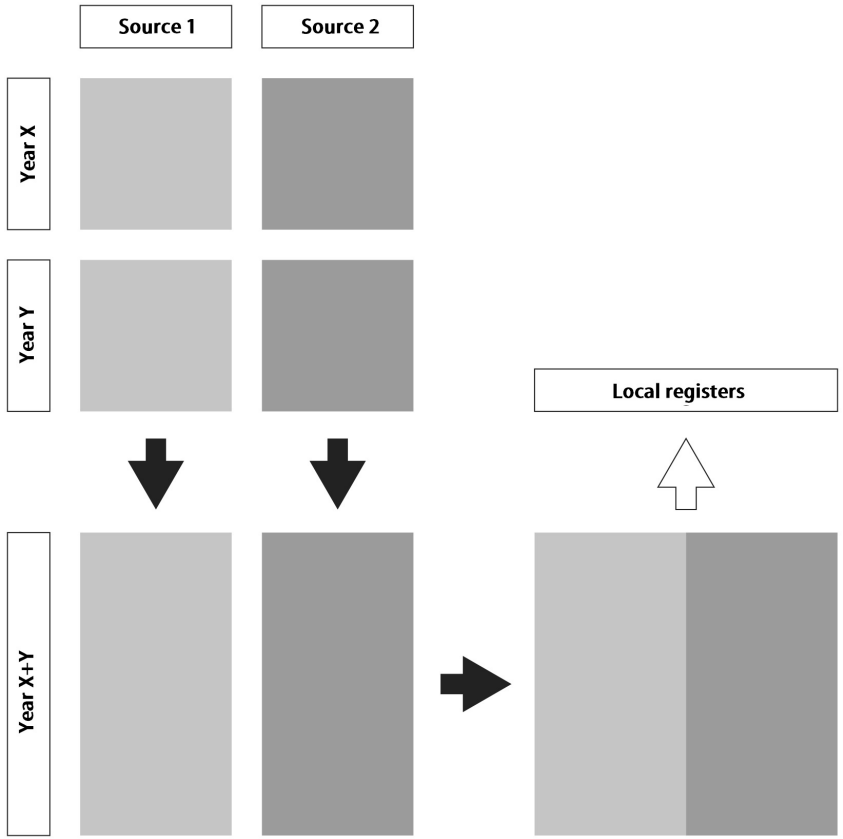
Data and record linkage

Record linkage

We have linked the data sources of the three years with the health registry using the patient unique identification number, reaching a high linkage percentage (between 85.2% and 92.6%).

Final dataset

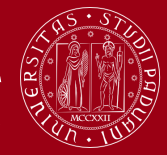
The final dataset contains all the relevant characteristics and events that happened to the considered population in the period 2012-2014.



The first approach: Frail people according to the Adjusted Clinical Groups (ACG) system

The Adjusted Clinical Groups (ACG) system by Johns Hopkins has been adopted in Veneto in 2012.
It is a *"case-mix grouper"* and it provides the *Medically Frail Condition Marker*.
The **Medically Frail Condition Marker** is a **dichotomous variable** that indicates whether an enrollee over the age of 18 has a **diagnosis** falling within anyone of **10 clusters** that represent medical problems associated with frailty.

The first approach: Frail people according to the Adjusted Clinical Groups (ACG) system



Some examples of diagnoses from the frailty condition list according to ACG are:

Malnutrition and/or Catabolic Nutritional Illness Nutritional marasmus, Failure to thrive

Dementia Senile dementia with delusional or depressive features, Senile dementia with delirium

Severe Vision Impairment Profound impairment in both eyes, Moderate or severe impairment

Decubitus Ulcer Decubitus Ulcer

Major Problems of Urine Retention or Control Incontinence without sensory awareness, Continuous leakage

The first approach: Frail people according to the Adjusted Clinical Groups (ACG) system

Loss of Weight Abnormal loss of weight and underweight, Feeding difficulties and mismanagement

Absence of Fecal Control Incontinence of feces

Social Support Needs Lack Of Housing, Inadequate Housing, Inadequate material resources

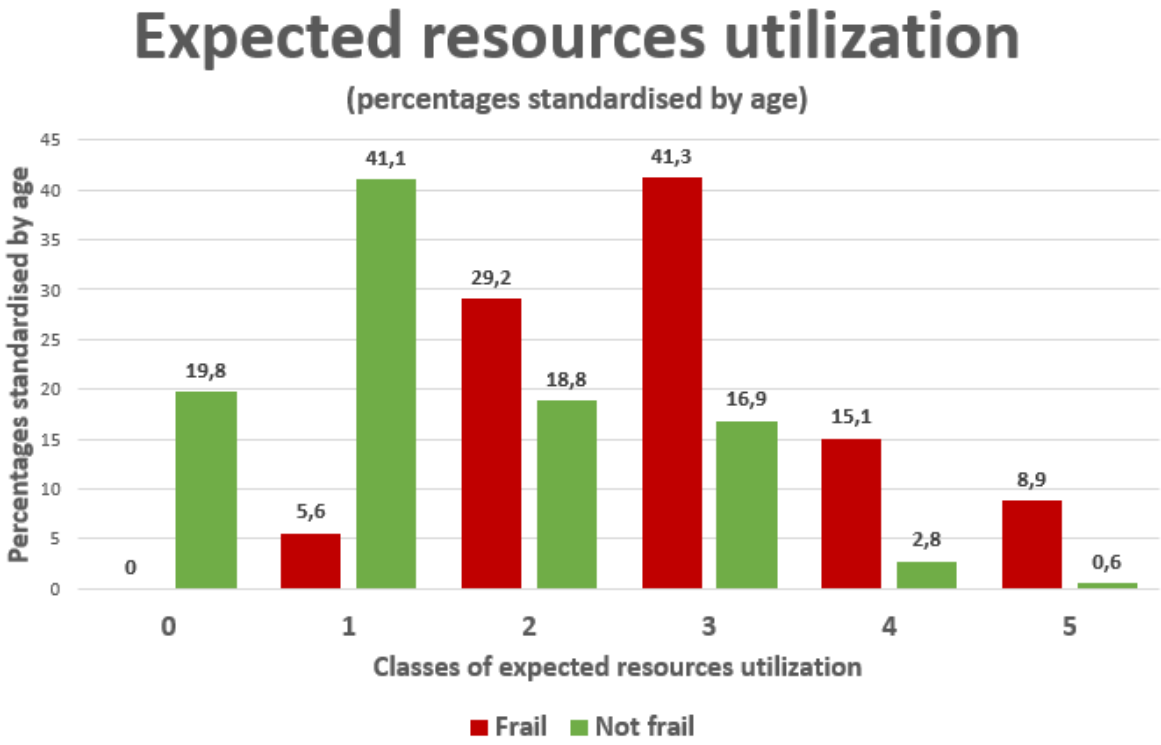
Difficulty in Walking Difficulty in walking, Abnormality of gait

Fall Fall On Stairs Or Steps, Fall From Wheelchair

The first approach: Frail people according to the Adjusted Clinical Groups (ACG) system

1531 frail people in ULSS15 in 2013:

- More serious health conditions
- Higher expected resources utilization .



