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Complete List of Authors:	Balzi, Daniela; 1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy Carreras, Giulia; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Tonarelli, Francesco; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Degli Esposti, Luca; CliCon S.r.l, Health, Economics and Outcomes Research, Michelozzi, Paola; Lazio Region, Epidemiology Ungar, Andrea; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Gabbani, Luciano; Careggi Hospital, Unit of Geriatrics Benvenuti, Enrico; Azienda USL Toscana centro, Department of Internal Medicine, Landini, Giancarlo; Azienda USL Toscana centro, Department of Internal Medicine, Bernabei, Roberto ; Fondazione Policlinico Agostino Gemelli IRCCS Marchionni, Niccolò; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Di Bari, Mauro; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine
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Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk: Development and Validation of the Dynamic Silver Code

Daniela Balzi, BSc [1]

Giulia Carreras, PhD [2]

Francesco Tonarelli, MD [2]

Luca Degli Esposti, EconD, PhD [3]

Paola Michelozzi, BSc, MS [4]

Andrea Ungar, MD, PhD [2, 5]

Luciano Gabbani, MD [6]

Enrico Benvenuti, MD [7]

Giancarlo Landini, MD [8]

Roberto Bernabei, MD [9]

Niccolò Marchionni, MD [2, 10]

Mauro Di Bari, MD, PhD [2, 5]

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

9. Fondazione Policlinico Agostino Gemelli IRCCS, Rome, Italy
10. Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy.

Corresponding Author

Mauro Di Bari, MD, PhD

Research Unit of Medicine of Aging

Department of Experimental and Clinical Medicine

University of Florence

Viale G. Pieraccini, 18

50139 Florence, Italy

E-mail: mauro.dibari@unifi.it

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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.

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

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 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

provide, thanks to on-demand linkage of the different archives involved, the information required to obtain the DSC. The score was then in real-time calculated and shown, together with the corresponding risk class, onto the computer screen. The lag time between occurrence of events contributing to the DSC (hospitalizations and drug prescriptions) and their registration in the healthcare data repository was approximately two weeks.

Participants' selection

The SCNP selected only records of subjects aged 75+ years, residing in the area where the study was conducted, who consecutively accessed the ED of the participating hospitals in the specified time windows and were eventually admitted to Internal Medicine or Geriatrics wards. Conversely, the AIDEA study enrolled all the residents aged 75+ years consecutively accessing the ED in the specified time periods, independent of the outcome (hospitalization or discharge) of their access to the ED.

Ethics

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

Patient and public involvement

Given the largely retrospective nature of the study, it was not possible to involve patients or the public in the design or conduct of our research. Reporting was provided as requested by the funding Institutions. Dissemination to the public was obtained through lay press.

Analytic procedures

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

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

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

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

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

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

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

A two-tailed *p* value less than 0.05 was considered statistically significant.

RESULTS

Participants in the SCNP

Out of the 281,321 records in the SCNP, 180,079 (64.01%) pertained to a single hospitalization, the 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.

	Overall (n=180,079)		Development subsample (n=90,039)		Validation subsample (n=90,040)		p
Variable	**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

<0.001), days from previous hospital admission (1-30 days: 34.5%, 31-180 days: 28.5%, p<0.001), or taking 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).

Risk models

Table 2 shows the results of Cox proportional hazard regression model in the SCNP development subsample. All the variables considered were significant predictors of 1-year mortality. Because the diagnostic groups of "cardiovascular disease" and "others" obtained similar HRs, they were combined into a single category, contrasted with "no previous hospital admission", "cancer" and "respiratory disease". The predictors "days from the previous hospital admission" and the associated "main diagnostic group" showed some multicollinearity, but the models with only one of those variables performed worse in terms of AIC: therefore, both variables were maintained in the final model. All predictors satisfied the assumption of proportional hazards.

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	*b* 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.

	SCNP		AIDEA	
DSC Class (score)	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

patient, thanks to an application implemented in the software routinely used for patients' clinical management in the EDs of Tuscany Region.

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

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

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

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

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

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

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

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

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CONFLICT OF INTEREST

All the authors had no financial relationships with organisations or other relationships that might appear to have influenced the submitted work.

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.

