Predicting Risks of Increased Morbidity among Atrial Fibrillation Patients using Consumption Classes

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Abstract: *Background*: Atrial fibrillation (AF) is the most common chronic cardiac arrhythmia. Predicting the risk of complications, or associated increases in healthcare costs, among AF patients is important for effective health care management.

Methods: A bivariate regression model including a latent morbidity index is used to predict both risk of transition to higher health costs, and mortality risk over a single year. A risk scoring algorithm for predicting transition to higher cost levels is then set out which incorporates the most significant risk factors from the regression.

Results: The regression analysis shows that in addition to age and comorbidities, baseline consumption category, ethnic group, metropolitan residence and Warfarin adherence are also significant influences on progression to increased health consumption, and relevant to assessing risk. The resulting risk scoring algorithm produces a higher AUC than the widely applied CHADS2 score.

Conclusions: The utility of a bivariate regression method with a latent morbidity index for predicting transition to worsening health status among AF patients is demonstrated. A risk scoring system based on this method outperforms an established risk score.

Keywords: Morbidity, Risk scores, Latent variable, Atrial fibrillation, Consumption class.

1. INTRODUCTION

Atrial fibrillation (AF) is the most common chronic cardiac arrhythmia (irregular heart rhythm). AF patients are at considerably elevated risk of stroke and other cardiovascular complications [1], and AF also constitutes a risk factor for elevated all-cause mortality [2]. Predicting deterioration of health status is important for planning patient care and for effective health care management, as is the development of simple risk scoring algorithms that can be used by administrators in allocating resources. It is advantageous for routine use by managers that such a risk score be readily calculated using routine administrative healthcare data. It is also advantageous to effective health care administration that the costs of health care are considered as an aspect of broadly conceived health risk.

The present study accordingly considers methods for predicting the risk of deteriorating health status among AF patients using administrative data on Medicare Beneficiaries in the US. The focus is on upward transition between consumption classes (i.e. shifts to increased healthcare costs) during a single calendar year, 2008. Using the consumption class methodology of Caballero *et al.* [3], patients are grouped into four consumption clusters: crisis consumers, heavy consumers, moderate consumers, and light/low consumers. Specifically the focus is on transition from low or light use (at end 2007) to moderate, heavy or crisis use (by end 2008). Data for the analysis are obtained from the Beneficiary Annual Summary File Data, which contains details of demographic status, service utilization, and history of chronic conditions for Medicare patients in the US.

The methodology has two aspects: regression to predict risk of transition to higher health consumption, and subsequent translation of the regression findings into a simplified risk scoring algorithm. The regression includes a latent morbidity index, contextual geographic factors (e.g. metropolitan residence, neighbourhood poverty), treatment (Warfarin) adherence and baseline consumption level. The regression is bivariate since as well as considering transition (or not) to higher cost levels, mortality as a possible subsequent or alternative outcome within the annual follow up period is also considered.

A number of risk scoring algorithms predict risk of complications or hospitalisation among AF patients [4-6], encapsulating the results of more complex regression findings. The most widely used scores summarise patient risk in terms of medical conditions, possibly adding age as an additional influence, as in the $CHADS_2$ score [7], or age and sex as in the CHA_2DS_2-VASC score [8]. These two scores do not

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E-ISSN: 1929-6029/14

adjust for ethnicity, treatment or prior health care usage. The present paper proposes a risk score including current health care costs (consumption category), ethnic group, and Warfarin adherence, as these were found relevant (in the regression) to predicting increased health consumption.

2. METHODS

In the full model estimated below, there are two outcomes to consider: shifts in consumption class during 2008, and mortality before the end of 2008, possibly after an earlier consumption shift. Around 6% (3252) of the 54765 subjects alive at the end of 2007 had died by end 2008. Among the 51513 survivors, around 68% stayed in low or light consumption, while 32% moved to a higher health consumption band. Of subjects dying before the end of 2008, the majority (78%) made upward cost transitions before death.

