

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk: Development and Validation of the Dynamic Silver Code

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-033374
Article Type:	Research
Date Submitted by the Author:	03-Aug-2019
Complete List of Authors:	<p>Balzi, Daniela; 1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy</p> <p>Carreras, Giulia; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Tonarelli, Francesco; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Degli Esposti, Luca; CliCon S.r.l, Health, Economics and Outcomes Research,</p> <p>Michelozzi, Paola; Lazio Region, Epidemiology</p> <p>Ungar, Andrea; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Gabbani, Luciano; Careggi Hospital, Unit of Geriatrics</p> <p>Benvenuti, Enrico; Azienda USL Toscana centro, Department of Internal Medicine,</p> <p>Landini, Giancarlo; Azienda USL Toscana centro, Department of Internal Medicine,</p> <p>Bernabei, Roberto ; Fondazione Policlinico Agostino Gemelli IRCCS</p> <p>Marchionni, Niccolò; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Di Bari, Mauro; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p>
Keywords:	Prognostic assessment, elderly, Emergency Department, Dynamic Silver Code, administrative data

SCHOLARONE™
Manuscripts

1
2
3 **Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk:**
4
5 **Development and Validation of the Dynamic Silver Code**
6
7
8
9

10 Daniela Balzi, BSc ¹

11 Giulia Carreras, PhD ²

12 Francesco Tonarelli, MD ²

13 Luca Degli Esposti, EconD, PhD ³

14 Paola Michelozzi, BSc, MS ⁴

15 Andrea Ungar, MD, PhD ^{2,5}

16 Luciano Gabbani, MD ⁶

17 Enrico Benvenuti, MD ⁷

18 Giancarlo Landini, MD ⁸

19 Roberto Bernabei, MD ⁹

20 Niccolò Marchionni, MD ^{2,10}

21 Mauro Di Bari, MD, PhD ^{2,5}

- 22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy
 2. Research Unit of Medicine of Aging, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy
 3. Clicon – Health, Economics & Outcome Research, Ravenna, Italy
 4. Department of Epidemiology, Lazio Region, Rome, Italy
 5. Unit of Geriatrics, Department of Medicine and Geriatrics, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
 6. Department of Medicine and Geriatrics, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
 7. Unit of Geriatrics, Department of Internal Medicine, Azienda USL Toscana Centro, Florence, Italy
 8. Department of Internal Medicine, Azienda USL Toscana Centro, Florence, Italy

1
2
3 9. Fondazione Policlinico Agostino Gemelli IRCCS, Rome, Italy
4

5 10. Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Careggi, Florence,
6
7 Italy.
8
9

10
11
12 **Corresponding Author**
13

14 Mauro Di Bari, MD, PhD

15
16 Research Unit of Medicine of Aging

17
18 Department of Experimental and Clinical Medicine

19
20 University of Florence

21
22 Viale G. Pieraccini, 18

23
24 50139 Florence, Italy

25
26 E-mail: mauro.dibari@unifi.it
27
28
29
30
31

32 **RUNNING TITLE:** Risk stratification of older patients in the ED
33
34
35

36 **ABSTRACT WORD COUNT:** 292
37

38 **WORD COUNT:** 3570 (including Introduction, Methods, Results, Discussion, Acknowledgments, Funding,
39
40 Conflict of interest, Author contributions and Data availability statement)
41
42

43 **NUMBER OF TABLES:** 4
44

45 **NUMBER OF FIGURES:** 1
46

47 **NUMBER OF REFERENCES:** 30
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60**ABSTRACT**

Objective: Identification of older patients at risk, among those accessing the Emergency Department (ED), may support clinical decision-making. To this purpose, we developed and validated the Dynamic Silver Code (DSC), a score based on real-time linkage of administrative data.

Design and Setting: The “Silver Code National Project (SCNP)”, a non-concurrent cohort study, was used for retrospective development and internal validation of the DSC. External validation was obtained in the “Anziani in DEA (AIDEA)”, a prospective cohort study where the DSC was generated by the software routinely used in the ED.

Participants: The SCNP contained records of 75+ years old residents from Tuscany and Lazio, Italy, admitted via the ED to Internal Medicine or Geriatrics units. The AIDEA study enrolled subjects aged 75+ years accessing two EDs in the area of Florence, Italy, independent of the outcome of their ED visit. 281,321 records (180,079 patients) were available in the SCNP, and 5,217 (4,425 patients) in AIDEA.

Interventions: None.

Outcome measures: Primary outcome: one-year mortality. Secondary outcomes: 7- and 30-day mortality and 1-year recurrent ED visits.

Results: Advancing age, male gender, previous hospital admission, discharge diagnosis, time from discharge, and polypharmacy predicted 1-year mortality and contributed to the DSC in the development subsample of the SCNP cohort. Based on score quartiles, participants were classified into low-, medium-, high-, and very high-risk classes. In the SCNP validation sample, mortality increased progressively across DSC classes (HR [95% CI] 1.92 [1.85-1.99], 2.71 [2.61-2.81], and 5.40 [5.21-5.59] in class II, III, and IV, vs. class I; $p < 0.001$). Findings were similar in AIDEA, where the DSC predicted also recurrent ED visits in one year. In both databases, the DSC predicted 7- and 30-day mortality.

Conclusions: The DSC, based on administrative data available in real-time, predicts prognosis of older patients and might improve their management in the ED.

KEYWORDS.

1
2
3 Prognostic assessment, elderly, Emergency Department, Dynamic Silver Code, administrative data.
4
5

6 **ARTICLE SUMMARY**

7

8 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

9

- 10 • The Dynamic Silver Code combines in real-time administrative data available in all Italian
11 regions, to automatically produce a score predicting 1-year mortality and other health
12 outcomes in older persons accessing the Emergency Department (ED).
13
14
- 15 • The tool was developed retrospectively and initially validated in a large, representative
16 cohort of patients aged 75+ years; it was further validated in a new cohort of subjects
17 prospectively recruited, where the tool was available in the software routinely used for
18 clinical management of patients in the ED.
19
20
- 21 • We did not include predictors such as data on outpatient services, functional status and
22 census, nor outcomes such as functional impairment, cognitive decline and
23 institutionalization.
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

INTRODUCTION

At the end of the disease era, when medical care is mostly directed towards management of chronic multimorbidity or non-disease-specific complaints in older persons,[1] a gear shift in the scope of, and the approach to, prognostic assessment is necessary. Besides survival, other goals should be pursued as outcomes of disease prevention and treatment, such as relief of symptoms, maintenance of personal autonomy, and preservation of quality of life, all of which may be targets of prognostic evaluation.[2] Focusing on one single disease is of limited value, when other coexistent illnesses, age-related physiological changes, and non-biological determinants of health may all affect prognosis. Patient's preferences and future perspectives must be valued: many older patients at the end of their life receive futile therapies for minor conditions,[3] whereas others with a reasonable disability-free life expectancy fail to receive appropriate treatments just because they are considered too old.[4]

Prognostic tools help clinicians optimize the benefit/burden ratio of medical interventions [2] and support their decision-making;[5] they may prove useful also in the health policy arena, to perform risk-adjustment when comparing clinical interventions or healthcare models.[2, 5, 6] Administrative data are increasingly used to this purpose, because of their variety, availability, low cost, and accuracy.[7-9] Such tools have been applied to screen in-patients,[10, 11] outpatients,[12] and free-living subjects [5, 12, 13] for mortality, hospitalization, or disease-specific outcomes, aiming to personalized cures.[14-16]

We have previously described the Silver Code (SC), which combines administrative data into a score predicting 1-year survival in subjects aged 75+ years, admitted to the hospital via the Emergency Department (ED).[17, 18] The Dynamic SC (DSC) presented here is an evolution of the original score, developed from a large administrative dataset and then applied prospectively in a new sample. Whereas the original SC was based on one single moment of observation, the DSC considers, for each individual, the dynamics of events occurring across time. The new tool has been implemented into the software routinely used in the ED of several hospitals in Tuscany, Italy, to provide automated, real-time risk stratification of older patients.

METHODS

Study design and data source

Two different studies contributed to the present investigation. The first was the “Silver Code National Project (SCNP)”, which was sponsored by the Centre for Disease Control of the Italian Ministry of Health in 2008.[19] The second was represented by the “Anziani in DEA (AIDEA)” (standing for “Older Persons in the ED”) study, jointly sponsored by the Italian Ministry of Health and by the Tuscany Region in 2010 (RF-2010-2321801). The SCNP was a non-concurrent cohort study, whereas AIDEA followed a prospective cohort study design.

The SCNP database,[19] representing the primary data source for the development and initial validation of the DSC, was obtained from the administrative archives of two Regions in Italy, Tuscany and Lazio, which deliver healthcare services to a total population of more than 9.6 million persons. The archives included data on demographics, hospitalizations, drug prescriptions, and deaths of beneficiaries aged 75+ years, who had been admitted via the ED to hospitals in the two Regions between April 2004 and December 2009. Data were linked using a numeric unique identifier, which allowed records anonymization before data processing to preserve beneficiaries’ confidentiality. Universal healthcare coverage in Italy allows completeness and comprehensiveness of the information contained in these databases, which have been used in previous epidemiological studies.[17, 20] The Italian Ministry of Health reported that Tuscany archives are 100% complete and 95% accurate.[21, 22]

Further validation of the score developed from the SCNP was subsequently obtained in a different sample, assembled in the AIDEA study, which was conducted in the ED of two hospitals in Florence, Italy, the Azienda Ospedaliero-Universitaria Careggi (AOUC), an academic tertiary hospital, and the Ospedale S. Maria Annunziata (OSMA), a large community hospital. Enrolment was consecutively conducted between June and August 2016 and again between February and March 2017 in the AOUC, and between August and September 2016 in the OSMA, for a total of 22 weeks. In AIDEA, an application generating the DSC was incorporated into the software routinely used in the ED of the hospitals of the Tuscany Region: as soon as an eligible patient was triaged, the repository of healthcare data of the Local Health Unit was queried to

1
2
3 provide, thanks to on-demand linkage of the different archives involved, the information required to obtain
4 the DSC. The score was then in real-time calculated and shown, together with the corresponding risk class,
5 onto the computer screen. The lag time between occurrence of events contributing to the DSC
6 (hospitalizations and drug prescriptions) and their registration in the healthcare data repository was
7 approximately two weeks.
8
9
10
11
12
13
14
15

16 **Participants' selection**

17
18 The SCNP selected only records of subjects aged 75+ years, residing in the area where the study
19 was conducted, who consecutively accessed the ED of the participating hospitals in the specified time
20 windows and were eventually admitted to Internal Medicine or Geriatrics wards. Conversely, the AIDEA
21 study enrolled all the residents aged 75+ years consecutively accessing the ED in the specified time periods,
22 independent of the outcome (hospitalization or discharge) of their access to the ED.
23
24
25
26
27
28
29
30
31

32 **Ethics**

33
34 Following the Italian legislation on observational studies using administrative databases in place at
35 the time of data acquisition, Ethics Committee approval and participants' subscription of informed consent
36 was waived in the SCNP, because only anonymized administrative data were extracted. The protocol of the
37 AIDEA study, which included also face-to-face interview (not reported in the present work), was approved
38 by the Ethics Committee of the AOU Careggi (976/13_AOUC).
39
40
41
42
43
44
45
46
47

48 **Patient and public involvement**

49
50 Given the largely retrospective nature of the study, it was not possible to involve patients or the
51 public in the design or conduct of our research. Reporting was provided as requested by the funding
52 Institutions. Dissemination to the public was obtained through lay press.
53
54
55
56
57
58

59 **Analytic procedures**

1
2
3 Statistical analysis was performed with SPSS for Mac v. 25 (IBM Corp., Armonk, NY, USA), STATA v.
4
5 15.1 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC), and R
6
7 3.5.0 (R Core Team, 2018).
8
9

10 A total of 281,321 records were available in the SCNP database to create the DSC and test its
11
12 validity. The χ^2 was used to test differences in relative frequencies and to identify bivariate predictors of
13
14 death, taking into account trends as appropriate.
15
16

17 The sample was randomly split into a development and a validation subsample. In the first
18
19 subsample, a Cox proportional hazards model was fit to estimate the association, expressed as hazard ratio
20
21 (HR) with 95% confidence interval (CI) of demographics and other variables on 1-year all-cause mortality
22
23 risk. Variables initially considered included age, gender, number of drugs prescribed in the previous 3
24
25 months as resulting from pharmacy claims (categorized as 0-3, 4-5, 6-8, and 9+), days from previous
26
27 hospital admission (no admission, 30-180 days, 0-30 days) and its associated main diagnostic group (cancer,
28
29 respiratory disease, cardiovascular disease, and other conditions). Compared to the original version of the
30
31 SC, previous admission to a day hospital was not considered, because availability and utilization of day
32
33 hospital service are not consistent across Regions in Italy. Marital status information was also omitted,
34
35 because it was frequently missing in the discharge summary and in preliminary analyses it contributed
36
37 marginally to the prediction of death. Differently from the SC, repeated hospitalizations were taken into
38
39 account to dynamically update patient's information at each new hospital admission. To this purpose, data
40
41 were arranged in order to have one observation per event or time interval, and the counting process
42
43 approach proposed by Andersen and Gill [23] was applied: this is a generalization of Cox's model, which
44
45 assumes that the correlation between event times for a person can be explained by past events. Thus, we
46
47 made the assumption that correlations among events for each individual were captured by appropriate
48
49 time-dependent covariates.
50
51
52
53

54 We evaluated the adherence of predictors to the assumption of proportional hazards and tested for
55
56 multicollinearity comparing different models in terms of Akaike information criteria.[24] We then assigned
57
58 each risk factor a score, calculated as the ratio, rounded to the nearest integer, between the regression b
59
60 coefficient for that variable and the smallest significant b coefficient (b_0) in the Cox model. We finally

1
2
3 computed the DSC as a summary point score, by adding the points individually assigned to each risk factor.
4
5 Four prognostic classes were then created from DSC quartiles.
6

7 In the validation data set, Harrell's C index of concordance was applied to evaluate model
8
9 performance, as a measure of the predictive power of Cox regression model.[25] Furthermore, the ability
10
11 of DSC classes to predict 1-year mortality was analysed after adjusting for Region of enrolment and
12
13 principal diagnosis at discharge. External validity of the DSC was performed in the AIDEA data set, using Cox
14
15 regression models and Harrell's C index of concordance to predict 1-year mortality, as well as the risk of
16
17 recurrent ED access after a first hospital admission.
18
19

20
21 Additional analyses were performed on both datasets, to verify the ability of the DSC to predict 7-
22
23 and 30-day mortality, two outcomes that are more immediate and potentially of greater clinical interest in
24
25 the perspective of application of the tool in the ED. Also these analyses were adjusted for main diagnostic
26
27 group at discharge and Region of enrolment.
28
29

30 A two-tailed p value less than 0.05 was considered statistically significant.
31
32
33

34 RESULTS

35
36
37
38

39 Participants in the SCNP

40

41 Out of the 281,321 records in the SCNP, 180,079 (64.01%) pertained to a single hospitalization, the
42
43 remaining to patients with multiple hospital admissions in the study period. The random split assigned
44
45 90,039 patients to the development and 90,040 to the validation subsample, with 140,716 and 140,605
46
47 records, respectively. As shown in **Table 1**, baseline characteristics of participants on their first hospital
48
49 admission were comparable between the two subsamples.
50
51
52
53
54
55
56
57
58
59
60

Table 1. Baseline characteristics of participants on their first hospital admission, in the entire sample and in the development and validation subsamples. The p value reported refers to the χ^2 test, for trend when appropriate.

Variable	Overall (n=180,079)		Development subsample (n=90,039)		Validation subsample (n=90,040)		p
	N	%	N	%	N	%	
Age (years)							0.348
75-79	52,196	29.0	25,974	28.9	26,222	29.1	
80-84	60,205	33.4	30,221	33.6	29,984	33.3	
85+	67,678	37.6	33,844	37.6	33,834	37.6	
Gender							0.639
Male	77,803	43.2	38,852	43.2	38,951	43.3	
Female	102,276	56.8	51,187	56.9	51,089	56.7	
Number of drugs in previous 3 months							0.268
0-3	57,859	32.1	28,995	32.2	28,864	32.1	
4-5	38,405	21.3	19,322	21.5	19,083	21.2	
6-8	46,754	26.0	23,222	25.8	23,532	26.1	
9+	37,061	20.6	18,500	20.6	18,561	20.6	
Main diagnostic group in previous (6 months) hospital admission							0.773
No previous hospital admission	146,562	81.4	73,241	81.3	73,321	81.4	
Cardiovascular disease	11,206	6.2	5,537	6.15	5,669	6.3	
Cancer	3,954	2.2	1,955	2.2	1,999	2.2	
Respiratory disease	3,171	1.8	1,585	1.8	1,586	1.8	
Others	15,186	8.4	7,721	8.6	7,465	8.3	
Days from previous (6 months) hospital admission							0.156
No previous hospital admission	146,562	81.4	73,241	81.3	73,321	81.4	
31-180	23,374	13.0	11,793	13.1	11,581	12.9	
0-30	10,143	5.6	5,005	5.6	5,138	5.7	

Predictors of 1-year mortality

From hospital admission through the following year, a total of 42,434 deaths were recorded; mortality was comparable in the development (21,250/90,039, 23.6%) and the validation (21,184/90,040, 23.5%) subsamples. In the development sample, bivariate predictors of death were older age (75–79 years: 16.4%, 80–84 years: 20.5%, 85+ years: 31.9%; $p=0.001$), gender (men: 24.8%, women: 22.7%; $p<0.001$), previous hospital admission with its corresponding main discharge diagnosis (no admission: 22.1%, cardiovascular disease: 23.5%, cancer: 49.1%, respiratory disease: 30.8%, other diagnoses: 30.2%; p

1
2
3 <0.001), days from previous hospital admission (1-30 days: 34.5%, 31-180 days: 28.5%, $p < 0.001$), or taking
4
5 more drugs prior to the index ED admission (0-3: 22.6%, 4-5: 22.9%, 6-8: 23.3%, 9+: 26.2%; $p < 0.001$).
6
7
8
9

10 Risk models

11
12 **Table 2** shows the results of Cox proportional hazard regression model in the SCNP development
13
14 subsample. All the variables considered were significant predictors of 1-year mortality. Because the
15
16 diagnostic groups of “cardiovascular disease” and “others” obtained similar HRs, they were combined into a
17
18 single category, contrasted with “no previous hospital admission”, “cancer” and “respiratory disease”. The
19
20 predictors “days from the previous hospital admission” and the associated “main diagnostic group” showed
21
22 some multicollinearity, but the models with only one of those variables performed worse in terms of AIC:
23
24 therefore, both variables were maintained in the final model. All predictors satisfied the assumption of
25
26 proportional hazards.
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 2. Multivariable *b* coefficients, obtained from Cox regression model predicting 1-year death, in the 90,039 participants in the development subsample, with scores associated.

