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## Two morbidity indices developed in a nationwide population permitted performant outcome-specific severity adjustment

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### ABSTRACT

**Objective:** The objective of the study was to develop and validate two outcome-specific **morbidity** indices in a population-based setting: the Mortality-Related Morbidity Index (MRMI) predictive of all-cause mortality and the Expenditure-Related Morbidity Index (ERMI) predictive of health care expenditure.

**Study Design and Setting:** A cohort including all beneficiaries of the main French health insurance scheme aged 65 years or older on December 31, 2013 ( $N = 7,672,111$ ), was randomly split into a development population for index elaboration and a validation population for predictive performance assessment. Age, gender, and selected lists of conditions identified through standard algorithms available in the French health insurance database (SNDS) were used as predictors for 2-year mortality and 2-year health care expenditure in separate models. Overall performance and calibration of the MRMI and ERMI were measured and compared to various versions of the Charlson Comorbidity Index (CCI).

**Results:** The MRMI included 16 conditions, was more discriminant than the age-adjusted CCI (c-statistic: 0.825 [95% confidence interval: 0.824–0.826] vs. 0.800 [0.799–0.801]), and better calibrated. The ERMI included 19 conditions, explained more variance than the cost-adapted CCI (21.8% vs. 13.0%), and was better calibrated.

**Conclusion:** The proposed MRMI and ERMI indices are performant tools to account for health-state severity according to outcomes of interest.

### 1. INTRODUCTION

The accurate characterization of health-state severity has been a central concern over the last decades. In a clinical context, risk profiles are being used to guide **clinical management**, whereas prognostic stratification of patients has been at the origin of **clinical epidemiology** [1] and still constitutes a major issue in comparative **effectiveness studies** [2]. From a health care regulator's perspective, information

about disease severity is essential for risk adjustment in performance measurements [3] or for designing and evaluating payment policies [4]. Health-state severity assessment is also used to tailor interventions for patients with specific health care needs in integrated care initiatives [5].

A common approach to take into account health-state severity is the use of summary measures (referred here as indices), based on predictive modeling methods including selected predictors and their association with a specific outcome of interest. With the increasing availability of routinely collected standardized data in medicoadministrative databases, such summary measures are more widely used for research purposes or to inform policy making [6]. Several indices have been developed to predict a wide array of medical or resource utilization outcomes [7], [8]. They are usually classified into diagnosis-based indices using the International Classification of Diseases (ICD) codes and medication-based indices that identify conditions through pharmacy claims, the former performing better in mortality prediction and the latter in **health care utilization** prediction [9], [10]. The most widely used measure is the diagnosis-based Charlson Comorbidity Index (CCI), initially developed to predict 1-year postadmission mortality in a cohort of hospitalized patients [11] and more recently adapted by the author to predict costs of care [12].

An early finding on health-state severity measures is that the predictive performance or confounding control ability of the conditions selected as predictors depend on the outcome and the population under study [13]. A measure should preferably be used to predict or control for the same outcome and in a similar population as for which it was developed [10], [14]. Furthermore, when considering a specific outcome such as mortality, predictive performance depends on the data used to identify conditions selected as predictors and can, for example, be enhanced when adding outpatient to inpatient diagnoses [15] or medication consumption data to **diagnostic codes** [14]. Another important feature of **morbidity** indices is their intended application, which should determine the choice of predictors to be considered in addition to morbidity information. Using a framework proposed by Ellis [16] (Fig. S1 as supplementary material), different information is suitable for a risk-adjustment measure to be used in payment models, a case-identification measure to identify, for example, individuals with expected high future expenditures or a severity-adjustment measure for confounding control or stratification in epidemiological and health services research. Finally, according to the population considered during index development, an index could be more suitable for comorbidity or **multimorbidity** measurement. While some studies explicitly adopted a comorbidity, hospital-based approach [13], [17], the specificity of multimorbidity is to consider co-occurring conditions without reference to an index disease [18], [19], which is a major concern for health systems at a nationwide level [20] and of special interest in primary care settings [21]. Multimorbidity is increasingly frequent with age [22] and has been shown to be associated with both medical outcomes such as mortality or disability [23], [24] and health care resource utilization or costs [25]. Existing indices, such as the different versions [12], [26], and updates [27], [28] of the CCI or adaptations of the Elixhauser measures [17], [29], have been successively developed in heterogeneous settings, predicting a single outcome, without reevaluating the list of conditions initially considered.

In France, public health insurance coverage is mandatory and the French National Health Insurance Information System (SNDS) contains extensive individual information for almost the entire French population. The availability of inpatient, outpatient, diagnostic, and medication data makes it a very appropriate source for predictive modeling of both medical and health care utilization outcomes. Our objective was to develop and to validate two outcome-specific morbidity indices: the Mortality-Related Morbidity Index (MRMI) predictive of all-cause mortality and the Expenditure-Related Morbidity Index (ERMI) predictive of health care expenditure, to be used as health-state severity-adjustment tools for research or policy making. We adopted a multimorbidity approach and applied a common methodological framework in a population-based cohort of health insurance beneficiaries aged 65 years and older, as both mortality and multimorbidity are rare events in younger populations. By applying a common framework, we also expected our work to (1) document the differential effect of multiple conditions on different outcomes and (2) provide insight into the determinants of predictive performance according to the outcome of interest.

