Characteristics of Under-Treated Hypertensives in the Veteran Population

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CERTIFICATE OF APPROVAL

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Abstract

Background: Executive performance summary statistics highlight preventive care outcomes for the Veteran Integrated Service Networks (VISN) on a monthly basis. One such outcome is the proportion of veterans with essential hypertension and blood pressure readings below 140/90 mmHg, a measure that has been consistently low and more frequently than not below benchmark. This finding, when coupled to recent evidence that reductions in cardio and cerebrovascular morbidity and mortality result as a function of tighter control of systolic and diastolic blood pressure serves to raise the question as to which characteristics distinguish well from under treated hypertensive patients.

Objective: To determine the characteristics of patients with under treated essential hypertension so that appropriate resources can be used to aid this population with achieving desired preventive care outcomes.

Design: Cross sectional study design.

Setting and Patients: This study makes use of computerized records from a CHIPS database which serves as a warehouse for over 200,000 veterans from Portland, Oregon of the Veteran Integrated Service Network 20 (VISN 20).

Methods: Of the 208,819 patients in the Portland VA Medical Center CHIPS database, 6,382 veteran patients with an ICD-9 diagnosis of hypertension and at least three vitals taken between January 1st, 2001 and April 24th, 2002 were selected using a Microsoft Access query of a CHIPS data warehouse of all computerized medical data for the Portland VAMC of Veteran Integrated Service Network 20. Uncontrolled hypertension was defined as both an average systolic blood pressure reading above 140 mmHg over the past fifteen months and a last systolic blood pressure reading of over 140 mmHg. 'Controlled' versus 'under controlled' hypertensive veteran patients were compared according to the following characteristics: Sex, marital status, race, age, body mass index, smoking status, alcohol history, medical history (history of congestive heart failure, renal disease, depression and/or diabetes mellitus), marital status, recent use of beta blocker, ace inhibitor, angiotensin receptor blocker, alpha blocker and/or nitrate therapy, number of blood pressure readings in the past fifteen months and disability status. A cross tab assessment of each categorical variable in a univariate analysis using the outcome of systolic hypertension was performed, followed by a univariate analysis of each continuous variable to choose variables of significance. A multivariate analysis was then used following the procedures set forth by Hosmer and Lemoshow[1] to yield a main effects model with significant interaction terms.

Results: The final model obtained found statistically significant associations between uncontrolled systolic hypertension and advancing age, diabetes mellitus, elevated body mass index, use of calcium channel blockers and non loop diuretics. For controlled systolic hypertension, significant associations were found with Veterans receiving more

frequent blood pressure readings, having a history of congestive heart failure and taking loop diuretics, nitrate agents or lipid lowering agents.

Conclusions: Within the Portland Veteran population between the dates of January 1st, 2001 and April 24th, 2002, those hypertensive Veterans achieving systolic blood pressure control of less than 140 as an average of all readings and on their last visit were more commonly of a younger age, of a lower body mass index, had their blood pressure read more frequently, had a history of congestive heart failure and were treated with loop diuretics, nitrates or lipid lowering agents (with an alpha of 0.05). Those Veterans from the same period who were less likely to be controlled were more commonly diabetic and treated with calcium channel blockers or non loop diuretic therapy. Thus more frequent monitoring and the use of more traditional antihypertensive agents is associated with better hypertensive control in the Veteran population.

BACKGROUND

The importance of adequate systolic blood pressure control cannot be understated. In an analysis of the Cardiovascular Health Study which included 5,888 adults aged 65 or more from 4 US centers, Psaty et al [2] found systolic blood pressure to be the single best predictor of adverse cardiovascular events. In a separate study from the same population, Psaty et al [3] found after a follow up of 4.8 years that systolic blood pressure elevated above 140 mm Hg was associated with one quarter of the coronary events and one third of the cerebrovascular events that occurred in the population studied. Perry et al [4] in their analysis of the Systolic Hypertension in the Elderly Program (SHEP) study found a significant reduction in stroke incidence when specific systolic blood pressure goals were obtained, lending further support for the control of this one variable to leverage secondary prevention of coronary and cerebrovascular events in an older population.[4]

The veteran population is one that closely monitors the proportion of subjects with adequate systolic blood pressure control. There are twenty-two Veteran Integrated Service Networks (VISNs) in the United States. Each VISN is 'graded' according to a set of guidelines established as markers for the provision of preventive services that closely parallel the HEDIS (health measures used in the private health care arena). One such performance outcome is the proportion of hypertensive veterans with blood pressure readings below 140/90 mmHg, a measure that has consistently shown more than half of veterans as being uncontrolled (approximately forty percent achieve control).[5] The proportion of veterans with controlled systolic hypertension may actually be higher than

that of the private sector where estimates from the 1988-1991 National Health and Nutrition Examination Survey (NHANES III) show as few as 24 percent of hypertensives are adequately treated.[6] Even more alarming is the fact that within both populations the proportion of adequately treated hypertensive patients is decreasing over time in spite of the advances in medical treatments.[5,6] These findings bring to focus an interest for the characteristics that distinguish well controlled from under controlled hypertensive patients.

Berlowitz et al. found that hypertensive control was directly related to physician intensity of treatment, concluding that as outcomes are influenced by physician behavior and performance, so should responsibility also fall in part on their shoulders.[7] They further found that patients with known coronary artery disease achieve better blood pressure control largely due to physician adherence to guidelines surrounding post ischemic care for this patient population.

Hyman et al. analyzed the third National Health and Nutrition Examination Survey and discovered that most cases of uncontrolled hypertension consist of isolated and mild elevations in systolic blood pressure.[8] They further found that patients with uncontrolled hypertension are primarily older adults with access to health care and frequent contacts with physicians throughout each year. They emphasized that patients with uncontrolled hypertension exist largely within the health care system and suggested that changes that address better identification and management by health care providers are paramount in increasing the proportion of patients with controlled hypertension.

Many additional questions remain, however, as to what additional characteristics are associated with uncontrolled hypertension. Possible predictors include depression, smoking, alcohol use, alcohol related disease, the number and class of blood pressure medicines taken, disability status and the frequency with which blood pressure measurements are made. This study proposes therefore to expand upon the findings of Hyman et al. through an investigation into additional characteristics of patients with uncontrolled hypertension that could be potentially helpful to health care providers, so that they may better identify and more aggressively manage such a population.

METHODS

This study made use of a veteran database warehouse that receives regular updates and imports from a computer based medical record system to study the characteristics of interest. Patient data reviewed were from the Portland VAMC of VISN 20 (the northwest region of the Veterans network). Microsoft Access and SQL Server were utilized to extract data. Interventional Review Board and Research and Development approval was obtained from the Portland VA Medical Center. Patient consent was not needed because the data was collected retrospectively without social security or name identification. Of the 208,819 veteran patients from the Portland VA Medical Center, 33,639 were identified as having an ICD-9 code for hypertension (401) or hypertension like diseases (401*). Of these 33,639 veterans, 6,382 had not deceased by the time of data extraction (April 24th, 2002) and had had at least three blood pressure

readings from January 1st, 2001 through April 24th. The characteristics shown in table I were collected from the 6,382 records.