Variable	<i>b</i> Coefficient	p-value	Score
Age (years)			
75-79	Ref.		0
80-84	0.2871	<0.001	8
85+	0.8259	<0.001	23
Gender			
Female	Ref.		0
Male	0.1875	<0.001	5
Number of drugs in previous 3 months			
0-3	Ref.		0
4-5	0.0364	0.0320	1
6-8	0.0732	<0.001	2
9+	0.2173	<0.001	6
Main diagnostic group in previous (6 months) hospital admission			
No admission	Ref.		0
Cardiovascular disease / Others	0.6944	<0.001	19
Cancer	1.5218	<0.001	42
Respiratory disease	1.0357	<0.001	28
Days from previous (6 months) hospital admission			
No admission	Ref.		0
30-180	0.2763	<0.001	8
0-30	0.000		0

The smallest significant *b* coefficient in the Cox model resulted to be associated with 4-5 drugs prescribed in the previous 3 months ($b_0 = 0.0364$). Thus, each significant predictor was assigned a score by rounding the ratio between the corresponding *b* coefficient in the regression model and b_0 up to the nearest integer (**Table 2**). The DSC was finally calculated as summation of all scores.

Participants were classified into low-, medium-, high-, and very high-risk classes, based upon DSC quartiles. One-year risk of death increased significantly from the first to the fourth DSC class (**Figure 1**), with almost identical hazard ratios in both subsamples (**Table 3**). In the validation subsample, the performance of the risk scoring system, assessed with Harrell's C index, was 0.668 (95% CI 0.665- 0.672). The ability of the DSC to predict 1-year mortality persisted after controlling for main diagnostic group at discharge and Region of enrolment (Tuscany vs. Lazio), as shown by HR (95% CI) of 1.93 (1.88-1.98), 2.71 (2.64-2.78), and 5.00 (4.88-5.13) for class II, III, and IV, respectively, compared to class I ($p<0.001$) (**Figure 1**).

Table 3. One-year mortality and corresponding hazard ratios by DSC class, separately in the development and validation subsamples.

DSC Class (score)	Development subsample (n=90,039)			Validation subsample (n=90,040)		
	Participants	Deaths	HR (95% CI)	Participants	Deaths	HR (95% CI)
I (≤ 10)	29,880	4,303	Ref.	29,798	4,291	Ref.
II (11-25)	32,712	8,127	1.93 (1.86-2.00)	32,775	8,082	1.92 (1.85-1.99)
III (26-34)	17,391	5,180	2.73 (2.64-2.84)	17,439	5,126	2.71 (2.61-2.81)
IV (≥ 35)	10,056	3,640	5.37 (5.18-5.56)	10,028	3,685	5.40 (5.21-5.59)
Total	90,039	21,250		90,040	21,184	

External validity

External validity of the DSC was ascertained in the AIDEA sample, which included 5,217 records for 4,425 subjects, of whom 1,292 died and 465 had a new ED admission within one year. Mortality increased progressively across DSC classes, with HR (95% CI) of 2.06 (1.68-2.53), 3.32 (2.74-4.03), and 5.28 (4.37-6.39) in class II, III, and IV, vs. class I ($p<0.001$) and a Harrell's C index of 0.660 (95% CI 0.641-0.678). Also 1-year risk of recurrent ED access increased significantly across DSC classes, with HR (95% CI) of 1.46 (1.11-1.93), 1.45 (1.10-1.92), 2.60 (1.99-3.40) in class II, III, and IV, vs. class I ($p=0.007$, 0.009 and <0.001 , respectively) and a Harrell's C index of 0.604 (95% CI 0.573-0.634).

Prediction of short-term mortality

The DSC was able to predict also 7- and 30-day mortality in both databases. In the SCNP database as a whole, 20,297 and 27,812 participants died within 7 and 30 days, respectively, out of the 180,079 enrolled at baseline. In AIDEA, the analysis on 7- and 30-day mortality included 4,425 participants, of whom 102 and 345 died within 7 and 30 days, respectively. In both databases and for both follow-up times, short-term mortality increased significantly across DSC classes ($p < 0.001$) (**Table 4**). Harrell's C index was 0.623 (95% CI 0.618-0.627) and 0.639 (95% CI 0.635-0.643) for 7- and 30-day mortality in the SCNP and 0.690 (95% CI 0.619-0.761) and 0.683 (95% CI 0.645-0.721) in AIDEA.

Table 4. Prediction of 7- and 30-day mortality by DSC class in the complete SCNP and in the AIDEA databases.

DSC Class (score)	SCNP		AIDEA	
	7-day mortality HR (95% CI) *	30-day mortality HR (95% CI) *	7-day mortality HR (95% CI)	30-day mortality HR (95% CI)
I (≤ 10)	Ref.	Ref.	Ref.	Ref.
II (11-25)	1.83 (1.76-1.91)	1.92 (1.85-1.99)	2.24 (1.06-4.76)	1.74 (1.14-2.65)
III (26-34)	2.41 (2.31-2.52)	2.53 (2.43-2.62)	2.73 (1.33-5.64)	3.17 (3.17-4.64)
IV (≥ 35)	3.30 (3.15-3.45)	3.98 (3.84-4.14)	5.57 (2.78-11.15)	5.58 (3.85-8.09)

* Adjusted for main diagnostic group at discharge and Region of enrolment (Tuscany vs. Lazio).

DISCUSSION

Using the SCNP large, representative cohort of older persons accessing the ED and then admitted to hospitals in two Italian Regions, we developed the DSC, which combines simple variables, extracted from administrative databases, into a score predicting 1-year mortality. The score was validated against mortality in a random subset of the same cohort, and then its external validity was proven in the newly enrolled sample of the AIDEA study. Remarkably, whereas in the SCNP cohort the DSC was obtained from off-line processing of consolidated archives, in AIDEA it was generated in real-time on arrival of each eligible

1
2
3 patient, thanks to an application implemented in the software routinely used for patients' clinical
4
5 management in the EDs of Tuscany Region.
6

7
8 Instruments for the screening of older persons in the ED based on comprehensive geriatric
9
10 assessment do exist,[26] but are not used routinely in clinical practice, as they require some expertise and
11
12 are time consuming. In the assumption that simple administrative data might facilitate prognostic
13
14 assessment in such a difficult setting, we have previously developed the SC, which was shown to predict
15
16 long-term mortality [17, 18] and hospitalizations of older persons in the ED [18] in two different cohorts,
17
18 with a discrimination ability comparable to that of other tools requiring face-to-face interview.[18]
19
20 Moreover, the SC allowed risk stratification when comparing the effects of different therapeutic
21
22 approaches.[17, 27] However, the algorithm to develop the SC relied only upon the first ED admission, so
23
24 that the score remained constant throughout the following observation time, independently of new
25
26 hospitalizations or drug prescriptions. To overcome this limitation of the parent tool, the DSC was
27
28 developed by taking into account each hospital admission as the unit of analysis. This would allow the score
29
30 to reflect more closely the dynamics of risk status of older patients, changing after each hospitalization or
31
32 new drug prescription.
33
34
35

36
37 The estimates we obtained are robust, because they were based on high-quality data from a large,
38
39 randomly split population-based cohort, thus overcoming the problem of overestimation typical of small
40
41 sample size datasets.[28] The predictive ability of the tool persisted even after controlling for discharge
42
43 diagnosis. As a further confirm, external validation was achieved in the new sample of the AIDEA study,
44
45 whose participants might be hospitalized or not after the index ED access. It should be emphasized that the
46
47 DSC predicted also short-term mortality and, at least in AIDEA, recurrent hospitalizations, outcomes for
48
49 which it had not been created. In terms of Harrell's C index, the discrimination of the DSC was only
50
51 moderate, similar in the internal and external validation cohorts. Thus, although predictive at the group
52
53 level, its ability to predict prognosis at an individual level is suboptimal. A possible, partial explanation for
54
55 this finding is that the DSC might misclassify subjects defined at low risk, if they reached the ED with acute
56
57 life-threatening conditions. On the other hand, comparable performances have been reported for other
58
59 tools, proposed in the literature for prognostic assessment in acute care settings, such as the Identification
60

1
2
3 of Seniors At Risk [26] (C statistics of 0.65 for 6-month mortality) or the Hospital Frailty Risk Score [29] (C
4 statistics of 0.60 for 30-day mortality), or widely used to drive clinical decisions in selected clinical
5
6
7 conditions, such as the TIMI risk score (C statistics of 0.65 for a 14-day composite endpoint).[30]
8
9

10 A 2012 systematic review on prognostic indices for older adults [2] reported only one article – our
11 original publication on the parent instrument –[17] that focused on ED triage of older persons using
12 administrative data, but not in a real-time application. Although other, more recent studies dealing with
13 prognostic issues around older persons in an acute hospital setting can be found, none of them was
14 developed for use in the ED nor proposed real-time linkage of administrative data. Thus, to the best of our
15 knowledge, the DSC represents the first example in the literature of real-time utilization of administrative
16 data for prognostic purposes, at least in – but probably not limited to – older persons accessing the ED.
17
18
19
20
21
22
23
24

25 Several strengths of the DSC should be highlighted. First, it predicts short- and long-term prognosis
26 and risk of hospitalizations combining with a simple calculation a limited set of variables, obtained from
27 administrative data: thus, it is objective, does not rely on patient's collaboration, which is sometime
28 difficult to obtain in the presence of cognitive decline or communication barriers. Second, as the AIDEA
29 study shows, it can be calculated in real-time, being therefore immediately available to the ED staff as soon
30 as a target patient is triaged, even before any clinical assessment and with no need of dedicated human
31 resources to gather information. To our knowledge, this represents a unique example of clinical utilization
32 of administrative data, which might be easily replicated in other hospitals, at least in Italy. Third, it is a non-
33 disease specific tool, an important characteristic allowing its universal application in older patients, in
34 whom multimorbidity and atypical symptoms presentation make clinical and prognostic assessment
35 challenging. Fourth, similar to other prognostic tools based on administrative data, it can be applied also to
36 obtain risk adjustment in the healthcare policy arena: to our knowledge, no previous prognostic tools have
37 been developed to pursue both clinical and epidemiological purposes.
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53

54 Study limitations are to be acknowledged. The original SCNP dataset is relatively old: however, the
55 validity of the score was confirmed in the definitively more recent AIDEA cohort. The score was developed
56 based on data obtained only in subjects admitted to Internal Medicine or Geriatrics units: nonetheless, its
57 validity was confirmed in a completely different series, which included patients visiting the ED for a variety
58
59
60

1
2
3 of reasons and most of times discharged from the ED. The data so far available did not consent considering
4
5 other predictors (e.g., claims for specialized visits or other services, or census data), neither different
6
7 outcomes besides mortality, such as functional or cognitive decline and institutionalization, which are
8
9 highly relevant in geriatric patients. However, we are confident that the increasing availability of other
10
11 administrative databases will allow incorporating a wider set of predictors as well as of endpoints in the
12
13 next future.
14
15

16 In conclusion, the DSC, a simple prognostic tool based on administrative data, available in real-time
17
18 in the software used in the ED of Italian hospitals, offers a valid prognostic assessment of older patients,
19
20 virtually at no additional costs, once the system has been set. This might support clinical decision-making
21
22 and improve the quality of the care provided. Future studies are needed to assess whether these
23
24 expectations will be satisfied.
25
26
27
28
29

30 **ACKNOWLEDGMENTS**

31
32 Not applicable.
33
34
35

36 **FUNDING**

37
38 The “Silver Code National Project” was funded by the Centre for Disease Control of the Italian
39
40 Ministry of Health. The “Anziani in DEA” study was jointly funded by the Italian Ministry of Health and by
41
42 the Tuscany Region (RF-2010-2321801). The funders had no role in study design, data collection and
43
44 analysis, decision to publish, or preparation of the manuscript. All the authors were independent from
45
46 funders, had access to all of the data and can take responsibility for the integrity of the data and the
47
48 accuracy of the data analysis.
49
50
51
52
53

54 **CONFLICT OF INTEREST**

55
56 All the authors had no financial relationships with organisations or other relationships that might
57
58 appear to have influenced the submitted work.
59
60

AUTHOR CONTRIBUTIONS

DB conceived the study, conducted data management and analysis, and contributed drafting the manuscript. GC conducted data analysis and contributed drafting the manuscript. FT contributed obtaining the data and drafting the manuscript. LDE and PM obtained the data and contributed to data management. AU and EB contributed obtaining the data and provided institutional support. LG and GL provided institutional support. RB and NM provided institutional support and contributed developing the research question. MDB conceived the study, wrote the protocol, supervised analyses, and drafted the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

Study protocol and data may be obtained from the authors on reasonable request, provided that consent is released by the funding Institutions.

REFERENCES

1. Tinetti ME, Fried T. The end of the disease era. *Am J Med.* 2004;116(3):179–85.
2. Yourman LC, Lee SJ, Schonberg MA, et al. Prognostic indices for older adults: a systematic review. *JAMA.* 2012;307(2):182–92.
3. Walter LC, Covinsky KE. Cancer Screening in Elderly Patients. *JAMA.* 2001;285(21):2750.
4. Mehta KM, Fung KZ, Kistler CE, et al. Impact of Cognitive Impairment on Screening Mammography Use in Older US Women. *Am J Public Health.* 2010;100(10):1917–23.
5. Wallace E, Stuart E, Vaughan N, et al. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. *Med Care.* 2014;52(8):751–65.
6. Galvin R, Gilleit Y, Wallace E, et al. Editor's Choice: Adverse outcomes in older adults attending emergency departments: A systematic review and meta-analysis of the identification of Seniors at risk (ISAR) screening tool. *Age Ageing.* 2017;46(2):179–86.
7. Dagan N, Cohen-Stavi C, Leventer-Roberts M, et al. External validation and comparison of three prediction tools for risk of osteoporotic fractures using data from population based electronic health

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

records: retrospective cohort study. *BMJ*. 2017;i6755.

8. Albaba M, Cha SS, Takahashi PY. The Elders risk assessment index, an electronic administrative database-derived frailty index, can identify risk of hip fracture in a cohort of community-dwelling adults. *Mayo Clin Proc*. 2012;87(7):652–8.
9. Simpson AN, Wilmskoetter J, Hong I, et al. Stroke Administrative Severity Index: using administrative data for 30-day poststroke outcomes prediction. *J Comp Eff Res*. 2018;7(4):293–304.
10. Mahajan SM, Heidenreich P, Abbott B, et al. Predictive models for identifying risk of readmission after index hospitalization for heart failure: A systematic review. *Eur J Cardiovasc Nurs*. 2018;17(8):675–89.
11. Taylor RA, Pare JR, Venkatesh AK, et al. Prediction of In-hospital Mortality in Emergency Department Patients With Sepsis: A Local Big Data-Driven, Machine Learning Approach. *Acad Emerg Med*. 2016;23(3):269–78.
12. Clegg A, Bates C, Young J, et al. Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age Ageing*. 2016;45(3):353–60.
13. Corrao G, Rea F, Di Martino M, et al. Developing and validating a novel multisource comorbidity score from administrative data: a large population-based cohort study from Italy. *BMJ Open*. 2017;7(12):e019503.
14. Davoudi A, Ozrazgat-Baslanti T, Ebadi A, et al. Delirium Prediction using Machine Learning Models on Predictive Electronic Health Records Data. *Proc IEEE Int Symp Bioinformatics Bioeng*. 2018: 568–73.
15. Corey KM, Kashyap S, Lorenzi E, et al. Development and validation of machine learning models to identify high-risk surgical patients using automatically curated electronic health record data (Pythia): A retrospective, single-site study. *PLoS Med*. 2018;15(11):e1002701.
16. Rahimian F, Salimi-Khorshidi G, Payberah AH, et al. Predicting the risk of emergency admission with machine learning: Development and validation using linked electronic health records. *PLoS Med*. 2018;15(11):e1002695.
17. Di Bari M, Balzi D, Roberts AT, et al. Prognostic stratification of older persons based on simple

- 1
2
3 administrative data: development and validation of the “Silver Code,” to be used in emergency
4 department triage. *J Gerontol A Biol Sci Med Sci*. 2010;65(2):159–64.
5
6
7
8 18. Di Bari M, Salvi F, Roberts AT, et al. Prognostic stratification of elderly patients in the emergency
9 department: a comparison between the “Identification of Seniors at Risk” and the “Silver Code”. *J*
10 *Gerontol A Biol Sci Med Sci*. 2012;67(5):544–50.
11
12
13
14 19. Centro Nazionale per la Prevenzione e il Controllo delle Malattie. Modelli innovativi per la presa in
15 carico del paziente anziano fragile nella transizione dall’ ospedale al territorio e dal territorio all’
16 ospedale: Case Management e qualità della vita. Available at: [http://www.ccm-](http://www.ccm-network.it/progetto.jsp?id=node/1353&idP=740)
17 [network.it/progetto.jsp?id=node/1353&idP=740](http://www.ccm-network.it/progetto.jsp?id=node/1353&idP=740).
18
19
20
21
22
23 20. Simonato L, Baldi I, Balzi D, et al. Objectives, tools and methods for an epidemiological use of
24 electronic health archives in various areas of Italy. *Epidemiol Prev*. 2008;32(3 Suppl):5-14.
25
26
27
28 21. Ministero del Lavoro, della Salute e delle Politiche Sociali. Rapporto annuale sulla attività di ricovero
29 ospedaliero–Anno . 2005. Available at:
30 <http://www.ministerosalute.it/programmazione/sdo/sezDocumenti.jsp?id=148&label=osp>.
31
32
33 Consultation date April 10, 2019.
34
35
36
37 22. Ministero della Salute. Rapporto Annuale sull’attività di ricovero ospedaliero. Dati SDO 2017. 2019.
38 Available at: http://www.salute.gov.it/portale/temi/p2_4.jsp?lingua=italiano&tema=Assistenza,
39 [ospedale e territorio&area=ricoveriOspedalieri](http://www.salute.gov.it/portale/temi/p2_4.jsp?lingua=italiano&tema=Assistenza,). Consultation date April 10, 2019.
40
41
42
43
44 23. Andersen PK, Gill RD. Cox’s regression model for counting processes: A large sample study. *Annals of*
45 *Statistics* 1982;10:1100-1120.
46
47
48
49 24. Akaike H. A New Look at the Statistical Model Identification. *IEEE Transaction Autom Contr*.
50 1974;19(6):716-23.
51
52
53
54 25. Harrell FE, Califf RM, Pryor DB, et al. Evaluating the Yield of Medical Tests. *JAMA*.
55 1982;247(18):2543-6.
56
57
58
59 26. McCusker J, Bellavance F, Cardin S, et al. Detection of Older People at Increased Risk of Adverse
60 Health Outcomes After an Emergency Visit: The ISAR Screening Tool. *J Am Geriatr Soc*.
1999;47(10):1229–37.