ACG validation: first regression

Dependent variable

$$y = \begin{cases} 1 & \text{dead or emergency hospitalized in 2014} \\ 0 & \text{otherwise} \end{cases}$$

Independent variables

Frailty according to the Medically Frail Condition Marker (dichotomous variable) by ACG

Remarks

- Balanced sample of data with respect to y.
- Sensitivity 4%.

The Medically Frail Condition Marker is **not enough** to predict frailty negative outcomes.

ACG validation: second regression

Dependent variable

$$y = \begin{cases} 1 & \text{dead or emergency hospitalized in 2014} \\ 0 & \text{otherwise} \end{cases}$$

Independent variables

- Frailty according to ACG;
- Age as an **ordinal** variable: young (age$\leq$20), adult (21$<$age$<$69), elderly (age$\geq$70);
- Gender;
- Other risk factors.

ACG validation: second regression

Variable	Odds Ratio	CI 95%
Frailty according to ACG	1,531**	1,035-2,264
Gender (men vs women)	0,687***	0,647-0,729
Home care services	2,039***	1,622-2,562
Charlson Index	1,863***	1,501-2,313
Poliprescription	1,630***	1,489-1,785
Disability	2,102***	1,865-2,370
Hospitalization	1,717***	1,543-1,910
First Aid	1,617***	1,494-1,749
Psychiatric services	2,090***	1,703-2,566
Young (vs Adult)	0,470***	0,430-0,515
Elderly (vs Adult)	2,563***	2,351-2,794
3 + Diagnosis	1,442**	1,091-1,906
Cancer	1,516***	1,182-1,944
Probability Level	0,4	
Correctly classified	69%	
Sensitivity	65,7%	
Specificity	72,3%	
False positive	29.8%	
False negative	32.1%	
ROC Area	0,762	
Pseudo R^2	0.2093	

Logistic regression on a balanced sample of data with respect to the dependent variable (dead or emergency hospitalized in 2014). (Significance levels: ***=0.01, **=0.05, *=0.1)

- The Medically Frail Condition Marker has a significant impact in this model.
- **Other risk factors have higher impact than the MFCM.**

Combined Statistical Model (MoSaiCo) from ULSS of Ravenna (Falasca et al., 2011)

Dependent variable

$$y = \begin{cases} 1 & \text{dead or emergency hospitalized} \\ 0 & \text{otherwise} \end{cases}$$

Independent variables

31 independent variables selected from a set of 57

Remarks

- Reasonable predictive power (ROC Area 0.774).
- Large number of independent variables.
- Some variables have a low impact or are unavailable in ULSS15.

The application of the MoSaiCo in a reduced form, in ULSS15

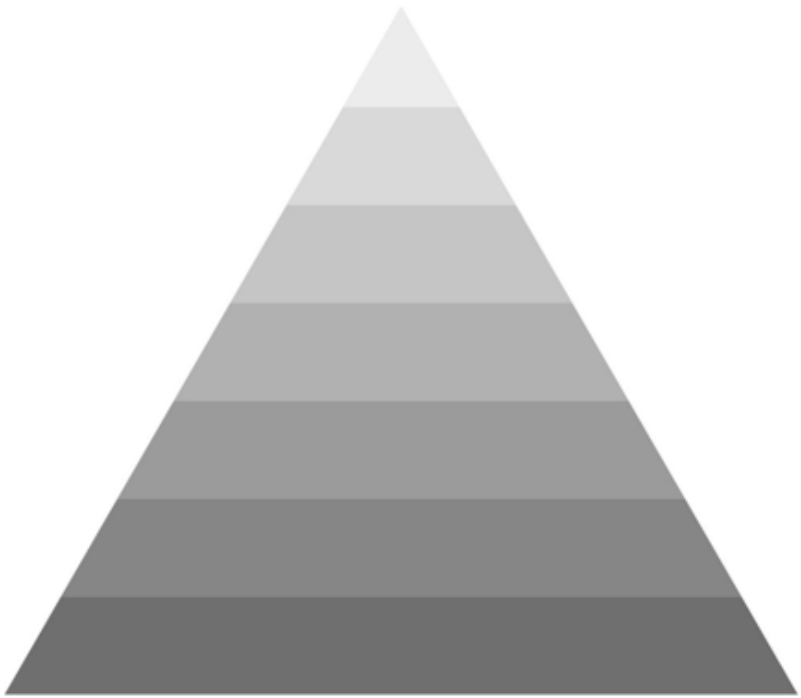
Variable	Odds Ratio	IC 95%	Entrance
Adult (vs Young)	0.458***	0.419-0.502	1
Elderly (vs Young)	2.764***	2.534-3.014	1
Home care services	1,990***	1,589-2,491	8
Cancer	1,648***	1,280-2,121	12
Charlson Index	1,714***	1,370-2,143	7
Congestive heart failure	1,614**	1,092-2,388	11
3 + Diagnosis	1,573***	1,191-2,077	10
Poliprescription	1,657***	1,514-1,815	4
Disability	1,849***	1,644-2,081	3
Hospitalization	1,708***	1,535-1,900	2
First Aid	1,503***	1,390-1,625	6
Psychiatric services	1,862***	1,532-2,262	9
Deprivation Index	1,087**	1,009-1,172	13
Gender (men vs women)	0,673***	0,634-0,715	5
Probability Level	0,42		
Correctly classified	62.9%		
Sensitivity	67,7%		
Specificity	70.7%		
False positive	30.2%		
False negative	31.4%		
ROC Area	0,764		
Pseudo R^2	0.210		

Logistic regression on a balanced sample of data with respect to the dependent variable (dead or emergency hospitalized in 2014). (Significance levels: ***=0.01, **=0.05, *=0.1)

- Sample: 11130 cases and 11130 controls.
- More thrifty (only 13 variables).
- Area under ROC curve close to the ULSS of Ravenna.

Stratification of users according to the risk of negative outcomes

Using predicted values, we created 9 risk levels of negative outcomes related to the frailty condition:



Level	Predicted values	Subjects
9	[0.9; 1)	4.282
8	[0.8; 0.9)	6.524
7	[0.7; 0.8)	9.743
6	[0.6; 0.7)	14.382
5	[0.5; 0.6)	22.699
4	[0.4; 0.5)	76.351
1, 2, 3	(0; 0.4)	115.665

A new approach to measure frailty, based on partially ordered sets (Poset)

- We need a frailty measure.
- A measure that should be robust for more than one **outcome**.
- Considering together **ordinal and dichotomous** variables.
- Considering together variables that represent **both events and characteristics**.
- An index of frailty based on the sum of events (such as Rockwood frailty index, Rockwood & Mitnitski (2007)) is not appropriate.