TABLE I: Variable Definitions

Variable	Definition
Race	White, Black, Hispanic, American Indian or Alaskan Native, Asian or Pacific Islander, Black Hispanic, Unknown
Body Mass Index	Kg/M^2
Systolic Blood Pressure	Continuous in mmHg
Smoking status (h/o or active)	Current, former or never smoked
Marital Status	Married, Divorced, Widow/Widower, Never Married, Unknown
Sex	Male or Female
Age	Continuous Variable
Number of blood pressure readings from January 1st, 2001 until April 24th, 2002	Continuous Variable
H/O Etoh Related Disease	Yes or No
Etoh Use Status	Yes or No (active drinker?)
Disability Status	Yes or No
Disability Status by percent service connected	Continuous as percentage
H/O Non Loop Diuretic therapy	Yes or No
H/O Ace Inhibitor Therapy	Yes or No
H/O Loop Diuretic therapy	Yes or No
H/O Angiotensin II Inhibitor therapy	Yes or No
H/O Lipid Lowering Agent (statin and/or other agent)	Yes or No
H/O Nitrate Therapy	Yes or No
H/O Beta Blocker therapy	Yes or No
H/O Renal Disease	Yes or No
H/O Congestive Heart Failure	Yes or No
H/O Diabetes Mellitus	Yes or No
Number of Cardio Vascular Medicines	Zero through Eight

H/O = History of

Systolic blood pressure control served as the outcome measure of interest for this study. Only living patients with at least three blood pressure readings over the study period of fifteen months were included. All non-diabetic patients were defined as controlled when both their last systolic blood pressure reading and average systolic blood pressure reading over the past fifteen months (from January 1st, 2001 through April 24th, 2002) were below 140 mmHg. All diabetic patients in the study were labeled as controlled if both their last systolic blood pressure reading and average systolic blood pressure reading over the past fifteen months (from January 1st, 2001 through April 24th, 2002) fell below 130 mmHg. This criteria was chosen to be accordance with that of the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI).[9] The use of both last and average blood pressure readings for definition of control offered the advantage of combining short with long term markers of blood pressure readings in this population.

A logistic regression analysis was performed making use of our dichotomous outcome of systolic blood pressure control. The mathematical model is of the form:

$$\text{Ln}\,[p/(1-p)] = a_0 + a_1x_1 + a_2x_2 + \ldots\, a_kx_k$$

Where p is the probability of an event, uncontrolled systolic blood pressure, as previously defined, the x's are the predictor variables, and the a's are the coefficients for the predictor variables. A univariate analysis of each categorical predictor variable with systolic control was made and all variables with a Chi-square significance of $p<0.20$ were included into a main effects model. Continuous variables were graphed and analyzed according to the strength of their individual Wald statistic when either the raw values

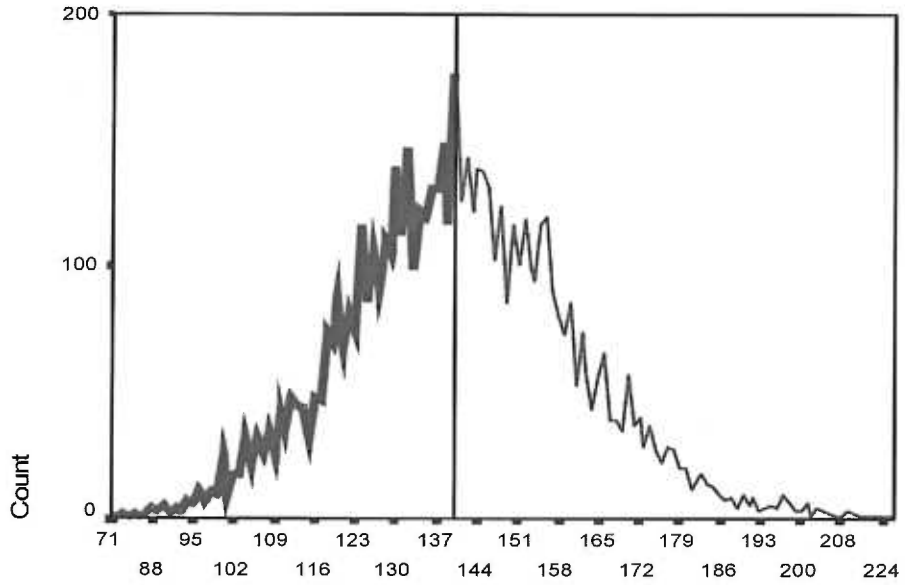
were used or they were re-defined in ways that made more clinical sense or more closely represented the distribution of data found. All significant predictors (of $p<0.20$) were combined in a multivariate logistical regression output with systolic control as the outcome variable. Only those variables of significance (at the $p<0.05$ level) within the model were maintained to generate a main effects model. Consideration was next given to adjustment for potential confounding between variables in the main effects model. Those variables possessing high correlation coefficients together and significant associations with systolic control of hypertension were identified as potential confounding variables and maintained within the final model for adjustment purposes. Lastly, consideration for interaction was given for each potential combination of predictor variables within the main effects model. Those interactions that created a statistically significant rise in the -2loglikelihood value were considered closely and those which remained significant when included with the main effects model and altered the odds ratio values for the predictor variables were maintained to generate a final model.

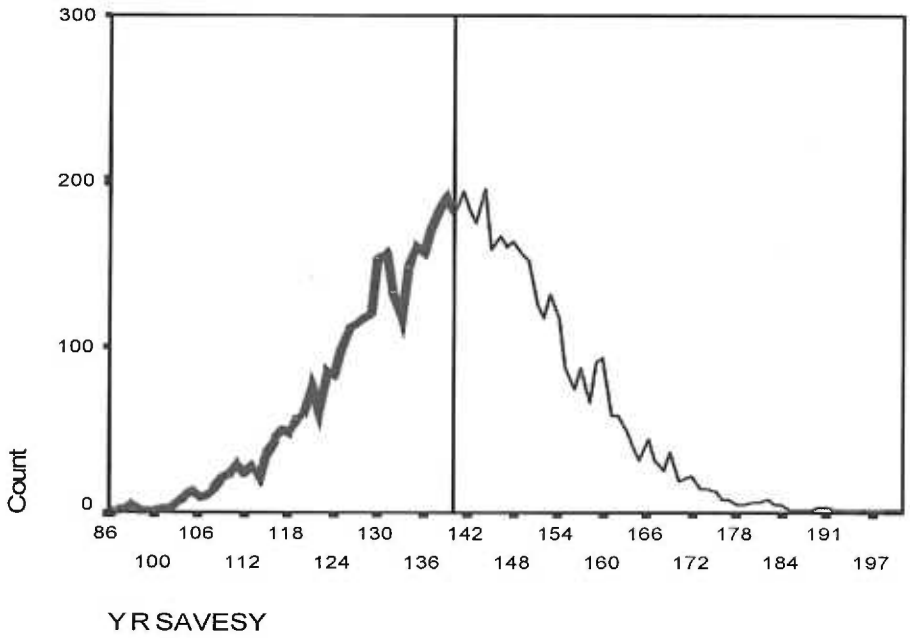
RESULTS

Distribution of Systolic Blood Pressure

Figure 1 below represents the distribution of the systolic blood pressures recorded at each subject's last visit and the average of all systolic blood pressure readings over a fifteen month study, respectively.

Figure I: Distribution SBP Readings at Last Visit (Above) and 15 Month Average (Below)





Roughly half of our population of hypertensive patients were uncontrolled at the time of their last blood pressure reading as well as over a fifteen month study period.

