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Mild Cognitive Impairment And Risk of Critical Illness

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Abstract

Objective—Approximately half of intensive care unit admissions are comprised of patients older than 65 year of age. Mild cognitive impairment (MCI) is a common disorder affecting 10-20% of patients in that same age group. A need exists for exploring MCI and risk of critical illness. As MCI may be a contributor to poorer overall health or be a result of it, we sought to determine whether the presence of MCI independently increases the risk of critical illness admissions.

Design—Data from the Mayo Clinic Study of Aging (MCSA) was analyzed. All study participants underwent prospective comprehensive cognitive testing and expert panel consensus diagnosis of both cognitive function and clinical state at baseline and subsequent visits. Comparisons were made between those with normal cognitive function and MCI regarding baseline health and frequency of critical illness.

Setting—Single-center population-based cohort out of Olmsted County, Minnesota.

Participants—All individuals aged 70-89 years were screened for prospective enrollment in MCSA. Patients with pre-existing dementia and intensive care unit (ICU) admission within 3 years of entry to the study were excluded from this analysis.

Measurements and Main Results—Of 2425 analyzed from MCSA, 1734 (71%) were included in the current study. Clinical factors associated with baseline MCI included age, male gender, stroke, and poorer health self-rating. Using a Cox regression model adjusting for these and a priori variables of baseline health, the presence of MCI remained a significant predictor of ICU admission (HR 1.50 (1.15-1.96), P = 0.003).

Conclusions and Relevance—The presence of MCI is independently associated with increased incidence of critical illness admission. Further prospective studies are needed to analyze the impact of critical illness on cognitive function.

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Keywords

mild cognitive impairment; critical illness

Introduction

Mild cognitive impairment (MCI) is an intermediate state of cognitive dysfunction defined by impairment in one or more cognitive domains including memory, attention, executive function, language, or visuospatial skills, but not generally meeting the criteria for dementia (1). Approximately 10-20% of the general population over 65 years of age have MCI and are at an increased risk for developing dementia, with 5-10% of MCI patients advancing to dementia each year compared with 1-2% of the normal population (1).

Patients over the age of 65 comprise approximately half of all intensive care unit (ICU) admissions with the number of geriatric ICU admissions expected to increase over the next several decades (2). Advances in critical care medicine have allowed for a growing number of critical illness survivors, with elderly patients making up a large proportion. Studies have shown approximately 63-85% of elderly patients admitted to the ICU will survive to hospital discharge (3-6). However, these survivors face increased risk of physical, emotional, and neurocognitive deficits, may have diminished quality of life, and utilize a disproportionate amount of healthcare resources after hospital discharge (7-9).

As MCI may be a reflection of overall poorer health, risk of critical illness may be increased reflective of this alone. Nonetheless, the same mechanisms that lead to declining health may also be worsened further by the presence of MCI and therefore increase the risk of critical illness. We hypothesize that MCI may independently increase critical illness risk despite similar baseline health among elderly patients. We also wished to avoid the confounding associated with prior critical illness and its contribution to long term cognitive decline or deficiency. Unfortunately, there are few studies assessing cognitive function prior to ICU admission, since critical illness often occurs emergently with little time to screen for baseline impairment (10). Using a prospective, population-based cohort, we identified patients assessed in a systematic manner with and without MCI at baseline, and studied their risk for ICU admission and critical illness.

Methods

Study of Aging Design

Data from the previously described Mayo Clinic Study of Aging (MCSA) was analyzed for admission or transfer to an ICU (11, 12). Enrollment began on October 1, 2004, with a rolling enrollment protocol designed to continually add patients to the study. A prospective cohort was constructed that consisted of patients aged 70-89 residing in Olmsted County, Minnesota. A sampling frame of 9,953 unique individuals who had been in contact with the health care system in Olmsted County within 3 years of the start of the study were identified by use of the medical records-linkage system from the Rochester Epidemiology Project (13). Based on census data, it was determined that nearly all Olmsted County residents aged

70-89 were identified with 5,233 persons randomly selected for the first round of recruitment.