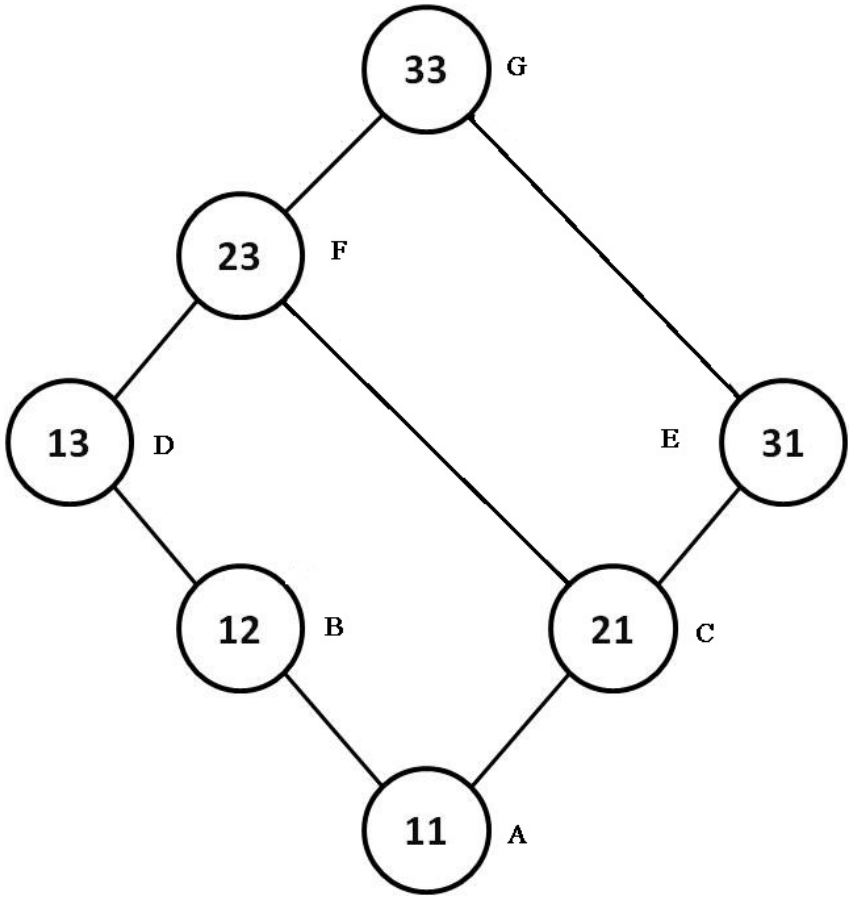
A new approach to measure frailty, based on partially ordered set (Poset)

We proposed a new approach to measure frailty, based on partially ordered sets (Poset) to use the entire amount of ordinal information from our data. With this method we are not strictly bound to one outcome, and we do not add arbitrary choices.
Brüggemann & Carlsen (2011), Brüggemann & Patil (2011), Caperna (2016).
Each subject is identified by a **profile** corresponding to its own characteristics with respect to the considered set of variables.

Partially ordered set

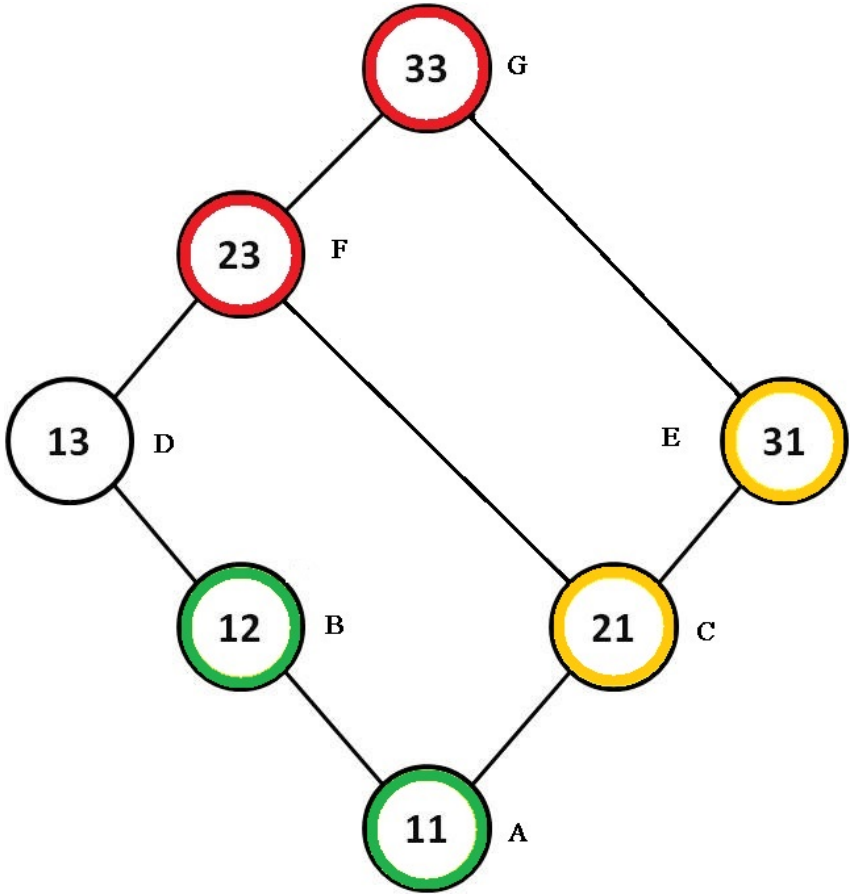
A toy example to introduce some theorical ideas about partially ordered set.
The considered variables should have the same direction.

Subject	Drugs	First Aid
A	1	1
B	1	2
C	2	1
D	1	3
E	3	1
F	2	3
G	3	3



Key concepts

- **Down Set**
  $O(x) := \{y \in X : y \leq x\}$.
- **Successor Set**
  $S(x) := O(x) - \{x\}$.
  (**D**'s Successor Set)
- **Up Set** $F(x) := \{y \in X : x \leq y\}$.
- **Predecessor Set**
  $P(x) := F(x) - \{x\}$.
  (**D**'s Predecessor Set)
- Set of **comparable objects**
  $C(x) = F(x) \cup O(x)$.
- Set of **incomparable objects**
  $U(x) := \{y \in X : y || x\}$
  (Objects incomparable with **D**) .



Linear extensions

G	G	G	G	G	G	G	G	G
E	E	E	F	F	F	F	F	F
F	F	F	E	E	E	D	D	D
C	D	D	C	D	D	B	E	E
D	C	B	D	C	B	E	B	C
B	B	C	B	B	C	C	C	B
A	A	A	A	A	A	A	A	A

G	$\Rightarrow$	7	$\Rightarrow$	1
F	$\Rightarrow$	5.67	$\Rightarrow$	0.78
E	$\Rightarrow$	4.89	$\Rightarrow$	0.65
D	$\Rightarrow$	4.11	$\Rightarrow$	0.52
C	$\Rightarrow$	2.78	$\Rightarrow$	0.30
B	$\Rightarrow$	2.56	$\Rightarrow$	0.26
A	$\Rightarrow$	1	$\Rightarrow$	0

- It is possible to get **many combinations**, bacause the relative positions of two incomparable subjects are interchangeable.
- The **average rank** becomes a measure of the vulnerability of individuals.

Approximations for the calculation of average ranks

- **Problem:** with many profiles the computation of the average rank is very intensive.
- There are manly two approaches to solve this problem:
  - Sampling of linear extentions (Fattore (2015) and others)
  - Approximation of average rank (Brüggemann & Carlsen (2011) and others)

Approximation of average rank: extended Local Partial Order Model (Brüggemann & Carlsen, 2011)

$$H(x) = ||O(x)|| + \sum_{y \in U(x)} \frac{||O(x) \cap U(y)||}{||O(x) \cap U(y)|| + ||F(x) \cap U(y)||}$$

- The first part of the equation describes the lowest possible height of x, according to the number of Down Set elements.
- The sum quantifies the contribution of each object of U(x).
- The quotient can be interpreted as probability that an object $y \in U(x)$ finds a position below x in a linear extension. So, any object $y \in U(x)$ contributes to H(x) according to its probability to be ranked below x in a linear extension.