Population Characteristics

Table II shows comparisons of the variable among those patients with or without systolic hypertension control:

Table II:

Variable	Controlled Patients N = 3258	Uncontrolled Patients N = 3129	P Value
	Mean +/- SD	***Mean +/- SD***	
Age *	66.3 +/- 11.9	67.1 +/- 11.7	0.01
No. BP Readings *	16.7 +/- 31.8	11.3 +/- 19.1	<0.00
Number of cardiovascular agents	2.0 +/- 1.5	2.0 +/- 1.4	0.40
Body Mass Index (Kg/M^2)*	30.1 +/- 6.3	30.8 +/- 6.3	<0.00
Percent of Service Connection *	23.4 +/- 33.5	20.9 +/- 31.8	0.00
	n (%)	***n (%)***	
Gender (Males)	3114 (95.7)	2989 (95.5)	0.69
Marital Status			0.45
Married	1715 (52.7)	1685 (53.9)	
Divorced	887 (27.3)	813 (26.0)	
Widowed	288 (8.9)	297 (9.5)	
Never Married	74 (2.3)	80 (2.6)	
Unknown	289 (8.9)	254 (8.1)	
Race +			<0.00
White	2334 (71.7)	2041 (65.2)	
Black	97 (3.0)	106 (3.4)	
Hispanic	35 (1.1)	46 (1.5)	
American Indian Or Alaskan Native	30 (0.9)	52 (1.7)	
Asian or Pacific Islander	30 (0.9)	28 (0.9)	
Black Hispanic	26 (0.8)	35 (1.1)	
Unknown	701 (21.5)	821 (26.2)	
Service Connected	1711 (52.6)	1603 (51.2)	0.27
Depression *	631 (19.4)	477 (15.2)	<0.00
Diabetes Mellitus *	87 (26.8)	1449 (46.3)	<0.00
Chronic Renal Failure	213 (6.5)	186 (5.9)	0.32
Congestive Heart Failure *	525 (16.1)	291 (9.3)	<0.00
Etoh Use	1647 (50.6)	1586 (50.7)	0.96

EtohICD9 Dx	*	362 (11.1)	298 (9.5)	0.04
Tobacco Hx	*			0.00
Current		1253 (38.6)	1113 (35.8)	
Former		1913 (59.0)	1888 (60.7)	
Never		78 (2.4)	110 (3.5)	
Ace Inhibitor	*	1105 (34.0)	1232 (39.4)	<0.00
Beta Blocker		1271 (39.1)	1192 (38.1)	0.42
Alpha Blocker	*	318 (9.8)	350 (11.2)	0.07
Non Loop Diuretic	*	619 (19.0)	725 (23.2)	<0.00
CaChannelBlocker	*	701 (21.5)	885 (28.3)	<0.00
AngiotensinIIBlock	*	130 (4.0)	150 (4.8)	0.12
Nitrate	*	677 (20.8)	439 (14.0)	<0.00
Lipid Agent	*	1103 (33.9)	971 (31.0)	0.01
Loop Diuretic	*	496 (15.2)	327 (10.5)	<0.00

* Variable included in the multivariate logistic model

\+ Race not included in multivariate logistic model due to high proportion of unknowns

Logistic Regression Modeling

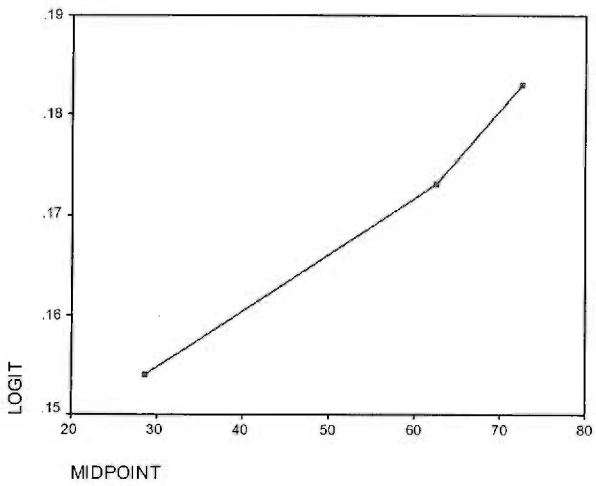
Selection of Candidate Variables

Logistic regression modeling followed procedures outline by Hosmer and Lemeshow, Chapter 4.[1] We began with a selection of candidate variables using a cross tab assessment and Chi-square univariate analysis of each categorical variable using the outcome of systolic hypertension previously described. The goal was to choose those variables at a significance level of 0.20 or less as candidates for the model. Table II (above) denotes those variables significant at this level with an asterisk after the variable name. Race was not included in the multivariate logistic model in spite of its significance due to the low proportion of non-white veterans as well as high proportion of veterans within the unknown race category making generalizations of findings from the data to non-white races highly susceptible to selection bias.

Assessing the Linearity of Continuous Variables

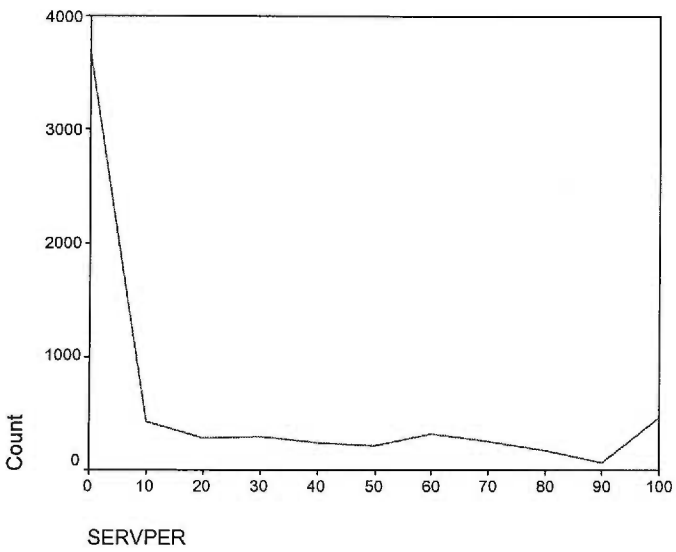
Age was divided into quartiles and the midpoint of each quartile was plotted against the logit [ln (p/(1-p))] of the proportion of patients with uncontrolled hypertension in the quartiles. Figure II shows the plot to be linear so that age is entered into the model as a continuous variable. Since the distribution of age in our population is older, AGE is defined as AGE-50 in order to facilitate clinical interpretation of the findings.

Figure II. LOGIT versus midpoints of AGE quartiles



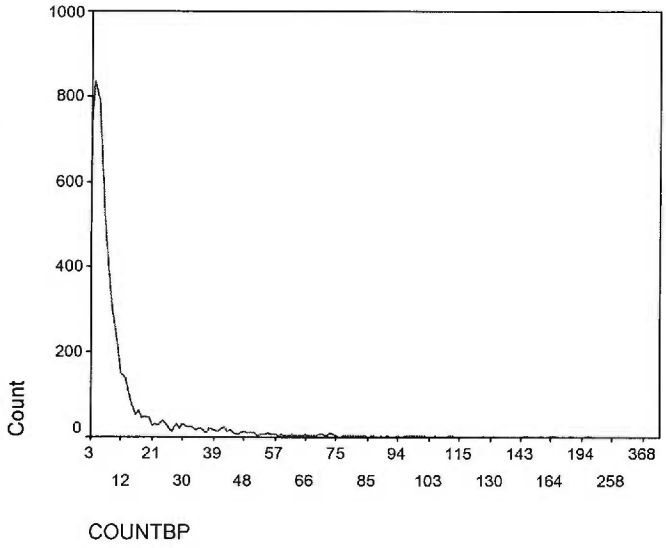
Percent of Service Connection was considered next. Figure III depicts the distribution of data for this variable. Percent of Service Connection was entered into the model as a categorical variable due the lack of linear relationship demonstrated and significance found of $p<0.20$ when considered as categorical (in Table II above).

Figure III: Distribution of Percent Service Connected



The number of blood pressure readings in the study period is considered next. The distribution of COUNTBP is depicted in figure IV.

Figure IV: Distribution of Number of Blood Pressure Readings



We see a drop off in the number of readings that is rather abrupt. We therefore grouped the number of blood pressure readings into evenly distributed categorical variables as follow, which served to strengthen the association found with systolic blood pressure control when entered into the model:

No. of Readings	Categorical Variables
3-4	0
5-6	1
7-11	2
12 or more	3

Body mass index (BMI) is considered next. Figure V depicts the distribution of BMI in our population.