Regarding shifts in consumption class, let y_{1i} denote consumption class (with J=4 ranked categories) at end 2008: y_1=1 for patients remaining in the low or light use class at end 2008; y_1=2 for patients moving to moderate consumption; y_1=3 for patients moving to heavy use; and y_1=4 for patients moving to crisis use. The ordinal observations y_{1i} represent realisations of a process on an underlying continuous scale z, with

$$z_i=R_i+\varepsilon_i$$

where R_i represents total risk, ε_i denotes an error term with distribution function $F(\varepsilon)$, and with cutpoints (θ_0=-∞, $\theta_1,\ldots,\ \theta_{J-1},\ \theta_J$=$\infty$) on the z scale. A multinomial likelihood is then defined, namely

$$y_{1i} \sim Mult(\pi_{i1},\ldots,\pi_{iJ}) \quad (1.1)$$

with

$$\pi_{ij}=Pr(y_{1i}=j)=Pr(\theta_{j-1}\leq z_i\leq\theta_j)=F(\theta_j-R_i)-F(\theta_{j-1}-R_i)=S_{ij}-S_{i,j-1}$$

where

$$S_{ij}=Pr(y_{1i}\leq j)=F(\theta_j-R_i), \quad j=1,..,J-1$$

are cumulative probabilities over ranked categories. Assuming logistic errors ε_i, one has

$$logit(S_{ij})=\theta_j-R_i. \quad (1.2)$$

Influences on risk R_i are taken to be individual morbidity M_i, contextual risk factors C_i (e.g. region, local poverty), and treatment variables T_i. Morbidity M_i is regarded as a latent variable in the sense used by Rabe-Hesketh and Skrondal [9], namely an unobserved random variable measured by different indicators, as opposed to repeats or replicates of a single indicator. Specifically M_i is measured both by reflective indicators, denoted $\{D_{1i},..,D_{Ki}\}$ (e.g. pre-existing medical conditions, medical care history), and by causative risk factors, denoted $X_i=(X_{1i},..,X_{Li})$ such as age and ethnicity. There may in be additional directly observed morbidity indicators V_i, such as measures of functional status or perceived health state [10,11], so that total risk is

$$R_i=\alpha_1 M_i+\delta_1 C_i+\psi_1 V_i+\gamma T_i. \quad (1.3)$$

Appendix 1 sets out details of the indicators and predictors used in the study.

The outcome frame of reference is extended to include mortality between end 2007 and end 2008 (y_{2i}=1 for death, y_{2i}=0 otherwise). The mortality outcome provides additional information relevant to measuring patient morbidity (higher morbidity subjects are more likely to die earlier), so latent morbidity M_i is shared across the two outcomes, namely

$$y_{2i} \sim Bern(\phi_i) \quad (2.1)$$

$$logit(\phi_i)=\zeta+\alpha_2 M_i+\delta_2 C_i+\psi_2 V_i \quad (2.2)$$

It is assumed that the latent variable M_i in (1.3) and (2.2) is normal with mean zero $X_i\beta$ and unknown variance σ_M^2. All reflective indicators are binary, so with $Bern(p)$ denoting a Bernoulli density with probability p, one has

$$M_i \sim N(X_i\beta,\ \sigma_M^2)$$

$$D_{ki} \sim Bern(\rho_{ki}), \quad k=1,..,K$$

$$logit(\rho_{ki})=\kappa_k+\lambda_k M_i,$$

For scale identification, the loadings λ_k $(k=2,..,K)$ are taken as unknown, but λ_1=1 [9]. For location identifiability, the X variables omit an intercept.

The impact of Warfarin adherence is assumed to vary by year of age. So with ages denoted a (=65,66,…,84,85+), the treatment effect in (1.3) consists of random effects γ_a following a second order random walk evolution

$$\gamma_a \sim N(2\gamma_{a-1}-\gamma_{a-2}, 1/\tau_\gamma),$$

where τ_γ is an unknown precision parameter.