## 2. METHODS

### 2.1. Data source: the French National Health Insurance information system (SNDS)

French National Health Insurance provides mandatory coverage through three main schemes, depending on occupational class, that cover the entire population. The main scheme covers more than 57 million people, 87% of the French population. Individual-level information from administrative forms and reimbursement claims are prospectively recorded in a common data warehouse since 2003, the “*Système National des Données de Santé, SNDS*”, formerly named “*SNIRAM*” [30]. The SNDS warehouse contains demographic data including vital status and exhaustive information on pharmacy claims and the type of outpatient services or procedures reimbursed (without their results). Diagnostic physician-reported information is available in outpatient settings only for beneficiaries under the “*Affection Longue Durée*” status that waives copayments related to the treatment of specific long-term diseases (LTD). The SNDS also includes the French Hospital Discharge Database (“*Programme de Médicalisation des Systèmes d’Information, PMSI*”), containing inpatient diagnoses and procedures. Overall, information from pharmacy claims and utilization of both ambulatory and inpatient health care services, including related expenditure, is available. Diagnoses (LTD and PMSI) are recorded according to the ICD 10th Revision (ICD-10) codes and drugs according to the Anatomical Therapeutic Chemical (ATC) classification. All data are anonymous and individually linkable. Access to data is subject to prior training and authorization and has received approval from the French independent data protection administrative authority (“*Commission Nationale de l’Informatique et des Libertés, CNIL*”).

### 2.2. Morbidity and expenditure measurement: the SNDS mapping tool

Based on SNDS data, the National Health Insurance has developed a standardized tool to analyze and monitor morbidity burden through health care utilization. A summary presentation of the morbidity identification algorithms and of the expenditure items considered for the SNDS mapping tool is available in the Appendix. Detailed methodology is publicly available in French at

<http://www.ameli.fr.proxy.library.uu.nl/l-assurance-maladie/statistiques-et-publications/etudes-en-sante-publique/cartographie-des-pathologies-et-des-dependances/methodologie.php>.

### 2.2.1. Morbidity measurement

Algorithms combining inpatient diagnoses, LTD information, and pharmacy reimbursement claims have been defined to identify a list of 56 conditions. These algorithms are applied annually to each beneficiary of the main scheme to determine whether they have received care, within a given year, for any of the defined conditions. Exclusion criteria or hierarchical rules apply to some algorithms, and some conditions are therefore mutually exclusive (e.g., acute **ischemic heart disease** is prioritized over chronic ischemic heart disease and, for a given location, currently treated cancer over history of cancer). All algorithms have been submitted to expert review.

### 2.2.2. Expenditure measurement

Total expenditure directly attributable to care provided within a given year is calculated, from a National Health Insurance perspective, for each beneficiary and summarized into three categories: outpatient care, hospital care, and cash benefits administered by the National Health Insurance (not considered in our study). Expenditure related to outpatient care is directly available from individual reimbursement data, and expenditure related to hospital care is computed through diagnosis-related group-specific costs of each hospital stay.

## 2.3. Study population

All beneficiaries of the main scheme with at least one reimbursement during 2013 and who were alive and aged 65 years or older in December 31, 2013, were considered. We excluded beneficiaries with no reimbursement from the main scheme in 2014 or in 2015 (approximately 214,000 individuals) to ensure complete follow-up for the entire study population. This cohort ( $N = 7,672,111$ ) was randomly split into a development population for elaboration of the weighted indices ( $n_{\text{development}} = 3,836,056$ ) and a validation population for assessment of their predictive performance ( $n_{\text{validation}} = 3,836,055$ ).

## 2.4. Outcomes to predict

The two outcomes were measured at the end of a 2-year follow-up period. Mortality (binary outcome variable) was defined as death from any cause within 2 years after December 31st, 2013. Expenditure (continuous outcome variable) was defined as the total health care expenditure during the 2-year follow-up period, for all services covered by the main scheme, excluding cash benefits. For individuals who died during the follow-up period, expenditure was set at the total expenditure until death.

## 2.5. Predictor selection strategy

Consistently with the intended use of the MRMI and ERMI indices as severity-adjustment variables, we exclusively used health-state information, alongside age and gender, for the prediction models.

We first reviewed the 56 available morbidity algorithms to select variables measuring specific conditions (e.g., **diabetes** or multiple sclerosis) or homogeneous groups of conditions (e.g., **inflammatory bowel diseases** or cerebrovascular disease).

Variables subject to hierarchical rules were combined (e.g., ischemic heart disease including acute or chronic disease). We then performed pairwise and multivariate correlation analyses to combine highly correlated conditions within disease categories. Such data reduction procedures reduce the number of parameters to include in the final model and prevent multicollinearity, without information loss. This preliminary selection resulted in an initial list of 29 potential predictors for both outcomes, presented as supplementary material in [Table S1](#).