Figure V: Distribution of BMI in Study Population

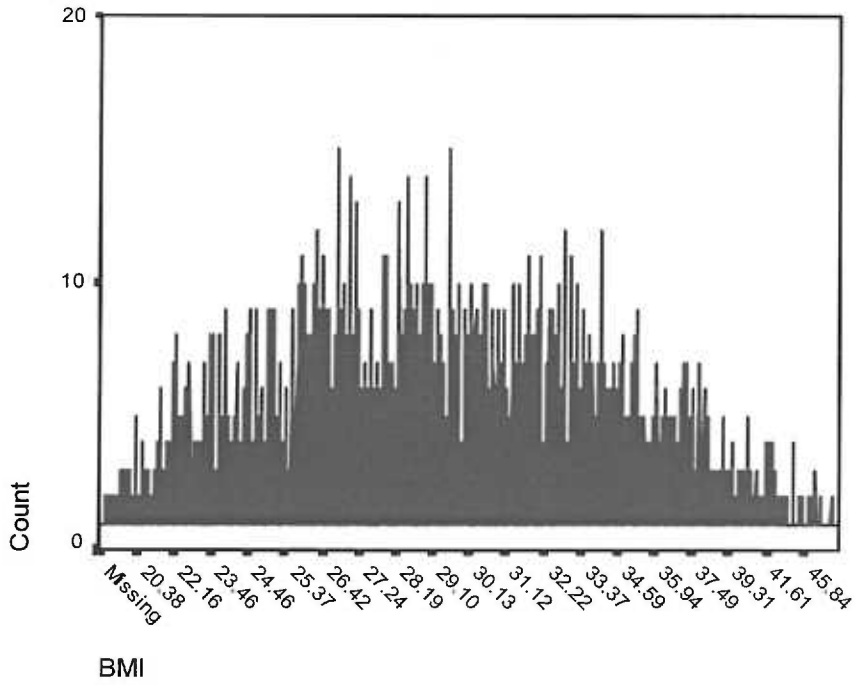
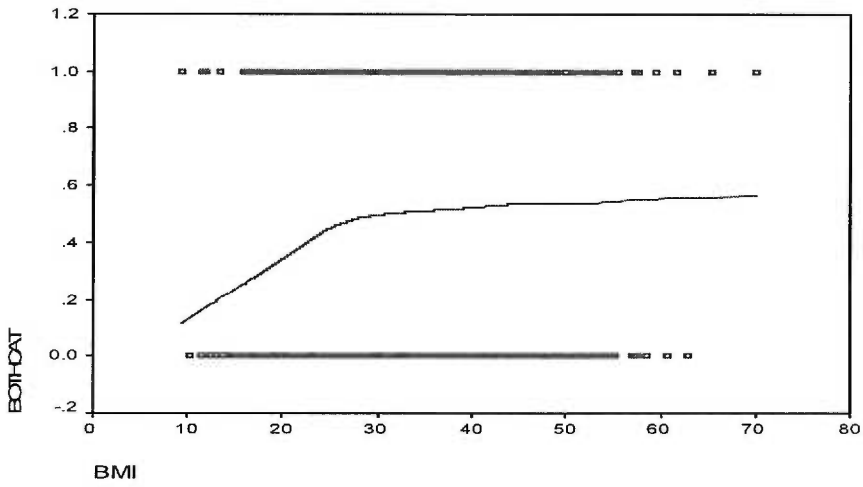


Figure VI compares BMI with control of systolic blood pressure and we see that there appears to be a linear relationship between BMI and lack of blood pressure control until a point when it tapers off.

Figure VI: BMI and Systolic Blood Pressure Control



BMI was therefore considered as a categorical variable with one category to represent those with a BMI at or beyond the cut off point (when less of a linear relationship is noted) while maintaining the previous portion of the graph as quintiles. The referent category was defined as subjects of normal weight with those who are under weight used as the first comparison variable (and then those of progressive weight thereafter).

BMI Range	Categorical Variable
23.9 to 26.2	0
<23.9	1
26.2 to 28.1	2
28.1 to 30.0	3
30.0 to 32.0	4
>32.0	5

Due to the low numbers of veterans with BMI values above the point where the linear relationship diminishes, a benefit for maintaining BMI as a continuous variable was discovered. These more obese veterans therefore pull the distribution to the right and in effect 'level' out the slope of the line, when in fact a linear distribution of the majority of subjects best represents the distribution of BMI in our population. To make more clinically useful BMI as a continuous variable, it is computed as BMI-25 for our analysis.

The Number of Cardiovascular Medications taken is next considered. We considered keeping the data as a continuous (ordinal) variable versus collapsing the rows to create a final category of those taking three or more cardiovascular medicines:

MEDCOUNT

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	1039	16.3	16.3	16.3
	1	1578	24.7	24.7	41.0
	2	1642	25.7	25.7	66.7
	3	1111	17.4	17.4	84.1
	4	655	10.3	10.3	94.4
	5	277	4.3	4.3	98.7
	6	70	1.1	1.1	99.8
	7	9	.1	.1	100.0
	8	1	.0	.0	100.0
	Total	6382	100.0	100.0	

Collapsing the 4^{th} to 8^{th} rows:

MEDCAT

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	1039	16.3	16.3	16.3
	1	1578	24.7	24.7	41.0
	2	1642	25.7	25.7	66.7
	3	2123	33.3	33.3	100.0
	Total	6382	100.0	100.0	

A statistical benefit was noted for considering the Number of Cardiovascular Medicines taken (MEDCOUNT) as a categorical variable and this more evenly

distributed distribution was used for modeling. We summarize how the above continuous variables will be used in the analysis and proceed with our modeling:

AGE as continuous and as AGE-50
BMI as continuous and as BMI-25
COUNTBP as categorical
MEDCOUNT as categorical
SERPER as categorical

Multivariate Logistic Model

Each of the significant categorical variables in Table III above are combined into a multivariate model with those continuous variables as redefined above to yield the multivariate logistic regression model shown in Table IV.

Table IV: Multivariate Logistic Model with Candidate Variables

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	AGE50	.013	.003	23.196	1	.000	1.013	1.008	1.018
	SERVCON(1)	.017	.054	.099	1	.753	1.017	.916	1.129
	DEPRESSI(1)	-.153	.074	4.263	1	.039	.858	.742	.992
	DM(1)	1.012	.060	288.690	1	.000	2.751	2.448	3.092
	CHF(1)	-.592	.092	41.014	1	.000	.553	.462	.663
	ETOHICD9(1)	.054	.091	.357	1	.550	1.056	.884	1.261
	TOBACCO			6.723	2	.035			
	TOBACCO(1)	-.072	.060	1.468	1	.226	.930	.828	1.046
	TOBACCO(2)	.315	.161	3.821	1	.051	1.370	.999	1.880
	COUNTQUA			46.608	3	.000			
	COUNTQUA(1)	-.009	.076	.015	1	.904	.991	.853	1.151
	COUNTQUA(2)	-.168	.074	5.140	1	.023	.845	.730	.977
	COUNTQUA(3)	-.473	.079	36.282	1	.000	.623	.534	.727
	BMI25	.015	.005	10.202	1	.001	1.015	1.006	1.025
	ACE(1)	.147	.070	4.333	1	.037	1.158	1.009	1.329
	ALPHA(1)	.076	.094	.651	1	.420	1.078	.898	1.296
	NONLOOP(1)	.176	.077	5.179	1	.023	1.192	1.025	1.387
	CHANNELB(1)	.372	.072	26.686	1	.000	1.450	1.259	1.670
	ANGIIBLO(1)	.198	.145	1.868	1	.172	1.219	.918	1.619
	NITRATES(1)	-.414	.085	23.976	1	.000	.661	.560	.780
	LOOP(1)	-.324	.098	10.872	1	.001	.723	.597	.877
	LIPID(1)	-.150	.073	4.268	1	.039	.861	.746	.992
	MEDCAT			1.822	3	.610			
	MEDCAT(1)	.089	.092	.940	1	.332	1.093	.913	1.309
	MEDCAT(2)	.015	.112	.018	1	.894	1.015	.815	1.264
	MEDCAT(3)	-.015	.158	.008	1	.927	.986	.723	1.344
	Constant	-.476	.098	23.521	1	.000	.621		

a. Variable(s) entered on step 1: AGE50, SERVCON, DEPRESSI, DM, CHF, ETOHICD9, TOBACCO, COUNTQUA, BMI25, ACE, ALPHA, NONLOOP, CHANNELB, ANGIIBLO, NITRATES, LOOP, LIPID, MEDCAT.

b. For DM, CHF, ACE, NONLOOP, CHANNELB, NITRATES, LOOP, LIPID, DEPRESSI, ALPHA, ANGIIBLO and ETOHICD9 indicates the presences of the effect compared to the absence of the effect (reference). TOBACCO(1) corresponds to former smoker and TOBACCO(2) to never smoked, each compared to current smoker (reference). For COUNTQUA, (1), (2), and (3) corresponds to blood pressure counts of 5-6, 7-11, and 12+ respectively, compared to the reference count of 3-4. For MEDCAT, (1), (2) and (3) corresponds to 1,2, and 3+ cardiovascular medications compared to the reference of no such medications. These codings also apply to subsequent logistic model tables.