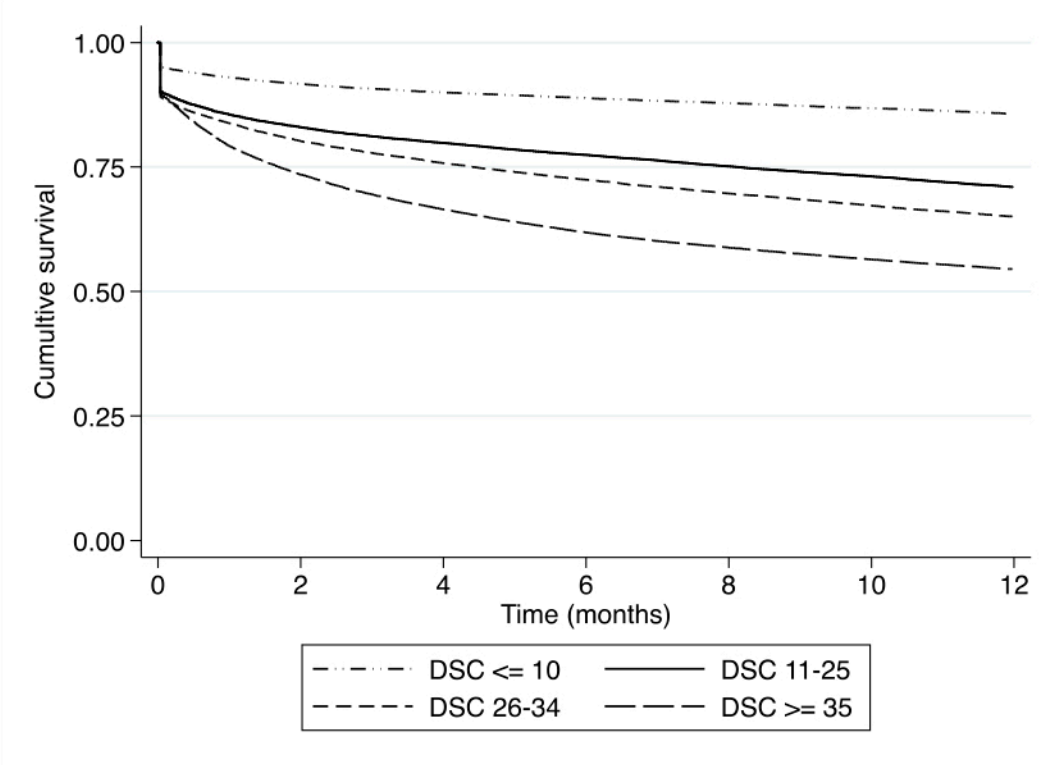
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

27. Di Bari M, Balzi D, Fracchia S, et al. Decreased usage and increased effectiveness of percutaneous coronary intervention in complex older patients with acute coronary syndromes. *Heart*. 2014;100(19):1537–42.
28. Royston P, Moons KGM, Altman DG, et al. Prognosis and prognostic research: Developing a prognostic model. *BMJ*. 2009;338:b604.
29. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet*. 2018;391:1775-1782.
30. Antman EM, Cohen M, Bernink PJLM, et al. The TIMI Risk Score for Unstable Angina/Non–ST Elevation MI. *JAMA*. 2000;284(7):835-42.

1
2
3 **Figure 1.** Survival curves for cumulative risk of death within 1 year after first hospitalization by class of
4 Dynamic Silver Code (DSC) in the validation sample (n=90,040). Cox proportional hazards regression,
5 adjusting for Region of residence and main discharge diagnostic group, with p for trend <0.001.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the TRIPOD reporting guidelines, and cite them as:

Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

	Reporting Item	Page Number
Title		
	#1 Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract		
	#2 Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction		
	#3a Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5
	#3b Specify the objectives, including whether the study describes the	5

development or validation of the model or both.

Methods

1				
2				
3	Methods			
4				
5	Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
6				
7				
8				
9				
10	Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
11				
12				
13				
14	Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	7
15				
16				
17				
18	Participants	#5b	Describe eligibility criteria for participants.	7
19				
20	Participants	#5c	Give details of treatments received, if relevant	NA
21				
22	Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	8
23				
24				
25				
26	Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.	NA
27				
28				
29	Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured	8
30				
31				
32				
33				
34	Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
35				
36				
37				
38	Sample size	#8	Explain how the study size was arrived at.	6
39				
40	Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
41				
42				
43				
44				
45	Statistical analysis methods	#10a	If you are developing a prediction model describe how predictors were handled in the analyses.	7-8
46				
47				
48				
49	Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	8
50				
51				
52				
53				
54	Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.	8
55				
56				
57				
58	Statistical analysis	#10d	Specify all measures used to assess model performance and, if relevant,	8
59				
60				

1	methods	to compare multiple models.	
2	Statistical analysis	#10e If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	NA
3	methods		
4			
5			
6	Risk groups	#11 Provide details on how risk groups were created, if done.	8
7			
8	Development vs.	#12 For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8
9	validation		
10			
11			
12	Results		
13			
14			
15	Participants	#13a Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9
16			
17			
18			
19			
20	Participants	#13b Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	10
21			
22			
23			
24			
25	Participants	#13c For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	10
26			
27			
28			
29			
30			
31	Model	#14a If developing a model, specify the number of participants and outcome events in each analysis.	10
32	development		
33			
34			
35	Model	#14b If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	11
36	development		
37			
38			
39	Model	#15a If developing a model, present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12
40	specification		
41			
42			
43			
44	Model	#15b If developing a prediction model, explain how to use it.	13
45	specification		
46			
47			
48	Model	#16 Report performance measures (with CIs) for the prediction model.	13
49	performance		
50			
51			
52	Model-updating	#17 If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	14
53			
54			
55	Discussion		
56			
57			
58	Limitations	#18 Discuss any limitations of the study (such as nonrepresentative sample,	16
59			
60			

few events per predictor, missing data).

1				
2				
3	Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	15
4				
5				
6	Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
7				
8				
9				
10	Implications	#20	Discuss the potential clinical use of the model and implications for future research	16
11				
12				
13				
14	Other			
15	information			
16				
17				
18	Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	18
19				
20				
21	Funding	#22	Give the source of funding and the role of the funders for the present study.	17
22				
23				
24				

The TRIPOD checklist is distributed under the terms of the Creative Commons Attribution License CC-BY.

This checklist was completed on 01. August 2019 using <https://www.goodreports.org/>, a tool made by the

[EQUATOR Network](#) in collaboration with [Penelope.ai](#)

BMJ Open

Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk: Development and Validation of the Dynamic Silver Code

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-033374.R1
Article Type:	Original research
Date Submitted by the Author:	07-Oct-2019
Complete List of Authors:	<p>Balzi, Daniela; 1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy</p> <p>Carreras, Giulia; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Tonarelli, Francesco; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Degli Esposti, Luca; CliCon S.r.l, Health, Economics and Outcomes Research,</p> <p>Michelozzi, Paola; Lazio Region, Epidemiology</p> <p>Ungar, Andrea; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Gabbani, Luciano; Careggi Hospital, Unit of Geriatrics</p> <p>Benvenuti, Enrico; Azienda USL Toscana centro, Department of Internal Medicine,</p> <p>Landini, Giancarlo; Azienda USL Toscana centro, Department of Internal Medicine,</p> <p>Bernabei, Roberto ; Fondazione Policlinico Agostino Gemelli IRCCS</p> <p>Marchionni, Niccolò; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Di Bari, Mauro; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p>
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Emergency medicine, Health informatics
Keywords:	Prognostic assessment, elderly, Emergency Department, Dynamic Silver Code, administrative data

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



1
2
3 **Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk:**
4
5 **Development and Validation of the Dynamic Silver Code**
6
7
8
9

10 Daniela Balzi, BSc ¹

11 Giulia Carreras, PhD ²

12 Francesco Tonarelli, MD ²

13 Luca Degli Esposti, EconD, PhD ³

14 Paola Michelozzi, BSc, MS ⁴

15 Andrea Ungar, MD, PhD ^{2,5}

16 Luciano Gabbani, MD ⁶

17 Enrico Benvenuti, MD ⁷

18 Giancarlo Landini, MD ⁸

19 Roberto Bernabei, MD ⁹

20 Niccolò Marchionni, MD ^{2,10}

21 Mauro Di Bari, MD, PhD ^{2,5}

- 22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy
 2. Research Unit of Medicine of Aging, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy
 3. Clicon – Health, Economics & Outcome Research, Ravenna, Italy
 4. Department of Epidemiology, Lazio Region, Rome, Italy
 5. Unit of Geriatrics, Department of Medicine and Geriatrics, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
 6. Department of Medicine and Geriatrics, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
 7. Unit of Geriatrics, Department of Internal Medicine, Azienda USL Toscana Centro, Florence, Italy
 8. Department of Internal Medicine, Azienda USL Toscana Centro, Florence, Italy

1
2
3 9. Fondazione Policlinico Agostino Gemelli IRCCS, Rome, Italy
4

5 10. Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Careggi, Florence,
6
7 Italy.
8
9

10
11
12 **Corresponding Author**
13

14 Mauro Di Bari, MD, PhD

15
16 Research Unit of Medicine of Aging

17
18 Department of Experimental and Clinical Medicine

19
20 University of Florence

21
22 Viale G. Pieraccini, 18

23
24 50139 Florence, Italy

25
26 E-mail: mauro.dibari@unifi.it
27
28
29
30
31

32 **RUNNING TITLE:** Risk stratification of older patients in the ED
33
34
35

36 **ABSTRACT WORD COUNT:** 292
37

38 **WORD COUNT:** 3995
39

40 **NUMBER OF TABLES:** 4
41

42 **NUMBER OF FIGURES:** 1
43

44 **NUMBER OF REFERENCES:** 33
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ABSTRACT

Objective: Identification of older patients at risk, among those accessing the Emergency Department (ED), may support clinical decision-making. To this purpose, we developed and validated the Dynamic Silver Code (DSC), a score based on real-time linkage of administrative data.

Design and Setting: The “Silver Code National Project (SCNP)”, a non-concurrent cohort study, was used for retrospective development and internal validation of the DSC. External validation was obtained in the “Anziani in DEA (AIDEA)”, a prospective cohort study where the DSC was generated by the software routinely used in the ED.

Participants: The SCNP contained records of 75+ years old residents from Tuscany and Lazio, Italy, admitted via the ED to Internal Medicine or Geriatrics units. The AIDEA study enrolled subjects aged 75+ years accessing two EDs in the area of Florence, Italy, independent of the outcome of their ED visit. 281,321 records (180,079 patients) were available in the SCNP, and 5,217 (4,425 patients) in AIDEA.

Interventions: None.

Outcome measures: Primary outcome: one-year mortality. Secondary outcomes: 7- and 30-day mortality and 1-year recurrent ED visits.

Results: Advancing age, male gender, previous hospital admission, discharge diagnosis, time from discharge, and polypharmacy predicted 1-year mortality and contributed to the DSC in the development subsample of the SCNP cohort. Based on score quartiles, participants were classified into low-, medium-, high-, and very high-risk classes. In the SCNP validation sample, mortality increased progressively across DSC classes (HR [95% CI] 1.92 [1.85-1.99], 2.71 [2.61-2.81], and 5.40 [5.21-5.59] in class II, III, and IV, vs. class I; $p < 0.001$). Findings were similar in AIDEA, where the DSC predicted also recurrent ED visits in one year. In both databases, the DSC predicted 7- and 30-day mortality.

Conclusions: The DSC, based on administrative data available in real-time, predicts prognosis of older patients and might improve their management in the ED.

KEYWORDS.

1
2
3 Prognostic assessment, elderly, Emergency Department, Dynamic Silver Code, administrative data.
4
5

6 **ARTICLE SUMMARY**
7

8 **STRENGTHS AND LIMITATIONS OF THIS STUDY**
9

- 10
11 • The Dynamic Silver Code combines in real-time administrative data available in all Italian
12 regions, to automatically produce a score predicting 1-year mortality and other health
13 outcomes in older persons accessing the Emergency Department (ED).
14
15
16
17
18 • The tool was developed retrospectively and initially validated in a large, representative
19 cohort of patients aged 75+ years; it was further validated in a new cohort of subjects
20 prospectively recruited, where the tool was available in the software routinely used for
21 clinical management of patients in the ED.
22
23
24
25
26
27 • We did not include predictors such as data on outpatient services, functional status and
28 census, nor outcomes such as functional impairment, cognitive decline and
29 institutionalization.
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

INTRODUCTION

At the end of the disease era, when medical care is mostly directed towards management of chronic multimorbidity or non-disease-specific complaints in older persons,[1] a gear shift in the scope of, and the approach to, prognostic assessment is necessary. Besides survival, other goals should be pursued as outcomes of disease prevention and treatment, such as relief of symptoms, maintenance of personal autonomy, and preservation of quality of life, all of which may be targets of prognostic evaluation.[2] Focusing on one single disease is of limited value, when other coexistent illnesses, age-related physiological changes, and non-biological determinants of health may all affect prognosis. Patient's preferences and future perspectives must be valued: many older patients at the end of their life receive futile therapies for minor conditions,[3] whereas others with a reasonable disability-free life expectancy fail to receive appropriate treatments just because they are considered too old.[4]

Prognostic tools have the potential to help clinicians optimize the benefit/burden ratio of medical interventions [2] and support their decision-making;[5] they may prove useful also in the health policy arena, to perform risk-adjustment when comparing clinical interventions or healthcare models.[2, 5, 6] Administrative data are increasingly used to this purpose, because of their variety, availability, low cost, and accuracy.[7-9] Such tools have been applied to screen in-patients,[10, 11] outpatients,[12] and free-living subjects [5, 12, 13] for mortality, hospitalization, or disease-specific outcomes, aiming to personalized cures.[14-16]

We have previously described the Silver Code (SC), which combines administrative data into a score predicting 1-year survival in subjects aged 75+ years, admitted to the hospital via the Emergency Department (ED).[17, 18] The Dynamic SC (DSC) presented here is an evolution of the original score, developed from a large administrative dataset and then applied prospectively in a new sample. Whereas the original SC was based on one single moment of observation, the DSC considers, for each individual, the dynamics of events occurring across time. The new tool has been implemented into the software routinely used in the ED of several hospitals in Tuscany, Italy, to provide automated, real-time risk stratification of older patients.

METHODS

The DSC was obtained following the same general approach used for the SC, i.e. combining into a score variables from healthcare administrative archives, to predict long-term survival of older persons admitted to the hospital. Compared with the SC, the cohort used to develop and validate the DSC was much larger and representative of the general older population. Moreover, important computational differences were introduced and external validation in a completely new cohort was obtained.

Study design and data source

Two different studies contributed to the present investigation. The first was the “Silver Code National Project (SCNP)”, which was sponsored by the Centre for Disease Control of the Italian Ministry of Health in 2008.[19] The second was represented by the “Anziani in DEA (AIDEA)” (standing for “Older Persons in the ED”) study, jointly sponsored by the Italian Ministry of Health and by the Tuscany Region in 2010 (RF-2010-2321801). The SCNP was a non-concurrent cohort study, whereas AIDEA followed a prospective cohort study design.