We then excluded conditions that were either not associated with the outcomes (e.g., ankylosing spondylitis) or that were associated with a decreased mortality risk or total expenditure (e.g., hypertension) in univariate analyses ( $P$ -value threshold of 0.05 for statistical significance).

Finally, we applied outcome-specific inclusion criteria. For the MRMI, we excluded conditions with less than 500 observed deaths to ensure a minimum of approximately 20 events per variable, commonly considered as a valid threshold for stability of logistic regression models [31] or with very small sample sizes (less than 0.2% of the population). For the ERMI, we excluded conditions with very low explained variance of total reimbursed expenditure ( $<0.1\%$ ) in age- and gender-adjusted analyses. Explained variance was calculated as  $1 - (\text{deviance of [condition-age-gender-adjusted model]} / \text{deviance of age-gender-adjusted model})$  [12].

## 2.6. Predictor effect estimation and weighting rule

We used generalized linear models (GLM) adjusted for age, gender, and the selected lists of conditions for both indices.

For the MRMI, we estimated the effect of predictors on 2-year mortality using a logistic regression.

For the ERMI, we used a GLM model with a log link function and a gamma response probability distribution to obtain unbiased estimates. We chose to model the raw-scale expenditure rather than the log-transformed scale after examining heteroscedasticity according to the framework proposed by Manning and Mullahy [32]. GLM models have previously been shown suited to model [health expenditure](#) in SNDS data [33].

To convert the estimated coefficients in weights, we applied for both indices a weighting rule proposed in the [Framingham risk score](#) context [34], with additional points reflecting risk associated with a 5-year age increase. For that, we recoded age before inclusion in the multivariate models and then divided each estimated coefficient by the age coefficient and rounded to the nearest integer. We conducted two series of sensitivity analyses to test the stability of the weights when accounting for effect modification due to age and gender or to associations of conditions, by adding to the final list of selected conditions (1) 10 mutually exclusive age/gender indicators (e.g., male aged 65–69 years; female aged 65–69 years) and (2) interaction terms for the most prevalent dyads of conditions (diabetes/ischemic heart disease; diabetes/chronic [respiratory disease](#); heart failure/ischemic heart disease; diabetes/heart failure; diabetes/history of cancer; chronic respiratory disease/heart failure). Finally, for the ERMI, we assessed the stability of weights when accounting for death during follow-up.

## 2.7. Validation

We assessed the predictive performance of the indices in the validation population: each individual was assigned a value for the MRMI and another for the ERMI,

according to age, gender, and morbidity status, and we then measured overall performance and calibration for the two indices.

For the MRMI, we assessed discrimination using a logistic regression model with the index as unique predictor of 2-year mortality and computing the concordance statistic (c-statistic, equivalent to the area under the Receiver Operating Characteristic curve). For the ERMI, we measured the explained variance of a GLM model with the index as unique predictor of 2-year expenditure. Overall performance of the two indices was also assessed using a 10-fold **cross-validation** strategy, in 10% random samples of the validation population.

Calibration was assessed, for both indices, by comparing predictions with observations among individuals with the same index value [29], [35]. Each index was introduced as a continuous variable for calculation of predicted mortality probability and predicted mean expenditure.

## 2.8. Comparative performance

We computed different versions of the CCI: the original index [11], the age-adjusted index [26], recently shown to have the highest discrimination for mortality prediction in the French context [27], and the cost-adapted CCI [12]. We also computed the index adaptation of the Elixhauser measures proposed by van Walraven et al. [17]. Although the Elixhauser measures were initially developed as a set of independent comorbidity variables adapted to in-hospital outcomes, they have been shown to be more performant for 1-year mortality prediction than the CCI [36]. To discuss the determinants of predictive performance and to assess the importance of using outcome-specific measures, the performance of all indices and of models including only age and gender was measured for both mortality and expenditure prediction.

## 3. RESULTS

### 3.1. Description of the study cohort

Mean age of the 7,672,111 individuals included was 75.3 years and 59.4% were women (Table 1). Overall observed 2-year mortality was 7.2% and increased linearly from 2.3% for beneficiaries aged 65–69 years to over 28% for beneficiaries aged 90–94 years. Mean expenditure for the 2-year follow-up period was €10,124 and increased linearly with age (€7,392–€13,994, respectively) with increasing expenditure variability (except for the most elderly aged 95 years and above).

[TABLE 1]

### 3.2. Mortality prediction

Weights for the final list of predicting conditions, calculated in the development population, are presented in Table 2. Three conditions were weighted “0”: **ischemic heart disease**, history of cancer, and **inflammatory bowel diseases**. Adjusted **odds ratios** ranged from 1.34 [95% CI: 1.31–1.37] for depression and mood disorders and 1.36 [1.32–1.39] for **rheumatoid arthritis** or **systemic diseases** to 3.79 [3.62–3.97] for **end-stage renal disease** and 4.09 [4.04–4.15] for cancer.