We see from this multivariate analysis, that the following variables may be removed from the model because they have a p value > 0.05: ETOHICD9, ALPHA blocker use, Angiotensin II blocker use, MEDCAT and SERVPER to yield the following model in Table V.

Table V: Multivariate Logistic Model with Significant Candidate Variables

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	AGE50	.013	.003	24.242	1	.000	1.013	1.008	1.018
	DM(1)	1.015	.059	292.762	1	.000	2.759	2.457	3.100
	CHF(1)	-.592	.092	41.222	1	.000	.553	.462	.663
	TOBACCO			6.812	2	.033			
	TOBACCO(1)	-.075	.059	1.616	1	.204	.928	.826	1.042
	TOBACCO(2)	.312	.161	3.774	1	.052	1.366	.997	1.871
	ACE(1)	.125	.056	4.915	1	.027	1.133	1.015	1.265
	NONLOOP(1)	.167	.065	6.531	1	.011	1.182	1.040	1.343
	CHANNELB(1)	.363	.062	34.526	1	.000	1.438	1.274	1.623
	NITRATES(1)	-.434	.074	34.820	1	.000	.648	.561	.748
	LOOP(1)	-.330	.091	12.989	1	.000	.719	.601	.860
	LIPID(1)	-.168	.058	8.366	1	.004	.845	.754	.947
	COUNTQUA			46.497	3	.000			
	COUNTQUA(1)	-.008	.076	.011	1	.918	.992	.854	1.152
	COUNTQUA(2)	-.163	.074	4.824	1	.028	.850	.735	.983
	COUNTQUA(3)	-.470	.078	36.076	1	.000	.625	.536	.728
	DEPRESSI(1)	-.149	.073	4.201	1	.040	.861	.747	.993
	BMI25	.015	.005	10.593	1	.001	1.015	1.006	1.025
	Constant	-.407	.080	25.620	1	.000	.666		

a. Variable(s) entered on step 1: AGE50, DM, CHF, TOBACCO, ACE, NONLOOP, CHANNELB, NITRATES, LOOP, LIPID, COUNTQUA, DEPRESSI, BMI25.

To ensure ourselves that the model is not improved by any of these variables removed, we now calculate the likelihood ratio tests resulting from the difference between models for each variable as they are reapplied to the model:

> G = -2 (the difference in likelihood ratios between models) = a value compared to a Chi-square distribution with one degree of freedom (except MEDCAT has 3 degrees of freedom):

Variable	G	P-value[10]
ETOHICD9	0.67	0.41
ALPHA	0.46	0.50
ANGIOBLO	2.87	0.09
MEDCAT	2.38	0.41
SERVPER	3.38	0.07

We therefore proceed with using the model above without the inclusion of these statistically insignificant variables.

Correlation/Confounding

Next, consideration is given to correlation between variables. A Pearson's correlation coefficient is generated between each variable in the model to see if two variables are so highly correlated with one another to allow for the omission of such 'duplicate' and, therefore, less predictive variables (Table VII). Table VI shows the output for those variables with the strongest associations represented by a Pearson's coefficient of > 0.20.

Table VI.

Variables	Pearson's Correlation
CHF and LOOP	0.440
CHF and COUNTQUA	0.210
Depression and AGE50	-0.233
Tobacco and AGE50	0.246
AGE and BMI25	-0.305

Table VII. Correlation Coefficients Between Predictor Variables in Table V

Correlations

		AGE50	DEPRESS	DM	CHF	TOBACCC	COUNTQUA	BMI25	ACE	NONLOOP	CHANNEL	NITRATES	LOOP	LIPID
AGE50	Pearson Correl	1	-.233	.005	.173	.246	.062	-.305	.041	.038	.062	.099	.127	.010
	Sig. (2-tailed)	.	.000	.675	.000	.000	.000	.000	.001	.002	.000	.000	.000	.417
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
DEPRESS	Pearson Correl	-.233	1	.010	.001	-.098	.137	.067	-.051	-.036	-.027	.026	-.008	.005
	Sig. (2-tailed)	.000	.	.415	.960	.000	.000	.000	.000	.004	.030	.035	.497	.676
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
DM	Pearson Correl	.005	.010	1	.131	.071	.139	.199	.182	-.026	.042	.069	.141	.113
	Sig. (2-tailed)	.675	.415	.	.000	.000	.000	.000	.000	.035	.001	.000	.000	.000
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
CHF	Pearson Correl	.173	.001	.131	1	.026	.210	.038	.073	-.054	.002	.170	.440	.068
	Sig. (2-tailed)	.000	.960	.000	.	.039	.000	.002	.000	.000	.899	.000	.000	.000
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
TOBACCC	Pearson Correl	.246	-.098	.071	.026	1	-.018	.104	.026	.023	-.002	-.016	.031	.008
	Sig. (2-tailed)	.000	.000	.000	.039	.	.146	.000	.039	.072	.864	.189	.015	.544
	N	6355	6355	6355	6355	6355	6355	6338	6355	6355	6355	6355	6355	6355
COUNTQU	Pearson Correl	.062	.137	.139	.210	-.018	1	-.011	.031	-.022	.031	.124	.193	.059
	Sig. (2-tailed)	.000	.000	.000	.000	.146	.	.382	.013	.078	.014	.000	.000	.000
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
BMI25	Pearson Correl	-.305	.067	.199	.038	.104	-.011	1	.075	.042	.010	.005	.114	.058
	Sig. (2-tailed)	.000	.000	.000	.002	.000	.382	.	.000	.001	.448	.664	.000	.000
	N	6365	6365	6365	6365	6338	6365	6365	6365	6365	6365	6365	6365	6365
ACE	Pearson Correl	.041	-.051	.182	.073	.026	.031	.075	1	.025	.025	.063	.098	.099
	Sig. (2-tailed)	.001	.000	.000	.000	.039	.013	.000	.	.049	.046	.000	.000	.000
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
NONLOOI	Pearson Correl	.038	-.036	-.026	-.054	.023	-.022	.042	.025	1	.062	-.031	-.089	.003
	Sig. (2-tailed)	.002	.004	.035	.000	.072	.078	.001	.049	.	.000	.012	.000	.832
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
CHANNEL	Pearson Correl	.062	-.027	.042	.002	-.002	.031	.010	.025	.062	1	.044	.059	.058
	Sig. (2-tailed)	.000	.030	.001	.899	.864	.014	.448	.046	.000	.	.000	.000	.000
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
NITRATES	Pearson Correl	.099	.026	.069	.170	-.016	.124	.005	.063	-.031	.044	1	.170	.192
	Sig. (2-tailed)	.000	.035	.000	.000	.189	.000	.664	.000	.012	.000	.	.000	.000
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
LOOP	Pearson Correl	.127	-.008	.141	.440	.031	.193	.114	.098	-.089	.059	.170	1	.095
	Sig. (2-tailed)	.000	.497	.000	.000	.015	.000	.000	.000	.000	.000	.000	.	.000
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382
LIPID	Pearson Correl	.010	.005	.113	.068	.008	.059	.058	.099	.003	.058	.192	.095	1
	Sig. (2-tailed)	.417	.676	.000	.000	.544	.000	.000	.000	.832	.000	.000	.000	.
	N	6382	6382	6382	6382	6355	6382	6365	6382	6382	6382	6382	6382	6382

As a result of the uniformly low correlation coefficients found, the variables appear to be independent of one another.