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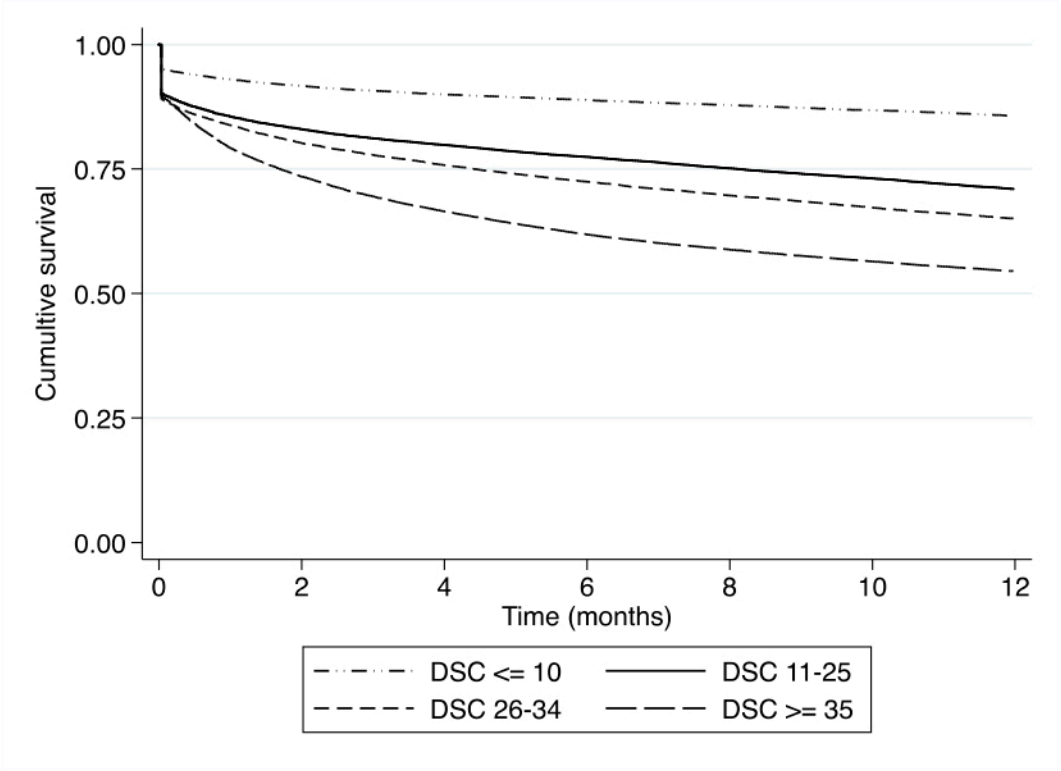
Figure 1. Survival curves for cumulative risk of death within 1 year after first hospitalization by class of Dynamic Silver Code (DSC) in the validation sample (n=90,040). Cox proportional hazards regression, adjusting for Region of residence and main discharge diagnostic group, with p for trend <0.001.


1.00
0.75
0.50
0.25
0.00
Cumultive survival
0
2
4
6
8
10
12
Time (months)
DSC <= 10
DSC 11-25
DSC 26-34
DSC >= 35

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.

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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

methods		to compare multiple models.	
Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	NA
Risk groups	#11	Provide details on how risk groups were created, if done.	8
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8
Results			
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
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
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	10
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	10
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	11
Model specification	#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
Model specification	#15b	If developing a prediction model, explain how to the use it.	13
Model performance	#16	Report performance measures (with CIs) for the prediction model.	13
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	14
Discussion			
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample,	16

		few events per predictor, missing data).	
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	15
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
Implications	#20	Discuss the potential clinical use of the model and implications for future research	16
Other information			
Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	18
Funding	#22	Give the source of funding and the role of the funders for the present study.	17

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

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

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Complete List of Authors:	Balzi, Daniela; 1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy Carreras, Giulia; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Tonarelli, Francesco; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Degli Esposti, Luca; CliCon S.r.l, Health, Economics and Outcomes Research, Michelozzi, Paola; Lazio Region, Epidemiology Ungar, Andrea; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Gabbani, Luciano; Careggi Hospital, Unit of Geriatrics Benvenuti, Enrico; Azienda USL Toscana centro, Department of Internal Medicine, Landini, Giancarlo; Azienda USL Toscana centro, Department of Internal Medicine, Bernabei, Roberto ; Fondazione Policlinico Agostino Gemelli IRCCS Marchionni, Niccolò; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Di Bari, Mauro; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine
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Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk: Development and Validation of the Dynamic Silver Code