[TABLE 2]

Index values in the validation population were monotonically related to observed mortality with approximately 45% separation between the groups with the lowest (0.5% for index value “0”) and the highest (45.1% for index value “9 and above”) values (Table S2 in Supplementary material).

Discrimination for mortality prediction is summarized in Table 3. The MRMI was the most discriminant (c-statistic: 0.825 [95% CI: 0.824–0.826]) and the original CCI, the less discriminant (c-statistic: 0.674 [0.673–0.675]). Ten-fold cross-validation yielded similar results. Age and gender alone were more discriminant than indices that did not include age (original CCI, cost-prediction-adapted CCI, and index adaptation of Elixhauser measures). A graphical comparison of calibration for the MRMI and the age-adjusted CCI is presented in Fig. 1. For each value of the two indices, predicted probability is plotted against observed mortality. The calibration slope was closer to 1 for the MRMI than for the age-adjusted CCI, indicating better calibration.

[TABLE 3][FIGURE 1]

### 3.3. Expenditure prediction

Weights for the final list of predicting conditions, calculated in the development population, are presented in Table 4. All conditions had an effect on 2-year expenditure at least twice as important as a 5-year age increase. Multiple sclerosis or paraplegia, HIV/AIDS, and end-stage renal disease had the highest effect.

[TABLE 4]

Index values in the validation population were monotonically related to mean expenditure with a 10-fold increase between the groups with the lowest (€3,632 for index value “0”) and the highest (€35,439 for index value “15 and above”) values (Table S2 in Supplementary material).

Explained variance for expenditure models is summarized in Table 3. Maximum explained variance was obtained with the ERMI (21.8% of total expenditure variance). Performance of all other indices was similar but lower, ranging from 12.1% to 15.4% explained total variance. Ten-fold cross-validation yielded similar results. The calibration slope (Fig. 1) was closer to 1 for the ERMI than for the cost-adapted CCI.

### 3.4. Summary of weights and robustness analyses

Table 5 summarizes the predictors considered and the corresponding weights for the two proposed indices. Cancer, multiple sclerosis or paraplegia and end-stage renal disease were important predictors for both indices, whereas the burden of dementia was considerably greater for mortality and the burden of schizophrenia or HIV/AIDS for expenditure.

[TABLE 5]

The MRMI weights were robust to our two series of sensitivity analyses. The ERMI weights were not affected when adding age/gender indicators and were marginally affected when taking into account the most prevalent associations of conditions: applying the scoring rule resulted in a one unit weight increase for three conditions

due to rounding. ERMI weights were stable when adding a variable to account for death during first or second year of follow-up and were marginally modified when computed over 1 year of follow-up or when total expenditure was deflated by the fraction of the study period during which each person remained alive. Modifications were minimal and no particular pattern emerged (results available upon request).

#### 4. DISCUSSION

We developed and internally validated two performant outcome-specific indices for health-state severity-adjustment, by modeling mortality and total health care-related expenditure over a 2-year period in a nationwide cohort of health insurance beneficiaries aged 65 years and older. The MRMI performed better than the age-adjusted CCI and the ERMI explained substantially more variance than the cost-prediction-adapted CCI. The joint development of two indices permitted us to show that health-state severity adjustment is more performant when an index is chosen accordingly to the outcome under study and to discuss the relative contribution of age and of multiple conditions to predictive performance.

##### 4.1. Predictive performance

For mortality prediction models, age variability in the study population is an important determinant of performance. Recent studies have reported c-statistics approaching [29] or exceeding [27], [38] 0.900. Such performances were achieved in settings including all individuals aged 18 years and older [27], [38], where predictive performance of age and gender alone is already very close to 0.900 [38]. In individuals aged 65 years and older, discrimination of mortality prediction decreased with follow-up from a 0.860 c-statistic at 30 days to 0.788 at 1 year [29]. The MRMI index had comparably high performance, among older individuals with lower age variability and longer follow-up.

For models predicting future health care expenditure, morbidity information is more important than age. In the work updating the *Chronic Disease Score*, Huber et al. showed that performance for total expenditure prediction was relatively low, especially in individuals aged 65 years or older, but that adding morbidity information to age and insurance coverage type doubled the amount of explained variance from 7% to 14% [39]. Outcome specificity of a morbidity index also determines performance for expenditure prediction. In a study comparing different predictive models in adults with a *diagnosis of hypertension* [40], age and gender accounted for 2% of total explained variance, indices initially developed to predict mortality explained 9% and indices specifically developed to predict costs explained 13%. Performance exceeded 20% of explained variance only when information about prior resource utilization was added to the morbidity indices. In our study, the ERMI performance also exceeded 20% of explained variance, including exclusively age and morbidity information.