Confounding is now considered. In order to be considered confounders, variables must be associated with systolic blood pressure control as well as with one another (yet not exist within the causal pathway). Variables not included within the main effects model above are, therefore, not considered as confounders, given their lack of association with systolic blood pressure control. Variables within the main effects model and with known associations for one another are considered as potential confounders. We choose this time to use less selective criteria and test all variables with a Pearson's coefficient of >=0.10:

Interaction Terms	Pearson's Correlation
CHF and LOOP	0.440
CHF and COUNTQUA	0.232
CHF and DM	0.131
CHF and Nitrates	0.170
CHF and Age50	0.173
AGE50 and Depression	0.233
AGE50 and Tobacco Status	0.246
AGE50 and BMI25	0.305
AGE50 and Loop	0.127
Depression and Countqua	0.113
DM and ACE	0.182
DM and Loop	0.141
DM and BMI25	0.199
DM and Countqua	0.128
Nitrate and Loop	0.170
Nitrate and Countqua	0.125
Loop and Countqua	0.199

Each variable with an apparent association is added to a model containing the confounding term to assess for a change in the crude odds ratio of greater than 15 percent. Table VIII summarizes those variables that demonstrated such a change in their crude odds ratio and thus serve as confounding variables in our study and are maintained within the model.

Table VIII: Crude and Adjusted Odds Ratios Due to Confounding

Variables (and Crude Univariate OR)	Adjusted Odds Ratios
CHF (0.53) and LOOP (0.65)	CHF (0.58) and LOOP (0.82)
CHF (0.53) and DM (2.35)	CHF (0.43) and DM (2.58)
AGE (1.005) and BMI25 (1.02)	AGE (1.009) and BMI25 (1.24)
DM (2.35) and ACE (1.26)	DM (2.31) and ACE (1.09)
DM (2.35) and Loop (0.65)	DM (2.53) and Loop (0.52)
DM (2.35) and Countqua(3) (0.62) *	DM (2.58) and Countqua(3) (0.51) *

* Countqua(3) represents 12+ blood pressure readings

Stepwise Regression

Before testing for potential interaction terms, we ensure that our main effects model is final. We run a forward conditional stepwise model using a probability for stepwise entry of $p = 0.01$ and for removal $p = 0.05$ to reduce the model in the context of our large sample size. From this, we notice that TOBACCO, ACE and DEPRESSION drop out resulting in the model in Table IX.

Table IX: Conditional Stepwise Logistic Regression Model

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	AGE50	.013	.002	28.915	1	.000	1.013	1.008	1.018
	DM(1)	1.035	.058	313.758	1	.000	2.815	2.510	3.156
	CHF(1)	-.603	.092	43.040	1	.000	.547	.457	.655
	COUNTQUA			51.631	3	.000			
	COUNTQUA(1)	-.021	.076	.077	1	.781	.979	.844	1.136
	COUNTQUA(2)	-.177	.073	5.835	1	.016	.837	.725	.967
	COUNTQUA(3)	-.495	.077	41.157	1	.000	.610	.524	.709
	BMI25	.014	.005	9.280	1	.002	1.014	1.005	1.023
	NONLOOP(1)	.178	.065	7.468	1	.006	1.195	1.052	1.357
	CHANNELB(1)	.363	.062	34.815	1	.000	1.438	1.275	1.622
	NITRATES(1)	-.429	.073	34.368	1	.000	.651	.564	.752
	LOOP(1)	-.305	.091	11.237	1	.001	.737	.616	.881
	LIPID(1)	-.164	.058	8.046	1	.005	.849	.758	.951
	Constant	-.412	.074	30.628	1	.000	.662		

a. Variable(s) entered on step 1: AGE50, DM, CHF, COUNTQUA, BMI25, NONLOOP, CHANNELB, NITRATES, LOOP, L

A comparison of the final model in Table V with the stepwise final model of Table IX shows little advantage for keeping in the three variables that dropped out of the model as a result of the stepwise analysis and, most importantly, little change in the Wald significance for each remaining variable. Moreover, all potential confounding variables remain in the main effects model. Table X looks at several goodness of fit statistics in comparing the two main effect models.

Table X: Goodness of Fits Statistics of Main effects and Stepwise Models

Final Main Effects Model	Stepwise Final Model
Chi square: 593.03 with 16 df	578.14 with 12 df
-2loglike: 8190.47	8243.17
Hosmer Lemoshow test for goodness of fit:	
5.82 (p-value = 0.667)	12.41 (p-value = 0.13)

We therefore conclude that our main effect model is sufficiently represented by the variables: AGE50, BMI50, COUNTQUA, DM, CHF, LOOP, NONLOOP, NITRATE, LIPIDS, CHANNELB.

Interactions

There are numerous potential interactions between the variables involved. In order to assess for this possibility, we begin by entering each potential interaction into the main effects model to assess the significance of the Chi-square value generated. All possible interactions are tested; those with significance are listed in Table XI.

Table XI: Possible Interactions Between Main Effects Variables

Interaction	Chi Square	Df	P value	B (coefficient)
Diabetes x Lipids	4.76	1	0.03	0.25
CHF x Calcium Ch Blockers	5.55	1	0.02	0.00
CHF x Nitrates	5.41	1	0.02	0.42
CHF x Lipids	5.38	1	0.02	0.39
Loop x Nitrate	5.94	1	0.02	0.44
Loop x CaCHannel	6.82	1	0.01	0.45

We choose to add all of the above variables into our model except for CHF x Calcium Ch Blockers because of its small B coefficient and, therefore, its small influence upon main effect variables that appear in Table X. The model with main effects and interactions is shown in Table XII.

Table XII: Main Effects Logistic Regression Model with Interactions

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B) Lower	Upper
Step 1[a]	AGE50	.014	.002	31.398	1	.000	1.014	1.009	1.018
	DM(1)	.971	.072	183.374	1	.000	2.640	2.294	3.038
	CHF(1)	-.774	.124	38.941	1	.000	.461	.362	.588
	COUNTQUA			51.564	3	.000			
	COUNTQUA(1)	-.012	.076	.027	1	.870	.988	.851	1.147
	COUNTQUA(2)	-.175	.074	5.657	1	.017	.839	.727	.970
	COUNTQUA(3)	-.492	.077	40.457	1	.000	.611	.525	.712
	BMI25	.014	.005	9.668	1	.002	1.014	1.005	1.023
	NONLOOP(1)	.175	.065	7.192	1	.007	1.191	1.048	1.354
	CHANNELB(1)	.302	.067	20.534	1	.000	1.353	1.187	1.542
	NITRATES(1)	-.534	.085	39.541	1	.000	.586	.496	.692
	LOOP(1)	-.549	.122	20.311	1	.000	.578	.455	.733
	LIPID(1)	-.279	.076	13.605	1	.000	.757	.652	.877
	DM(1) by LIPID(1)	.204	.118	2.965	1	.085	1.226	.972	1.547
	CHF(1) by NITRATES(1)	.252	.203	1.535	1	.215	1.286	.864	1.915
	CHF(1) by LIPID(1)	.263	.172	2.341	1	.126	1.301	.929	1.822
	LOOP(1) by NITRATES(1	.289	.199	2.105	1	.147	1.336	.904	1.974
	CHANNELB(1) by LOOP(1)	.442	.174	6.444	1	.011	1.556	1.106	2.188
	Constant	-.366	.076	23.413	1	.000	.694		

a. Variable(s) entered on step 1: DM * LIPID , CHF * NITRATES , CHF * LIPID , LOOP * NITRATES , CHANNELB * LOOP .