3. RESULTS

3.1. Regression Models

Two models are analysed, in order to show the benefit of a bivariate model: model 1 is the full bivariate response model, whereas model 2 considers change in consumption y_{1i} as a univariate response only. A Bayesian estimation and inference approach uses the BUGS software [12]. Thus Normal N(0,100) priors are assumed for unknown fixed effect parameters, while precisions (inverse variances) are assigned gamma priors with shape 1 and index 0.01. For the ordinal regression thresholds the re-parameterisation

$$\theta_j=\theta_{j-1}+exp(\Delta_j) \quad j=2,\ldots,J-1$$

$$\theta_1=\Delta_1$$

is adopted, with the Δ parameters taken as unconstrained normal with N(0,100) priors. Inferences are based on the second halves of two chain runs of 20000 iterations with convergence assessed using Gelman-Rubin statistics [13].

Model fit is assessed using the Deviance Information Criterion [14], and in terms of accurately predicting transition status. The latter is represented by a binary indicator s_i, with s_i=1 if a patient makes an upward cost transition (if $y_{1i}\geq 2$), while s_i=0 if a patient remains in low-light use throughout 2008. The area under the receiver operating curve (AUC) is often used to measure predictive success [4], but in view of potential drawbacks [15,16], also considered is comparative sensitivity at a set false positive rate [17,18]. For example, Pepe *et al.* [19] mention sensitivity at low false positive rates (e.g. FPR=0.2) is typically of interest.

Table **1** shows a lower DIC, and higher AUC, for the full bivariate model 1. Model 1 also has a significantly higher sensitivity at a set FPR of 0.2. Table **2** shows parameter summaries for this model, except for Warfarin adherence, the impact of which is represented graphically (Figure **1**).

Panel C of Table **2** shows that all K=7 reflective indicators are relevant to defining morbidity. The highest loadings are for heart failure, ischaemic heart disease, and inpatient spell. The β parameters (representing formative influences) show increased age, black and Hispanic ethnicity are most significantly associated with elevated morbidity. There is also a gender effect, albeit less pronounced, with females at lower risk.

Regression effects for consumption transition and mortality are in panels A and B of Table **2**. These show

Table 1: Fit and Predictive Accuracy, Upward Consumption Transitions

	DIC (Consumption Category Transition)	AUC for all upward transitions (and 95% interval)	Sensitivity for FPR=0.2 (and 95% interval)
Model 1 (Bivariate)	95915	0.737 (0.732, 0.741)	0.511 (0.503, 0.522)
Model 2 (Univariate)	97940	0.610 (0.605, 0.614)	0.306 (0.299, 0.316)

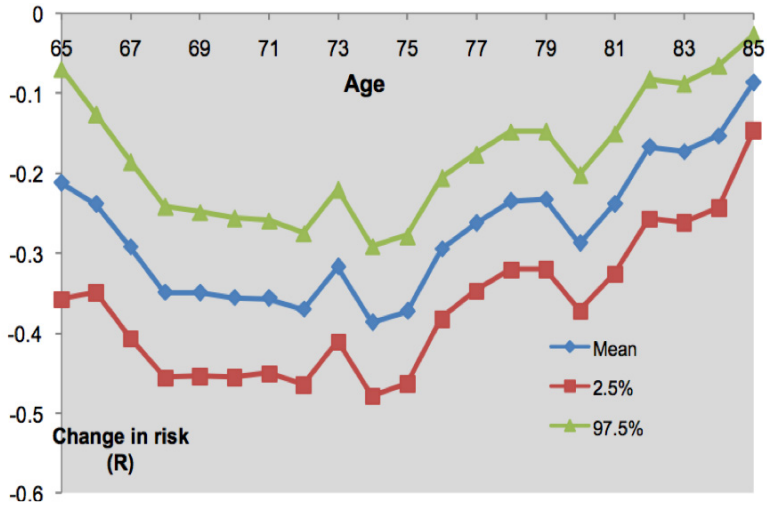

Figure 1: Treatment Effect by Age.