Charts of selected patients were examined and patients initially excluded if they had a prior diagnosis of dementia. Dementia was confirmed by standard neurologic assessment established in the medical record prior to the initiation of MCSA. Those without established diagnosis of dementia were contacted and scheduled for an in-person or structured telephone interview. Participants who were evaluated in-person underwent extensive assessment which included meeting with a nurse or study coordinator, neurologic examination by a physician, and neuropsychological testing by a psychometrist. A nurse or study coordinator gathered detailed information that included demographics, past medical history, family history, and a self-reported overall wellness rating (based on a 1-5 scale). A physician and psychometrist administered and performed a complete neurological examination and neuropsychological testing. For neurologic assessment, testing included the Short Test of Mental Status, Modified Hachinski Scale, Prime MD, and neurologic interview and examination. Neuropsychologic testing included assessment of memory (Logical memory, Visual Reproduction, and Adult Video Learning Test (AVLT)), executive function (Trails A and B, Digit Symbol Substitution), visuospatial (Picture Completion, Block Design), and language (Boston Naming Test, Category Fluency) domains. Each study evaluator (nurse, study coordinator, physician, or psychometrist) reached an independent preliminary impression of every study participant prior to reaching a consensus diagnosis of normal cognitive function, MCI, or dementia. Patients were reevaluated approximately every 15 months. A consensus diagnosis of normal, MCI, or dementia was again made during each subsequent visit.

Current Study Design

IRB approval was obtained for analysis of ICU admissions (Mayo Clinic IRB 10-000328). Data from MCSA October 1, 2004, to December 31, 2010, were analyzed. The previously described ICU DataMart, developed as part of the Multidisciplinary Epidemiology and Translational Research in Intensive Care (METRIC) program at Mayo Clinic, was utilized to obtain ICU admission dates for subjects enrolled in MCSA (14, 15). Reason for admission to an ICU was documented and categorized via manual chart review by a blinded physician researcher.

Patients from MCSA who were found to have dementia on initial visit were excluded. As survivors of critical illness have previously been shown to have neurocognitive deficits following discharge, study subjects who were admitted to an ICU within 3 years of entering the study were also excluded (7-9).

Patients with normal cognitive function and those diagnosed with MCI were followed at study entry through December 31, 2010. Incidence of ICU admission between patients with normal cognitive function and those with subsequent MCI were compared, along with baseline demographics and medical comorbidities. Patients dying before ICU admission (not in the ICU) were censored for the purposes of this analysis.

When patients were enrolled into MCSA, baseline health inclusive of comorbidities, laboratory, and vital signs were obtained. Sixteen variables were selected for this analysis

based on their plausible contribution to increased risk of MCI and critical illness. These included age, gender, race, years of education, self-reported health status, smoking history, diabetes, hypertension, congestive heart failure (CHF), hypercholesterolemia, stroke, myocardial infarction (MI), atrial fibrillation, prior coronary bypass (CABG), and prior angioplasty.

Statistical Analysis

Continuous data were presented as mean values $\pm$ standard deviation when normally distributed or median with 25% to 75% interquartile ranges (IQRs) otherwise. Categorical data were presented as counts with percentages. Continuous variables were compared by using either Student *t* test or Wilcoxon rank-sum based on parametric or non-parametric characteristics. χ^2 or Fisher exact test was used to compare categorical variables. A Cox proportional hazards regression model correcting for a priori variables plausibly contributing to increased risk of developing MCI was used. These covariables included age, male gender, health self-rating, and years of education. A composite score for coronary heart disease was used for combining covariables of MI, prior CABG, and angioplasty for the purposes of univariable and multivariable Cox regression. As 'immortal time bias' may be of concern, only those risk factors known at baseline (study enrollment) were used, including the exclusion of those who developed incident MCI after enrollment. P-values less than 0.05 were considered significant. All statistical analysis was performed using JMP 10.0 (SAS Institute, Inc., Cary, NC).

Results

Of 2425 MCSA patients enrolled, 1734 (71%) were included in the current study (Figure 1). Four hundred and eighty one subjects were excluded including 419 who had previous ICU admission within 3 years of entry to MCSA and 62 who were identified as having dementia at baseline. MCI was identified at MCSA study enrollment in 306 individuals with exclusion of 210 developing incident MCI after baseline assessment. A total of 1428 patients were deemed to have normal cognitive function at MCSA study entry. Median follow-up in those with ICU admission (n= 296) was 2.2 years vs 4.1 years in those without. One hundred seven patients died before incident ICU admission with their follow-up censored for Log rank analysis.