Due to its significance, we choose to leave ChannelB x LOOP in the model but remove the other interactions, generating the final model depicted in Table XIII.

Table XIII: Final Logistic Regression Model

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	AGE50	.013	.002	29.073	1	.000	1.013	1.008	1.018
	DM(1)	1.037	.058	314.591	1	.000	2.821	2.515	3.163
	CHF(1)	-.589	.092	40.890	1	.000	.555	.463	.664
	COUNTQUA			51.854	3	.000			
	COUNTQUA(1)	-.015	.076	.039	1	.843	.985	.849	1.143
	COUNTQUA(2)	-.178	.073	5.875	1	.015	.837	.725	.966
	COUNTQUA(3)	-.494	.077	40.895	1	.000	.610	.525	.710
	BMI25	.014	.005	9.481	1	.002	1.014	1.005	1.023
	NONLOOP(1)	.184	.065	7.981	1	.005	1.202	1.058	1.366
	CHANNELB(1)	.297	.066	19.925	1	.000	1.346	1.181	1.533
	NITRATES(1)	-.428	.073	34.117	1	.000	.652	.565	.752
	LOOP(1)	-.456	.109	17.626	1	.000	.634	.512	.784
	LIPID(1)	-.166	.058	8.258	1	.004	.847	.756	.949
	CHANNELB(1) by LOOP(1)	.454	.174	6.791	1	.009	1.574	1.119	2.215
	Constant	-.402	.075	29.078	1	.000	.669		

a. Variable(s) entered on step 1: CHANNELB * LOOP .

Characteristics for Blood Pressure Control

We conclude that the characteristics of veterans who lack systolic blood pressure control include diabetes mellitus, advancing age, higher body mass and current use of calcium channel blockers or non-loop diuretic medications. Those variables predictive of systolic blood pressure control in this same population include those receiving twelve or more blood pressure readings over a fifteen month time period, and those veterans taking nitrates, loop diuretics or lipid agent medications. Moreover, those taking loop diuretic medication appear to lose the beneficial effect of this medication class when concurrently taking calcium channel antagonist medications.

Table XIV: Summary of Characteristics with Significance

Variables Predicting SBP Control	Variables Predicting Elevated SBP
More BP readings	Diabetes Mellitus
Nitrate Medication Use	Advancing Age
Loop Diuretic Use	Obesity
Lipid Agent Use	Non Loop Diuretic Use
Congestive Heart Failure	Calcium Channel Blocker Use

COMMENTS

It is the intention of this study to shed further light into the characteristics of hypertensive adults so as to enable better identification and thus more adequate treatment of such a large 'under treated' population. Of the ten variables found to have significant associations with systolic blood pressure control, diabetes mellitus was found to carry the strongest association with a lack of control of systolic hypertension for the veteran population. As somewhat of a surprise, it is how hypertension is defined in this population (due to the increase in morbidity and mortality that occurs at lower systolic levels) that creates the strength of the association found. In fact, if one were to redefine systolic control as <140 for diabetics, one would find no association at all between diabetes and control of one's systolic hypertension (OR 0.93 with p value of 0.22). As a result, the highly elevated odds ratio associated with diabetic veterans and uncontrolled systolic blood pressure is more a reflection of a lack of ability on the part of providers to bring under more strict control the blood pressure of a population thought to experience morbidity and mortality at a lower systolic blood pressure threshold. Redefining the culture of blood pressure considerations in the management of diabetics would therefore

seem to represent the greatest potential for gain in reversing the large association found between two prevalent subgroups of the population studied.

Not surprisingly, advancing age was found to be associated with poor systolic control. As older age is an established risk factor for the development of hypertension, this finding does little more than to lend external validity to the model and reemphasize the importance for a more meticulous and thorough treatment of older hypertensive patients.[11] According to the adjusted odds ratio for age in the population above, there exists a 14% increase in odds that patients will be under-controlled for every decade lived. The importance of frequent monitoring and adequate treatment therefore increases with age, and clinicians can benefit from the knowledge that elevated systolic readings in their older population is less likely circumstantial, and more likely to only progress with time unless appropriate interventions are made

Research surrounding obesity and systolic hypertension has demonstrated similar yet stronger associations between the two as evidenced most recently from the Second National Health and Nutrition Examination Survey (NHANES II) data.[12] This study showed that obese persons were 3 times as likely as non obese persons to have hypertension, with obese young adults carrying a 5.5-fold higher risk and obese adults (between 45 and 75) carrying a 1.9-fold higher risk.[12] Additional risk estimates derived from the Framingham study suggest that as much as 78% of essential hypertension in men and 65% in women can be attributed to obesity and that each 10% gain in weight is associated with a 6.5 mm Hg increase in systolic BP.[13] While these estimates may be on

the high side, so might the estimates from this study be on the low side due to the mean weight of the subjects studied (208.1 pounds), and consequential smaller referent population of normal weight (more than eighty percent have a BMI of > 25). Estimates of magnitude aside, the importance of a more targeted and directed treatment course for those patients who are overweight cannot be over emphasized. This study places a small yet significantly elevated estimate of risk for each unit rise in body mass index to be associated with poorly controlled systolic hypertension, and thus adds further evidence towards the body of knowledge surrounding obesity and hypertension.

A diagnosis of congestive heart failure is intuitively associated with systolic blood pressure control as hypertension is a known major risk factor for the development of congestive heart failure.[9] What is interesting is how in this study heart failure was significantly associated with control of systolic hypertension after consideration was given to those variables likely to serve as confounders or effect modifiers (specifically loop diuretics, beta blockers and nitrates). The question is therefore raised as to what should represent a goal systolic blood pressure for patients with congestive heart failure? Is the higher proportion of controlled hypertensives with congestive heart failure reflective of a population in need of redefined clinical guidelines so as to prevent further cardiovascular morbidity and mortality or merely a reflection of disease patho-physiology and a decreased ejection fraction. For this reason, further study looking at outcomes related to lower blood pressure levels for patients with congestive heart failure are needed so as to guide the medical management of this population.

An important if not unique factor that demonstrates a strong association with systolic hypertension control in this study is the frequency with which veterans are monitored. The importance of this observation cannot be understated as it seems to suggest that the system itself is more capable of assisting patients with achieving blood pressure control when presented with more opportunities to witness blood pressure readings. The strength of the association found is enforced by the progressive significance for more frequent categories of monitoring found (and thus internal validity is noted). There appears to exist a threshold effect in that a lack of control is more common unless patients are monitored approximately every other week. Of further interest is the progressive improvement in control as the number of readings increase to where those veterans monitored more than eleven times (roughly once every five weeks) achieve the highest association with systolic control. These findings would suggest that there may exist a threshold or minimum frequency by which to guide care for the hypertensive population in order to optimize the care that is received. Such interventions as home blood pressure monitoring, more frequent non-provider ambulatory visits where blood pressure readings alone can be performed, or the encouragement of more provider visits for patients experiencing persistently elevated systolic blood pressure measurements each would seem to carry the potential to bring a large proportion of veterans under control who previously were not.

A great deal of focus in this study has been applied to which medications are associated with systolic hypertension control. The challenges that are inherent with such an analysis include a lack of information about patient compliance with medication use,

strength of medicine taken and duration of treatment course. Moreover there is a strong potential for interaction and confounding to distort the results generated from a cross sectional analysis when attempting to draw conclusions from a 'window in time' snapshot approach. Furthermore, many of the previous trials and meta-analyses have looked at end points related to the use of various drug classes and based their conclusions on reductions in cardiovascular morbidity and mortality rather than drop in systolic blood pressure.[9] For this reason conclusions drawn from this study say nothing about the utility of drug classes in reducing important cardiovascular outcomes nor influencing other potentially beneficial clinical results (i.e. alpha blockers and prostatic hypertrophy). The conclusions of this study rather bring into focus a need to look prospectively at the role of medication classes in systolic blood pressure control while offering 'blue prints' upon which to base future studies that build upon and more closely examine the associations discovered.