Daniela Balzi, BSc [1]

Giulia Carreras, PhD [2]

Francesco Tonarelli, MD [2]

Luca Degli Esposti, EconD, PhD [3]

Paola Michelozzi, BSc, MS [4]

Andrea Ungar, MD, PhD [2, 5]

Luciano Gabbani, MD [6]

Enrico Benvenuti, MD [7]

Giancarlo Landini, MD [8]

Roberto Bernabei, MD [9]

Niccolò Marchionni, MD [2, 10]

Mauro Di Bari, MD, PhD [2, 5]

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

9. Fondazione Policlinico Agostino Gemelli IRCCS, Rome, Italy
10. Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy.

Corresponding Author

Mauro Di Bari, MD, PhD

Research Unit of Medicine of Aging

Department of Experimental and Clinical Medicine

University of Florence

Viale G. Pieraccini, 18

50139 Florence, Italy

E-mail: mauro.dibari@unifi.it

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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.

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

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. 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 provide, thanks to on-demand linkage of the different archives involved, the information required to obtain the DSC. The score was then in real-time calculated and shown, together with the corresponding risk class, onto the computer screen. The lag time between occurrence of events contributing to the DSC (hospitalizations and drug prescriptions) and their registration in the healthcare data repository was approximately two weeks.

Participants' selection

The SCNP selected only records of subjects aged 75+ years, residing in the area where the study was conducted, who consecutively accessed the ED of the participating hospitals in the specified time windows and were eventually admitted to Internal Medicine or Geriatrics wards. Conversely, the AIDEA study enrolled all the residents aged 75+ years consecutively accessing the ED in the specified time periods, independent of the outcome (hospitalization or discharge) of their access to the ED.

Ethics

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

Patient and public involvement

Patients or the public were not involved in the design or conduct of our research, partially because of its retrospective nature. Patients' associations will be involved in the upcoming, large-scale application of the DSC in hospitals of the Tuscany Region. Reporting was provided as requested by the funding Institutions. Dissemination to the public was obtained through lay press.

Analytic procedures

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

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

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

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

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

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

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

A two-tailed *p* value less than 0.05 was considered statistically significant.

RESULTS

Participants in the SCNP

Out of the 281,321 records in the SCNP, 180,079 (64.01%) pertained to a single hospitalization, the 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.

	Overall (n=180,079)		Development subsample (n=90,039)		Validation subsample (n=90,040)		p
Variable	**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* <0.001), days from previous hospital admission (1-30 days: 34.5%, 31-180 days: 28.5%, p<0.001), or taking 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).

Risk models

Table 2 shows the results of Cox proportional hazard regression model in the SCNP development subsample. All the variables considered were significant predictors of 1-year mortality. Because the diagnostic groups of "cardiovascular disease" and "others" obtained similar HRs, they were combined into a single category, contrasted with "no previous hospital admission", "cancer" and "respiratory disease". The predictors "days from the previous hospital admission" and the associated "main diagnostic group" showed some multicollinearity, but the models with only one of those variables performed worse in terms of AIC: therefore, both variables were maintained in the final model. All predictors satisfied the assumption of proportional hazards.

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	*b* 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.

	Development subsample (n=90,039)				Validation subsample (n=90,040)			
DSC Class (score)	**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	

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 (per 1000 p-y)	HR (95% CI) *	Rate (per 1000 p-y)	HR (95% CI) *	Rate (per 1000 p-y)	HR (95% CI)	Rate (per 1000 p-y)	HR (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

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

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

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

planned at the end of the index hospitalization (e.g. to complete diagnostics or treatments) from those occurring because of clinical instability.

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

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

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

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

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

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

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

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

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funders, had access to all of the data and can take responsibility for the integrity of the data and the accuracy of the data analysis.

CONFLICT OF INTEREST

All the authors had no financial relationships with organisations or other relationships that might appear to have influenced the submitted work.

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.