Equivalence classes and a LPOMext modification (Caperna, 2016)

- It is possible to deal with identical rows in the data matrix as they are equivalent objects, making **equivalence classes**.
- According to LPOMext, an average rank is associated with each equivalence class without taking into account the **size** of the latter.
- It seems appropriate to take into account also the value of the **frequency** of each equivalence class of f(x) in the average rank computation (Caperna, 2016).

Equivalence classes and a LPOMext modification

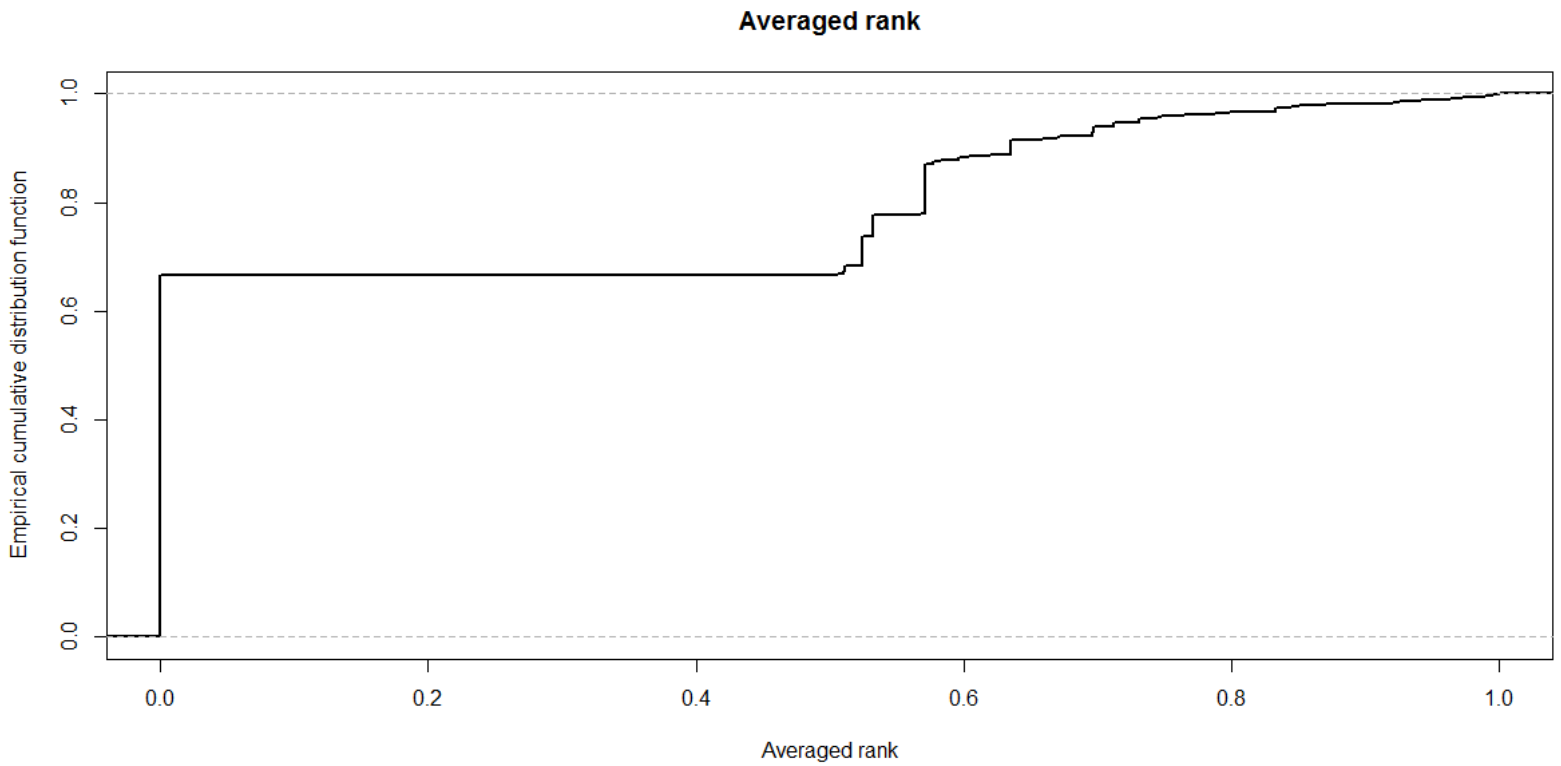
$$H(x) = max\{1, f(O(x)) - \frac{1}{2}f(x)\}+$$
$$+ \sum_{y \in U(x)} \frac{||O(x) \cap U(y)||}{||O(x) \cap U(y)|| + ||F(x) \cap U(y)||} \cdot f(y)$$

- The first part of the equation describes the lowest possible height of x on average, according to the number of Down Set elements.
- The second part weights the contribution of incomparable objects with their frequencies.