What this study is able to offer in light of these limitations comes from what it is able to measure, adjust for and thus overcome in order to yield meaningful results. The opportunity to use an outcome that is based upon both a current as well as average of recent blood pressure readings renders a boost in accuracy that minimizes measurement bias inherent in other cross sectional studies. The ability to extract information about medication prescription fills around the time of the last blood pressure readings more closely ties the use of a particular medicine with its effect. And an ability to adjust for medical co-morbidities and use of other medications enables one to use statistical tools to minimize the distorting effects of confounding and interaction.

Hildebrandt and Tuxen[14] examined the effects of "newer" drugs (angiotensin-converting enzyme inhibitors, calcium antagonists, and alpha-blockers) compared to "older" well-proven drug (thiazide diuretics, and beta-blockers) in the treatment of essential hypertension. They combined 58,000 middle aged or elderly subjects from five prospective and randomized clinical trials (CAPPP, STOP-2, NORDIL, INSIGHT, and one arm of ALLHAT), looking at the primary outcomes of stroke, myocardial infarction, composite cardiovascular (CV) death, and fatal coronary heart disease to find that the prevention of these complications depends more on the lowering of blood pressure with well-tolerated medication, irrespective of class. These findings therefore lend importance and significance to the associations that exist between blood pressure control and class of medication.

The medication classes found to be associated with systolic hypertension control in this study are nitrates, loop diuretics, lipid lowering agents, calcium channel blockers and non-loop diuretics. There are practical limitations to the findings that nitrates are associated with controlled systolic hypertension due to the inability for many patients to tolerate these medications because of their side effects and short half-life, making them unrealistic agents for monotherapy or as first line agents. This class of medication has, however, become reformulated into the use of longer acting and better tolerated applications (i.e. through use with a patch) to where clinicians may feel more comfortable supplementing care for patients with persistent or refractory systolic hypertension with this type of medication. Moreover, as a result of the systolic control associated with

nitrate use in this study, further investigation into this medication class as a form of hypertension management is needed as a means to better understand all ways of approaching hypertensive patient.

Loop and non loop diuretic therapy is considered first line treatment for systolic hypertension and has been shown to be associated with a reduction in many adverse cardiovascular outcomes.[9] The associations discovered in this study between loop diuretics and systolic control yet not between non-loop diuretics, however, raise important questions. Do non-loop diuretics reduce morbidity and mortality through mechanisms other than the lowering of one's blood pressure? As nearly twice as many hypertensive veterans in our population take non loop diuretics than loop diuretics (21.1 percent versus 12.9 percent), is there a benefit to be gained from a greater dependence upon diuretics of the loop variety?

Findings supportive of an association between lipid lowering medication use and control of systolic hypertension make intuitive sense as hyperlipidemia is a known risk factor for systolic hypertension.[9] The fact that those hypertensive patients taking lipid lowering agents were more often controlled than those not taking this class of medication begs the question as to whether there is a potential for both primary and secondary prevention to result from the use of these agents. The importance of screening for hyperlipidemia in hypertensive patients is emphasized as well given the potential benefit rendered upon systolic control should lipid lowering agents be indicated. There does exist the potential for misclassification bias with regard to lipid lowering agents due to

the inclusion of different mechanisms of actions of the drugs included in this variable category, as the benefits may be more or less attributed to one particular agent and thus further research is needed to isolate and investigate these variables.

A lack of systolic control with calcium channel blockers lends further evidence against the use of a class of medicines which have raised concerns for sudden cardiac death in the treatment of hypertensive emergencies.[9] The lack of strong evidence supportive of calcium channel blockers and the prevention of cardiovascular morbidity and mortality coupled to findings that they may be associated with patients with uncontrolled hypertension raises many question surrounding the benefits of this class of medication. Further, findings of an interaction between loop diuretics and calcium channel blockers to where the benefits of loop diuretics are lost in the presence of calcium channel antagonists heightens the call for a deeper understanding of the role of calcium channel antagonists in the treatment of systolic hypertension.

The findings consistent with a lack of association between systolic blood pressure control and medication class, in particular beta blockers and ace inhibitors, are as useful as those demonstrating an association in the study. The high proportion of use of ace inhibitors in the population studied (37 %) makes it unlikely that a lack of blood pressure control had occurred due to insufficient time on these newer medications. Moreover, a correction for interaction and confounding reduces the likelihood that those patients with a higher likelihood of poor control are taking ACE inhibitors or beta blockers. In fact, a sub analysis performed using this data set found no statistically significant difference in

the proportion of veterans on ace inhibitors or beta blockers and those with congestive heart failure, diabetes mellitus and chronic renal failure. It remains possible, however that the dose of ace inhibitor or beta blocker taken is sub therapeutic and therefore poorly reflective of the pressure lowering potential. More likely, however, is the possibility that too often clinicians associate blood pressure control with the 'power' of these agents and conclude that less medication manipulation is needed in such patients as a result. The importance of the role of beta blockers and ace inhibitors in reducing cardiovascular morbidity and mortality[9] is not challenged by this study, yet the assumptions that they are synonymous with blood pressure control may need to be considered more carefully.

In spite of the consistent and technical nature of this study's data collection, redundancy of its measurements, and large sample size of similar patients within one system of care, there are several limitations that deserve mention. This study is limited by the lack of data that exists on other known risk factors of systolic hypertension that include how sedentary one's lifestyle is, stress levels and intake of salt, potassium and calcium, and family history of hypertension. Further limiting is the ability to compare races due to the low numbers of non-white Veterans as well as high number of unknowns in the race category data set (raising the potential for a misclassification bias above the utility of analyzing race as a variable). Race therefore was left out of the model limiting the ability to draw conclusions about races known to be associated with a lack of control and disallowing an opportunity to adjust for the influence of this important variable. For similar reasons, the low numbers of women in the dataset make the drawing of important conclusions surrounding sex differences and hypertension impossible.

This study is further limited by the quality of data surrounding several of the variables measured. The potential exists for an underreporting of such measured quantities as alcohol use or tobacco history to where true associations are hidden by a misclassification. This miscoding is felt to be more likely than for other variables in the analysis such as congestive heart failure, renal failure or diabetes mellitus which come from a more objective source (ICD or International Code of Disease definition). Next, as the older age of the veteran population in our sample (mean age is 66.7) limits our ability to generalize the findings of this study to patients younger than fifty years of age. And lastly, the potential for a high proportion of undiagnosed hypertensives in any population gives rise to the potential for many hypertensive veterans to have been falsely excluded from this data selection.

CONCLUSIONS

Veteran patients with adequately controlled systolic hypertension are more likely to be younger, more frequently monitored and taking loop diuretics, nitrates or lipid lowering agents. Veteran patients with congestive heart failure are less likely to have uncontrolled systolic hypertension. Veteran patients who have uncontrolled systolic hypertension are more likely older, diabetic, obese and taking calcium channel blocker or non loop diuretics medications. Loop diuretics may offer more of a benefit to the Veteran population than do non-loop diuretics in controlling systolic hypertension, and this benefit may be lost with the concurrent use of calcium channel blocker medication.

Further investigation into the role of nitrates, loop diuretic therapy and lipid lowering agents for hypertensive management is needed given their association with systolic blood pressure control. Prospective studies of the influence of medication classes upon systolic blood pressure control are needed to build upon the evidence for and against control generated from this study. The frequency with which clinicians monitor hypertensive blood pressure levels has a strong association with how well controlled each patient's systolic blood pressure is.

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