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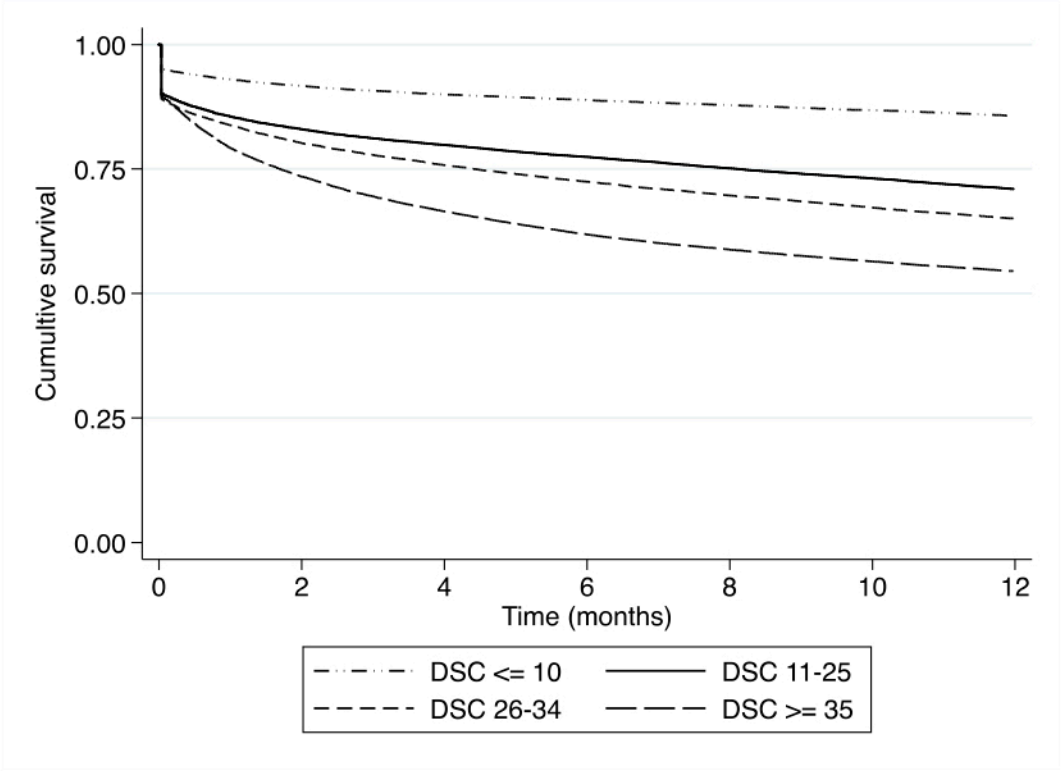
Figure 1. Survival curves for cumulative risk of death within 1 year after first hospitalization by class of Dynamic Silver Code (DSC) in the validation sample (n=90,040). Cox proportional hazards regression, adjusting for Region of residence and main discharge diagnostic group, with p for trend <0.001.


1.00
0.75
0.50
0.25
0.00
Cumultive survival
0
2
4
6
8
10
12
Time (months)
DSC <= 10
DSC 11-25
DSC 26-34
DSC >= 35

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.

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		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

methods		to compare multiple models.	
Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	NA
Risk groups	#11	Provide details on how risk groups were created, if done.	8
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8
Results			
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
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
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	10
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	10
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	11
Model specification	#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
Model specification	#15b	If developing a prediction model, explain how to the use it.	13
Model performance	#16	Report performance measures (with CIs) for the prediction model.	13
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	14
Discussion			
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample,	16

		few events per predictor, missing data).	
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	15
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
Implications	#20	Discuss the potential clinical use of the model and implications for future research	16
Other information			
Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	18
Funding	#22	Give the source of funding and the role of the funders for the present study.	17

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

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Complete List of Authors:	Balzi, Daniela; 1. Epidemiology, Azienda USL Toscana Centro, Florence, Italy Carreras, Giulia; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Tonarelli, Francesco; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Degli Esposti, Luca; CliCon S.r.l, Health, Economics and Outcomes Research, Michelozzi, Paola; Lazio Region, Epidemiology Ungar, Andrea; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Gabbani, Luciano; Careggi Hospital, Unit of Geriatrics Benvenuti, Enrico; Azienda USL Toscana centro, Department of Internal Medicine, Landini, Giancarlo; Azienda USL Toscana centro, Department of Internal Medicine, Bernabei, Roberto ; Fondazione Policlinico Agostino Gemelli IRCCS Marchionni, Niccolò; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine Di Bari, Mauro; University of Florence and Careggi Hospital, Research Unit of Medicine of Aging, Department of Clinical and Experimenal Medicine
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Real-time Utilization of Administrative Data in the ED to Identify Older Patients at Risk: Development and Validation of the Dynamic Silver Code