Our results show that age is the most important predictor for long-term mortality and that the method to summarize morbidity also counts, as the MRMI outperformed the ERMI. When the outcome of interest concerns expenditure or resource utilization, our results suggest that a specific index like the ERMI should be considered for severity adjustment. The proposed indices integrate the effect of age on each outcome. Alternatively, index values can be calculated by assigning only morbidity weights and then jointly adjusting on indices and age.



## 4.2. Index elaboration

Considering conditions associated with an increased risk of mortality or expenditure led to the exclusion of hypertension and **dyslipidemia**. These were the two most prevalent conditions in our study population (**Table S1**), consistently with results reported in different settings [20], [41], [42]. Although there is no consensus on whether to adjust or not for conditions associated with a decreased outcome risk in prediction models [29], [38], [43], we excluded them for several reasons. First, it has been argued that they may reflect selective coding, if such conditions are more frequently recorded for patients without additional more severe diagnoses [13], [17]. In our study, coding bias is not likely, as both conditions were identified exclusively through pharmacy data; healthier individuals are however selected as both algorithms have exclusion criteria (**Table A1** in Appendix). Second, including predictors carrying a negative weight could result in an index without monotonical association between index values and outcome, leading to suboptimal analytical properties [4]. Finally, we considered that the content validity of an index was higher when containing only conditions associated with outcome's increase.

Normalizing estimated coefficients on a 5-year age increase did not introduce bias as the effect of age was approximately linear in our study population and presented the advantage of legibility and comparability between outcomes. For mortality prediction (MRMI model), although the range of weights was smaller than the range of estimates, predictive performance was similar when compared with alternate weighting rules preserving more variability between conditions, such as normalizing on the weakest predictor [17] or rescaling the estimates [44]. Availability of estimates in **Table 2**, **Table 4** allows choosing any alternative weighting rule. We recommend the use of regression-based scoring rules as they are both theoretically correct and more performant than risk ratio-based rules [45].

## 4.3. Generalizability

We used nationwide quasiexhaustive data, applied a rigorous predictor selection strategy resulting in a limited number of predictors for each index, and internally validated the proposed indices with both split sample and ten-fold **cross-validation** techniques. Our results are therefore less subject to overfitting and could be consistent in external validation studies, among populations drawn from comparable health care settings, aged 65 years and older and not selected upon a specific disease. However, the predictive performance of the MRMI and ERMI indices should be assessed using alternate morbidity identification methods (sometimes referred to as methodologic transportability [46]). The combination of diagnosis-based and medication-based information and the important lookback periods is an important feature of the SNDS algorithms that enhances sensitivity of condition identification but that may limit exact reproducibility. Although algorithms are defined using internationally standardized codes (ICD-10 and ATC), the combination of diagnosis-based and medication-based information and the historical depth may not be available in different settings. Availability of weights permitting simple calculation of the indices facilitates such transportability assessments.

The use of a predefined set of conditions for predictor selection can also be seen as a limitation. As there is no consensual list of conditions to consider in studies dealing with health-state severity-adjustment or **multimorbidity**, initial selection often depends on setting-specific considerations of data availability and reproducibility [20], [47]. The resulting heterogeneity in health-state severity measurement,

especially in multimorbidity approaches among elderly individuals not selected upon an index disease, has been underlined in a review by Diederichs et al. [8]. In line with the authors, we believe that defining criteria for inclusion of relevant conditions in multimorbidity measures would be useful. Assessing which are the most frequently considered conditions [48], which conditions are identified through metrologically valid methods [49], or assessing the proportion of an outcome effectively captured by included conditions (content validity) could be examples of such criteria. Predictors considered in our study met these requirements, and the associations measured for the MRMI and ERMI indices could contribute to defining a list of conditions to consider.

## 5. CONCLUSION

We proposed two performant indices to be used as outcome-specific severity-adjustment variables in population-based settings and discussed the determinants of predictive performance according to the outcome under study. In particular, when the outcome of interest concerns resource utilization, the use of a specific index like the ERMI is more performant and should be considered. Transportability of our methodological framework and of our results should be assessed in different settings.

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## TABLES, BOX AND FIGURES

Wat is new?

### Key findings•

- The outcome-specific Mortality-Related **Morbidity** Index (MRMI) and Expenditure-Related Morbidity Index (ERMI), predictive of mortality and of health care expenditure, respectively, were developed and validated in a nationwide population of people aged 65 years and older, with better overall performance and better calibration than comparable Charlson indices.
- The MRMI was more performant than the ERMI for mortality prediction, and the ERMI was more performant than the MRMI for expenditure prediction

### What this adds to what was known?

- Conditions included as predictors in the MRMI and ERMI indices were identified through standard algorithms combining outpatient and inpatient information, medication consumption data, and **diagnostic codes**.
- By applying a common framework in a nationwide population and by comparing predictive models, this work documents (1) the outcome-specific adjusted effect of selected conditions in population-based settings and (2) the relative contribution of age and of multiple conditions to predictive performance according to the outcome of interest.

### What is the implication and what should change now?

- Morbidity indices should be chosen accordingly to the outcome of interest for a more performant adjustment on health-state severity.