The SCNP database,[19] representing the primary data source for the development and initial validation of the DSC, was obtained from the administrative archives of two Regions in Italy, Tuscany and Lazio, which deliver healthcare services to a total population of more than 9.6 million persons. The archives included data on demographics, hospitalizations, drug prescriptions, and deaths of beneficiaries aged 75+ years, who had been admitted via the ED to hospitals in the two Regions between April 2004 and December 2009. Data were linked using a numeric unique identifier, which allowed records anonymization before data processing to preserve beneficiaries’ confidentiality. Universal healthcare coverage in Italy allows completeness and comprehensiveness of the information contained in these databases, which have been used in previous epidemiological studies.[17, 20] The Italian Ministry of Health reported that Tuscany archives are 100% complete and 95% accurate.[21, 22]

Further validation of the score developed from the SCNP was subsequently obtained in a different sample, assembled in the AIDEA study, which was conducted in the ED of two hospitals in Florence, Italy,

1
2
3 the Azienda Ospedaliero-Universitaria Careggi (AOUC), an academic tertiary hospital, and the Ospedale S.
4 Maria Annunziata (OSMA), a large community hospital. Enrolment was consecutively conducted between
5 June and August 2016 and again between February and March 2017 in the AOUC, and between August and
6 September 2016 in the OSMA, for a total of 22 weeks. In AIDEA, an application generating the DSC was
7 incorporated into the software routinely used in the ED of the hospitals of the Tuscany Region: as soon as
8 an eligible patient was triaged, the repository of healthcare data of the Local Health Unit was queried to
9 provide, thanks to on-demand linkage of the different archives involved, the information required to obtain
10 the DSC. The score was then in real-time calculated and shown, together with the corresponding risk class,
11 onto the computer screen. The lag time between occurrence of events contributing to the DSC
12 (hospitalizations and drug prescriptions) and their registration in the healthcare data repository was
13 approximately two weeks.
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29

30 **Participants' selection**

31
32 The SCNP selected only records of subjects aged 75+ years, residing in the area where the study
33 was conducted, who consecutively accessed the ED of the participating hospitals in the specified time
34 windows and were eventually admitted to Internal Medicine or Geriatrics wards. Conversely, the AIDEA
35 study enrolled all the residents aged 75+ years consecutively accessing the ED in the specified time periods,
36 independent of the outcome (hospitalization or discharge) of their access to the ED.
37
38
39
40
41
42
43
44
45
46
47

48 **Ethics**

49 Following the Italian legislation on observational studies using administrative databases in place at
50 the time of data acquisition, Ethics Committee approval and participants' subscription of informed consent
51 was waived in the SCNP, because only anonymized administrative data were extracted. The protocol of the
52 AIDEA study, which included also face-to-face interview (not reported in the present work), was approved
53 by the Ethics Committee of the AOU Careggi (976/13_AOUC).
54
55
56
57
58
59
60

Patient and public involvement

1
2
3 Patients or the public were not involved in the design or conduct of our research, partially because
4
5 of its retrospective nature. Patients' associations will be involved in the upcoming, large-scale application of
6
7 the DSC in hospitals of the Tuscany Region. Reporting was provided as requested by the funding
8
9 Institutions. Dissemination to the public was obtained through lay press.
10
11
12
13

14 **Analytic procedures**

15
16 Statistical analysis was performed with SPSS for Mac v. 25 (IBM Corp., Armonk, NY, USA), STATA v.
17
18 15.1 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC), and R
19
20 3.5.0 (R Core Team, 2018).
21
22

23 A total of 281,321 records were available in the SCNP database to create the DSC and test its
24
25 validity. The χ^2 was used to test differences in relative frequencies and to identify bivariate predictors of
26
27 death, taking into account trends as appropriate.
28
29

30 The sample was randomly split into a development and a validation subsample. In the first
31
32 subsample, a Cox proportional hazards model was fit to estimate the association, expressed as hazard ratio
33
34 (HR) with 95% confidence interval (CI) of demographics and other variables on 1-year all-cause mortality
35
36 risk. Variables initially considered, by definition limited to those available prior to the index ED visit,
37
38 included age, gender, number of drugs prescribed in the previous 3 months as resulting from pharmacy
39
40 claims (categorized as 0-3, 4-5, 6-8, and 9+), days from previous hospital admission (no admission, 30-180
41
42 days, 0-30 days) and its associated main diagnostic group (cancer, respiratory disease, cardiovascular
43
44 disease, and other conditions), which were selected as the most frequently observed, in the study cohort,
45
46 among those included in the ICD-9 classification. Compared to the original version of the SC, previous
47
48 admission to a day hospital was not considered, because availability and utilization of day hospital service
49
50 are not consistent across Regions in Italy. Marital status information was also omitted, because it was
51
52 frequently missing in the discharge summary and in preliminary analyses it contributed marginally to the
53
54 prediction of death. Differently from the SC, repeated hospitalizations were taken into account to
55
56 dynamically update patient's information at each new hospital admission. To this purpose, data were
57
58 arranged in order to have one observation per event or time interval, and the counting process approach
59
60

1
2
3 proposed by Andersen and Gill [23] was applied: this is a generalization of Cox's model, which assumes that
4
5 the correlation between event times for a person can be explained by past events. Thus, we made the
6
7 assumption that correlations among events for each individual were captured by appropriate time-
8
9 dependent covariates.
10

11
12 We evaluated the adherence of predictors to the assumption of proportional hazards and tested for
13
14 multicollinearity comparing different models in terms of Akaike information criteria.[24] We then assigned
15
16 each risk factor a score, calculated as the ratio, rounded to the nearest integer, between the regression b
17
18 coefficient for that variable and the smallest significant b coefficient (b_0) in the Cox model. We finally
19
20 computed the DSC as a summary score, by adding the points individually assigned to each risk factor. Four
21
22 prognostic classes were then created from DSC quartiles.
23

24
25 In the validation data set, Harrell's C index of concordance was applied to evaluate model
26
27 performance, as a measure of the predictive power of Cox regression model.[25] Furthermore, the ability
28
29 of DSC classes to predict 1-year mortality was analysed after adjusting for Region of enrolment and ICD-9
30
31 coded principal diagnosis at discharge after the index hospitalization. External validity of the DSC was
32
33 performed in the AIDEA data set, using Cox regression models and Harrell's C index of concordance to
34
35 predict 1-year mortality and the risk of recurrent ED access after a first hospital admission.
36
37

38
39 Additional analyses were performed to verify the ability of the DSC to predict 7- and 30-day
40
41 mortality, two outcomes that are more immediate and potentially of greater clinical interest in the
42
43 perspective of application of the tool in the ED. Also these analyses were adjusted for main diagnostic
44
45 group at discharge and Region of enrolment.
46

47
48 A two-tailed p value less than 0.05 was considered statistically significant.
49
50

51 52 **RESULTS**

53 54 55 56 **Participants in the SCNP**

57
58
59 Out of the 281,321 records in the SCNP, 180,079 (64.01%) pertained to a single hospitalization, the
60
remaining to patients with multiple hospital admissions in the study period. The random split assigned

90,039 patients to the development and 90,040 to the validation subsample, with 140,716 and 140,605 records, respectively. As shown in **Table 1**, baseline characteristics of participants on their first hospital admission were comparable between the two subsamples.

Table 1. Baseline characteristics of participants on their first hospital admission, in the entire sample and in the development and validation subsamples. The p value reported refers to the χ^2 test, for trend when appropriate.

Variable	Overall (n=180,079)		Development subsample (n=90,039)		Validation subsample (n=90,040)		p
	N	%	N	%	N	%	
Age (years)							0.348
75-79	52,196	29.0	25,974	28.9	26,222	29.1	
80-84	60,205	33.4	30,221	33.6	29,984	33.3	
85+	67,678	37.6	33,844	37.6	33,834	37.6	
Gender							0.639
Male	77,803	43.2	38,852	43.2	38,951	43.3	
Female	102,276	56.8	51,187	56.9	51,089	56.7	
Number of drugs in previous 3 months							0.268
0-3	57,859	32.1	28,995	32.2	28,864	32.1	
4-5	38,405	21.3	19,322	21.5	19,083	21.2	
6-8	46,754	26.0	23,222	25.8	23,532	26.1	
9+	37,061	20.6	18,500	20.6	18,561	20.6	
Main diagnostic group in previous (6 months) hospital admission							0.773
No previous hospital admission	146,562	81.4	73,241	81.3	73,321	81.4	
Cardiovascular disease	11,206	6.2	5,537	6.15	5,669	6.3	
Cancer	3,954	2.2	1,955	2.2	1,999	2.2	
Respiratory disease	3,171	1.8	1,585	1.8	1,586	1.8	
Others	15,186	8.4	7,721	8.6	7,465	8.3	
Days from previous (6 months) hospital admission							0.156
No previous hospital admission	146,562	81.4	73,241	81.3	73,321	81.4	
31-180	23,374	13.0	11,793	13.1	11,581	12.9	
0-30	10,143	5.6	5,005	5.6	5,138	5.7	

Predictors of 1-year mortality

From hospital admission through the following year, a total of 42,434 deaths were recorded; mortality was comparable in the development (21,250/90,039, 23.6%) and the validation (21,184/90,040,

1
2
3 23.5%) subsamples. In the development sample, bivariate predictors of death were older age (75–79 years:
4 16.4%, 80–84 years: 20.5%, 85+ years: 31.9%; $p=0.001$), gender (men: 24.8%, women: 22.7%; $p<0.001$),
5
6 previous hospital admission with its corresponding main discharge diagnosis (no admission: 22.1%,
7
8 cardiovascular disease: 23.5%, cancer: 49.1%, respiratory disease: 30.8%, other diagnoses: 30.2%; p
9
10 <0.001), days from previous hospital admission (1–30 days: 34.5%, 31–180 days: 28.5%, $p<0.001$), or taking
11
12 more drugs prior to the index ED admission (0–3: 22.6%, 4–5: 22.9%, 6–8: 23.3%, 9+: 26.2%; $p<0.001$).
13
14
15
16
17

18 Risk models

19
20
21 **Table 2** shows the results of Cox proportional hazard regression model in the SCNP development
22
23 subsample. All the variables considered were significant predictors of 1-year mortality. Because the
24
25 diagnostic groups of “cardiovascular disease” and “others” obtained similar HRs, they were combined into a
26
27 single category, contrasted with “no previous hospital admission”, “cancer” and “respiratory disease”. The
28
29 predictors “days from the previous hospital admission” and the associated “main diagnostic group” showed
30
31 some multicollinearity, but the models with only one of those variables performed worse in terms of AIC:
32
33 therefore, both variables were maintained in the final model. All predictors satisfied the assumption of
34
35 proportional hazards.
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 2. Multivariable *b* coefficients, obtained from Cox regression model predicting 1-year death, in the 90,039 participants in the development subsample, with scores associated.

Variable	<i>b</i> Coefficient	p-value	Score
Age (years)			
75-79	Ref.		0
80-84	0.2871	<0.001	8
85+	0.8259	<0.001	23
Gender			
Female	Ref.		0
Male	0.1875	<0.001	5
Number of drugs in previous 3 months			
0-3	Ref.		0
4-5	0.0364	0.0320	1
6-8	0.0732	<0.001	2
9+	0.2173	<0.001	6
Main diagnostic group in previous (6 months) hospital admission			
No admission	Ref.		0
Cardiovascular disease / Others	0.6944	<0.001	19
Cancer	1.5218	<0.001	42
Respiratory disease	1.0357	<0.001	28
Days from previous (6 months) hospital admission			
No admission	Ref.		0
30-180	0.2763	<0.001	8
0-30	0.000		0

The smallest significant *b* coefficient in the Cox model resulted to be associated with 4-5 drugs prescribed in the previous 3 months ($b_0 = 0.0364$). Thus, each significant predictor was assigned a score by rounding the ratio between the corresponding *b* coefficient in the regression model and b_0 up to the nearest integer (**Table 2**). The DSC was finally calculated as summation of all scores.

Participants were classified into low-, medium-, high-, and very high-risk classes, based upon DSC quartiles. One-year risk of death increased significantly from the first to the fourth DSC class, with almost identical hazard ratios in both subsamples (**Table 3**). In the validation subsample, the performance of the risk scoring system, assessed with Harrell's C index, was 0.668 (95% CI 0.665- 0.672). The ability of the DSC to predict 1-year mortality persisted controlling for main diagnostic group at discharge after the index hospitalization and Region of enrolment (Tuscany vs. Lazio), as shown by HR (95% CI) of 1.93 (1.88-1.98), 2.71 (2.64-2.78), and 5.00 (4.88-5.13) for class II, III, and IV, respectively, compared to class I ($p < 0.001$) (**Figure 1**).

Table 3. One-year mortality and corresponding hazard ratios by DSC class, separately in the development and validation subsamples.

DSC Class (score)	Development subsample (n=90,039)				Validation subsample (n=90,040)			
	Participants	Deaths	Rate (per 1,000 p-y)	HR (95% CI)	Participants	Deaths	Rate (per 1000 p- y)	HR (95% CI)
I (≤ 10)	29,880	4,303	144	Ref.	29,798	4,291	144	Ref.
II (11-25)	32,712	8,127	248	1.93 (1.86-2.00)	32,775	8,082	247	1.92 (1.85-1.99)
III (26-34)	17,391	5,180	298	2.73 (2.64-2.84)	17,439	5,126	294	2.71 (2.61-2.81)
IV (≥ 35)	10,056	3,640	362	5.37 (5.18-5.56)	10,028	3,685	367	5.40 (5.21-5.59)
Total	90,039	21,250	236		90,040	21,184	235	

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

External validity

External validity of the DSC was ascertained in the AIDEA sample, which included 5,217 records for 4,425 subjects, of whom 1,292 died and 465 had a new ED admission within one year. Mortality increased progressively across DSC classes, with HR (95% CI) of 2.06 (1.68-2.53), 3.32 (2.74-4.03), and 5.28 (4.37-6.39) in class II, III, and IV, vs. class I ($p < 0.001$) and a Harrell's C index of 0.660 (95% CI 0.641-0.678). Also 1-year risk of recurrent ED access increased significantly across DSC classes, with HR (95% CI) of 1.46 (1.11-1.93), 1.45 (1.10-1.92), 2.60 (1.99-3.40) in class II, III, and IV, vs. class I ($p = 0.007$, 0.009 and < 0.001 , respectively) and a Harrell's C index of 0.604 (95% CI 0.573-0.634).

Prediction of short-term mortality

The DSC predicted also 7- and 30-day mortality in both databases. In the SCNP database as a whole, 20,297 and 27,812 participants died within 7 and 30 days, respectively, out of the 180,079 enrolled. In AIDEA, the analysis on 7- and 30-day mortality included 4,425 participants, of whom 102 and 345 died within 7 and 30 days, respectively. In both databases and for both follow-up times, short-term mortality increased significantly across DSC classes ($p < 0.001$) (**Table 4**). Harrell's C index was 0.623 (95% CI 0.618-0.627) and 0.639 (95% CI 0.635-0.643) for 7- and 30-day mortality in the SCNP and 0.690 (95% CI 0.619-0.761) and 0.683 (95% CI 0.645-0.721) in AIDEA.

Table 4. Prediction of 7- and 30-day mortality by DSC class in the complete SCNP and in the AIDEA databases.

DSC Class (score)	SCNP				AIDEA			
	7-day mortality		30-day mortality		7-day mortality		30-day mortality	
	Rate	HR	Rate	HR	Rate	HR	Rate	HR
	(per 1000 p-y)	(95% CI) *	(per 1000 p-y)	(95% CI) *	(per 1000 p-y)	(95% CI)	(per 1000 p-y)	(95% CI)
I (≤ 10)	64	Ref.	81	Ref.	8	Ref.	28	Ref.
II (11-25)	113	1.83 (1.76- 1.91)	145	1.92 (1.85- 1.99)	19	2.24 (1.06- 4.76)	46	1.74 (1.14- 2.65)
III (26-34)	144	2.41 (2.31- 2.52)	178	2.53 (2.43- 2.62)	22	2.73 (1.33- 5.64)	84	3.17 (3.17- 4.64)
IV (≥ 35)	189	3.30 (3.15- 3.45)	234	3.98 (3.84- 4.14)	45	5.57 (2.78- 11.15)	136	5.58 (3.85- 8.09)

* Adjusted for main diagnostic group at discharge and Region of enrolment (Tuscany vs. Lazio).

DISCUSSION

Using the SCNP large, representative cohort of older persons accessing the ED and then admitted to hospitals in two Italian Regions, we developed the DSC, which combines simple variables, extracted from administrative databases, into a score predicting 1-year mortality. The score was validated against mortality in a random subset of the same cohort, and then its external validity was proven in the newly enrolled sample of the AIDEA study. Remarkably, whereas in the SCNP cohort the DSC was obtained from off-line processing of consolidated archives, in AIDEA it was generated in real-time on arrival of each eligible patient, thanks to an application implemented in the software routinely used for patients' clinical management in the EDs of Tuscany Region.

In older persons, because of coexisting chronic comorbidities and diminished life expectancy, fully informed clinical decision making requires adequate knowledge of patient's prognosis. In the presence of any given acute condition, comprehensive care planning should be carefully performed, by considering life expectancy, as well as pre-morbid functional and cognitive status.[26] Nevertheless, accurate prognostic

1
2
3 assessment of complex older patients is frequently overlooked in clinical practice, especially in the busy
4
5 daily practice of an ED, where geriatric patients often arrive with non-specific complaints, such as
6
7 worsening functional status, confusion, dizziness or fall. Their clinical presentation is frequently
8
9 characterized not by a single, well-defined disease, but rather by an entangled combination of age-related
10
11 changes, comorbidity, functional and cognitive impairment, polypharmacy, and social problems. As a
12
13 consequence, the risk of wrong triage, incorrect diagnosis and treatment, prolonged ED stay and
14
15 inappropriate destination is substantial.[27] Worsening disability, institutionalization or death shortly after
16
17 the ED access may be ultimate consequences.[28]

20
21 Instruments to screen older persons in the ED, based on comprehensive geriatric assessment, do
22
23 exist,[29] but are not used routinely in clinical practice, as they require some expertise and are time
24
25 consuming. Thus, in spite of their inherent limitations, simple administrative data are increasingly explored
26
27 as an attractive contribution to prognostic assessment, because they are accurate, objective and easily
28
29 available at a low cost.[7-9] Along this track, we have previously developed the SC, which was shown to
30
31 predict long-term mortality [17, 18] and hospitalizations of older persons in the ED [18] in two different
32
33 cohorts, with a discrimination ability comparable to that of other tools requiring face-to-face interview.[18]
34
35 Moreover, the SC allowed risk stratification when comparing the effects of different therapeutic
36
37 approaches.[17, 30] However, the algorithm to develop the SC relied only upon the first ED admission, so
38
39 that the score remained constant throughout the following observation time, independently of new
40
41 hospitalizations or drug prescriptions. To overcome this limitation of the parent tool, the DSC was
42
43 developed by taking into account each hospital admission as the unit of analysis. This would allow the score
44
45 to reflect more closely the dynamics of risk status of older patients, changing after each hospitalization or
46
47 new drug prescription.