Baseline characteristics of cognitively normal patients versus those with MCI are presented in Table 1. Subjects with MCI were older, more likely to be male, and had similar total years of education. Prior stroke history appeared to be the only statistically significant variable (9.6% vs 22.8%, $P < 0.001$) between normal vs MCI subjects. When self-rating their own health, patients with MCI were more likely to rate their health as poor (19.9% vs 8.4%, $P < 0.001$).

The incidence of ICU admission in patients with MCI was significantly higher than in cognitively normal patients (27.1% vs. 14.9% < 0.0001). Indications for ICU admission are presented in Table 2. Planned procedures with related post-operative ICU monitoring or complications were the most frequent admission type in each group (33% and 21% respectively). In patients with MCI, ischemic cardiovascular disease (including ST-elevation

myocardial infarctions) accounted for 17% of ICU admissions while severe sepsis and septic shock and respiratory failure accounting for 11% and 10% respectively. There was overall no statistically significant difference in terms of admission types between the two groups ($P = 0.42$).

Univariable and multivariable Cox regression models for predictors of ICU admission adjusted for a priori covariables of age, gender, smoker status, years of post-secondary education, and health self-report status are presented in Table 3. Notable predictors after adjustment include ischemic heart disease (CHD composite factor), other heart disease including CHF and atrial fibrillation, and BMI. MCI was an independent predictor of ICU admission on both univariable and multivariable analysis (HR 1.50 (1.15-1.96), $P = 0.03$). Kaplan-Meier analysis (Figure 2) demonstrated increased incidence of ICU admission over a 4 year timeline in those with MCI compared to normal (Log rank <0.0001).

Discussion

In this population-based, prospective study of cognitive function and aging, MCI appears to be independently associated with increased risk of ICU admission. To our knowledge, this is the first study to systematically evaluate baseline cognitive function and other clinical risk factors for transition to MCI and dementia over time prior to incidence of critical illness. Patients with MCI at study enrollment had twice the incidence of ICU admission during a 4 year follow-up time frame (27.1% vs 14.9%, $P < 0.0001$). They were older and male with prior history of stroke and worse health self-rating. Baseline comorbid conditions such as diabetes, ischemic heart disease (previous MI, CABG, or angioplasty), congestive heart failure, atrial fibrillation, and hypertension, were not statistically different. As there may be 'immortal bias' for those living to ICU admission vs those who died beforehand, only incident MCI at enrollment was followed. A multivariable Cox regression model controlling for a priori clinical covariables found MCI remained an independent predictor of ICU admission. While other comorbidities and characteristics were also associated with increased ICU admission, only poor health self-rating, age, and male gender, were associated with increased MCI. Stroke was not predictive on multivariable Cox analysis for ICU admission though associated with MCI risk.

Reason for ICU admission did not vary statistically between those with and without MCI. A third (33%) of patients with normal cognitive function and 21% of MCI patients were admitted to an ICU following a planned procedure that typically necessitated post-operative ICU management (such as cardiac valve replacement or coronary artery bypass grafting) or as a direct complication of such procedure. Cognitive impairment may have played a role in overall decision making regarding higher risk treatment options outside of any increased procedural risk, though this was not well documented in the medical record. We speculate that more conservative treatment options may have been recommended to patients with cognitive impairment and thus a smaller percentage underwent planned procedures. As well, MCI is known to be associated with a higher number of medical comorbidities, with such comorbidities perhaps influencing the decision to pursue elective procedures. A recent study by Kazmierski et al. suggested baseline MCI increases the likelihood of postoperative delirium, adding to the morbidity of a procedure. They noted that pre and postoperative

inflammatory markers and cortisol levels were higher in those with diagnosed MCI compared to non-MCI patients (16). These findings suggest perhaps increased complication rate in procedures both elective and non-elective for patients with suspected MCI, which may influence decision-making for planned procedures.