Table 2: Parameter Summary, Posterior Means and 95% Credible Intervals, Model 1 (Bivariate Response)

A) Upward Consumption Transition				
	Parameter	**Mean**	**2.5%**	**97.5%**
Intercepts (Cutpoints)	θ_1	2.3	2.1	2.4
	θ_2	3.6	3.4	3.8
	θ_3	6.2	6.0	6.4
ZIP Poverty (C_1)	δ_{11}	0.02	-0.01	0.05
Metro Area (C_2)	δ_{12}	0.08	0.03	0.12
Mid-West (C_3=2)	δ_{13}	0.01	-0.05	0.07
South (C_3=3)	δ_{14}	-0.01	-0.06	0.04
West (C_3=4)	δ_{15}	-0.08	-0.14	-0.02
Frailty (M)	α_1	4.6	3.5	5.8
Base Consumption (V)	ψ_1	-0.54	-0.58	-0.50
B) Mortality				
Intercept	ζ	-7.2	-7.7	-6.9
ZIP Poverty (C_1)	δ_{21}	0.07	0.00	0.14
Metro Area (C_2)	δ_{22}	0.11	0.01	0.21
Mid-West (C_3=2)	δ_{23}	0.10	-0.01	0.22
South (C_3=3)	δ_{24}	-0.03	-0.14	0.08
West (C_3=4)	δ_{25}	0.03	-0.10	0.16
Frailty (M)	α_2	8.9	6.9	11.3
Base Consumption (V)	ψ_2	0.03	-0.06	0.11
C) Latent Morbidity				
Reflective Indicators				
Myocardial infarct (D_1)	λ_1	1		
Heart failure (D_2)	λ_2	11.7	9.2	14.8
Diabetes (D_3)	λ_3	2.8	2.2	3.6
Ischaemic heart disease (D_4)	λ_4	6.8	5.3	9.0
Stroke/TIA (D_5)	λ_5	3.3	2.5	4.3
Inpatient in 2007 (D_6)	λ_6	5.2	4.1	6.7
2+ Years with AF (D_7)	λ_7	2.4	1.8	3.1
Formative Indicators				
Female (X_1)	β_1	-0.02	-0.02	-0.01
Black non-Hispanic (X_2=2)	β_{22}	0.07	0.05	0.09
Hispanic (X_2=3)	β_{23}	0.05	0.03	0.07
Other (X_2=4)	β_{24}	0.02	0.01	0.03
Age (X_3)	β_3	0.53	0.42	0.67

strong morbidity effects on both outcomes, with α coefficients highly significant. Baseline consumption is only significant for upward consumption transition, which is less likely to occur for patients classed as low users at end 2007 (with 95% interval for ψ_1 from -0.58 to -0.50). Upward consumption transition is higher in metropolitan areas, and lower in the West region. Both effects may reflect differences between rural and urban hospital access, access to specialist care, etc.

The nonlinear treatment (Warfarin adherence) effect in reducing upward consumption transition is strongest at ages between 67 and 77. This is apparent from Figure **1**, which plots the estimated γ_a parameters (posterior means and 95% credible intervals).

3.2. Predictive Risk Scoring

Translating statistical results into simple scoring algorithms is an area of on-going research [20], and we