51
52 The variables contributing to the DSC can be all recognized as meaningful predictors of prognosis.
53
54 Yet, because short-term re-hospitalization usually indicates clinical instability, it is somewhat unexpected
55
56 that, in the multivariable model reported in Table 2, a previous hospital admission between 0 and 30 days
57
58 had a b coefficient of zero, comparable to no admission. However, the Italian hospital discharge coding
59
60 system does not allow distinguishing, among short-term re-hospitalizations, those that might have been

1
2
3 planned at the end of the index hospitalization (e.g. to complete diagnostics or treatments) from those
4
5 occurring because of clinical instability.
6

7 The estimates we obtained are robust, because they were based on high-quality data from a large,
8
9 randomly split population-based cohort, thus overcoming the problem of overestimation typical of small
10
11 sample size datasets.[31] The predictive ability of the tool persisted even after controlling for discharge
12
13 diagnosis. As a further confirm, external validation was achieved in the new sample of the AIDEA study,
14
15 whose participants might be hospitalized or not after the index ED access. It should be emphasized that the
16
17 DSC predicted also short-term mortality and, at least in AIDEA, recurrent hospitalizations, outcomes for
18
19 which it had not been created. As suggested by the lower short-term mortality rates reported in Table 4,
20
21 the AIDEA cohort was substantially healthier than the SCNP cohort: this is to be expected, as AIDEA
22
23 enrolled also participants that were immediately discharged from the ED, without being hospitalised.
24
25 Nevertheless, the incremental risk across DSC classes was comparable in the two studies. Moreover, short-
26
27 and long-term mortality rate figures in the AIDEA cohort compare well to those reported by Tanderup et
28
29 al.: in a Danish study on 3775 subjects aged 65+ years accessing the ED, 30-day and 1-year cumulative
30
31 mortality increased progressively, from 2.2% to 10.6% and from 8% to 39%, respectively, with the number
32
33 of geriatric conditions (from 0 to 4), identified on the basis of comprehensive geriatric assessment.[27] The
34
35 similarity between Tanderup's and ours estimates seems to provide further, indirect support to the validity
36
37 of the DSC.
38
39
40
41
42

43 In terms of Harrell's C index, the discrimination of the DSC was only moderate, similar in the
44
45 internal and external validation cohorts. Thus, although predictive at the group level, its ability to predict
46
47 prognosis at an individual level is suboptimal. A possible, partial explanation for this finding is that the DSC
48
49 might misclassify subjects defined at low risk, if they reached the ED with acute life-threatening conditions.
50
51 Also nursing home residents with severe disability or dementia might be erroneously considered as at low
52
53 risk by the DSC, if they had no hospital admissions in the previous year: other administrative archives
54
55 collecting data on nursing home services, which are expected to become promptly available in Tuscany,
56
57 should eliminate this source of misclassification. On the other hand, comparably suboptimal performances
58
59 have been reported for other tools, proposed in the literature for prognostic assessment in the ED, such as
60

1
2
3 the Identification of Seniors At Risk [29, 18] (C statistics of 0.65 for 6-month mortality) or the Hospital
4 Frailty Risk Score [32] (C statistics of 0.60 for 30-day mortality), or widely used to drive clinical decisions in
5 acute coronary syndromes, such as the TIMI risk score (C statistics of 0.65 for a 14-day composite
6 endpoint).[33] This may reflect the fact that, as pointed out by other authors,[32] individual outcomes are
7 inherently unpredictable in acute settings, even when risk status is well characterized at a cohort level. This
8 does not detract from the clinical impact of the DSC and similar scores, which help delivery targeted
9 interventions to groups of patients with specific characteristics, whereas, at an individual level, should be
10 used to support, not to substitute clinical judgment.

11
12
13
14
15
16
17
18
19
20
21 A 2012 systematic review on prognostic indices for older adults [2] reported only one article – our
22 original publication on the parent instrument –[17] that focused on ED triage of older persons using
23 administrative data, but not in a real-time application. Although other, more recent studies dealing with
24 prognostic issues around older persons in an acute hospital setting can be found, none of them was
25 developed for use in the ED nor proposed real-time linkage of administrative data. Thus, to the best of our
26 knowledge, the DSC represents the first example in the literature of real-time utilization of administrative
27 data for prognostic purposes, at least in – but probably not limited to – older persons accessing the ED.

28
29
30
31
32
33
34
35
36
37 Several strengths of the DSC should be highlighted. First, it predicts short- and long-term prognosis
38 and risk of hospitalization combining with a simple calculation a limited set of variables, obtained from
39 administrative data: thus, it is objective and does not rely on patient's collaboration, which is sometime
40 difficult to obtain in the presence of cognitive decline or communication barriers. Second, as the AIDEA
41 study shows, it can be calculated in real-time, being therefore immediately available to the ED staff as soon
42 as a target patient is triaged, even before any clinical assessment and with no need of dedicated human
43 resources to gather information. To our knowledge, this represents a unique example of clinical utilization
44 of administrative data, which might be easily replicated in other hospitals, at least in Italy. Third, it is a non-
45 disease specific tool, an important characteristic allowing its universal application in older patients, in
46 whom multimorbidity and atypical symptoms presentation make clinical and prognostic assessment
47 challenging. Fourth, similar to other prognostic tools based on administrative data, it can be applied also to
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 obtain risk adjustment in the healthcare policy arena: to our knowledge, no previous prognostic tools have
4
5 been developed to pursue both clinical and epidemiological purposes.
6

7 Study limitations are to be acknowledged. The original SCNP dataset is relatively old: however, the
8
9 validity of the score was confirmed in the definitively more recent AIDEA cohort. The score was developed
10
11 based on data obtained only in subjects admitted to Internal Medicine or Geriatrics units: nonetheless, its
12
13 validity was confirmed in a completely different series, which included patients visiting the ED for a variety
14
15 of reasons and most of times discharged from the ED. The data so far available did not consent considering
16
17 other predictors (e.g., claims for specialized visits or other services, or census data), neither different
18
19 outcomes besides mortality, such as functional or cognitive decline and institutionalization, which are
20
21 highly relevant in geriatric patients. However, we are confident that the increasing availability of other
22
23 administrative databases, as suggested above in reference to nursing home services, will allow
24
25 incorporating a wider set of predictors as well as of endpoints in the next future.
26
27
28

29 In conclusion, the DSC, a simple prognostic tool based on administrative data, available in real-time
30
31 in the software used in the ED of Italian hospitals, offers a valid prognostic assessment of older patients,
32
33 virtually at no additional costs, once the system has been set. This might support clinical decision-making
34
35 and improve the quality of the care provided. Future studies are needed to assess whether these
36
37 expectations will be satisfied.
38
39
40

41 42 43 **ACKNOWLEDGMENTS**

44
45 Not applicable.
46
47
48
49

50 51 **FUNDING**

52 The “Silver Code National Project” was funded by the Centre for Disease Control of the Italian
53
54 Ministry of Health. The “Anziani in DEA” study was jointly funded by the Italian Ministry of Health and by
55
56 the Tuscany Region (RF-2010-2321801). The funders had no role in study design, data collection and
57
58 analysis, decision to publish, or preparation of the manuscript. All the authors were independent from
59
60

1
2
3 funders, had access to all of the data and can take responsibility for the integrity of the data and the
4
5 accuracy of the data analysis.
6
7
8
9

10 **CONFLICT OF INTEREST**

11 All the authors had no financial relationships with organisations or other relationships that might
12
13 appear to have influenced the submitted work.
14
15
16
17

18 **AUTHOR CONTRIBUTIONS**

19
20 DB conceived the study, conducted data management and analysis, and contributed drafting the
21
22 manuscript. GC conducted data analysis and contributed drafting the manuscript. FT contributed obtaining
23
24 the data and drafting the manuscript. LDE and PM obtained the data and contributed to data management.
25
26 AU and EB contributed obtaining the data and provided institutional support. LG and GL provided
27
28 institutional support. RB and NM provided institutional support and contributed developing the research
29
30 question. MDB conceived the study, wrote the protocol, supervised analyses, and drafted the manuscript.
31
32 All authors read and approved the final manuscript.
33
34
35
36
37
38

39 **DATA AVAILABILITY STATEMENT**

40
41 Study protocol and data may be obtained from the authors on reasonable request, provided that
42
43 consent is released by the funding Institutions.
44
45
46
47

48 **REFERENCES**

- 49
50 1. Tinetti ME, Fried T. The end of the disease era. *Am J Med.* 2004;116(3):179–85.
51
52 2. Yourman LC, Lee SJ, Schonberg MA, et al. Prognostic indices for older adults: a systematic review.
53
54 *JAMA.* 2012;307(2):182–92.
55
56 3. Walter LC, Covinsky KE. Cancer Screening in Elderly Patients. *JAMA.* 2001;285(21):2750.
57
58 4. Mehta KM, Fung KZ, Kistler CE, et al. Impact of Cognitive Impairment on Screening Mammography
59
60 Use in Older US Women. *Am J Public Health.* 2010;100(10):1917–23.

- 1
2
3 5. Wallace E, Stuart E, Vaughan N, et al. Risk prediction models to predict emergency hospital
4 admission in community-dwelling adults: a systematic review. *Med Care*. 2014;52(8):751–65.
5
6
- 7 6. Galvin R, Gillett Y, Wallace E, et al. Editor’s Choice: Adverse outcomes in older adults attending
8 emergency departments: A systematic review and meta-analysis of the Identification of Seniors At
9 Risk (ISAR) screening tool. *Age Ageing*. 2017;46(2):179–86.
10
11
- 12 7. Dagan N, Cohen-Stavi C, Leventer-Roberts M, et al. External validation and comparison of three
13 prediction tools for risk of osteoporotic fractures using data from population based electronic health
14 records: retrospective cohort study. *BMJ*. 2017;i6755.
15
16
- 17 8. Albaba M, Cha SS, Takahashi PY. The Elders risk assessment index, an electronic administrative
18 database-derived frailty index, can identify risk of hip fracture in a cohort of community-dwelling
19 adults. *Mayo Clin Proc*. 2012;87(7):652–8.
20
21
- 22 9. Simpson AN, Wilmskoetter J, Hong I, et al. Stroke Administrative Severity Index: using administrative
23 data for 30-day poststroke outcomes prediction. *J Comp Eff Res*. 2018;7(4):293–304.
24
25
- 26 10. Mahajan SM, Heidenreich P, Abbott B, et al. Predictive models for identifying risk of readmission
27 after index hospitalization for heart failure: A systematic review. *Eur J Cardiovasc Nurs*.
28 2018;17(8):675–89.
29
30
- 31 11. Taylor RA, Pare JR, Venkatesh AK, et al. Prediction of In-hospital Mortality in Emergency Department
32 Patients With Sepsis: A Local Big Data-Driven, Machine Learning Approach. *Acad Emerg Med*.
33 2016;23(3):269–78.
34
35
- 36 12. Clegg A, Bates C, Young J, et al. Development and validation of an electronic frailty index using
37 routine primary care electronic health record data. *Age Ageing*. 2016;45(3):353–60.
38
39
- 40 13. Corrao G, Rea F, Di Martino M, et al. Developing and validating a novel multisource comorbidity
41 score from administrative data: a large population-based cohort study from Italy. *BMJ Open*.
42 2017;7(12):e019503.
43
44
- 45 14. Davoudi A, Ozrazgat-Baslanti T, Ebadi A, et al. Delirium Prediction using Machine Learning Models
46 on Predictive Electronic Health Records Data. *Proc IEEE Int Symp Bioinformatics Bioeng*. 2018: 568–
47 73.
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

15. Corey KM, Kashyap S, Lorenzi E, et al. Development and validation of machine learning models to identify high-risk surgical patients using automatically curated electronic health record data (Pythia): A retrospective, single-site study. *PLoS Med.* 2018;15(11):e1002701.
16. Rahimian F, Salimi-Khorshidi G, Payberah AH, et al. Predicting the risk of emergency admission with machine learning: Development and validation using linked electronic health records. *PLoS Med.* 2018;15(11):e1002695.
17. Di Bari M, Balzi D, Roberts AT, et al. Prognostic stratification of older persons based on simple administrative data: development and validation of the “Silver Code,” to be used in emergency department triage. *J Gerontol A Biol Sci Med Sci.* 2010;65(2):159–64.
18. Di Bari M, Salvi F, Roberts AT, et al. Prognostic stratification of elderly patients in the emergency department: a comparison between the “Identification of Seniors at Risk” and the “Silver Code”. *J Gerontol A Biol Sci Med Sci.* 2012;67(5):544–50.
19. Centro Nazionale per la Prevenzione e il Controllo delle Malattie. Modelli innovativi per la presa in carico del paziente anziano fragile nella transizione dall’ ospedale al territorio e dal territorio all’ ospedale: Case Management e qualità della vita. Available at: <http://www.ccm-network.it/progetto.jsp?id=node/1353&idP=740>.
20. Simonato L, Baldi I, Balzi D, et al. Objectives, tools and methods for an epidemiological use of electronic health archives in various areas of Italy. *Epidemiol Prev.* 2008;32(3 Suppl):5-14.
21. Ministero del Lavoro, della Salute e delle Politiche Sociali. Rapporto annuale sulla attività di ricovero ospedaliero—Anno . 2005. Available at: <http://www.ministerosalute.it/programmazione/sdo/sezDocumenti.jsp?id=148&label=osp>. Consultation date April 10, 2019.
22. Ministero della Salute. Rapporto Annuale sull’attività di ricovero ospedaliero. Dati SDO 2017. 2019. Available at: [http://www.salute.gov.it/portale/temi/p2_4.jsp?lingua=italiano&tema=Assistenza, ospedale e territorio&area=ricoveriOspedalieri](http://www.salute.gov.it/portale/temi/p2_4.jsp?lingua=italiano&tema=Assistenza,ospedale%20e%20territorio&area=ricoveriOspedalieri). Consultation date April 10, 2019.
23. Andersen PK, Gill RD. Cox’s regression model for counting processes: A large sample study. *Annals of Statistics* 1982;10:1100-1120.

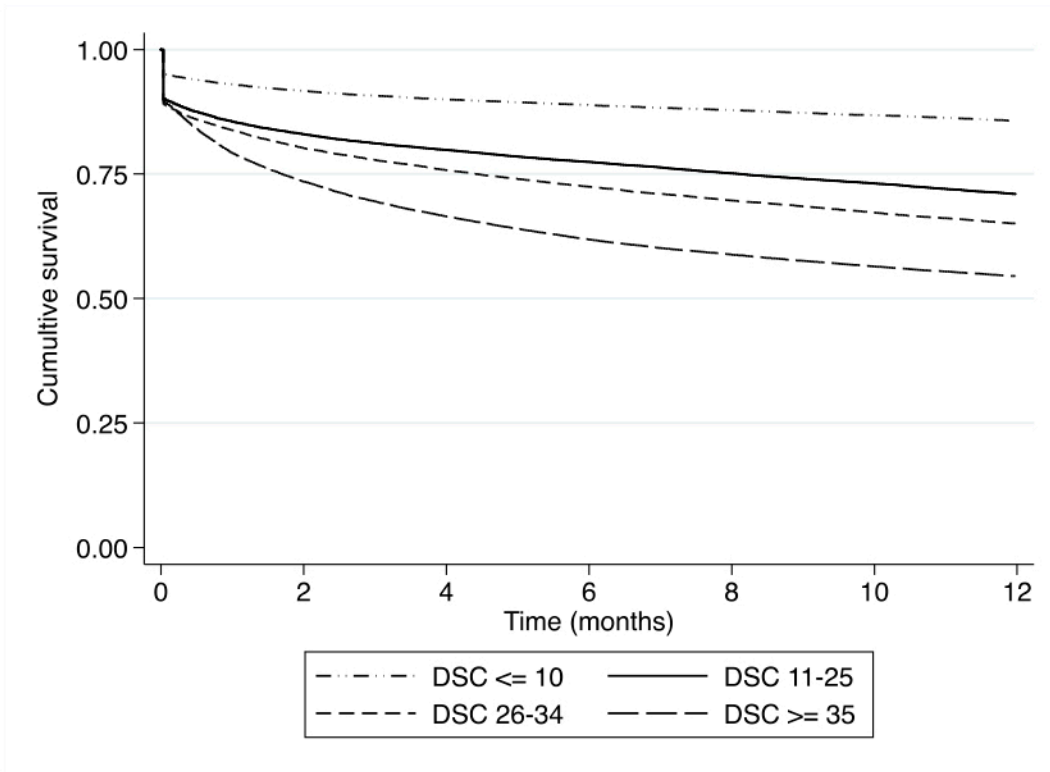
- 1
2
3 24. Akaike H. A New Look at the Statistical Model Identification. *IEEE Transaction Autom Contr.*
4
5 1974;19(6):716-23.
6
- 7 25. Harrell FE, Califf RM, Pryor DB, et al. Evaluating the Yield of Medical Tests. *JAMA.*
8
9 1982;247(18):2543-6.
10
- 11 26. Gill TM. The central role of prognosis in clinical decision making. *JAMA* 2012; 307(2): 199–200.
12
- 13 27. Tanderup A, Lassen AT, Rosholm JU, Ryg J. Disability and morbidity among older patients in the
14 emergency department: a Danish population-based cohort study. *BMJ Open* 2018;8:e023803.
15
16 doi:10.1136/bmjopen-2018-023803.
17
- 18 28. Salvi F, Morichi V, Grilli A, et al. The elderly in the emergency department: a critical review of
19 problems and solutions. *Intern Emerg Med.* 2007;2(4):292-301.
20
- 21 29. McCusker J, Bellavance F, Cardin S, et al. Detection of Older People at Increased Risk of Adverse
22 Health Outcomes After an Emergency Visit: The ISAR Screening Tool. *J Am Geriatr Soc.*
23
24 1999;47(10):1229–37.
25
- 26 30. Di Bari M, Balzi D, Fracchia S, et al. Decreased usage and increased effectiveness of percutaneous
27 coronary intervention in complex older patients with acute coronary syndromes. *Heart.*
28
29 2014;100(19):1537–42.
30
- 31 31. Royston P, Moons KGM, Altman DG, et al. Prognosis and prognostic research: Developing a
32 prognostic model. *BMJ.* 2009;338:b604.
33
- 34 32. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score
35 focusing on older people in acute care settings using electronic hospital records: an observational
36
37 study. *Lancet.* 2018;391:1775-1782.
38
- 39 33. Antman EM, Cohen M, Bernink PJLM, et al. The TIMI Risk Score for Unstable Angina/Non–ST
40
41 Elevation MI. *JAMA.* 2000;284(7):835-42.
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. Survival curves for cumulative risk of death within 1 year after first hospitalization by class of Dynamic Silver Code (DSC) in the validation sample (n=90,040). Cox proportional hazards regression, adjusting for Region of residence and main discharge diagnostic group, with p for trend <0.001.