Few studies have prospectively examined the risk of ICU admission in patients with established MCI. Pandharipande and colleagues evaluated by short questionnaire (IQCODE) the baseline cognitive function of 821 patients and their long term cognitive outcomes after critical illness, noting approximately 6% of critically ill patients met criteria for cognitive impairment at the time of critical illness admission (17). They ultimately found profound effects of delirium on long term cognitive function, even in younger patients not expected to have baseline cognitive disease. Although attempts at measuring baseline cognitive function at the time of study enrollment (admission to the ICU) were made, more extensive or comprehensive assessment was not feasible even in those at increased risk of subclinical disease. Of 296 ICU admissions in our study, MCI was established or existed in 28% by comprehensive pre-illness assessment. Explanation for the discrepancy in frequencies in our two studies include vastly different study populations (all ICU admission age groups vs older patients >70 years of age already at increased risk of MCI in our study), and different methodologies for establishing MCI diagnosis. Two population-based prospective cohorts analyzing baseline cognitive health pre and post critical illness noted worsening of tested cognitive function after critical illness admission(8, 10). Their baseline assessment of cognitive health included biannual recorded surveys as part of larger health group assessments and proxy interviews where available. While methodologies for assessing baseline cognitive health were less extensive than ours, they were able to establish baseline criteria for dysfunction and graded progression over time. Ehlenbach and colleagues included dementia patients and all ICU admissions(10), while Iwashyna studied severe sepsis survivors(8). Our cohort using the MCSA database, whose intent was to follow risk and presentation of MCI and dementia itself, did not assess primarily the effects of critical illness, but more so reflected on an extensive prospective assessment of cognitive health. We then followed risk of critical illness as stratified by the presence or absence of MCI at baseline. However, it should be highlighted that the timing and establishing of a comprehensive diagnosis of MCI is important to delineating interactions of cognitive health with critical illness and other daily comorbidities. Subclinical undiagnosed disease may have a profound effect on hospital course including incidence and duration of delirium, as well as contribute to more rapid cognitive decline after critical illness.

While work establishing pre-illness MCI as a risk factor for critical illness is currently limited, prior studies have examined risk of hospital admission in patients with dementia. In a retrospective cohort analysis, Phelan and colleagues showed that incident dementia significantly increased the risk of hospitalization in the elderly and potentially preventable admissions (18). Similarly, a study examining claims-based data found that Medicare beneficiaries with dementia had more than three times the risk of being hospitalized as compared to cognitively normal patients (19). Ehlenbach and colleagues also studied and noted the increased prevalence of dementia after admission for critical illness(10).

Establishing a link between MCI and ICU admission is important in several ways. First, post hospitalization care may be provided in a more directed and resource-focused manner. For example, recognizing pre-existing MCI at the time of admission may increase awareness of increased morbidity and related post-admission complications. Such patients may require extra assistance with medication management or be candidates for cognitive rehabilitation programs (1). Extra surveillance in these cognitive domains hopefully may reduce potentially preventable readmissions (18). Understanding future risk of readmission or risk of cognitive debility may also prompt important discussions regarding end-of-life care prior to and after critical illness. Indeed if MCI increases the likelihood of critical illness, improving management of baseline health with more directed primary or preventive care measures such as better medication compliance, social support, and home safety standards, may reduce the frequency and related costs of more expensive ICU admissions. A first approach may be recognizing the significance of baseline cognitive impairment as a premorbid condition contributing to not only increased risk of critical illness, but perhaps to longer or more severe disease presentation.

Our study has several important limitations. The population consisted of only patients from Olmsted County, Minnesota, with the vast majority of participants identifying themselves as Caucasian. While we found an association of MCI with critical illness, MCI may indeed be a surrogate of overall generally poorer health, rather than an independent mechanism leading to increased risk of ICU admission. Patients with MCI may be theoretically unable to provide appropriate self-care, such as timely adherence to prescribed medications or keeping up with health appointments. In the same vein, diseases such as stroke may increase the likelihood of MCI at the same time as contribute to increased likelihood of critical illness, confounding contribution of MCI to critical illness. Despite controlling for these factors in our analysis, it is still a possibility that MCI's contribution to critical illness may be more indirectly related to lowering overall health status or be a result of it than independently adding to severity of ICU disease frequency, presentation, or outcome. Finally, criteria for ICU admission are not standardized and admission is often determined by institutional policies and the discretion of the treating provider. We did not intend to study severity of illness or duration of hospitalization as a direct result of baseline MCI, but instead review the influence of pre-existing cognitive dysfunction in the context of a patient's overall health as risk a factor for critical illness. Studies delineating survival or morbidity of hospital course are needed in a cohort of patients with well-established and comprehensive pre-critical illness disease.

In conclusion, risk of ICU admission is significantly associated with mild cognitive impairment. As there is an ever-growing population of elderly patients with established MCI who survive critical illness, future prospective cohort studies are needed to analyze the impact of critical illness on further cognitive function.