Table 1. Observed outcomes for the study population by age class (SNDS data, years 2013–2015)

Study population	n	%	% Male	1-yr mortality (%)	2-yr mortality <sup>b</sup> (%)	1-yr expenditure		2-yr expenditure <sup>b</sup>	
						Mean	IQR <sup>c</sup>	Mean	IQR <sup>c</sup>
Entire cohort <sup>a</sup>	7,672,111	100	40.7	3.55	7.24	€5,074	€3,799	€10,124	€9,165
<b>Age classes</b>									
65 to 69	2,309,569	30.1	45.8	1.14	2.32	€3,648	€2,176	€7,392	€4,983
70 to 74	1,594,682	20.8	44.9	1.67	3.47	€4,456	€2,874	€9,047	€6,952
75 to 79	1,452,921	18.9	41.2	2.63	5.52	€5,326	€3,868	€10,747	€9,499
80 to 84	1,199,022	15.6	36.2	4.67	9.73	€6,324	€5,808	€12,613	€13,187
85 to 89	732,492	9.6	30.6	8.51	17.45	€7,155	€7,829	€13,912	€15,850
90 to 94	320,658	4.2	24.0	14.57	28.87	€7,484	€8,902	€13,994	€16,337
95 and more	62,767	0.8	15.9	25.41	46.22	€6,959	€8,493	€12,103	€14,385

<sup>a</sup> This cohort was randomly split into a development sample and a validation sample.

<sup>b</sup> Outcomes were defined over the 2-yr follow-up period.

<sup>c</sup> Inter quartile range (IQR) (Q3–Q1).

Table 2. Logit model to predict 2-yr mortality in the development population (SNDS data)

Parameter (p)	Estimate (β)	SE	P-value	OR	95% CI	β <sub>p</sub> /β <sub>age</sub>	Weight
Intercept	-4.9188	0.0063	<sup>a</sup>	–	–	–	–
Gender (ref: male)	0.3331	0.00459	<sup>a</sup>	1.40	1.38–1.41	0.60	1
Age (continuous, 5-yr scale)	0.5512	0.00147	<sup>a</sup>	1.74	1.73–1.74	1	1
Ischemic heart disease	0.1899	0.0059	<sup>a</sup>	1.21	1.20–1.22	0.34	0
Cerebrovascular disease	0.4657	0.00785	<sup>a</sup>	1.59	1.57–1.62	0.84	1
Heart failure or arrhythmias or valve diseases	0.6586	0.00503	<sup>a</sup>	1.93	1.91–1.95	1.19	1
Peripheral vascular disease	0.5442	0.00806	<sup>a</sup>	1.72	1.70–1.75	0.99	1
Diabetes	0.327	0.00521	<sup>a</sup>	1.39	1.37–1.40	0.59	1
Cancer	1.4095	0.00638	<sup>a</sup>	4.09	4.04–4.15	2.56	3
History of cancer	0.2652	0.00643	<sup>a</sup>	1.30	1.29–1.32	0.48	0
Schizophrenia and delusional diseases	0.7703	0.0195	<sup>a</sup>	2.16	2.08–2.24	1.40	1
Depression and mood disorders	0.2916	0.013	<sup>a</sup>	1.34	1.31–1.37	0.53	1
Substance abuse disorders	0.9039	0.0291	<sup>a</sup>	2.47	2.33–2.61	1.64	2
Dementia (including Alzheimer's disease)	1.144	0.00647	<sup>a</sup>	3.14	3.10–3.18	2.08	2
Parkinson disease	0.7896	0.0112	<sup>a</sup>	2.20	2.15–	1.43	1

Parameter (p)	Estimate (β)	SE	P-value	OR	95% CI	β <sub>p</sub> /β <sub>age</sub>	Weight
					2.25		
Multiple sclerosis or Paraplegia or tetraplegia	0.9998	0.0357	<sup>a</sup>	2.72	2.53–2.92	1.81	2
Epilepsy	0.5567	0.019	<sup>a</sup>	1.75	1.68–1.81	1.01	1
Chronic respiratory diseases (including asthma and COPD)	0.5597	0.00575	<sup>a</sup>	1.75	1.73–1.77	1.02	1
Inflammatory bowel diseases	0.1153	0.0327	<sup>a</sup>	1.12	1.05–1.20	0.21	0
Rheumatoid arthritis or systemic and connective tissue diseases	0.3046	0.014	<sup>a</sup>	1.36	1.32–1.39	0.55	1
End-stage renal disease	1.3326	0.0231	<sup>a</sup>	3.79	3.62–3.97	2.42	2
Liver and pancreas diseases (including chronic and acute failures)	0.8703	0.0128	<sup>a</sup>	2.39	2.33–2.45	1.58	2

*Abbreviations:* COPD, chronic obstructive pulmonary disease; MRMI, Mortality-Related Morbidity Index; OR, odds ratio; SE, standard error.