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the TRIPOD reporting guidelines, and cite them as:

Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

	Reporting Item	Page Number
Title		
	#1 Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract		
	#2 Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction		
	#3a Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5
	#3b Specify the objectives, including whether the study describes the	5

development or validation of the model or both.

Methods

1			
2			
3	Methods		
4			
5	Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.
6			6
7			
8			
9			
10	Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.
11			6
12			
13			
14	Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.
15			7
16			
17			
18	Participants	#5b	Describe eligibility criteria for participants.
19			7
20	Participants	#5c	Give details of treatments received, if relevant
21			NA
22			
23	Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.
24			8
25			
26	Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.
27			NA
28			
29	Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured
30			8
31			
32			
33			
34	Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.
35			NA
36			
37			
38	Sample size	#8	Explain how the study size was arrived at.
39			6
40	Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.
41			NA
42			
43			
44			
45	Statistical analysis methods	#10a	If you are developing a prediction model describe how predictors were handled in the analyses.
46			7-8
47			
48			
49	Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.
50			8
51			
52			
53			
54	Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.
55			8
56			
57			
58	Statistical analysis	#10d	Specify all measures used to assess model performance and, if relevant,
59			8
60			

1	methods		to compare multiple models.	
2	Statistical analysis	#10e	If you are validating a prediction model, describe any model updating	NA
3	methods		(e.g., recalibration) arising from the validation, if done	
4				
5				
6	Risk groups	#11	Provide details on how risk groups were created, if done.	8
7				
8	Development vs.	#12	For validation, identify any differences from the development data in	8
9	validation		setting, eligibility criteria, outcome, and predictors.	
10				
11				
12	Results			
13				
14	Participants	#13a	Describe the flow of participants through the study, including the	9
15			number of participants with and without the outcome and, if applicable,	
16			a summary of the follow-up time. A diagram may be helpful.	
17				
18	Participants	#13b	Describe the characteristics of the participants (basic demographics,	10
19			clinical features, available predictors), including the number of	
20			participants with missing data for predictors and outcome.	
21				
22	Participants	#13c	For validation, show a comparison with the development data of the	10
23			distribution of important variables (demographics, predictors and	
24			outcome).	
25				
26	Model	#14a	If developing a model, specify the number of participants and outcome	10
27	development		events in each analysis.	
28				
29	Model	#14b	If developing a model, report the unadjusted association, if calculated	11
30	development		between each candidate predictor and outcome.	
31				
32	Model	#15a	If developing a model, present the full prediction model to allow	12
33	specification		predictions for individuals (i.e., all regression coefficients, and model	
34			intercept or baseline survival at a given time point).	
35				
36	Model	#15b	If developing a prediction model, explain how to the use it.	13
37	specification			
38				
39	Model	#16	Report performance measures (with CIs) for the prediction model.	13
40	performance			
41				
42	Model-updating	#17	If validating a model, report the results from any model updating, if	14
43			done (i.e., model specification, model performance).	
44				
45				
46	Discussion			
47				
48	Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample,	16
49				
50				

few events per predictor, missing data).

1			
2			
3	Interpretation	#19a	For validation, discuss the results with reference to performance in the 15
4			development data, and any other validation data
5			
6	Interpretation	#19b	Give an overall interpretation of the results, considering objectives, 16
7			limitations, results from similar studies, and other relevant evidence.
8			
9			
10	Implications	#20	Discuss the potential clinical use of the model and implications for 16
11			future research
12			
13			
14	Other		
15	information		
16			
17			
18	Supplementary	#21	Provide information about the availability of supplementary resources, 18
19	information		such as study protocol, Web calculator, and data sets.
20			
21	Funding	#22	Give the source of funding and the role of the funders for the present 17
22			study.
23			
24			

The TRIPOD checklist is distributed under the terms of the Creative Commons Attribution License CC-BY.

This checklist was completed on 01. August 2019 using <https://www.goodreports.org/>, a tool made by the

[EQUATOR Network](#) in collaboration with [Penelope.ai](#)

BMJ Open

Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk: Development and Validation of the Dynamic Silver Code

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-033374.R2
Article Type:	Original research
Date Submitted by the Author:	09-Nov-2019
Complete List of Authors:	<p>Balzi, Daniela; 1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy</p> <p>Carreras, Giulia; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Tonarelli, Francesco; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Degli Esposti, Luca; CliCon S.r.l, Health, Economics and Outcomes Research,</p> <p>Michelozzi, Paola; Lazio Region, Epidemiology</p> <p>Ungar, Andrea; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Gabbani, Luciano; Careggi Hospital, Unit of Geriatrics</p> <p>Benvenuti, Enrico; Azienda USL Toscana centro, Department of Internal Medicine,</p> <p>Landini, Giancarlo; Azienda USL Toscana centro, Department of Internal Medicine,</p> <p>Bernabei, Roberto ; Fondazione Policlinico Agostino Gemelli IRCCS</p> <p>Marchionni, Niccolò; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p> <p>Di Bari, Mauro; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimental Medicine</p>
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Emergency medicine, Health informatics
Keywords:	Prognostic assessment, elderly, Emergency Department, Dynamic Silver Code, administrative data

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



1
2
3 **Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk:**
4
5 **Development and Validation of the Dynamic Silver Code**
6
7
8
9

10 Daniela Balzi, BSc ¹

11 Giulia Carreras, PhD ²

12 Francesco Tonarelli, MD ²

13 Luca Degli Esposti, EconD, PhD ³

14 Paola Michelozzi, BSc, MS ⁴

15 Andrea Ungar, MD, PhD ^{2,5}

16 Luciano Gabbani, MD ⁶

17 Enrico Benvenuti, MD ⁷

18 Giancarlo Landini, MD ⁸

19 Roberto Bernabei, MD ⁹

20 Niccolò Marchionni, MD ^{2,10}

21 Mauro Di Bari, MD, PhD ^{2,5}

- 22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy
 2. Research Unit of Medicine of Aging, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy
 3. Clicon – Health, Economics & Outcome Research, Ravenna, Italy
 4. Department of Epidemiology, Lazio Region, Rome, Italy
 5. Unit of Geriatrics, Department of Medicine and Geriatrics, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
 6. Department of Medicine and Geriatrics, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy
 7. Unit of Geriatrics, Department of Internal Medicine, Azienda USL Toscana Centro, Florence, Italy
 8. Department of Internal Medicine, Azienda USL Toscana Centro, Florence, Italy

1
2
3 9. Fondazione Policlinico Agostino Gemelli IRCCS, Rome, Italy
4

5 10. Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Careggi, Florence,
6
7 Italy.
8
9

10
11
12 **Corresponding Author**
13

14 Mauro Di Bari, MD, PhD

15
16 Research Unit of Medicine of Aging

17
18 Department of Experimental and Clinical Medicine

19
20 University of Florence

21
22 Viale G. Pieraccini, 18

23
24 50139 Florence, Italy

25
26 E-mail: mauro.dibari@unifi.it
27
28
29
30
31

32 **RUNNING TITLE:** Risk stratification of older patients in the ED
33
34
35

36 **ABSTRACT WORD COUNT:** 290
37

38 **WORD COUNT:** 4072
39

40 **NUMBER OF TABLES:** 4
41

42 **NUMBER OF FIGURES:** 1
43

44 **NUMBER OF REFERENCES:** 33
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ABSTRACT

Objective: Identification of older patients at risk, among those accessing the Emergency Department (ED), may support clinical decision-making. To this purpose, we developed and validated the Dynamic Silver Code (DSC), a score based on real-time linkage of administrative data.

Design and Setting: The “Silver Code National Project (SCNP)”, a non-concurrent cohort study, was used for retrospective development and internal validation of the DSC. External validation was obtained in the “Anziani in DEA (AIDEA)” concurrent cohort study, where the DSC was generated by the software routinely used in the ED.

Participants: The SCNP contained 281,321 records of 180,079 75+ years old residents from Tuscany and Lazio, Italy, admitted via the ED to Internal Medicine or Geriatrics units. The AIDEA study enrolled 4,425 subjects aged 75+ years (5,217 records) accessing two EDs in the area of Florence, Italy.

Interventions: None.

Outcome measures: Primary outcome: one-year mortality. Secondary outcomes: 7- and 30-day mortality and 1-year recurrent ED visits.

Results: Advancing age, male gender, previous hospital admission, discharge diagnosis, time from discharge, and polypharmacy predicted 1-year mortality and contributed to the DSC in the development subsample of the SCNP cohort. Based on score quartiles, participants were classified into low-, medium-, high-, and very high-risk classes. In the SCNP validation sample, mortality increased progressively, from 144 to 367 per 1,000 person-years, across DSC classes, with HR (95% CI) of 1.92 (1.85-1.99), 2.71 (2.61-2.81), and 5.40 (5.21-5.59) in class II, III, and IV vs. class I ($p < 0.001$). Findings were similar in AIDEA, where the DSC predicted also recurrent ED visits in one year. In both databases, the DSC predicted 7- and 30-day mortality.

Conclusions: The DSC, based on administrative data available in real-time, predicts prognosis of older patients and might improve their management in the ED.

KEYWORDS.

Prognostic assessment, elderly, Emergency Department, Dynamic Silver Code, administrative data.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ARTICLE SUMMARY

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The Dynamic Silver Code combines in real-time administrative data available in all Italian regions, to automatically produce a score predicting 1-year mortality and other health outcomes in older persons accessing the Emergency Department (ED).
- The tool was developed retrospectively and initially validated in a large, representative cohort of patients aged 75+ years; it was further validated in a new cohort of subjects prospectively recruited, where the tool was available in the software routinely used for clinical management of patients in the ED.
- We did not include predictors such as data on outpatient services, functional status and census, nor outcomes such as functional impairment, cognitive decline and institutionalization.

INTRODUCTION

At the end of the disease era, when medical care is mostly directed towards management of chronic multimorbidity or non-disease-specific complaints in older persons,[1] a gear shift in the scope of, and the approach to, prognostic assessment is necessary. Besides survival, other goals should be pursued as outcomes of disease prevention and treatment, such as relief of symptoms, maintenance of personal autonomy, and preservation of quality of life, all of which may be targets of prognostic evaluation.[2] Focusing on one single disease is of limited value, when other coexistent illnesses, age-related physiological changes, and non-biological determinants of health may all affect prognosis. Patient's preferences and future perspectives must be valued: many older patients at the end of their life receive futile therapies for minor conditions,[3] whereas others with a reasonable disability-free life expectancy fail to receive appropriate treatments just because they are considered too old.[4]

Prognostic tools have the potential to help clinicians optimize the benefit/burden ratio of medical interventions [2] and support their decision-making;[5] they may prove useful also in the health policy arena, to perform risk-adjustment when comparing clinical interventions or healthcare models.[2, 5, 6] Administrative data are increasingly used to this purpose, because of their variety, availability, low cost, and accuracy.[7-9] Such tools have been applied to screen in-patients,[10, 11] outpatients,[12] and free-living subjects [5, 12, 13] for mortality, hospitalization, or disease-specific outcomes, aiming to personalized cures.[14-16]

We have previously described the Silver Code (SC), which combines administrative data into a score predicting 1-year survival in subjects aged 75+ years, admitted to the hospital via the Emergency Department (ED).[17, 18] The Dynamic SC (DSC) presented here is an evolution of the original score, developed from a large administrative dataset and then applied prospectively in a new sample. Whereas the original SC was based on one single moment of observation, the DSC considers, for each individual, the dynamics of events occurring across time. The new tool has been implemented into the software routinely used in the ED of several hospitals in Tuscany, Italy, to provide automated, real-time risk stratification of older patients.

METHODS

The DSC was obtained following the same general approach used for the SC, i.e. combining into a score variables from healthcare administrative archives, to predict long-term survival of older persons admitted to the hospital. Compared with the SC, the cohort used to develop and validate the DSC was much larger and representative of the general older population. Moreover, important computational differences were introduced and external validation in a completely new cohort was obtained.

Study design and data source

Two different studies contributed to the present investigation. The first was the “Silver Code National Project (SCNP)”, which was sponsored by the Centre for Disease Control of the Italian Ministry of Health in 2008.[19] The second was represented by the “Anziani in DEA (AIDEA)” (standing for “Older Persons in the ED”) study, jointly sponsored by the Italian Ministry of Health and by the Tuscany Region in 2010 (RF-2010-2321801). The SCNP was a non-concurrent cohort study, whereas AIDEA followed a prospective cohort study design.

The SCNP database,[19] representing the primary data source for the development and initial validation of the DSC, was obtained from the administrative archives of two Regions in Italy, Tuscany and Lazio, which deliver healthcare services to a total population of more than 9.6 million persons. The archives included data on demographics, hospitalizations, drug prescriptions, and deaths of beneficiaries aged 75+ years, who had been admitted via the ED to hospitals in the two Regions between April 2004 and December 2009. Data were linked using a numeric unique identifier, which allowed records anonymization before data processing to preserve beneficiaries’ confidentiality. Universal healthcare coverage in Italy allows completeness and comprehensiveness of the information contained in these databases, which have been used in previous epidemiological studies.[17, 20] The Italian Ministry of Health reported that Tuscany archives are 100% complete and 95% accurate.[21, 22]

Further validation of the score developed from the SCNP was subsequently obtained in a different sample, assembled in the AIDEA study, which was conducted in the ED of two hospitals in Florence, Italy, the Azienda Ospedaliero-Universitaria Careggi (AOUC), an academic tertiary hospital, and the Ospedale S.

1
2
3 Maria Annunziata (OSMA), a large community hospital. Enrolment was consecutively conducted between
4
5 June and August 2016 and again between February and March 2017 in the AOUC, and between August and
6
7 September 2016 in the OSMA, for a total of 22 weeks. In AIDEA, an application generating the DSC was
8
9 incorporated into the software routinely used in the ED of the hospitals of the Tuscany Region: as soon as
10
11 an eligible patient was triaged, the repository of healthcare data of the Local Health Unit was queried to
12
13 provide, thanks to on-demand linkage of the different archives involved, the information required to obtain
14
15 the DSC. The score was then in real-time calculated and shown, together with the corresponding risk class,
16
17 onto the computer screen. The lag time between occurrence of events contributing to the DSC
18
19 (hospitalizations and drug prescriptions) and their registration in the healthcare data repository was
20
21 approximately two weeks.
22
23
24
25
26
27

28 **Participants' selection**

29
30 The SCNP selected only records of subjects aged 75+ years, residing in the area where the study
31
32 was conducted, who consecutively accessed the ED of the participating hospitals in the specified time
33
34 windows and were eventually admitted to Internal Medicine or Geriatrics wards. Conversely, the AIDEA
35
36 study enrolled all the residents aged 75+ years consecutively accessing the ED in the specified time periods,
37
38 independent of the outcome (hospitalization or discharge) of their access to the ED.
39
40
41
42

43 **Ethics**

44
45 Following the Italian legislation on observational studies using administrative databases in place at
46
47 the time of data acquisition, Ethics Committee approval and participants' subscription of informed consent
48
49 was waived in the SCNP, because only anonymized administrative data were extracted. The protocol of the
50
51 AIDEA study, which included also face-to-face interview (not reported in the present work), was approved
52
53 by the Ethics Committee of the AOU Careggi (976/13_AOUC).
54
55
56
57
58

59 **Patient and public involvement**

60

1
2
3 Patients or the public were not involved in the design or conduct of our research, partially because
4
5 of its retrospective nature. Patients' associations will be involved in the upcoming, large-scale application of
6
7 the DSC in hospitals of the Tuscany Region. Reporting was provided as requested by the funding
8
9 Institutions. Dissemination to the public was obtained through lay press.
10
11
12
13

14 **Analytic procedures**

15
16 Statistical analysis was performed with SPSS for Mac v. 25 (IBM Corp., Armonk, NY, USA), STATA v.
17
18 15.1 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC), and R
19
20 3.5.0 (R Core Team, 2018).
21
22

23 A total of 281,321 records were available in the SCNP database to create the DSC and test its
24
25 validity. The χ^2 was used to test differences in relative frequencies and to identify bivariate predictors of
26
27 death, taking into account trends as appropriate.
28
29

30 The sample was randomly split into a development and a validation subsample. In the first
31
32 subsample, a Cox proportional hazards model was fit to estimate the association, expressed as hazard ratio
33
34 (HR) with 95% confidence interval (CI) of demographics and other variables on 1-year all-cause mortality
35
36 risk. Variables initially considered, by definition limited to those available prior to the index ED visit,
37
38 included age, gender, number of drugs prescribed in the previous 3 months as resulting from pharmacy
39
40 claims (categorized as 0-3, 4-5, 6-8, and 9+), days from previous hospital admission (no admission, 30-180
41
42 days, 0-30 days) and its associated main diagnostic group (cancer, respiratory disease, cardiovascular
43
44 disease, and other conditions), which were selected as the most frequently observed, in the study cohort,
45
46 among those included in the ICD-9 classification. Compared to the original version of the SC, previous
47
48 admission to a day hospital was not considered, because availability and utilization of day hospital service
49
50 are not consistent across Regions in Italy. Marital status information was also omitted, because it was
51
52 frequently missing in the discharge summary and in preliminary analyses it contributed marginally to the
53
54 prediction of death. Differently from the SC, repeated hospitalizations were taken into account to
55
56 dynamically update patient's information at each new hospital admission. To this purpose, data were
57
58 arranged in order to have one observation per event or time interval, and the counting process approach
59
60

1
2
3 proposed by Andersen and Gill [23] was applied: this is a generalization of Cox's model, which assumes that
4
5 the correlation between event times for a person can be explained by past events. Thus, we made the
6
7 assumption that correlations among events for each individual were captured by appropriate time-
8
9 dependent covariates.
10

11
12 We evaluated the adherence of predictors to the assumption of proportional hazards and tested for
13
14 multicollinearity comparing different models in terms of Akaike information criteria.[24] We then assigned
15
16 each risk factor a score, calculated as the ratio, rounded to the nearest integer, between the regression b
17
18 coefficient for that variable and the smallest significant b coefficient (b_0) in the Cox model. We finally
19
20 computed the DSC as a summary score, by adding the points individually assigned to each risk factor. Four
21
22 prognostic classes were then created from DSC quartiles.
23

24
25 In the validation data set, Harrell's C index of concordance was applied to evaluate model
26
27 performance, as a measure of the predictive power of Cox regression model.[25] Furthermore, the ability
28
29 of DSC classes to predict 1-year mortality was analysed after adjusting for Region of enrolment and ICD-9
30
31 coded principal diagnosis at discharge after the index hospitalization. External validity of the DSC was
32
33 performed in the AIDEA data set, using Cox regression models and Harrell's C index of concordance to
34
35 predict 1-year mortality and the risk of recurrent ED access after a first hospital admission.
36
37

38
39 Additional analyses were performed to verify the ability of the DSC to predict 7- and 30-day
40
41 mortality, two outcomes that are more immediate and potentially of greater clinical interest in the
42
43 perspective of application of the tool in the ED. Also these analyses were adjusted for main diagnostic
44
45 group at discharge and Region of enrolment.
46

47
48 A two-tailed p value less than 0.05 was considered statistically significant.
49
50

51 52 **RESULTS**

53 54 55 56 **Participants in the SCNP**

57
58
59 Out of the 281,321 records in the SCNP, 180,079 (64.01%) pertained to a single hospitalization, the
60
remaining to patients with multiple hospital admissions in the study period. The random split assigned

90,039 patients to the development and 90,040 to the validation subsample, with 140,716 and 140,605 records, respectively. As shown in **Table 1**, baseline characteristics of participants on their first hospital admission were comparable between the two subsamples.