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References

1. Petersen RC. Clinical practice. Mild cognitive impairment. *N Engl J Med*. 2011; 364(23):2227–2234. [PubMed: 21651394]
2. Carson SS. The epidemiology of critical illness in the elderly. *Crit Care Clin*. 2003; 19(4):605–617, v. [PubMed: 14601710]
3. Sacanella E, Perez-Castejon JM, Nicolas JM, et al. Mortality in healthy elderly patients after ICU admission. *Intensive Care Med*. 2009; 35(3):550–555. [PubMed: 18982308]
4. Kaarlola A, Tallgren M, Pettila V. Long-term survival, quality of life, and quality-adjusted life-years among critically ill elderly patients. *Crit Care Med*. 2006; 34(8):2120–2126. [PubMed: 16763517]
5. Bo M, Massaia M, Raspo S, et al. Predictive factors of in-hospital mortality in older patients admitted to a medical intensive care unit. *J Am Geriatr Soc*. 2003; 51(4):529–533. [PubMed: 12657074]
6. Sprung CL, Artigas A, Kesecioglu J, et al. The Eldicus prospective, observational study of triage decision making in European intensive care units. Part II: intensive care benefit for the elderly. *Crit Care Med*. 2012; 40(1):132–138. [PubMed: 22001580]
7. Hopkins RO, Weaver LK, Collingridge D, et al. Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2005; 171(4):340–347. [PubMed: 15542793]
8. Iwashyna TJ, Ely EW, Smith DM, et al. Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA*. 2010; 304(16):1787–1794. [PubMed: 20978258]
9. Jackson JC, Mitchell N, Hopkins RO. Cognitive functioning, mental health, and quality of life in ICU survivors: an overview. *Crit Care Clin*. 2009; 25(3):615–628, x. [PubMed: 19576534]
10. Ehlenbach WJ, Hough CL, Crane PK, et al. Association between acute care and critical illness hospitalization and cognitive function in older adults. *JAMA*. 2010; 303(8):763–770. [PubMed: 20179286]
11. Petersen RC, Roberts RO, Knopman DS, et al. Prevalence of mild cognitive impairment is higher in men. The Mayo Clinic Study of Aging. *Neurology*. 2010; 75(10):889–897. [PubMed: 20820000]
12. Roberts RO, Geda YE, Knopman DS, et al. The Mayo Clinic Study of Aging: design and sampling, participation, baseline measures and sample characteristics. *Neuroepidemiology*. 2008; 30(1):58–69. [PubMed: 18259084]
13. Melton LJ 3rd. History of the Rochester Epidemiology Project. *Mayo Clin Proc*. 1996; 71(3):266–274. [PubMed: 8594285]
14. Cartin-Ceba R, Kojacic M, Li G, et al. Epidemiology of critical care syndromes, organ failures, and life-support interventions in a suburban US community. *Chest*. 2011; 140(6):1447–1455. [PubMed: 21998258]
15. Li M, Pickering BW, Smith VD, et al. Medical informatics: an essential tool for health sciences research in acute care. *Bosn J Basic Med Sci*. 2009; 9(Suppl 1):34–39. [PubMed: 19912124]
16. Kazmierski J, Banyas A, Latek J, et al. Mild cognitive impairment with associated inflammatory and cortisol alterations as independent risk factor for postoperative delirium. *Dement Geriatr Cogn Disord*. 2014; 38(1-2):65–78. [PubMed: 24603477]
17. Pandharipande PP, Girard TD, Jackson JC, et al. Long-term cognitive impairment after critical illness. *The New England journal of medicine*. 2013; 369(14):1306–1316. [PubMed: 24088092]
18. Phelan EA, Borson S, Grothaus L, et al. Association of incident dementia with hospitalizations. *JAMA*. 2012; 307(2):165–172. [PubMed: 22235087]

19. Bynum JP, Rabins PV, Weller W, et al. The relationship between a dementia diagnosis, chronic illness, medicare expenditures, and hospital use. *J Am Geriatr Soc.* 2004; 52(2):187–194. [PubMed: 14728626]

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Figure 1.
Flowchart of Outcomes

Figure 2. Kaplan-Meier estimates of the probability of being free from ICU Admission after enrollment into the Mayo Clinic Study of Aging. (Log rank $P < 0.001$)