POSET approach to measure frailty

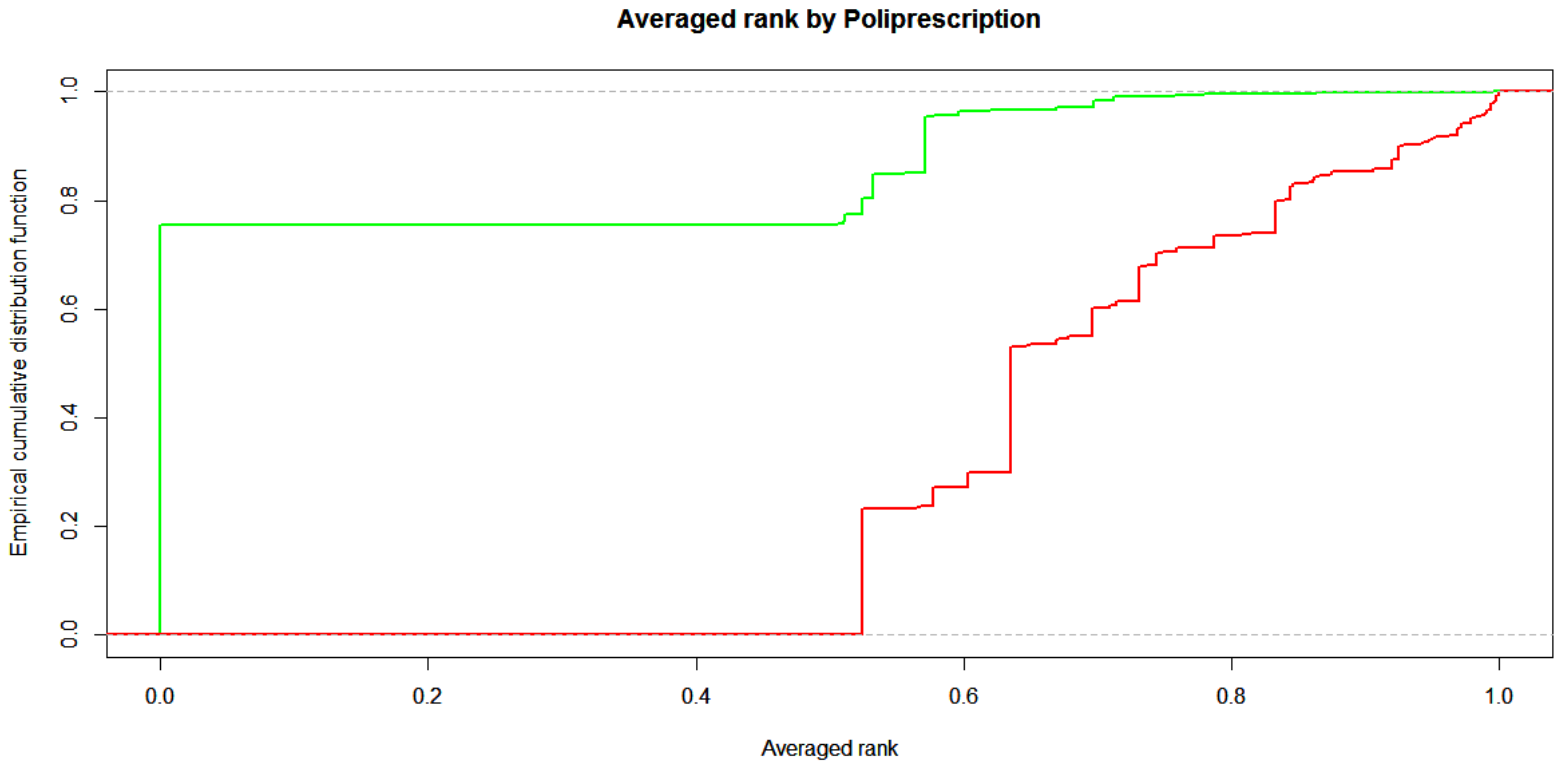
- We have chosen variables according to the **stepwise selection criteria** used in the logistic regression relative to frailty negative outcomes in ULSS15.
- We tested 5 subsets of variables.
- The selected subset contains **9 variables**: age, home care, disability, Poliprescription (Drugs), Charlson Index (comorbidities), First Aid, Hospitalization, Psychiatry and having 3 + diagnosis.
- The profiles are therefore $2^8 * 3 = 768$, of which 449 have non-zero elements.
- Average rank estimated was normalized using the values of minimum and maximum.

Average rank in the population



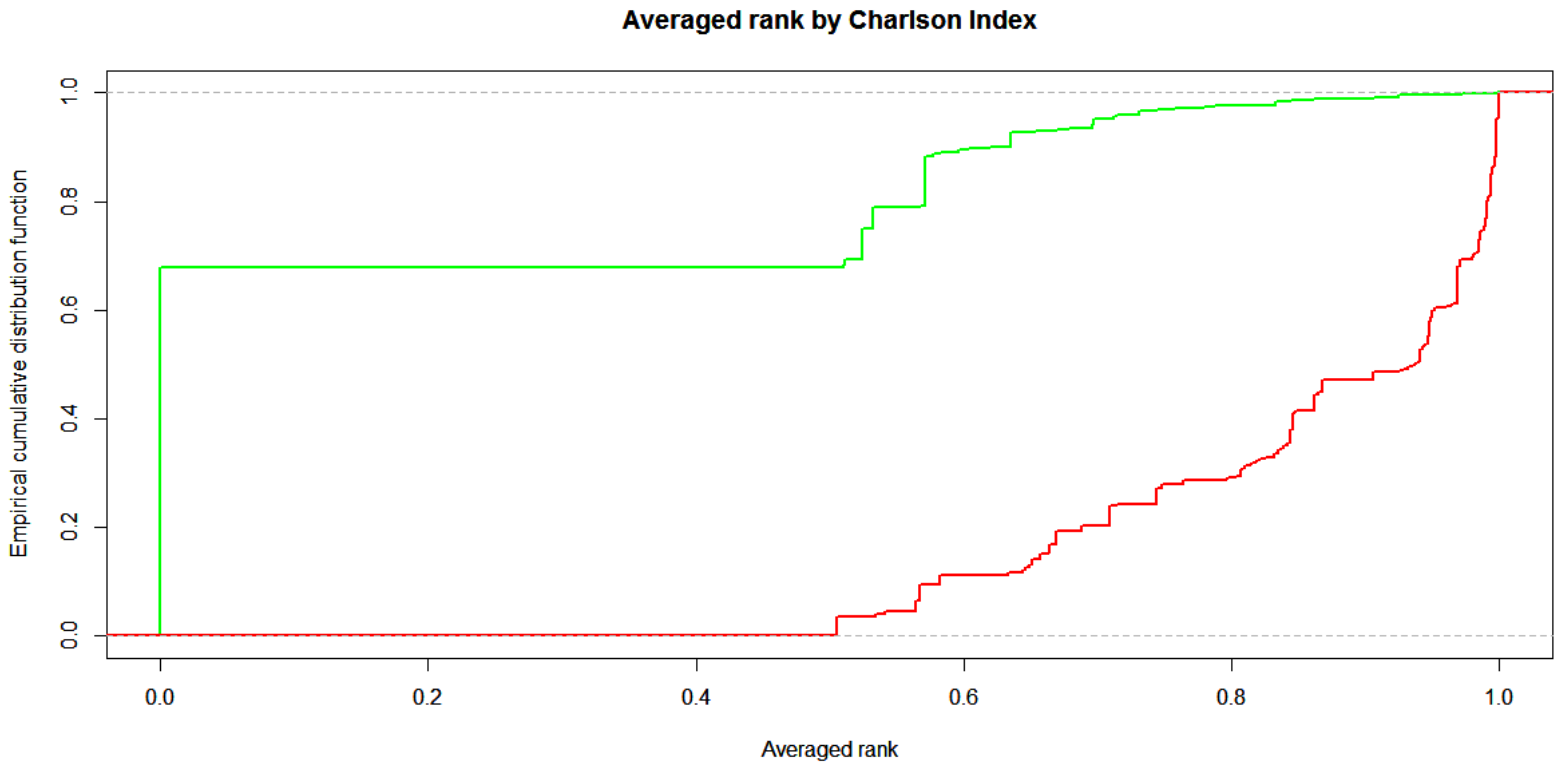
Average rank (computed with age as dichotomous variable) in the whole population.