Reading grid: Weights were computed according to the risk associated with a 5-yr age increase (weight of 1). We divided each coefficient by the age coefficient (0.5512) and rounded to the nearest integer. The adjusted effect of diabetes or male gender on 2-yr mortality is equivalent to a 5-yr age increase; dementia or multiple sclerosis has an effect equivalent to a 10-yr age increase.

Example: A 75-yr-old male beneficiary suffering from diabetes and chronic respiratory disease would have an MRMI value of 5 (2 + 1+1 + 1).

<sup>a</sup> P-value <.0001.

Table 3. Overall performance for mortality and expenditure prediction of different morbidity indices in the validation population (SNDS data)

Morbidity indices	Performance for mortality prediction <sup>a</sup>	Performance for expenditure prediction <sup>a</sup>	
	C-statistic [95% CI] (equivalent to the area under the ROC curve)	Model deviance	Explained variance <sup>b</sup>
<b>Reference models</b>			
Null model (intercept only)	–	1.8556	–
Age and gender adjusted model	0.761 [0.760–0.762]	1.7926	3.4%
<b>Mortality prediction indices</b>			
Original Charlson index <sup>c</sup>	0.674 [0.673–0.675]	1.6250	12.4%
Index adaptation of Elixhauser measures <sup>c</sup>	0.684 [0.683–0.685]	1.6309	12.1%
Age-adjusted Charlson index <sup>c</sup>	0.800 [0.799–0.801]	1.5886	14.4%
MRMI <sup>d</sup>	<b>0.825 [0.824–0.826]</b>	1.5701	15.4%
<b>Expenditure prediction indices</b>			
Adapted Charlson index <sup>c</sup>	0.681 [0.680–0.682]	1.6148	13.0%
ERMI <sup>d</sup>	0.797 [0.796–0.798]	1.4504	<b>21.8%</b>

*Abbreviations:* ERMI, Expenditure-Related Morbidity Index; MRMI, Mortality-Related Morbidity Index; ROC, receiver operating characteristic.

a For models including each index as unique predictor in the validation population.

b Computed for each model as follows: 1—deviance of the model of interest/deviance of the null model.

c Charlson et al. 1987 [11] for the original index; Charlson et al. 1994 [26] for the age-adjusted index; Charlson et al. 2008 [12] for the cost prediction adapted index; van Walraven et al. [17] for the index adaptation of the Elixhauser measures. All indices were computed using ICD-10 codes from Quan et al. 2005 [37] and screening all hospitalizations for years 2013 and 2012.

d MRMI and ERMI are the two indices developed in this study and both include age among predictors. Main results are in italics and bolded.

Fig. 1. Calibration of the MRMI and ERMI and of comparable versions of the CCI in the validation population (SNDS data). (A) Calibration of the MRMI and of the age-adjusted CCI. (B) Calibration of the ERMI and of the cost-adapted CCI. Observations are plotted against predictions within each value of the compared indices. The 45° dotted lines represent perfect calibration (slope of 1). Plain lines represent the calibration curves for each index. The MRMI and the ERMI (in red) are compared, respectively, to the age-adjusted CCI and to the cost-adapted CCI (in blue). CCI, Charlson comorbidity index; ERMI, Expenditure-Related Morbidity Index; MRMI, Mortality-Related Morbidity Index. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

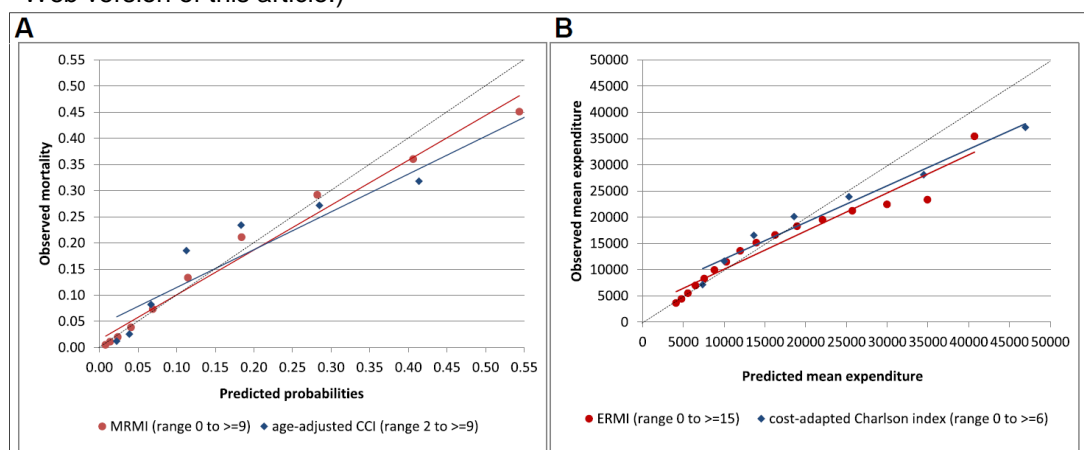


Table 4. Generalized linear model to predict 2-yr expenditures in the development population (SNDS data)