Table 1. Baseline characteristics of participants on their first hospital admission, in the entire sample and in the development and validation subsamples. The p value reported refers to the χ^2 test, for trend when appropriate.

Variable	Overall (n=180,079)		Development subsample (n=90,039)		Validation subsample (n=90,040)		p
	N	%	N	%	N	%	
Age (years)							0.348
75-79	52,196	29.0	25,974	28.9	26,222	29.1	
80-84	60,205	33.4	30,221	33.6	29,984	33.3	
85+	67,678	37.6	33,844	37.6	33,834	37.6	
Gender							0.639
Male	77,803	43.2	38,852	43.2	38,951	43.3	
Female	102,276	56.8	51,187	56.9	51,089	56.7	
Number of drugs in previous 3 months							0.268
0-3	57,859	32.1	28,995	32.2	28,864	32.1	
4-5	38,405	21.3	19,322	21.5	19,083	21.2	
6-8	46,754	26.0	23,222	25.8	23,532	26.1	
9+	37,061	20.6	18,500	20.6	18,561	20.6	
Main diagnostic group in previous (6 months) hospital admission							0.773
No previous hospital admission	146,562	81.4	73,241	81.3	73,321	81.4	
Cardiovascular disease	11,206	6.2	5,537	6.15	5,669	6.3	
Cancer	3,954	2.2	1,955	2.2	1,999	2.2	
Respiratory disease	3,171	1.8	1,585	1.8	1,586	1.8	
Others	15,186	8.4	7,721	8.6	7,465	8.3	
Days from previous (6 months) hospital admission							0.156
No previous hospital admission	146,562	81.4	73,241	81.3	73,321	81.4	
31-180	23,374	13.0	11,793	13.1	11,581	12.9	
0-30	10,143	5.6	5,005	5.6	5,138	5.7	

Predictors of 1-year mortality

From hospital admission through the following year, a total of 42,434 deaths were recorded; mortality was comparable in the development (21,250/90,039, 23.6%) and the validation (21,184/90,040,

1
2
3 23.5%) subsamples. In the development sample, bivariate predictors of death were older age (75–79 years:
4 16.4%, 80–84 years: 20.5%, 85+ years: 31.9%; $p=0.001$), gender (men: 24.8%, women: 22.7%; $p<0.001$),
5
6 previous hospital admission with its corresponding main discharge diagnosis (no admission: 22.1%,
7
8 cardiovascular disease: 23.5%, cancer: 49.1%, respiratory disease: 30.8%, other diagnoses: 30.2%; p
9
10 <0.001), days from previous hospital admission (1–30 days: 34.5%, 31–180 days: 28.5%, $p<0.001$), or taking
11
12 more drugs prior to the index ED admission (0–3: 22.6%, 4–5: 22.9%, 6–8: 23.3%, 9+: 26.2%; $p<0.001$).
13
14
15
16
17

18 Risk models

19
20
21 **Table 2** shows the results of Cox proportional hazard regression model in the SCNP development
22
23 subsample. All the variables considered were significant predictors of 1-year mortality. Because the
24
25 diagnostic groups of “cardiovascular disease” and “others” obtained similar HRs, they were combined into a
26
27 single category, contrasted with “no previous hospital admission”, “cancer” and “respiratory disease”. The
28
29 predictors “days from the previous hospital admission” and the associated “main diagnostic group” showed
30
31 some multicollinearity, but the models with only one of those variables performed worse in terms of AIC:
32
33 therefore, both variables were maintained in the final model. All predictors satisfied the assumption of
34
35 proportional hazards.
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 2. Multivariable *b* coefficients, obtained from Cox regression model predicting 1-year death, in the 90,039 participants in the development subsample, with scores associated.

Variable	<i>b</i> Coefficient	p-value	Score
Age (years)			
75-79	Ref.		0
80-84	0.2871	<0.001	8
85+	0.8259	<0.001	23
Gender			
Female	Ref.		0
Male	0.1875	<0.001	5
Number of drugs in previous 3 months			
0-3	Ref.		0
4-5	0.0364	0.0320	1
6-8	0.0732	<0.001	2
9+	0.2173	<0.001	6
Main diagnostic group in previous (6 months) hospital admission			
No admission	Ref.		0
Cardiovascular disease / Others	0.6944	<0.001	19
Cancer	1.5218	<0.001	42
Respiratory disease	1.0357	<0.001	28
Days from previous (6 months) hospital admission			
No admission	Ref.		0
30-180	0.2763	<0.001	8
0-30	0.000		0

The smallest significant *b* coefficient in the Cox model resulted to be associated with 4-5 drugs prescribed in the previous 3 months ($b_0 = 0.0364$). Thus, each significant predictor was assigned a score by rounding the ratio between the corresponding *b* coefficient in the regression model and b_0 up to the nearest integer (**Table 2**). The DSC was finally calculated as summation of all scores.

Participants were classified into low-, medium-, high-, and very high-risk classes, based upon DSC quartiles. One-year risk of death increased significantly from the first to the fourth DSC class, with almost identical rates and hazard ratios in the two subsamples (**Table 3**). In the validation subsample, the performance of the risk scoring system, assessed with Harrell's C index, was 0.668 (95% CI 0.665- 0.672). The ability of the DSC to predict 1-year mortality persisted controlling for main diagnostic group at discharge after the index hospitalization and Region of enrolment (Tuscany vs. Lazio), as shown by HR (95% CI) of 1.93 (1.88-1.98), 2.71 (2.64-2.78), and 5.00 (4.88-5.13) for class II, III, and IV, respectively, compared to class I ($p < 0.001$) (**Figure 1**).

Table 3. One-year mortality and corresponding hazard ratios by DSC class, separately in the development and validation subsamples.

DSC Class (score)	Development subsample (n=90,039)				Validation subsample (n=90,040)			
	Participants	Deaths	Rate (per 1,000 p-y)	HR (95% CI)	Participants	Deaths	Rate (per 1000 p- y)	HR (95% CI)
I (≤ 10)	29,880	4,303	144	Ref.	29,798	4,291	144	Ref.
II (11-25)	32,712	8,127	248	1.93 (1.86-2.00)	32,775	8,082	247	1.92 (1.85-1.99)
III (26-34)	17,391	5,180	298	2.73 (2.64-2.84)	17,439	5,126	294	2.71 (2.61-2.81)
IV (≥ 35)	10,056	3,640	362	5.37 (5.18-5.56)	10,028	3,685	367	5.40 (5.21-5.59)
Total	90,039	21,250	236		90,040	21,184	235	

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

External validity

External validity of the DSC was ascertained in the AIDEA sample, which included 5,217 records for 4,425 subjects, of whom 1,292 died and 465 had a new ED admission within one year. Mortality increased progressively across DSC classes, with rates of 106, 197, 303 and 412 per 1,000 person-years from class I through class IV, and HR (95% CI) of 2.06 (1.68-2.53), 3.32 (2.74-4.03) and 5.28 (4.37-6.39) in class II, III and IV vs. class I ($p < 0.001$). Harrell's C index for mortality was 0.660 (95% CI 0.641-0.678). Also 1-year risk of recurrent ED access increased significantly across DSC classes, with rates of 69, 93, 89 and 139 per 1,000 person-years from class I through class IV, and HR (95% CI) of 1.46 (1.11-1.93), 1.45 (1.10-1.92), 2.60 (1.99-3.40) in class II, III and IV vs. class I ($p = 0.007$, 0.009 and < 0.001 , respectively). For recurrent ED access, Harrell's C index was 0.604 (95% CI 0.573-0.634).

Prediction of short-term mortality

The DSC predicted also 7- and 30-day mortality in both databases. In the SCNP database as a whole, 20,297 and 27,812 participants died within 7 and 30 days, respectively, out of the 180,079 enrolled. In AIDEA, the analysis on 7- and 30-day mortality included 4,425 participants, of whom 102 and 345 died within 7 and 30 days, respectively. In both databases and for both follow-up times, short-term mortality increased significantly across DSC classes ($p < 0.001$) (**Table 4**). Harrell's C index was 0.623 (95% CI 0.618-0.627) and 0.639 (95% CI 0.635-0.643) for 7- and 30-day mortality in the SCNP and 0.690 (95% CI 0.619-0.761) and 0.683 (95% CI 0.645-0.721) in AIDEA.

Table 4. Prediction of 7- and 30-day mortality by DSC class in the complete SCNP and in the AIDEA databases.

DSC Class (score)	SCNP				AIDEA			
	7-day mortality		30-day mortality		7-day mortality		30-day mortality	
	Rate	HR	Rate	HR	Rate	HR	Rate	HR
	(per 1000 p-y)	(95% CI) *	(per 1000 p-y)	(95% CI) *	(per 1000 p-y)	(95% CI)	(per 1000 p-y)	(95% CI)
I (≤10)	64	Ref.	81	Ref.	8	Ref.	28	Ref.
II (11-25)	113	1.83 (1.76- 1.91)	145	1.92 (1.85- 1.99)	19	2.24 (1.06- 4.76)	46	1.74 (1.14- 2.65)
III (26-34)	144	2.41 (2.31- 2.52)	178	2.53 (2.43- 2.62)	22	2.73 (1.33- 5.64)	84	3.17 (3.17- 4.64)
IV (≥35)	189	3.30 (3.15- 3.45)	234	3.98 (3.84- 4.14)	45	5.57 (2.78- 11.15)	136	5.58 (3.85- 8.09)

* Adjusted for main diagnostic group at discharge and Region of enrolment (Tuscany vs. Lazio).

DISCUSSION

Using the SCNP large, representative cohort of older persons accessing the ED and then admitted to hospitals in two Italian Regions, we developed the DSC, which combines simple variables, extracted from administrative databases, into a score predicting 1-year mortality. The score was validated against mortality in a random subset of the same cohort, and then its external validity was proven in the newly enrolled sample of the AIDEA study. Remarkably, whereas in the SCNP cohort the DSC was obtained from off-line processing of consolidated archives, in AIDEA it was generated in real-time on arrival of each eligible patient, thanks to an application implemented in the software routinely used for patients' clinical management in the EDs of Tuscany Region.

In older persons, because of coexisting chronic comorbidities and diminished life expectancy, fully informed clinical decision making requires adequate knowledge of patient's prognosis. In the presence of any given acute condition, comprehensive care planning should be carefully performed, by considering life expectancy, as well as pre-morbid functional and cognitive status.[26] Nevertheless, accurate prognostic

1
2
3 assessment of complex older patients is frequently overlooked in clinical practice, especially in the busy
4
5 daily practice of an ED, where geriatric patients often arrive with non-specific complaints, such as
6
7 worsening functional status, confusion, dizziness or fall. Their clinical presentation is frequently
8
9 characterized not by a single, well-defined disease, but rather by an entangled combination of age-related
10
11 changes, comorbidity, functional and cognitive impairment, polypharmacy, and social problems. As a
12
13 consequence, the risk of wrong triage, incorrect diagnosis and treatment, prolonged ED stay and
14
15 inappropriate destination is substantial.[27] Worsening disability, institutionalization or death shortly after
16
17 the ED access may be ultimate consequences.[28]

20
21 Instruments to screen older persons in the ED, based on comprehensive geriatric assessment, do
22
23 exist,[29] but are not used routinely in clinical practice, as they require some expertise and are time
24
25 consuming. Thus, in spite of their inherent limitations, simple administrative data are increasingly explored
26
27 as an attractive contribution to prognostic assessment, because they are accurate, objective and easily
28
29 available at a low cost.[7-9] Along this track, we have previously developed the SC, which was shown to
30
31 predict long-term mortality [17, 18] and hospitalizations of older persons in the ED [18] in two different
32
33 cohorts, with a discrimination ability comparable to that of other tools requiring face-to-face interview.[18]
34
35 Moreover, the SC allowed risk stratification when comparing the effects of different therapeutic
36
37 approaches.[17, 30] However, the algorithm to develop the SC relied only upon the first ED admission, so
38
39 that the score remained constant throughout the following observation time, independently of new
40
41 hospitalizations or drug prescriptions. To overcome this limitation of the parent tool, the DSC was
42
43 developed by taking into account each hospital admission as the unit of analysis. This would allow the score
44
45 to reflect more closely the dynamics of risk status of older patients, changing after each hospitalization or
46
47 new drug prescription.

51
52 The variables contributing to the DSC can be all recognized as meaningful predictors of prognosis.
53
54 In particular, the main driving forces in the DSC are advanced age and severe comorbidity, two well known,
55
56 powerful prognostic factors. Yet, because short-term re-hospitalization usually indicates clinical instability,
57
58 it is somewhat unexpected that, in the multivariable model reported in Table 2, a previous hospital
59
60 admission between 0 and 30 days had a b coefficient of zero, comparable to no admission. However, the

1
2
3 Italian hospital discharge coding system does not allow distinguishing, among short-term re-
4 hospitalizations, those that might have been planned at the end of the index hospitalization (e.g. to
5 complete diagnostics or treatments) from those occurring because of clinical instability.
6
7
8

9
10 The estimates we obtained are robust, because they were based on high-quality data from a large,
11 randomly split population-based cohort, thus overcoming the problem of overestimation typical of small
12 sample size datasets.[31] The predictive ability of the tool persisted even after controlling for discharge
13 diagnosis. As a further confirm, external validation was achieved in the new sample of the AIDEA study,
14 whose participants might be hospitalized or not after the index ED access. It should be emphasized that the
15 DSC predicted also short-term mortality and, at least in AIDEA, recurrent hospitalizations, outcomes for
16 which it had not been created. As suggested by the lower short-term mortality rates reported in **Table 4**,
17 the AIDEA cohort was substantially healthier than the SCNP cohort: this is to be expected, as AIDEA
18 enrolled also participants that were immediately discharged from the ED, without being hospitalised.
19 Nevertheless, the incremental risk of death across DSC classes was comparable in the two studies.
20 Moreover, short- and long-term mortality rate figures in the AIDEA cohort compare well to those reported
21 by Tanderup et al.: in a Danish study on 3775 subjects aged 65+ years accessing the ED, 30-day and 1-year
22 cumulative mortality increased progressively, from 2.2% to 10.6% and from 8% to 39%, respectively, with
23 the number of geriatric conditions (from 0 to 4), identified on the basis of comprehensive geriatric
24 assessment.[27] The similarity between Tanderup's and our estimates provides further, indirect support to
25 the external validity of the DSC: the absolute mortality risk is indeed crucial, more than HR, to take
26 appropriate decisions on treatment level.
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

48 In terms of Harrell's C index, the discrimination of the DSC was only moderate, similar in the
49 internal and external validation cohorts. Thus, although predictive at the group level, its ability to predict
50 prognosis at an individual level is suboptimal. A possible, partial explanation for this finding is that the DSC
51 might misclassify subjects defined at low risk, if they reached the ED with acute life-threatening conditions.
52 Also nursing home residents with severe disability or dementia might be erroneously considered as at low
53 risk by the DSC, if they had no recent hospital admissions: other administrative archives collecting data on
54 nursing home services, which are expected to become promptly available at least in Tuscany, should
55
56
57
58
59
60

1
2
3 eliminate this source of misclassification. On the other hand, comparably suboptimal performances have
4
5 been reported for other tools, proposed in the literature for prognostic assessment in the ED, such as the
6
7 Identification of Seniors At Risk [29, 18] (C statistics of 0.65 for 6-month mortality) or the Hospital Frailty
8
9 Risk Score [32] (C statistics of 0.60 for 30-day mortality), or widely used to drive clinical decisions in acute
10
11 coronary syndromes, such as the TIMI risk score (C statistics of 0.65 for a 14-day composite endpoint).[33]
12
13 This may reflect the fact that, as pointed out by other authors,[32] individual outcomes are inherently
14
15 unpredictable in acute settings, even when risk status is well characterized at a cohort level. This does not
16
17 detract from the clinical impact of the DSC and similar scores, which help delivery targeted interventions to
18
19 groups of patients with specific characteristics, whereas, at an individual level, should be used to support,
20
21 not to substitute clinical judgment.
22
23

24
25 A 2012 systematic review on prognostic indices for older adults [2] reported only one article – our
26
27 original publication on the parent instrument –[17] that focused on ED triage of older persons using
28
29 administrative data, but not in a real-time application. Although other, more recent studies dealing with
30
31 prognostic issues around older persons in an acute hospital setting can be found, none of them was
32
33 developed for use in the ED nor proposed real-time linkage of administrative data. Thus, to the best of our
34
35 knowledge, the DSC represents the first example in the literature of real-time utilization of administrative
36
37 data for prognostic purposes, at least in – but probably not limited to – older persons accessing the ED.
38
39