Average rank by Poliprescription



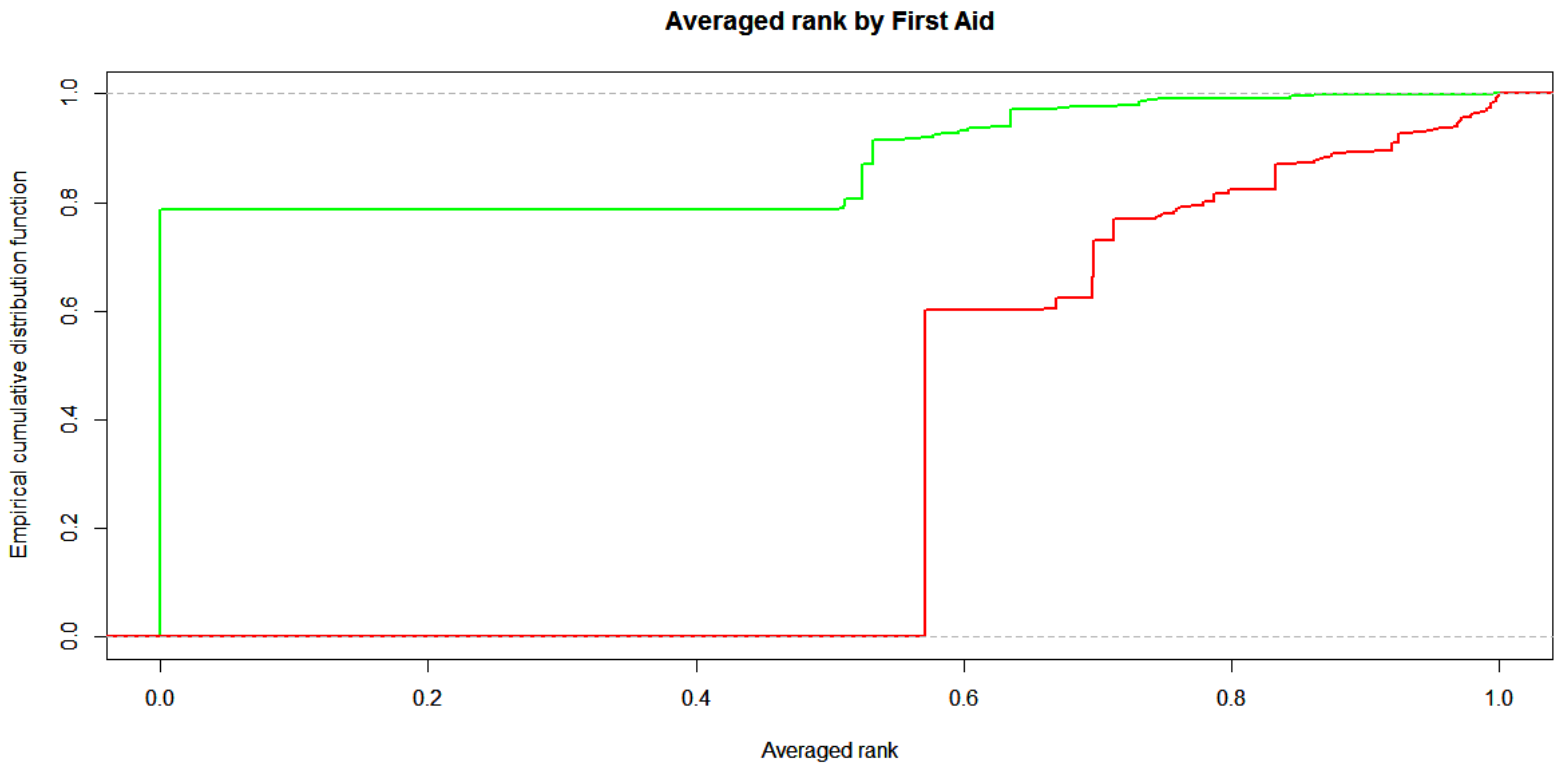
Where the red line represents people that had poliprescriptions in last 3 months of 2013, while the green line stands for all the other people.

Average rank by Charlson Index



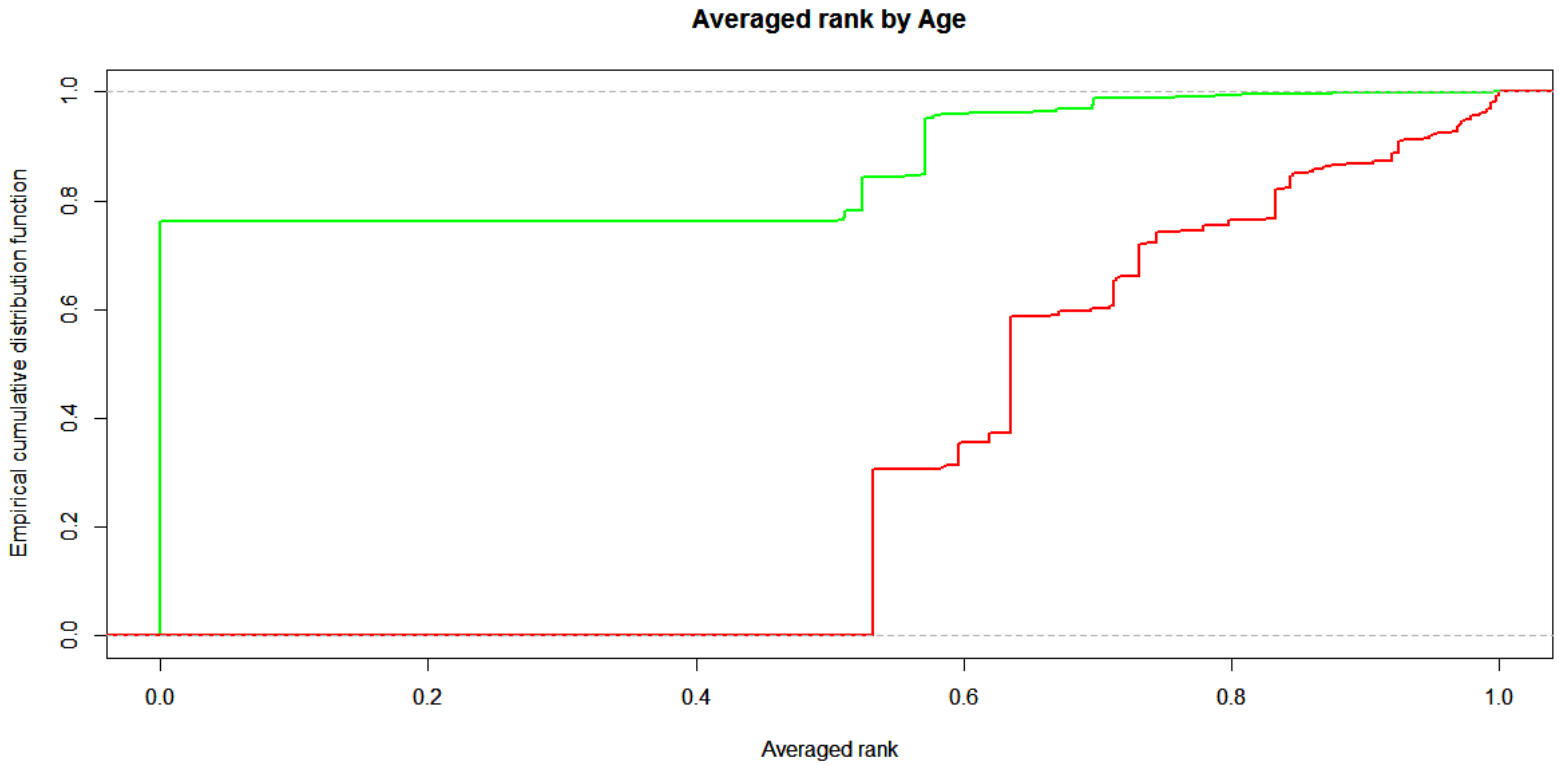
Where the green line represents people without comorbidities according to the Charlson Index and the red line stands for people with Charlson Index ≥ 1.