consider how the above regression findings may be included in a scoring algorithm. Accordingly, modelled transition probabilities $(\pi_{i2},\pi_{i3},\pi_{i4})$ to moderate, heavy and critical use, are averaged over patients within risk factor subgroups, and risk scores are based on comparing average probabilities. Consider how the covariate metropolitan residence (binary) affects transition to heavy consumption. Let A_i=1 and A_i=2 for patients resident in non-metro areas and metro areas respectively, with totals N_1 and N_2. Average transition probabilities $P_{3,non\text{-}met}$ and $P_{3,met}$ within the two levels of this covariate are obtained using posterior means $\bar{\pi}_{i3}$, namely $P_{3,non\text{-}met}=\sum_{A_i=1}\bar{\pi}_{i3}/N_1$ and $P_{3,met}=\sum_{A_i=2}\bar{\pi}_{i3}/N_2$. The ratio $P_{3,met}/P_{3,non\text{-}met}$ measures the impact of metropolitan residence on this particular transition. The model probabilities π_{ij}, being based on regression, control for the impact of other factors on transition rates. Analogous comparisons are made for patient age, ethnicity, co-morbidities, treatment status, each time with an appropriate reference group.

Scores are assigned as follows: a score of 0 if the relative transition ratio (the ratio comparing averaged modelled transition probability to that in the reference group) is between 1 and 1.1, a score of 1 for transition ratios between 1.1 and 1.25, a score of 2 for transition ratios between 1.25 and 1.5, and a score of 3 for transition ratios over 1.5. Scores are specific to destination (moderate, heavy, critical consumption). Table **3** summarises relative transition ratios and scores for predictors where effects are significant enough to produce at least one relative transition ratio exceeding 1.1. For example, effects of gender, region and ZIP poverty are not large enough to be included.

Mirroring the largest loadings on morbidity indicators in Table **2**, it can be seen from Table **3** that heart failure and IHD have the largest relative transition ratios (comparing patients with these conditions to patients without such conditions). Similarly, the strong age gradient apparent in the coefficient β_3 is reflected in the large relative transition ratios at ages 85+ in Table **3**. These ratios represent chances of moving to higher consumption for patients aged 85 and over as compared to patients aged 65-69. High scores also apply for patients in the light use consumption class at end 2007 as compared to the low use class.

Table 3: Relative Transition Risks and Risk Scores for Moves from Low-Light Consumption Category during 2008

		Ratio of transition probability (posterior mean) to reference group			Score for move to:		
		Consumption Category			Consumption Category		
Predictor or risk factor		Moderate	Heavy	Crisis	Moderate	Heavy	Crisis
Age (reference 65-69)	70-74	1.056	1.087	1.101	0	0	1
	75-79	1.150	1.248	1.296	1	1	2
	80-84	1.232	1.410	1.504	1	2	3
	85+	1.343	1.672	1.864	2	3	3
Race/Ethnicity (reference WNH)	BNH	1.121	1.235	1.298	1	1	2
	Hispanic	1.111	1.204	1.255	1	1	2
	North Amer Native	1.066	1.109	1.126	0	1	1
Myocardial Infarction during 2007		1.218	1.434	1.551	1	2	3
Heart Failure Diagnosis end 2007		1.442	1.892	2.153	2	3	3
Diabetes end 2007		1.140	1.257	1.317	1	2	2
Ischaemic Heart Disease end 2007		1.341	1.634	1.794	2	3	3
Stroke end 2007		1.154	1.299	1.379	1	2	2
Inpatient during 2007 (reference, not inpatient)		1.235	1.463	1.590	1	2	3
Atrial Fibrillation over 2+ years		1.084	1.150	1.185	0	1	1
Metro Area of Residence		1.047	1.084	1.103	0	0	1
Light User end 2007 (reference Low user)		1.393	1.749	1.948	2	3	3
Not Warfarin Adherent		1.106	1.178	1.211	1	1	1
Maximum Possible Score					14	23	27

Table 4: Risk Scores and Actual Transitions, Moves to Heavy Consumption

Risk Score for Move to Heavy Consumption	Total Patients	Total Moving to Heavy Consumption	Percent Transiting to Heavy Consumption
0	1388	61	4.4
1	1343	76	5.7
2	1693	102	6.0
3	3723	236	6.3
4	3100	247	8.0
5	3763	332	8.8
6	5201	466	9.0
7	4159	433	10.4
8	5059	551	10.9
9	5029	595	11.8
10	4159	547	13.2
11	4380	637	14.5
12	3663	579	15.8
13	3020	564	18.7
14	2324	475	20.4
15	1268	273	21.5
16+	1493	188	22.6
All	54765	6362	11.6
Score Ranges			
0-2	4424	239	5.4
3-9	30034	2860	10.0
10+	20307	3263	16.1