40
41 Several strengths of the DSC should be highlighted. First, it predicts short- and long-term prognosis
42
43 and risk of hospitalization combining with a simple calculation a limited set of variables, obtained from
44
45 administrative data: thus, it is objective and does not rely on patient's collaboration, which is sometime
46
47 difficult to obtain in the presence of cognitive decline or communication barriers. Second, as the AIDEA
48
49 study shows, it can be calculated in real-time, being therefore immediately available to the ED staff as soon
50
51 as a target patient is triaged, even before any clinical assessment and with no need of dedicated human
52
53 resources to gather information. To our knowledge, this represents a unique example of clinical utilization
54
55 of administrative data, which might be easily replicated in other hospitals, at least in Italy. Third, it is a non-
56
57 disease specific tool, an important characteristic allowing its universal application in older patients, in
58
59 whom multimorbidity and atypical symptoms presentation make clinical and prognostic assessment
60

1
2
3 challenging. Fourth, similar to other prognostic tools based on administrative data, it can be applied also to
4
5 obtain risk adjustment in the healthcare policy arena: to our knowledge, no previous prognostic tools have
6
7 been developed to pursue both clinical and epidemiological purposes.
8
9

10 Study limitations are to be acknowledged. The original SCNP dataset is relatively old: however, the
11
12 validity of the score was confirmed in the definitively more recent AIDEA cohort. The score was developed
13
14 based on data obtained only in subjects admitted to Internal Medicine or Geriatrics units: nonetheless, its
15
16 validity was confirmed in a completely different series, which included patients visiting the ED for a variety
17
18 of reasons and most of times discharged from the ED. The data so far available did not consent considering
19
20 other predictors (e.g., claims for specialized visits or other services, or census data), neither different
21
22 outcomes besides mortality, such as functional or cognitive decline and institutionalization, which are
23
24 highly relevant in geriatric patients. However, we are confident that the increasing availability of other
25
26 administrative databases, as suggested above in reference to nursing home services, will allow
27
28 incorporating a wider set of predictors as well as of endpoints in the next future.
29
30
31

32 In conclusion, the DSC, a simple prognostic tool based on administrative data, available in real-time
33
34 in the software used in the ED of Italian hospitals, offers a valid prognostic assessment of older patients,
35
36 virtually at no additional costs, once the system has been set. This might support clinical decision-making
37
38 and improve the quality of the care provided. Future studies are needed to assess whether these
39
40 expectations will be satisfied.
41
42
43
44

45 **ACKNOWLEDGMENTS**

46
47 Not applicable.
48
49
50
51

52 **FUNDING**

53
54 The “Silver Code National Project” was funded by the Centre for Disease Control of the Italian
55
56 Ministry of Health. The “Anziani in DEA” study was jointly funded by the Italian Ministry of Health and by
57
58 the Tuscany Region (RF-2010-2321801). The funders had no role in study design, data collection and
59
60 analysis, decision to publish, or preparation of the manuscript. All the authors were independent from

1
2
3 funders, had access to all of the data and can take responsibility for the integrity of the data and the
4
5 accuracy of the data analysis.
6
7
8
9

10 **CONFLICT OF INTEREST**

11 All the authors had no financial relationships with organisations or other relationships that might
12
13 appear to have influenced the submitted work.
14
15
16
17

18 **AUTHOR CONTRIBUTIONS**

19
20 DB conceived the study, conducted data management and analysis, and contributed drafting the
21
22 manuscript. GC conducted data analysis and contributed drafting the manuscript. FT contributed obtaining
23
24 the data and drafting the manuscript. LDE and PM obtained the data and contributed to data management.
25
26 AU and EB contributed obtaining the data and provided institutional support. LG and GL provided
27
28 institutional support. RB and NM provided institutional support and contributed developing the research
29
30 question. MDB conceived the study, wrote the protocol, supervised analyses, and drafted the manuscript.
31
32 All authors read and approved the final manuscript.
33
34
35
36
37
38

39 **DATA AVAILABILITY STATEMENT**

40
41 Study protocol and data may be obtained from the authors on reasonable request, provided that
42
43 consent is released by the funding Institutions.
44
45
46
47

48 **REFERENCES**

- 49
50 1. Tinetti ME, Fried T. The end of the disease era. *Am J Med.* 2004;116(3):179–85.
51
52 2. Yourman LC, Lee SJ, Schonberg MA, et al. Prognostic indices for older adults: a systematic review.
53
54 *JAMA.* 2012;307(2):182–92.
55
56 3. Walter LC, Covinsky KE. Cancer Screening in Elderly Patients. *JAMA.* 2001;285(21):2750.
57
58 4. Mehta KM, Fung KZ, Kistler CE, et al. Impact of Cognitive Impairment on Screening Mammography
59
60 Use in Older US Women. *Am J Public Health.* 2010;100(10):1917–23.

- 1
2
3 5. Wallace E, Stuart E, Vaughan N, et al. Risk prediction models to predict emergency hospital
4 admission in community-dwelling adults: a systematic review. *Med Care*. 2014;52(8):751–65.
5
6
- 7 6. Galvin R, Gillett Y, Wallace E, et al. Editor’s Choice: Adverse outcomes in older adults attending
8 emergency departments: A systematic review and meta-analysis of the Identification of Seniors At
9 Risk (ISAR) screening tool. *Age Ageing*. 2017;46(2):179–86.
10
11
- 12 7. Dagan N, Cohen-Stavi C, Leventer-Roberts M, et al. External validation and comparison of three
13 prediction tools for risk of osteoporotic fractures using data from population based electronic health
14 records: retrospective cohort study. *BMJ*. 2017;i6755.
15
16
- 17 8. Albaba M, Cha SS, Takahashi PY. The Elders risk assessment index, an electronic administrative
18 database-derived frailty index, can identify risk of hip fracture in a cohort of community-dwelling
19 adults. *Mayo Clin Proc*. 2012;87(7):652–8.
20
21
- 22 9. Simpson AN, Wilmskoetter J, Hong I, et al. Stroke Administrative Severity Index: using administrative
23 data for 30-day poststroke outcomes prediction. *J Comp Eff Res*. 2018;7(4):293–304.
24
25
- 26 10. Mahajan SM, Heidenreich P, Abbott B, et al. Predictive models for identifying risk of readmission
27 after index hospitalization for heart failure: A systematic review. *Eur J Cardiovasc Nurs*.
28 2018;17(8):675–89.
29
30
- 31 11. Taylor RA, Pare JR, Venkatesh AK, et al. Prediction of In-hospital Mortality in Emergency Department
32 Patients With Sepsis: A Local Big Data-Driven, Machine Learning Approach. *Acad Emerg Med*.
33 2016;23(3):269–78.
34
35
- 36 12. Clegg A, Bates C, Young J, et al. Development and validation of an electronic frailty index using
37 routine primary care electronic health record data. *Age Ageing*. 2016;45(3):353–60.
38
39
- 40 13. Corrao G, Rea F, Di Martino M, et al. Developing and validating a novel multisource comorbidity
41 score from administrative data: a large population-based cohort study from Italy. *BMJ Open*.
42 2017;7(12):e019503.
43
44
- 45 14. Davoudi A, Ozrazgat-Baslanti T, Ebadi A, et al. Delirium Prediction using Machine Learning Models
46 on Predictive Electronic Health Records Data. *Proc IEEE Int Symp Bioinformatics Bioeng*. 2018: 568–
47 73.
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

15. Corey KM, Kashyap S, Lorenzi E, et al. Development and validation of machine learning models to identify high-risk surgical patients using automatically curated electronic health record data (Pythia): A retrospective, single-site study. *PLoS Med.* 2018;15(11):e1002701.
16. Rahimian F, Salimi-Khorshidi G, Payberah AH, et al. Predicting the risk of emergency admission with machine learning: Development and validation using linked electronic health records. *PLoS Med.* 2018;15(11):e1002695.
17. Di Bari M, Balzi D, Roberts AT, et al. Prognostic stratification of older persons based on simple administrative data: development and validation of the “Silver Code,” to be used in emergency department triage. *J Gerontol A Biol Sci Med Sci.* 2010;65(2):159–64.
18. Di Bari M, Salvi F, Roberts AT, et al. Prognostic stratification of elderly patients in the emergency department: a comparison between the “Identification of Seniors at Risk” and the “Silver Code”. *J Gerontol A Biol Sci Med Sci.* 2012;67(5):544–50.
19. Centro Nazionale per la Prevenzione e il Controllo delle Malattie. Modelli innovativi per la presa in carico del paziente anziano fragile nella transizione dall’ ospedale al territorio e dal territorio all’ ospedale: Case Management e qualità della vita. Available at: <http://www.ccm-network.it/progetto.jsp?id=node/1353&idP=740>.
20. Simonato L, Baldi I, Balzi D, et al. Objectives, tools and methods for an epidemiological use of electronic health archives in various areas of Italy. *Epidemiol Prev.* 2008;32(3 Suppl):5-14.
21. Ministero del Lavoro, della Salute e delle Politiche Sociali. Rapporto annuale sulla attività di ricovero ospedaliero—Anno . 2005. Available at: <http://www.ministerosalute.it/programmazione/sdo/sezDocumenti.jsp?id=148&label=osp>. Consultation date April 10, 2019.
22. Ministero della Salute. Rapporto Annuale sull’attività di ricovero ospedaliero. Dati SDO 2017. 2019. Available at: [http://www.salute.gov.it/portale/temi/p2_4.jsp?lingua=italiano&tema=Assistenza, ospedale e territorio&area=ricoveriOspedalieri](http://www.salute.gov.it/portale/temi/p2_4.jsp?lingua=italiano&tema=Assistenza,ospedale%20e%20territorio&area=ricoveriOspedalieri). Consultation date April 10, 2019.
23. Andersen PK, Gill RD. Cox’s regression model for counting processes: A large sample study. *Annals of Statistics* 1982;10:1100-1120.

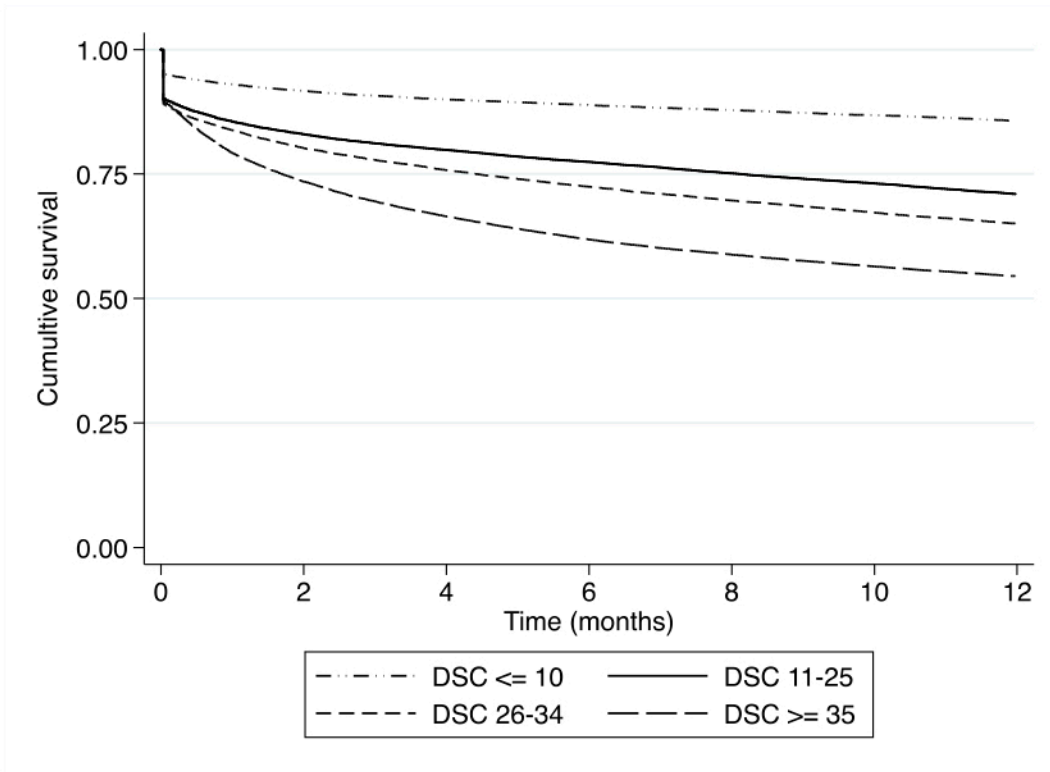
- 1
2
3 24. Akaike H. A New Look at the Statistical Model Identification. *IEEE Transaction Autom Contr.*
4
5 1974;19(6):716-23.
6
- 7 25. Harrell FE, Califf RM, Pryor DB, et al. Evaluating the Yield of Medical Tests. *JAMA.*
8
9 1982;247(18):2543-6.
10
- 11 26. Gill TM. The central role of prognosis in clinical decision making. *JAMA* 2012; 307(2): 199–200.
12
- 13 27. Tanderup A, Lassen AT, Rosholm JU, Ryg J. Disability and morbidity among older patients in the
14 emergency department: a Danish population-based cohort study. *BMJ Open* 2018;8:e023803.
15
16 doi:10.1136/bmjopen-2018-023803.
17
- 18 28. Salvi F, Morichi V, Grilli A, et al. The elderly in the emergency department: a critical review of
19 problems and solutions. *Intern Emerg Med.* 2007;2(4):292-301.
20
- 21 29. McCusker J, Bellavance F, Cardin S, et al. Detection of Older People at Increased Risk of Adverse
22 Health Outcomes After an Emergency Visit: The ISAR Screening Tool. *J Am Geriatr Soc.*
23
24 1999;47(10):1229–37.
25
- 26 30. Di Bari M, Balzi D, Fracchia S, et al. Decreased usage and increased effectiveness of percutaneous
27 coronary intervention in complex older patients with acute coronary syndromes. *Heart.*
28
29 2014;100(19):1537–42.
30
- 31 31. Royston P, Moons KGM, Altman DG, et al. Prognosis and prognostic research: Developing a
32 prognostic model. *BMJ.* 2009;338:b604.
33
- 34 32. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score
35 focusing on older people in acute care settings using electronic hospital records: an observational
36
37 study. *Lancet.* 2018;391:1775-1782.
38
- 39 33. Antman EM, Cohen M, Bernink PJLM, et al. The TIMI Risk Score for Unstable Angina/Non–ST
40
41 Elevation MI. *JAMA.* 2000;284(7):835-42.
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. Survival curves for cumulative risk of death within 1 year after first hospitalization by class of Dynamic Silver Code (DSC) in the validation sample (n=90,040). Cox proportional hazards regression, adjusting for Region of residence and main discharge diagnostic group, with p for trend <0.001.

For peer review only

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Reporting checklist for prediction model development and validation study.

Based on the TRIPOD guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the TRIPOD reporting guidelines, and cite them as:

Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.

	Reporting Item	Page Number
Title		
	#1 Identify the study as developing and / or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract		
	#2 Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	3
Introduction		
	#3a Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	5
	#3b Specify the objectives, including whether the study describes the	5

development or validation of the model or both.

Methods

Source of data	#4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
Source of data	#4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	#5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	7
Participants	#5b	Describe eligibility criteria for participants.	7
Participants	#5c	Give details of treatments received, if relevant	NA
Outcome	#6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	8
Outcome	#6b	Report any actions to blind assessment of the outcome to be predicted.	NA
Predictors	#7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured	8
Predictors	#7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	#8	Explain how the study size was arrived at.	6
Missing data	#9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	#10a	If you are developing a prediction model describe how predictors were handled in the analyses.	7-8
Statistical analysis methods	#10b	If you are developing a prediction model, specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	8
Statistical analysis methods	#10c	If you are validating a prediction model, describe how the predictions were calculated.	8
Statistical analysis	#10d	Specify all measures used to assess model performance and, if relevant,	8

1	methods	to compare multiple models.	
2	Statistical analysis	#10e If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	NA
3	methods		
4			
5			
6	Risk groups	#11 Provide details on how risk groups were created, if done.	8
7			
8	Development vs.	#12 For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8
9	validation		
10			
11			
12	Results		
13			
14	Participants	#13a Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	9
15			
16			
17	Participants	#13b Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	10
18			
19			
20	Participants	#13c For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	10
21			
22			
23	Participants	#14a If developing a model, specify the number of participants and outcome events in each analysis.	10
24			
25			
26	Model	#14b If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	11
27	development		
28			
29	Model	#15a If developing a model, present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	12
30	development		
31			
32	Model	#15b If developing a prediction model, explain how to the use it.	13
33	development		
34			
35	Model	#16 Report performance measures (with CIs) for the prediction model.	13
36	development		
37			
38	Model	#17 If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	14
39	specification		
40			
41	Model	#18 Discuss any limitations of the study (such as nonrepresentative sample,	16
42	specification		
43			
44	Model		
45	performance		
46			
47	Model		
48	performance		
49			
50	Model-updating		
51			
52			
53			
54			
55	Discussion		
56			
57	Limitations		
58			
59			
60			

few events per predictor, missing data).

1			
2			
3	Interpretation	#19a	For validation, discuss the results with reference to performance in the 15
4			development data, and any other validation data
5			
6	Interpretation	#19b	Give an overall interpretation of the results, considering objectives, 16
7			limitations, results from similar studies, and other relevant evidence.
8			
9			
10	Implications	#20	Discuss the potential clinical use of the model and implications for 16
11			future research
12			
13			
14	Other		
15	information		
16			
17			
18	Supplementary	#21	Provide information about the availability of supplementary resources, 18
19	information		such as study protocol, Web calculator, and data sets.
20			
21	Funding	#22	Give the source of funding and the role of the funders for the present 17
22			study.
23			
24			

The TRIPOD checklist is distributed under the terms of the Creative Commons Attribution License CC-BY.

This checklist was completed on 01. August 2019 using <https://www.goodreports.org/>, a tool made by the

[EQUATOR Network](#) in collaboration with [Penelope.ai](#)