Average rank by First Aid



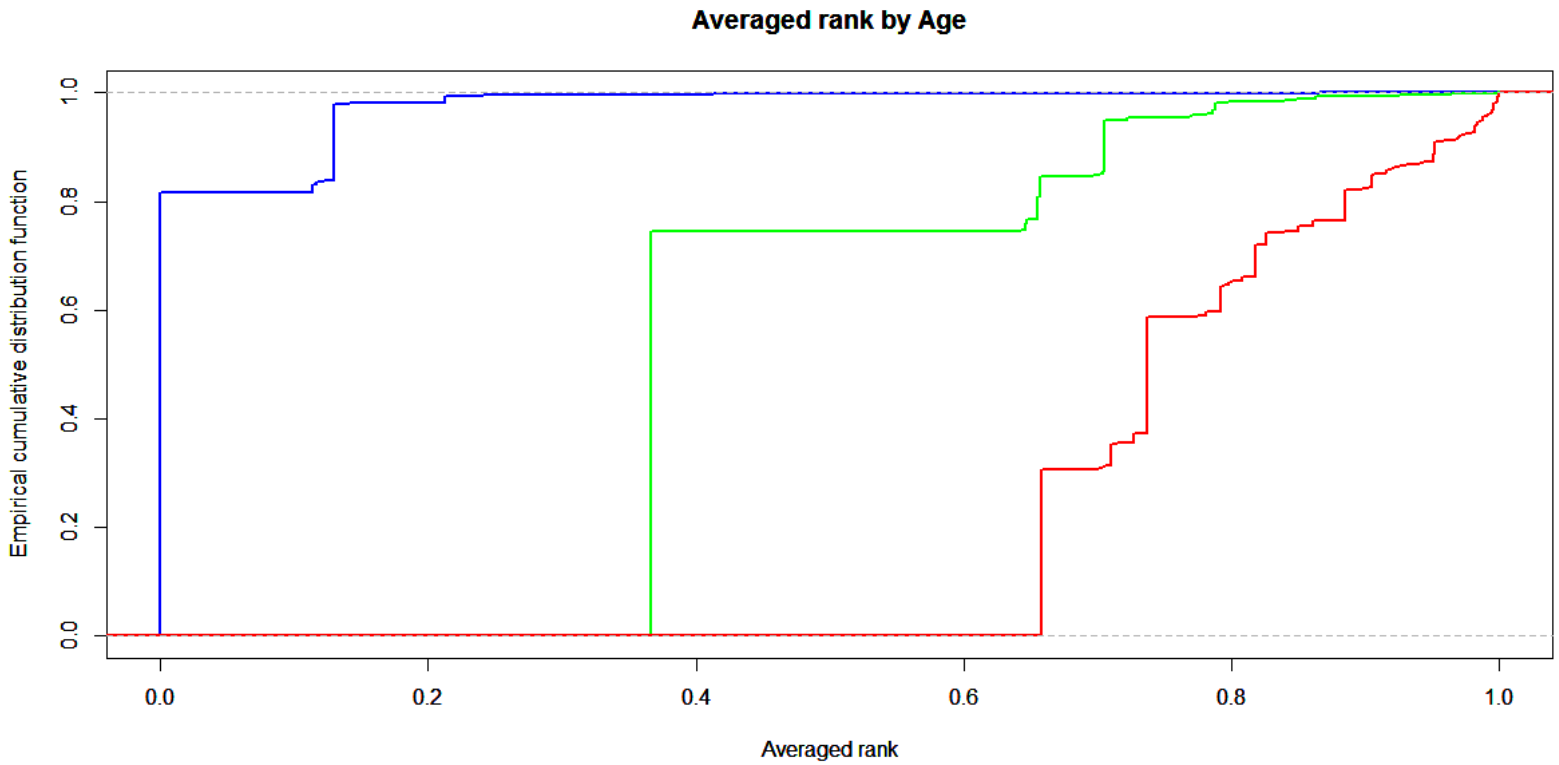
Where the red line represents people that acceded the First Aid in 2013, while the green line stands for all the other people.

Average rank by age, dichotomous



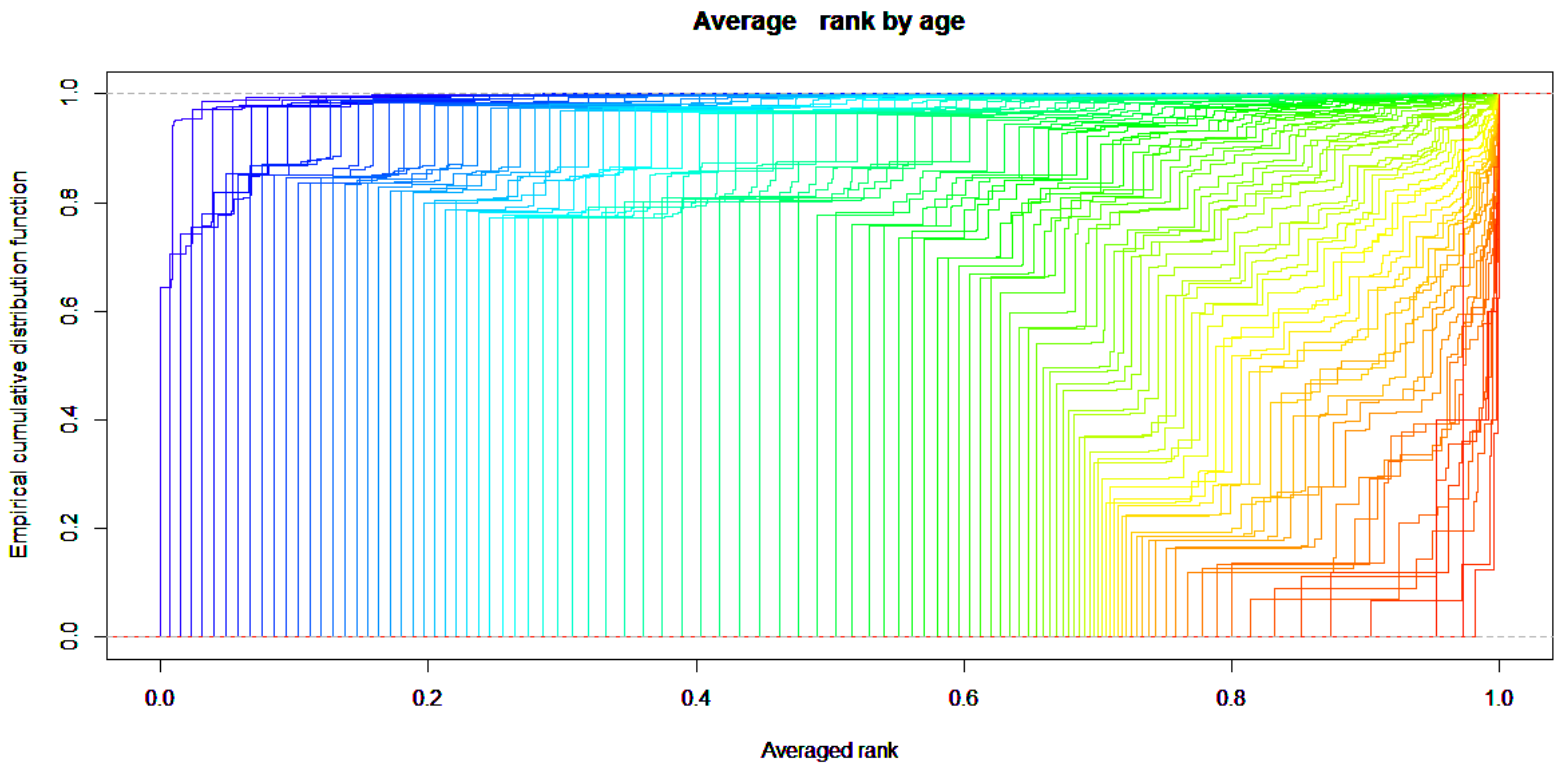
Where the green line represents young and adult people (age<70) and the red line stands for elderly (age≥ 70).