To illustrate how risk scores predict actual transitions, consider moves to heavy consumption. Table **4** and Figure **2** show observed transition behaviour at different scores. In predictive risk studies, thresholds are often assigned to distinguish low, intermediate and elevated risk. Table **4** accordingly also shows actual transition rates to heavy consumption for scores under 3, between 3 and 9, and over 10: respectively 5.4%, 10% and 16.1%. Figure **2** shows how actual transition rates to heavy consumption increase monotonically with the risk score.

The AUC and sensitivity at a FPR of 0.2 for the risk scores were evaluated for moves to heavy consumption, and compared with those obtained using the $CHADS_2$ score. The outcome here is relatively heterogeneous, namely deterioration in health resulting in increased health costs (usually from hospitalisation), rather than a single diagnosis. Hence AUC statistics are relatively low (Table **5**), though comparable to those reported by Hobbs *et al.* [4] and Philbin and DiSalvo [21]. Table **5** denotes the risk scores based on models of the present study as CC-Risk scores (CC for consumption class). The AUC for the CC-Risk score, namely 0.623 with 95% interval 0.616 to 0.630, is significantly above that of the $CHADS_2$ score, as is the sensitivity at an FPR of 0.2.

4. DISCUSSION

As compared to previous studies, the present study has detected a wider range of significant influences on increases in morbidity among AF patients. Such influences are relevant to future work on risk scoring algorithms for assessing worsening health status among cardiovascular patients. It has confirmed other studies in finding the morbidity risk among AF patients is related to age and comorbidities [7]. Existing risk scores (e.g. CHADS2, CHA2DS2-VASC) include these variables. However, the existing study also finds significant ethnic effects on increased health consumption, and shows improved risk score performance if ethnicity is included. Previous evidence

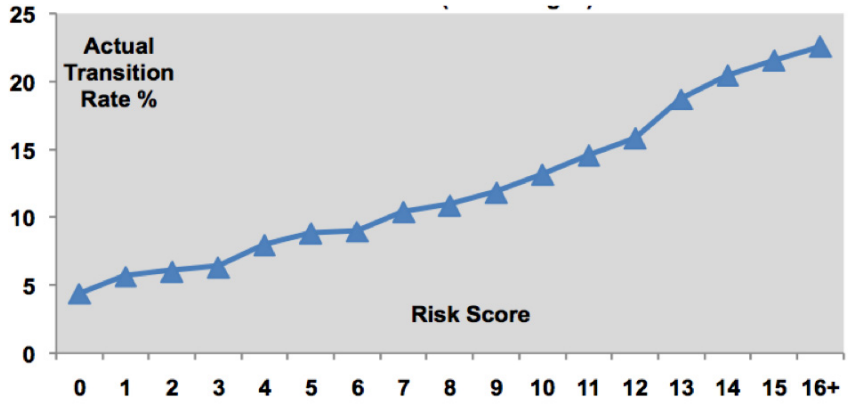

Figure 2: Transition to Heavy Consumption: Risk Score and Actual Transition (Percentages).

Table 5: Accuracy of Predictive Scores, Transitions to Heavy Consumption from Light-Low Consumption

	AUC (with 95% interval)	Sensitivity for FPR=0.2 (with 95% interval)
CC Risk	0.623 (0.616, 0.630)	0.326 (0.313, 0.339)
CHADS2	0.578 (0.570, 0.585)	0.174 (0.166, 0.183)

of ethnic differentials in increased morbidity among AF patients is limited, though Shen *et al.* [22] find elevated intracranial haemorrhage among black and Hispanic AF patients.