Daniela Balzi, BSc [1]

Giulia Carreras, PhD [2]

Francesco Tonarelli, MD [2]

Luca Degli Esposti, EconD, PhD [3]

Paola Michelozzi, BSc, MS [4]

Andrea Ungar, MD, PhD [2, 5]

Luciano Gabbani, MD [6]

Enrico Benvenuti, MD [7]

Giancarlo Landini, MD [8]

Roberto Bernabei, MD [9]

Niccolò Marchionni, MD [2, 10]

Mauro Di Bari, MD, PhD [2, 5]

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

9. Fondazione Policlinico Agostino Gemelli IRCCS, Rome, Italy
10. Cardiothoracic and Vascular Department, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy.

Corresponding Author

Mauro Di Bari, MD, PhD

Research Unit of Medicine of Aging

Department of Experimental and Clinical Medicine

University of Florence

Viale G. Pieraccini, 18

50139 Florence, Italy

E-mail: mauro.dibari@unifi.it

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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.

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.

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 provide, thanks to on-demand linkage of the different archives involved, the information required to obtain the DSC. The score was then in real-time calculated and shown, together with the corresponding risk class, onto the computer screen. The lag time between occurrence of events contributing to the DSC (hospitalizations and drug prescriptions) and their registration in the healthcare data repository was approximately two weeks.

Participants' selection

The SCNP selected only records of subjects aged 75+ years, residing in the area where the study was conducted, who consecutively accessed the ED of the participating hospitals in the specified time windows and were eventually admitted to Internal Medicine or Geriatrics wards. Conversely, the AIDEA study enrolled all the residents aged 75+ years consecutively accessing the ED in the specified time periods, independent of the outcome (hospitalization or discharge) of their access to the ED.

Ethics

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

Patient and public involvement

Patients or the public were not involved in the design or conduct of our research, partially because of its retrospective nature. Patients' associations will be involved in the upcoming, large-scale application of the DSC in hospitals of the Tuscany Region. Reporting was provided as requested by the funding Institutions. Dissemination to the public was obtained through lay press.

Analytic procedures

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

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

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

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

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

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

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

A two-tailed *p* value less than 0.05 was considered statistically significant.

RESULTS

Participants in the SCNP

Out of the 281,321 records in the SCNP, 180,079 (64.01%) pertained to a single hospitalization, the 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.

	Overall (n=180,079)		Development subsample (n=90,039)		Validation subsample (n=90,040)		p
Variable	**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 <0.001), days from previous hospital admission (1-30 days: 34.5%, 31-180 days: 28.5%, p<0.001), or taking 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).

Risk models

Table 2 shows the results of Cox proportional hazard regression model in the SCNP development subsample. All the variables considered were significant predictors of 1-year mortality. Because the diagnostic groups of “cardiovascular disease” and “others” obtained similar HRs, they were combined into a single category, contrasted with “no previous hospital admission”, “cancer” and “respiratory disease”. The predictors “days from the previous hospital admission” and the associated “main diagnostic group” showed some multicollinearity, but the models with only one of those variables performed worse in terms of AIC: therefore, both variables were maintained in the final model. All predictors satisfied the assumption of proportional hazards.

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	*b* 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.

	Development subsample (n=90,039)				**Validation subsample (n=90,040)**			
DSC Class (score)	**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	

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 (per 1000 p-y)	HR (95% CI) *	Rate (per 1000 p-y)	HR (95% CI) *	Rate (per 1000 p-y)	HR (95% CI)	Rate (per 1000 p-y)	HR (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

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

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

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

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

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

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

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

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

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

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

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

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

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funders, had access to all of the data and can take responsibility for the integrity of the data and the accuracy of the data analysis.

CONFLICT OF INTEREST

All the authors had no financial relationships with organisations or other relationships that might appear to have influenced the submitted work.

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.