Average rank by age, ordinal



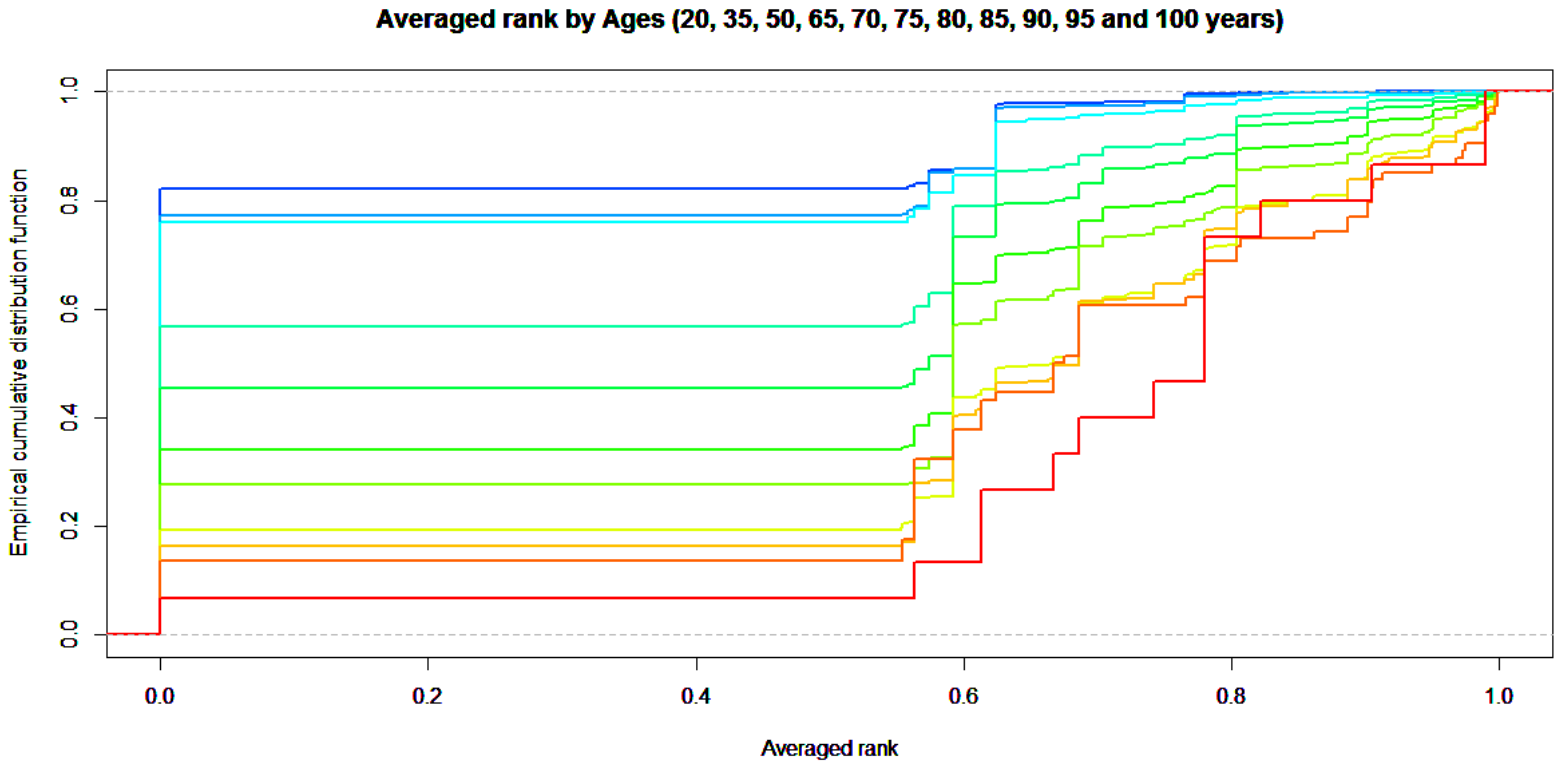
Where the blue line depicts young people (age$\leq$ 20), green line represents adult people (21 $\leq$age$\leq$ 69) and the red line stands for elderly (age$\geq$ 70).

Average rank by age



Where color shades from blue (young people) to red (elderly) represent the age variable.

Average rank by ages



Where the average rank is computed without the variable age and color shades from blue (young people) to red (elderly) represent the age variable.

Analysis of segmentation according to average rank

Age													N	Average	SD	Group
	Young	First Aid	No										45959	0,004	0,0285	23
			Yes	Hospital.	No								7794	0,133	0,0247	22
					Yes								784	0,261	0,1321	21
	Adult and Elderly	First Aid	No	Age	Adult	Polipresscrip.	No						132798	0,39	0,0802	20
							Yes	Hospital.	No	Invalidità	No		7036	0,658	0,0137	19
											Yes		1098	0,729	0,0491	16
									Yes				1305	0,775	0,0751	12
					Elderly	Polipresscrip.	No	Disability	No	Hospital.	No		9915	0,66	0,0098	18
											Yes		577	0,739	0,0329	14
									Yes				1699	0,734	0,0478	15
							Yes	Disability	No	Hospital.	No		7291	0,743	0,0232	13
											Yes		920	0,855	0,0466	7
									Yes	Home care	No		2229	0,836	0,0418	8
											Yes		830	0,925	0,0335	3
			Yes	Polipresscription	No	Age	Adult	Hospital.	No				16025	0,709	0,0173	17
									Yes				2404	0,805	0,0372	10
							Elderly	Hospital.	No				1938	0,81	0,0345	9
									Yes				736	0,917	0,0507	4
					Yes	Age	Adult	Hospital.	No				1865	0,804	0,0384	11
									Yes				1219	0,913	0,0503	5
							Elderly	Hospital.	No	Disability	No		1932	0,892	0,0207	6
											Yes		846	0,964	0,0176	2
									Yes				2446	0,981	0,0188	1

Conclusions

- We obtained a graduated classification of individuals that provides a simplification of a complex and multidimensional concept as the fragility is, without dichotomizing it (different levels of fragility).
- Using an approach based on poset, available information are fully exploited.
- Once you have the average rank, this becomes a variable to possibly use in further analysis.

Further Developments

It is possible to generalize and try to improve this frailty measure

- by increasing the set of considered **outcomes**.
- by running the analysis separately for **different age classes** (under and over 65 years).
- by changing and eventually increasing the set of **independent variables**, adapting them to the different outcomes.

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Thank you for your attention!