The present study also confirms the effect of anti-coagulant (Warfarin) therapy in reducing progression to increased costs, though not for very old patients. This confirms findings that such therapy reduces the risk of cardiovascular complications [23]. Atrial fibrillation is in itself a risk factor for excess morbidity and all-cause mortality [2,24], so if the condition is not managed with anti-coagulants, this may affect transitions to higher health spend categories (mainly hospitalisations) for a range of conditions, including non-cardiovascular conditions.

In line with the social model of health, the present study finds evidence that contextual factors may affect changes in morbidity status [25-26]. In particular transition to higher cost (usually due to hospitalisation) is higher in metropolitan areas, and lower in the West region (which includes sparsely populated rural areas). Access to hospital care suitable for critical or complex conditions may be lower in rural areas; for example, rural hospitals in the US are smaller than their urban counterparts [27,28], and geographic access issues include longer travel distances and lack of reliable transportation [29].

The present study benefits from a large sample size, and extensive information on pre-existing morbidity and service use. It focusses on health care spend as an indicator of morbidity, so contributing to a "longitudinal understanding of the resource burden" involved in the management of AF [30]. However, possible caveats to the analysis are the absence of information on personal or household income, which may affect access to care. A related possible drawback is absence of direct information on the quality of primary and community care preceding transition to higher costs, usually due to hospitalisation. Effective primary care can help reduce avoidable hospitalisations [31].

5. CONCLUSION

The analysis here seeks to demonstrate the potential of administrative patient databases for predicting risks of transition to increased health spend categories. A bivariate regression model including information on comorbidities, service use history, patient demography, baseline consumption and residential context has been estimated.

A risk scoring algorithm for predicting transition to higher consumption levels is then set out, including the most significant risk factors from the regression: in addition to age and comorbidities (as included in $CHADS_2$), baseline consumption category, ethnic group, metropolitan residence and Warfarin adherence are significant influences that contribute to defining a risk score. For moves to heavy consumption in particular, actual proportions of patients making the

transition increase monotonically with the risk score (see Figure **2**).

The risk scores in this application reflect the particular pattern of transition considered, namely from low or light use in 2007 to a higher level of health consumption a year later. Other types of transition may be considered, for example from low, light or moderate use combined to heavy or critical use. It would be expected that baseline consumption class level would again be important in any resulting risk scoring procedure.

APPENDIX 1 INDICATORS AND PREDICTORS

Reflective indicators of the latent morbidity index M_i are myocardial infarction (D_1=1 for MI during 2007, 0 otherwise), heart failure (D_2=1 or 0), diabetes (D_3=1 or 0), ischaemic heart disease (D_4=1 or 0), stroke/TIA (D_5=1 or 0), inpatient during 2007 (D_6=1 or 0), and years with AF (D_7=1 if over 2 years, 0 otherwise). Causative risk factors are gender (X_1, males as reference), ethnicity (X_2, with categories: white non-Hispanic as reference, black non-Hispanic, Hispanic, Other), and age in years divided by 100 (X_3).

There is also a directly observed index of health status, consumption class at end 2007, contrasting low users (V_i=1, first through 49th percentiles of aggregate Medicare payments), with light users (V_i=0, 50th through 74th percentiles of aggregate Medicare payments).

The treatment variable T_i is an indicator of Warfarin adherence: AF patients are considered to be receiving warfarin if they had three or more prothrombin test claims in the year ending 2007 [32].

Contextual variables (C_i) are poverty rate in ZIP Tract (micro-area) of residence (C_{1i}, log transform of percent poverty rate), metropolitan or non-metropolitan area of residence (C_{2i}=1 for metro areas, C_{2i}=0 for non-metro), and broad region (C_{3i}) with four categories: 1=North East (reference), 2=mid-West, 3=South, and 4=West.

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Received on 22-04-2014 Accepted on 22-05-2014 Published on 05-08-2014

http://dx.doi.org/10.6000/1929-6029.2014.03.03.4