Table 1

Baseline Characteristics of Patients with Normal Cognition vs. MCI

	Normal Cognition (n=1428)	MCI (n=306)	p-value
Sex (Male), n (%)	695 (48)	176 (58)	0.006
Age, median (IQR)	78.8 (70.5-90.8)	82.6 (70.7-91.8)	<0.001
Race (% White), n (%)	1417(98.5)	300 (98)	0.25
Education – years of education, median (IQR)	13 (12-16)	12 (12-15)	0.67
BMI, median (IQR)	27.2 (24.5-30.3)	26.9 (24.3-29.7)	0.67
Current or Previous Smoker, n (%)	684 (47.9)	147 (48)	1
Diabetes, n (%)	234 (16.3)	61 (19.9)	0.16
CHF, n (%)	83 (5.8)	21 (7)	0.54
Elevated Blood Pressure, n (%)	964 (67.5)	212 (69)	0.60
Elevated Cholesterol, n (%)	892 (62.6)	177 (58)	0.16
Previous Stroke, n (%)	136 (9.6)	70 (22.8)	<0.001
Previous MI, n (%)	169 (11.9)	70 (13.2)	0.60
Atrial Fibrillation, n (%)	176 (12.4)	47 (15.4)	0.18
Previous CABG, n (%)	108 (7.6)	32 (10.4)	0.12
Previous Angioplasty, n (%)	153 (10.8)	29 (9.5)	0.59
Poor Self Rating of Health, >3 (1 excellent, 5 poor), n (%)	120 (8.4)	61 (19.9)	<0.001

Table 2

Reason for Admission to ICU

	Cognitively Normal Group (n=213)	MCI Group (n=83)
Sepsis ^a , n (%)	17 (8)	9 (11)
Respiratory Failure ^b , n (%)	21 (10)	8 (10)
Gastrointestinal ^c , n (%)	19 (9)	8 (10)
Planned Procedure, n (%)	71 (33)	18 (21)
Unplanned Procedure, n (%)	13 (6)	4 (5)
Ischemic cardiac etiology, n (%)	25(12)	14 (17)
Other Cardiac ^d , n (%)	14 (7)	8(10)
Trauma, n (%)	20 (9)	5 (6)
Neurologic ^e , n (%)	11 (5)	6 (7)
Other ^f , n (%)	2 (1)	3 (4)

^aIncludes sepsis, severe sepsis, or septic shock

^bIncludes acute lung injury, acute respiratory distress syndrome, chronic obstructive pulmonary disease exacerbation, or pulmonary embolus

^cIncludes gastrointestinal bleeding or acute surgical abdomen

^dIncludes congestive heart failure exacerbation, cardiac tamponade, arrhythmia or conduction abnormality,

^eIncludes seizure, altered mental status, hemorrhagic and ischemic stroke, nontraumatic subdural hematoma, epidural hematoma, or intraparenchymal hemorrhage

^fIncludes allergic reaction, overdose, diabetic ketoacidosis, or hyperosmolar hyperglycemic nonketotic syndrome

Table 3

Univariable and multivariable Cox regression predictors of ICU Admission

	Univariable (HR, 95% CI)	P value	Multivariable * (HR, 95% CI)	P value
Age	1.04 (1.02-1.06)	0.0002	1.48 (1.17-1.87)	0.0012
Gender (male)	1.37 (1.08-1.72)	0.008	1.43 (1.14-1.81)	0.002
Health Self-rating	1.53 (1.35-1.73)	<0.0001	1.46 (1.28-1.66)	<0.0001
Education (years post-secondary)	0.93 (0.89-0.97)	0.0003	0.95 (0.92-0.99)	0.012
Diabetes	1.49 (1.13-1.96)	0.005	1.25 (0.95-1.66)	0.11
CHD composite	1.98 (1.56-2.51)	<0.0001	1.66 (1.29-2.31)	<0.0001
Stroke	1.46 (1.07-1.98)	0.016	1.12 (0.82-1.54)	0.47
CHF	2.26 (1.56-3.28)	<.0001	1.58 (1.07-2.32)	0.02
Atrial Fibrillation	1.9 (1.43-2.54)	<0.0001	1.55 (1.15-2.08)	0.004
Smoker History	1.41 (1.12-1.77)	0.003	1.25 (0.98-1.59)	0.072
BMI (obese)	1.36 (1.06-1.74)	0.013	1.31 (1.02-1.69)	0.03
MCI	1.95 (1.52-2.52)	<0.0001	1.50 (1.15-1.96)	0.003

* Corrected for a priori covariables of age, gender, smoker status, post-secondary years of education, and health self-rating.