Parameter (p)	Estimate (β)	SE	P-value	β <sub>p</sub> /β <sub>age</sub>	Weight
Intercept	8.3037	0.0012 <sup>a</sup>	—	—	—
Gender (ref: male)	0.0312	0.0012 <sup>a</sup>	0.23	0	
Age (continuous, 5-yr scale)	0.1385	0.0004 <sup>a</sup>	1	1	
Ischemic heart disease	0.2762	0.0019 <sup>a</sup>	1.99	2	
Cerebrovascular disease	0.4321	0.0029 <sup>a</sup>	3.12	3	
Heart failure or arrhythmias or valve diseases	0.4298	0.0018 <sup>a</sup>	3.10	3	
Peripheral vascular disease	0.4437	0.003 <sup>a</sup>	3.20	3	
Diabetes	0.5348	0.0015 <sup>a</sup>	3.86	4	
Cancer	0.9759	0.0025 <sup>a</sup>	7.05	7	
History of cancer	0.2762	0.0019 <sup>a</sup>	1.99	2	
Schizophrenia and delusional diseases	0.8298	0.0066 <sup>a</sup>	5.99	6	
Depression and mood disorders	0.6633	0.0041 <sup>a</sup>	4.79	5	



Parameter (p)	Estimate (β)	SE	P-value	β <sub>p</sub> /β <sub>age</sub>	Weight
Substance abuse disorders	0.6497	0.0102 <sup>a</sup>		4.69	5
Dementia (including Alzheimer's disease)	0.338	0.0028 <sup>a</sup>		2.44	2
Parkinson disease	0.7057	0.0045 <sup>a</sup>		5.10	5
Multiple sclerosis or Paraplegia or tetraplegia	1.2964	0.0117 <sup>a</sup>		9.36	9
Epilepsy	0.4292	0.0073 <sup>a</sup>		3.10	3
Chronic respiratory diseases (including asthma and COPD)	0.4629	0.0019 <sup>a</sup>		3.34	3
Rheumatoid arthritis or systemic and connective tissue diseases	0.6177	0.0043 <sup>a</sup>		4.46	4
HIV infection or AIDS	1.4277	0.0178 <sup>a</sup>		10.31	10
End-stage renal disease	2.2098	0.0101 <sup>a</sup>		15.96	16
Liver and pancreas diseases (including chronic and acute failures)	0.6702	0.0046 <sup>a</sup>		4.84	5
Scale	0.8079	0.0005	–	–	–

Abbreviation: COPD, chronic obstructive pulmonary disease; ERMI, Expenditure-Related Morbidity Index; SE, standard error.

Reading grid: Weights were computed according to the expenditure associated with a 5-yr age increase (weight of 1). We divided each coefficient by the age coefficient (0.1385) and rounded to the nearest integer. The adjusted effect of diabetes on 2-yr expenditure is fourfold the effect of a 5-yr age increase.

Example: A 75-yr-old male beneficiary suffering from diabetes and chronic respiratory disease would have an ERMI value of 9 (2 + 0 + 4 + 3).

<sup>a</sup> P-value <.0001.

Table 5. Summary of predictors and corresponding weights for the MRMI and ERMI indices (SNDS data)

Predictors	MRMI weights <sup>a</sup>	ERMI weights <sup>a</sup>
<b>Gender</b>		
male	1	–
<b>Age</b>	A 5-yr age increase is weighted “1”	
65–69	0	0
70–74	1	1
75–79	2	2
80–84	3	3
85–89	4	4
90–94	5	5
95–99	6	6
≥100	7	7
<b>Conditions<sup>b</sup></b>		
Ischemic heart disease	0	2
Cerebrovascular disease	1	3
Heart failure or arrhythmias or valve diseases	1	3
Peripheral vascular disease	1	3
Diabetes	1	4
Cancer	3	7
History of cancer	0	2
Schizophrenia and delusional diseases	1	6
Depression and mood disorders	1	5
Substance abuse disorders	2	5

Predictors	MRMI weights <sup>a</sup>	ERMI weights <sup>a</sup>
Dementia (including Alzheimer's disease)	2	2
Parkinson disease	1	5
Multiple sclerosis or paraplegia or tetraplegia	2	9
Epilepsy	1	3
Chronic respiratory diseases (including asthma and COPD)	1	3
Inflammatory bowel diseases <sup>c</sup>	0	–
Rheumatoid arthritis or systemic and connective tissue diseases	1	4
HIV infection or AIDS <sup>c</sup>	–	10
End-stage renal disease	2	16
Liver and pancreas diseases (including failures)	2	5

*Abbreviations:* COPD, chronic obstructive pulmonary disease; ERMI, Expenditure-Related Morbidity index; MRMI, Mortality-Related Morbidity Index.

a Derivation of weights from adjusted regression coefficients is presented in [Table 2](#), [Table 4](#).

b Identification algorithms are presented in [Table S1](#).

c Inflammatory bowel diseases and HIV/AIDS were not included among the final list of predictors for the expenditure-related morbidity index and the mortality-related morbidity index, respectively.