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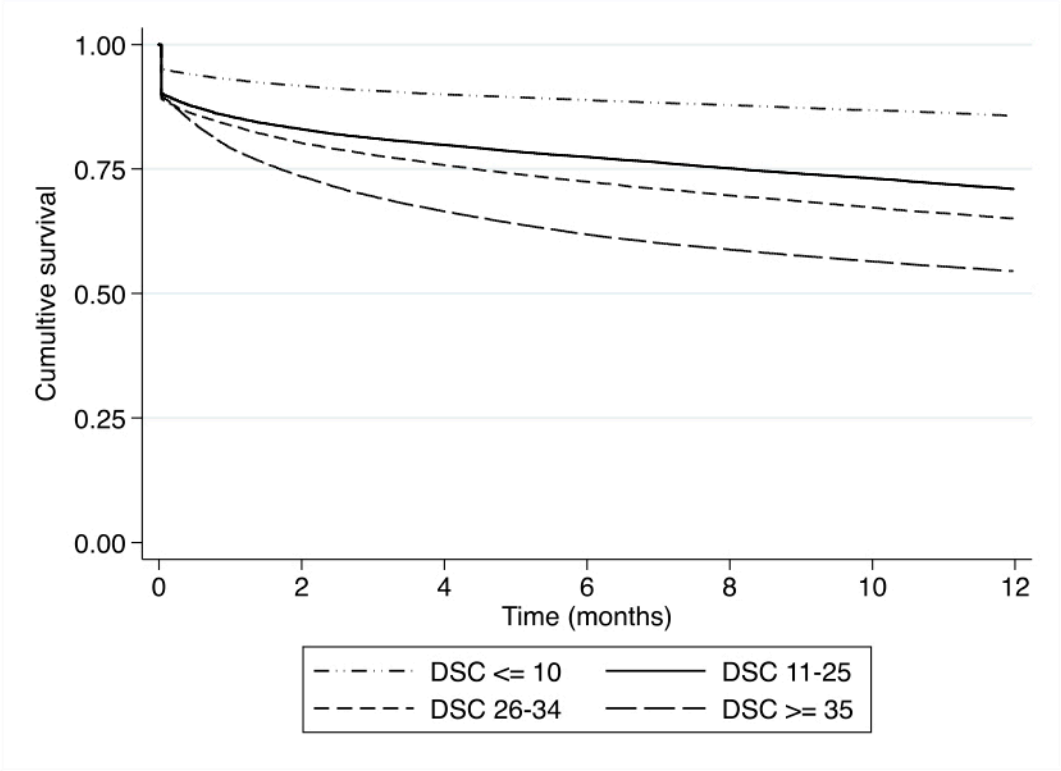
Figure 1. Survival curves for cumulative risk of death within 1 year after first hospitalization by class of Dynamic Silver Code (DSC) in the validation sample (n=90,040). Cox proportional hazards regression, adjusting for Region of residence and main discharge diagnostic group, with p for trend <0.001.


1.00
0.75
0.50
0.25
0.00
Cumultive survival
0
2
4
6
8
10
12
Time (months)
DSC <= 10
DSC 11-25
DSC 26-34
DSC >= 35

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.

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In your methods section, say that you used the TRIPODreporting 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

methods		to compare multiple models.	
Statistical analysis methods	#10e	If you are validating a prediction model, describe any model updating (e.g., recalibration) arising from the validation, if done	NA
Risk groups	#11	Provide details on how risk groups were created, if done.	8
Development vs. validation	#12	For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors.	8
Results			
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
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
Participants	#13c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome).	10
Model development	#14a	If developing a model, specify the number of participants and outcome events in each analysis.	10
Model development	#14b	If developing a model, report the unadjusted association, if calculated between each candidate predictor and outcome.	11
Model specification	#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
Model specification	#15b	If developing a prediction model, explain how to the use it.	13
Model performance	#16	Report performance measures (with CIs) for the prediction model.	13
Model-updating	#17	If validating a model, report the results from any model updating, if done (i.e., model specification, model performance).	14
Discussion			
Limitations	#18	Discuss any limitations of the study (such as nonrepresentative sample,	16

		few events per predictor, missing data).	
Interpretation	#19a	For validation, discuss the results with reference to performance in the development data, and any other validation data	15
Interpretation	#19b	Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence.	16
Implications	#20	Discuss the potential clinical use of the model and implications for future research	16
Other information			
Supplementary information	#21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	18
Funding	#22	Give the source of funding and the role of the funders for the present study.	17

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